THE PARADOX OF NUTRITIONAL ANEMIA IN INDIA: A CRITICAL ANALYSIS OF ITS EPIDEMIOLOGY AND INTERVENTIONS

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CERTIFICATE

I declare that the thesis entitled "**The paradox of nutritional anemia in India: a critical analysis of its epidemiology and interventions**" submitted by me in fulfilment of the requirements for the award of the degree of Doctor of Philosophy of Jawaharlal Nehru University is my original work and has not been submitted for any other degree of this University or any other university.

Rahul Rauny

We recommend that this thesis be placed before the examiners for evaluation.

Prof. Rajib Dasgupta	Dr. Nicholas Nisbett	Prof. Rajib Dasgupta
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LIST OF ABBREVIATIONS

ACD	Anemia of chronic disease
AI	Anemia of infections
AMB	Anemia Mukt Bharat
ANC	Antenatal clinics
ART	Artemisinin combination Therapy
ATP	Adenosine triphosphate
AWW	Anganwadi Worker
BCC	Behaviour Change Communication
BCCS	Behavioural Change Communication Strategies
BRINDA	Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia
CAP	Convergent action plan
CDA	Critical discourse analysis
CNNS	Comprehensive National Nutrition Survey
CSDH	Commission on social determinants of health
CSSMP	Child Survival and Safe Motherhood Programme
DCYTB	Duodenal cytochrome B reductase
DFS	Double fortified salt
DMT	Divalent metal transporter
eLENA	e-Library of evidence for nutrition action
EPO	Erythropoietin
ERFE	Erythroferrone
FPN	Ferroportin
GAIN	Global Alliance for Improved Nutrition
GBD	Global Burden of Disease
GDP	Gross domestic production
GLV	Green leafy vegetables
Hb	Haemoglobin
HDI	Human development index
HIV	Human Immune Virus
ICDS	Integrated child development scheme
ICMR	Indian council of Medical Research
ID	Iron deficiency
IDA	Iron deficiency anemia
IEC	Information, education, and communication
IFA	Iron folic acid
INACG	International Nutritional Anemia Consultative Group
IRIS	Institutional repository for information sharing
IRS	Indoor residual Spray
IUD	Intrauterine device acceptors
IYCF	Infant And Young Child Feeding Practices
JSY	Janani Suraksha Yojana
KII	Key Informant interview
LLIN	Long-lasting Insecticide Nets

MDM	Mid-day meal
MMN	Multiple micronutrients
MOHFW	Ministry of Health and family welfare
MWCD	Ministry of Women & child development
NFHS	National Family Health Surveys
NHANES	National Health and Nutrition Survey
NHS	National Health Services
NIN	National Institute of Nutrition
NIPI	National iron Plus Initiative
NITI	National Institution for Transforming India
NNACP	National Nutritional anemia control Programme
NNAPP	National Nutritional Anemia Prophylaxis Programme
NNM	National Nutrition Mission
NNMB	National Nutrition Monitoring Bureau
NNS	National Nutrition Strategy
NPPCF	National programme for prevention and control of Fluorosis
NRHM	National rural health Mission
NSSO	National sample survey office
NVBDCP	National vector-borne disease control program
OBC	other backward castes
PDS	Public Distribution System
PMMVY	Pradhan Mantri Matri Vandana Yojana
POSHAN	Prime Minister's Overarching Scheme for Holistic Nutrition
PSC	Pre-school children
RA	Retinoic acid
RBC	Red blood cells
RCH	Reproductive and Child Health
RCT	Randomized controlled trials
RDA	Recommended daily allowance
RDI	Recommended daily intake
RNI	recommended nutrient intakes
SBCC	social and behavioural change communication
SC	Schedule caste
SCD	Sickle cell disease
SES	Socioeconomic status
ST	Schedule tribe
STH	soil-transmitted helminths
T3	Test Treat Talk
TB	Tuberculosis
TFN	Tumor necrosis factor
UNICEF	United Nations International Children's Emergency Fund
UNU	United Nations University
UP	Uttar Pradesh
US	United States
USAID	United States Agency for International Development
VAD	Vitamin A deficiency
VHND	Village Health Nutrition Day
VHNSC	Village health sanitation and Nutrition Committee

WASH	Water, sanitation and hygiene
WHA	World health assembly
WHO	World health organisation
WRA	women of reproductive age

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ABSTRACT

Nutritional anemia is a challenging public health problem associated with significant morbidity and mortality in developing countries, including India. The leading causes are micronutrient deficiencies (iron, folate, vitamin B12 and A), infections, and genetic blood disorders. However, the distribution and contribution of causal factors in the population are little known. The traditional policy responses to control anemia, i.e., iron supplementation, food-based approaches including food fortification with iron, deworming, and behavioural change interventions, have had minimal impact. Anemia remains an ambiguous illness, with no consensus on its constitution, definition, causation, and intervention.

The thesis illuminates key aspects of the nature, causation, and programmatic approaches to explore the reasons for the high anemia prevalence. It used systematic narrative review methods, thematic content analysis and critical discourse analysis to unpack the diverse and contested theories regarding the nature and causation of anemia to situate the complexity in a broader perspective. The study primarily collected data from published literature, policy documents, and health and nutrition reports. In addition, key informants provided insights into the literature gaps and future recommendations.

The thesis found that a positivist biomedical construction of anemia transverses into the definition, constitution, causation, and intervention approaches. Within this discourse, anemia is defined narrowly within haematological parameters, the primacy given to individual risk factors such as micronutrient deficiencies, infections, and genetic disorders, without identifying the root causes. This study identified that caste, class, gender, and religion are the structural determinants, whereas food security, access to health services, education, occupation, and WASH are intermediate determinants of anemia. Structural and intermediate determinants are upstream factors that differentially impact biological factors.

Anemia is a biological embodiment of poverty, deprivation and social exclusion. It is a reflection of social inequities. The current programmatic approaches will have limited impact if more upstream determinants are not addressed through nutrition-sensitive intervention. The best approach would be to integrate the current intervention into the broader poverty alleviation, income generation, social safety nets programmes and interventions targeting the public provisioning of food, health services, safe drinking water, and a healthy environment.

Keywords: anemia, iron deficiency, infections, social inequities, poverty, and exclusion.

CHAPTER 1

"IT is important to end poverty, to end misery, but the most important thing is to offer power to the poor so that they can fight for themselves"

Hugo Chavez
Venezueala President

CHAPTER 1. HISTORICAL AND CONTEMPORARY APPROACHES TO ANEMIA

"You have to know the past to understand the present"

- Carl Sagan

1.1. INTRODUCTION

Health and nutritional problems, including nutritional anemia, are often the results of discourses evolving over the centuries. History is a valuable tool for public health to study continuities and shifts in discourse towards health problems. The historical approach enriches our understanding of a health problem by highlighting the importance of context, situating the health problem in the time frame and developing a critical perspective. This chapter is divided into two parts. The first part examines the key historical events that shaped our current understanding of nutritional anemia. A historical analysis of the construction, causes and strategies used to treat anemia can shed light on the embedded complexity of anemia. The second part introduces the key concepts and approaches concerning anemia at the global and national levels.

1.1.1. THE CHANGING DISEASE IDENTITY: CHLOROSIS TO ANEMIA

Anemia is considered a modern abbreviation of 'chlorosis', a disease prevalent among young girls and women in 17th-century Europe and America (Loudon, 1984). Chlorosis was a mysterious disease without a distinctive set of symptoms. A chlorotic girl was identified with paleness, sallowness of complexion, intense lethargy, headache, dyspnoea, palpitation, breathing on exertion, bloated appearance, loss of appetite, early ceasing of menses in many cases, loss of vigour and decolouration of blood (Poskitt, 2003). The construction of a chlorotic girl varied from novelists and philosophers to doctors, nurses, and family members. Novelists portrayed the chlorotic girl as an apathetic and enigmatic figure, characterised by vague symptoms. In the 16th and 17th centuries, physicians described chlorosis as a 'disease of virgins' in young girls and women who didn't adapt to the assigned familial and social mores such as marriage. It was believed to be caused by delayed or no marriage, perversion of diets, masturbation, unpredictable behaviours, use of corsets, and cured by expedient marriage and sex. Physicians of that era constructed the narrative of chlorosis, blamed the young's girl's

freedom, capricious and lax behaviour and loose morality for chlorosis and sought its cure in the moral management and control of womanhood. Chlorosis was a disease intricately linked to Victorian women's identity and daily life rituals (Wailoo, K, 1999, p. 30).

By the late nineteenth century, the definition of chlorosis experienced a marked shift; it seldom remained a ‘virgin’s disease’. Chlorosis now appeared in adolescent working girls, well-to-do married women, and all classes of women, reflecting the changing attitudes towards women and disease in the industrial revolution era. Others believed that the symptoms such as pallor, lethargy and menstrual abnormalities, characteristic of chlorosis, were caused due to hard labour and exploitative working conditions. The poor diets, poorly lighted and closed rooms, and other changing social demands acted as predisposing factors (Wailoo, K, 1999, p. 21). In his ‘Tale of two cities’, Charles Dickens characterised the poor hygienic conditions of Parsian streets in the 18th century and their association with the Chlorosis (Schümann & Solomons, 2017).

The Physicians almost always implicated puberty and recommended pubertal hygiene to treat chlorosis, thus invoking ‘hygiene discourse’. According to the ‘hygienic’ discourse, chlorosis was caused by contamination or loss of ‘pure’ blood through parasites in the peasant women, prompting physicians to emphasise the need to maintain the ‘hygiene of Puberty’(Trigo, 1999). For many physicians of this era, chlorosis was a haematological disorder. Even when physicians sought to treat the disease with haematological assessments and embraced clinical definition, they continued to believe in chlorosis's social and moral origins (Wailoo, K, 1999, p. 24).

By the middle of the twentieth century, with the rise of modern medicine and therapeutic iron, chlorosis essentially turned into an iron disorder that could be cured by iron supplementation and scientific improvements in iron metabolism (Stuart-Macadam & Kent, 1992).

1.1.2. THE DECLINE OF CHLOROSIS

Chlorosis occupied the central place in the medical consciousness till the 19th century and then underwent a slow demise in the 20th century in the face of changing technological and social relations. By the 1930s, chlorosis had disappeared from medical textbooks and consulting rooms. The stated reasons for its demise are not less controversial than the perceived causes.

Three dominant narratives, i.e., advancement of haematological diagnostic tools, therapeutic iron, and gender ideologies, shaped chlorosis's life and death stories.

1.1.2.1. RISE OF TECHNOLOGY

The growth of modern medicine and the corresponding change in the taxonomy of disease was the most significant factor in the disappearance of chlorosis. In the modern taxonomic classification, chlorosis paved the way for simple anemia, which was soon replaced by 'iron deficiency anemia' (IDA). In the twentieth century, chlorosis was merely seen as a simple problem of iron intake and iron metabolism, more prevalent in women because of their unique physiology. Lethargy and paleness were the outcomes of iron deficiency and reduced red blood cells.

The Victorian era moralist assumptions about capricious behaviour, illicit sexual practices, masturbation, moral degeneration, and failure of parents and family members to control young girls and women showed signs of weakening. The new emerging haematological thoughts and twin forces of diagnosis and iron therapy in the twentieth century threatened to make chlorosis obsolete by turning from social and moral management to more precise scientific management. The production of antibiotics during World War II emboldened the therapeutic management of diseases, including chlorosis. Iron pills were projected as the 'wonder' drug that could cure chlorosis.

1.1.2.2. USE OF IRON AS A THERAPEUTIC AGENT

"Those diseases which medicines do not cure, iron cures; those which iron cannot cure, fire cures; and those which fire cannot cure, are to be reckoned wholly incurable."- Hippocrates

Hippocrates long ago identified using the iron to treat Chlorosis (Poskitt, 2003). In the 17th century, scrapped rust from iron swords was mixed with wine to reinvent lost vigour and lost the colour of the blood of those listed as pale and weak. The earlier application of iron was symbolic because iron was considered a symbol that oozed strength. It seemed logical for a condition characterised by weakness and lethargy to be treated with a remedy providing strength and vigour (Haden, 1938). In the 17th century, Thomas Sydenham, a British physician, recommended iron chalybeate and Dr Blaud, a French Physician, in 1832 introduced ferrous

sulphate, popularly known as ‘Blaud pills’ for the treatment of chlorosis. As early as the 18th century, chlorosis was characterised by a lack of haemoglobin and iron deficiency. Still, a scientific rationale linking iron with chlorosis was not appreciated until the beginning of the twentieth century when Helen Mackay, a British physician, observed that insufficient dietary iron led to anemia in late infancy and anemia was preventable with supplementary iron. Iron may have reduced chlorotic conditions by chance rather than by design (Beutler, 2002).

1.1.2.2.1. THERAPEUTIC REDUCTIONISM OF IDA

By the middle of the twentieth century, the therapeutic potential of iron and the virtues of the new science of iron metabolism occupied a central place in shaping the identity of chlorosis. The iron-centric reconstruction of chlorosis built upon what physicians had long known. i.e., iron was limited in scope in the treatment of chlorosis. In the nineteenth century, physicians used iron as merely one component of the overall moral management of chlorotic subjects. Many were convinced that iron was no magic pill but was simply a part of an extended therapeutic mechanism (not even a necessary component). Gradually, because of the growing influence of pharmaceutical companies and physicians' inclination to use iron as a magic pill, it became appealing to prescribe higher iron doses for chlorosis (Wailoo, K, 1999, p. 40). In the 1930s and 1940s, physicians prescribed iron pills diagnostically instead of diagnosing blood deficiency through a hemocytometer. Iron pills replaced the hemoglobinometers and hemacytometers as a diagnostic tool of choice for many general practitioners. Subsequent studies placed women in the centre of contention and iron as the lead actor in studying iron metabolism concerning diet, lifestyle and physiology. Iron deficiency was characterised as a basic fact of womanhood, and knowledge of iron metabolism was considered essential in guiding the woman from perpetual sickness (Ridgway et al., 2019).

The newly constructed identity for chlorosis revealed less about chlorosis and more about the culture of haematological thought that emerged and expanded by the middle of the twentieth century. Within the new discourse, chlorosis was categorised as a blood disease that could be measured in haemoglobin values. The focus shifted from social vision to a narrowly defined haematological concept, from the complexities of illness to its symptom. Chlorosis was now described as a vague symptomatic approximation of several diseases and conditions.

Chlorosis was a disease of a different era, and modern physicians were poorly equipped to understand it. The relationship between technology and disease was vague to physicians of this era. Diseases evoked the image of vague symptoms with little variations from the norm. Moreover, the available diagnostic techniques and therapeutic drugs shaped the disease identity. The more accurate tools did not guarantee a reliable disease diagnosis, in many cases, added to the confusion. The technological innovation and haematological characterisation of chlorosis meant the focus shifted from the disease's epistemological, social, and psychological complexities to a narrow and unreliable taxonomy (Denic & Agarwal, 2007).

New haematological thoughts did not explain how and why chlorosis disappeared. The disease disappeared not because its symptoms ceased to exist but because the epistemological, social, and moral constitution was replaced with a ‘newer taxonomy. The characteristic symptoms of chlorosis such as lethargy, pallor, and menstrual disturbance continued to exist but were categorised into new disease constructs within a new style of scientific disease management. Chlorosis simply did not fit within the modern medical system; its demise was more rhetorical than in principle (Wailoo, K, 1999, p. 30). Modern clinicians ceased to recognise the existence of this disease. The new era gave a distinct identity to the malnutrition disorder called ‘Iron deficiency anemia’. Iron deficiency anemia emerged as a byproduct of new-age medicine devoid of social, cultural, and moral overtones (Brumberg, 2016).

1.1.2.3. GENDER AND CHLOROSIS

A group of physicians believed that the demise of chlorosis was not due to technological advancements but because of women’s emancipation and improved social status in western societies in the twentieth century. Ironically, freedom, lax and inconsistent behaviour, bringing political freedom and changing sexual mores, which were once blamed for chlorosis, was now associated with its demise. Some physicians believed that changing the social and political landscape, such as forming women’s unions, social reforms, and industrial health advocacy improved the women’s labour and overall living conditions (Sheftel et al., 2012). Chlorosis disappeared because of the availability of a nutritious diet, healthier and more accessible mode of life, better living places, shorter working hours, exercise, and disuse of tightly laced corsets. The social and political reforms led to the disappearance of the Victorian-era social assumptions and behaviours and improved the quality of life, followed by chlorosis decline (Trigo, 1999).

1.1.3. LEARNINGS FROM THE PAST

Almost 100 years after Mackay identified the linkages between dietary iron deficiency and anemia, nutritional anemia is the leading nutritional disorder worldwide; iron deficiency is the lead actor, and iron-centric approaches are the mainstay of anemia discourse. If history is anything to learn, the construction of chlorosis in varied time frames reveals telling stories of numerous identities of the disease. There was no single reality of chlorosis. The diverse narratives suggest that chlorosis meant many different things during the last century. The various ideas produced radically different and changing notions of womanhood, medicine, and disease (Wailoo, K, 1999, p. 43).

Often, its constitution and identity were contested and conflicted. Privileging one identity over another or assigning a universal identity to chlorosis negates the alternative realities essential to situate the complexity of the problem in the proper context and perspective. Without going into the validity of the claims of what chlorosis really was, examining stories and constructs concerning chlorosis reveals that the earlier construction (16^{th}-17^{th} century) of chlorosis was embedded in society's moral, environmental, and constitutional dimensions. On the other hand, by the middle of the twentieth century, chlorosis identity was confined to biological and bodily origins. The intersection of gender ideologies, technology, and changing culture of medicine, i.e., the culture of moral management, diagnostic techniques, iron pills and advocates of women's emancipation, shaped the changing identity of chlorosis (Wailoo, K, 1999, p. 44). In this context, the inherent complexities linked to the identity of the disease, anemia, must be examined. The past discourses can inform the present debates on the constitution, causes and approaches to addressing anemia.

1.2. INTRODUCTION

This section introduces the magnitude and prevalence, health consequences, causes and commonly used intervention strategies to control and prevent anemia.

1.2.1 MILD, MODERATE AND SEVERE ANEMIA

Anemia is defined as a "condition in which the number of red blood cells or their oxygen-carrying capacity is insufficient to meet the physiologic needs for oxygen delivery to the heart, muscles, brain, and other vital tissues. Haemoglobin is the primary oxygen-carrying molecule within the red blood cells; therefore, anemia is typically measured in terms of haemoglobin content and is diagnosed by low haemoglobin concentrations (WHO, 2011a).

The World Health Organization (WHO) classifies anemia into mild, moderate, and severe, based on haemoglobin cutoffs. Mild anemia corresponds to a level of haemoglobin concentration of 10.0-10.9 g/dl for pregnant women and children under the age of five years and 10.0-11.9 g/dl for nonpregnant women. For all the population groups, moderate anemia corresponds to 7.0-9.9 g/dl, while severe anemia corresponds to a level less than 7.0 g/dl (Table:1.1).

Table 1:1 Classification of anemia based on haemoglobin cutoffs

Population	*Non-anemia(g/dl)*	*Mild (g/dl)*	*Moderate (g/dl)*	*Severe (g/dl)*
Children 6 - 59 months of age	≥11.0	10.0-10.9	7.0-9.9	<7.0
Children 5 - 11 years of age	≥11.5	11.0-11.4	8.0-10.9	<8.0
Children 12 - 14 years of age	≥12.0	11.0-11.9	8.0-10.9	<8.0
Nonpregnant women (15 years of age and above)	≥12.0	11.0-11.9	8.0-10.9	<8.0
Pregnant women	≥11.0	10.0-10.9	7.0-9.9	<7.0
Men (15 years of age and above)	≥13.0	11.0-12.9	8.0-10.9	<8.0
Source: (WHO, 2011)				

The different regions or population groups have variable anemia prevalence. WHO has graded anemia based on its public health significance for the epidemiological mapping. Anemia is

considered a public health problem of mild, moderate, and severe importance if the prevalence in the population is 0-20 %, 21-40 % and > 40 %, respectively (WHO, 2011a) (Table:1.2).

Table 1:2 classification of anemia as a problem of public health significance

Prevalence of anemia	Category of public health significance
≤4.9	No public health problem
5.0-19.9	Mild public health problem
20.0-39.9	Moderate Public health problem
≥40	Severe public health problem
Source: (WHO, 2001)	

1.2.2. THE GLOBAL PREVALENCE OF ANEMIA

WHO defines anemia based on thresholds set at the fifth percentile of haemoglobin in a normal population appropriately adjusted for age and sex (WHO, 2011a). According to this definition, approximately one-third of the world's population is anemic. Children (6-59 months) and women (15-49 years) have the highest prevalence of anemia (40 % and 30 %, respectively) among all population groups[1].

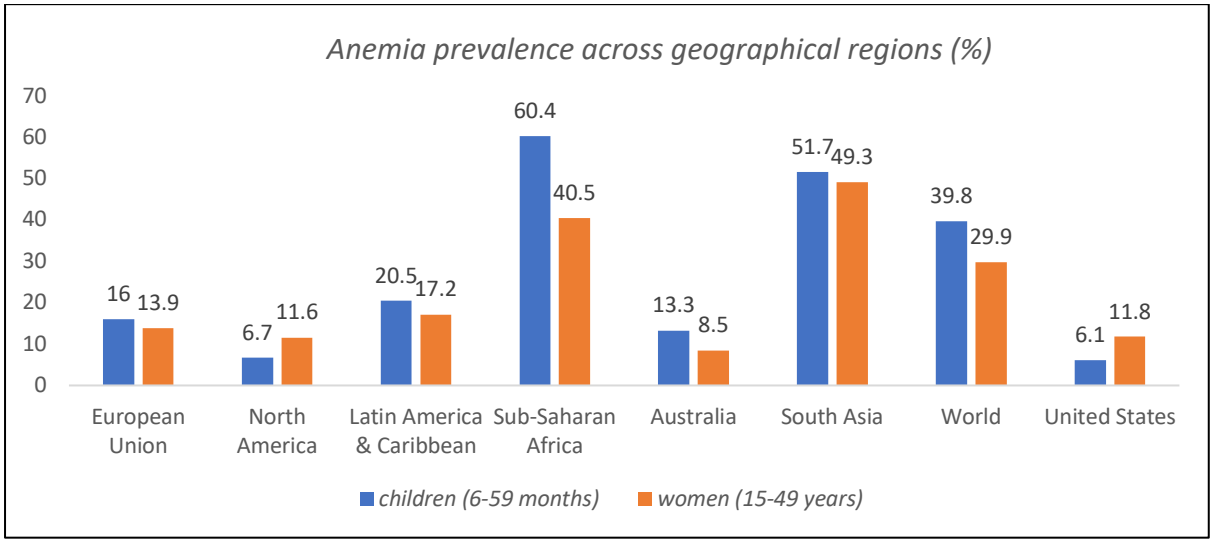
In terms of geographic regions, low-income and developing countries of Africa and Southeast Asia share the disproportionately highest burden of anemia. Asia and Africa accounted for more than 85% of the absolute anemia in high-risk groups in 2010 (Y. Balarajan et al., 2011). The anemia prevalence among children and women in Africa is 60 % & 41 %, whereas in Southeast Asia, 52 % & 50 %, respectively. (Fig:1.1)[2]. Anemia prevalence in children (60.4%) is highest in Africa, whereas among women, it is highest (49.3%) in South Asia. The children and women in the developed countries such as the United States (6 % &12 %), Australia (13 % & 9%), European Union (16 % & 14 %) have a reasonably lesser anemia prevalence than

[1] Global Health observatory, WHO Global anaemia estimates, 2021 edition, World Health Organization, 2021, https://www.who.int/data/gho/data/themes/topics/anaemia_in_women_and_children#:~:text=In%202019%2C%20global%20anaemia%20prevalence,39.1%25)%20in%20pregnant%20women. accessed on 03/01/2021

[2] https://www.who.int/data/gho/data/themes/topics/anaemia_in_women_and_children accessed on 11/04/2021

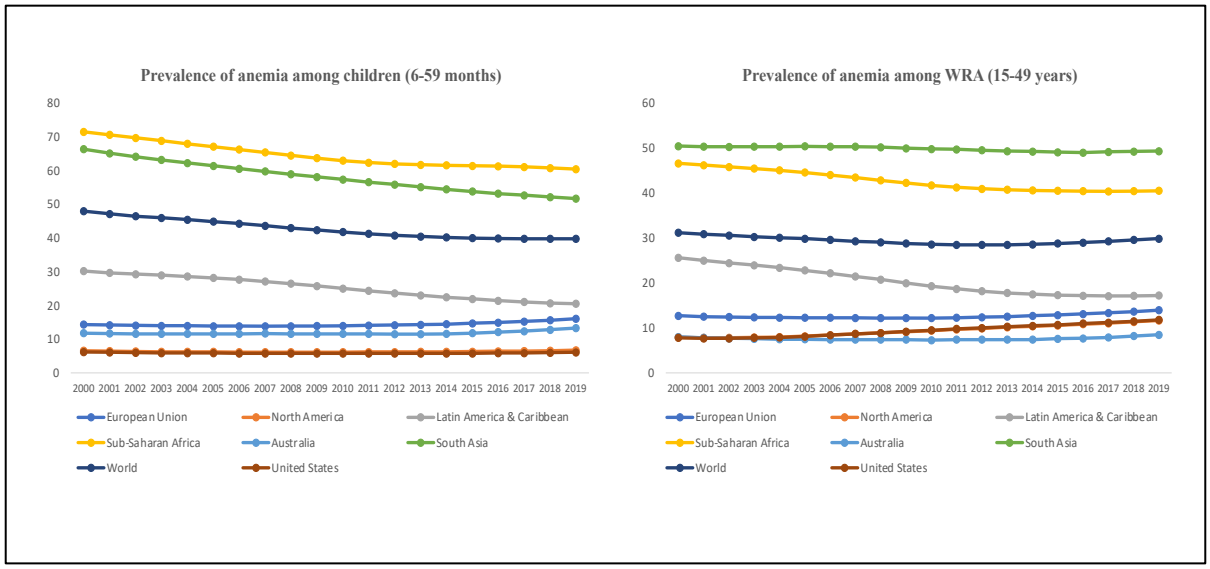
the global average (40 % & 30 %). Global anemia prevalence has remained almost unchanged in the past two decades, emphasising the scale and pernicious nature of the problem (Fig:1.2).

Figure 1:1 Anemia prevalence across geographical regions in 2019



Source: WHO, 2021[3]

Figure 1:2 Time Trends: Global prevalence of anemia among children and women



Source: WHO, 2021[3]

[3] WHO, 2021 edition. Global Health Observatory data repository. http://www.who.int/gho/en/. accessed on 03/01/2022

1.2.3. ANEMIA PREVALENCE IN INDIA'S NEIGHBOURING COUNTRIES

The respective anemia prevalence in children and women in South Asian countries of Afghanistan (44 % & 44 %), Bangladesh (56 % & 48%), Bhutan (55 % & 46%), Indonesia (32 % & 30 %), Nepal (51 % & 44 %), Srilanka (36 % & 25 %) and Thailand (29 % & 30 %) are high. The prevalence of anemia among children (59 %) and WRA (54%) in India are the highest among South Asian countries and the highest in the world (Table:1.3). With over 40 % of children (6-59 months) and WRA (15-49 years) anemic, India has a severe public health problem.

Table 1:3 Prevalence of anemia in children and women in South Asian countries

Country	Children (6-59 months)	Category of Public health significance	Women (15-49 years)	Category of Public health significance
Afghanistan	44	Severe	44	Severe
Bangladesh	56	Severe	48	Severe
Bhutan	55	Severe	46	Severe
India	***59***	***Severe***	***54***	***Severe***
Indonesia	32	Moderate	30	Moderate
Nepal	51	Severe	44	Severe
Pakistan	61	Severe	50	Severe
Srilanka	36	Moderate	25	Moderate
Thailand	29	Moderate	30	Moderate
Source: WHO, 2021[3]				

1.2.4. ANEMIA PREVALENCE IN INDIA

According to the fifth round of population-wide National Family Health Surveys (NFHS-5), 56.6 % of children (6-59 months) and 40.3 % of women (15-49 Years) in India are anemic (IIPS, 2020). According to the comprehensive National Nutrition Survey (CNNS), 41% of preschool children (1–4 years), 24% of school-age children (5–9 years), and 28% of adolescents (10–19 years) were anemic(MOHFW & UNICEF, 2019). The two national surveys show a marked difference in reported anemia prevalence.

1.2.5. HEALTH CONSEQUENCES OF ANEMIA

Anemia adversely affects health in numerous ways. It leads to malfunctioned clinical and cognitive functions, associated with enhanced morbidity and mortality. Anemia hampers human productivity and is directly related to economic losses.

1.2.5.1. CLINICAL AND COGNITIVE CONSEQUENCES

Anemia leads to impaired oxygen delivery to tissues, resulting in non-specific symptoms, including weakness, fatigue, lethargy, and decreased attention. Anemia associated with ischemic stroke can be a risk factor for other diseases such as tuberculosis and kidney and heart failure (Safiri et al., 2021). Maternal anemia can lead to adverse pregnancy outcomes, including stillbirth, low birth weight, preterm weight, and infant mortality. Anemia during pregnancy increases the risk of haemorrhage and maternal death. Post-partum anemia is linked to stress and depression (WHO, 2017). Anemia contributes to immune system dysfunction, disturbances in the gastrointestinal tract, impaired thermoregulation, neurocognitive function, and predisposition to infection. Iron is the primary etiology of anemia; iron deficiency exacerbates the risk of infections (WHO, 2017).

Anemia can reduce or delay children's cognitive and motor development and can impair adults' physical capacities. Iron deficiency anemia can cause irreversible brain structure and function alterations, which may not be cured even with iron treatment (WHO, 2017).

1.2.5.2. MORTALITY, MORBIDITY, AND ECONOMIC CONSEQUENCES

Anemia is among the leading causes of child and maternal mortality, attributed to more than 18 % of maternal deaths in low and middle-income countries (Y. S. Balarajan et al., 2013). In a study, haemoglobin concentrations below 50 g/L were linked to increased child mortality, and every 10 g/L increase in haemoglobin concentration was associated with a 24% reduction in risk of death (S. P. Scott et al., 2014).

Anemia shared nearly 9 % of the total global disability burden from all conditions and 18 % of all disability-adjusted life years in India in 2016. It was among the five leading causes of years lived with disability (YLD) in 2016 (Vos et al., 2017). Anemia is associated with reduced learning and work productivity. It has been estimated to cause a loss of 0.81% of gross domestic

product (GDP) in selected developing countries. In 2013 anemia contributed to an annual production loss equivalent to 1.3 % of India's gross domestic production (GDP). The Poor households of the developing countries bear the maximum brunt of these economic losses (WHO, 2017). Thus, anemia has significant consequences for health and social and economic development.

1.2.6. CAUSES OF ANEMIA

Anemia is considered to have a multifactorial etiology. The most common cause of anemia worldwide is a nutritional iron deficiency caused by inadequate dietary iron intake or absorption, increased need for iron during pregnancy or growth, and increased iron losses due to menstruation and infections (Kinyoki et al., 2021). An estimated 50% of anemia worldwide is due to iron deficiency (WHO, 2017). Other important causes of anemia worldwide include nutritional deficiencies of vitamin B12, folate, vitamin A, vitamin C, Zinc and copper, infections, chronic inflammations and genetic conditions including sickle cell disease and thalassaemia (WHO, 2016).

From a biological perspective, anemia occurs through three non-mutually exclusive pathways: blood loss, increased red blood cell destruction and inadequate red blood cell production, which leads to either less production of micronutrients or loss of micronutrients in the body (Kinyoki et al., 2021). Anemia is also associated with various biological, demographic, economic and social factors. The causes of anemia in the population and the linkages between multiple determinants are not well mapped.

1.2.7. INTERVENTION STRATEGIES FOR ANEMIA

Traditionally, the treatment of anemia involves identifying the etiology and treatment of underlying causes through appropriate interventions. At the immediate level, the scope of the treatment is to replenish iron stores to bring at normal levels and prevent future recurrence of micronutrient loss or deficiency through targeted interventions delivered to affected individuals throughout the life cycle. Several strategies are used to treat anemia - Iron and folic acid supplementation, food-based approaches such as food fortification with iron and other micronutrients, complementary feeding and exclusive breastfeeding, deworming, and behavioural change communication strategies.

1.2.7.1. IRON AND FOLIC ACID (IFA) SUPPLEMENTATION

WHO recommends iron supplementation as a therapeutic and preventive measure in populations at high risk of iron deficiency and anemia. IFA supplementation is the main pillar of India's response to control anemia among various age groups. The variable doses of elemental iron are recommended to different age and sex groups (WHO, 2017). Iron supplementation is considered an effective strategy to reduce the risk of anaemia (Gera et al., 2007).

1.2.7.2. FOOD-BASED APPROACHES

Food-based strategies to prevent anemia focus on improving the availability, access, and consumption of vitamin and mineral-rich foods. Three kinds of food bases strategies are used to address anemia:

1.2.7.2.1. DIETARY DIVERSIFICATION

Such strategies aim to increase the access of households and individuals, particularly those at most risk of anemia, to the diversified diets (increasing the variety and types of food consumed) and improve the year-round availability of micronutrient-rich foods. Food-based strategies also focus on improving the bioavailability of nutrients by including components in the diet that will enhance absorption or reduce the impact of antinutrient factors (Thompson, 2007).

1.2.7.2.2. INFANT AND YOUNG CHILD FEEDING PRACTICES (IYCF)

The promotion of appropriate feeding practices such as exclusive breastfeeding for six months and complementary feeding beginning at the age of six months until the age of two years is an important intervention strategy to meet the child's daily nutrient needs. IYCF is aimed at preventing anemia from being set on early in life in children under the age of two years.

1.2.7.2.3. FOOD FORTIFICATION

Fortification implies enriching foods with nutrients to improve the nutritional quality of diets. For decades, food fortification has been used to mitigate various nutritional deficiencies, including iron, in Europe and the United States (R. Hurrell et al., 2010). Food fortification has

gained momentum as an effective strategy to increase the iron and other micronutrient intakes at the population level. As a result, 91 countries so far have mandated wheat flour fortification. Under the food safety & standard regulation bill 2016, India introduced legislation to mandatorily fortify wheat flour with iron, folic acid, and vitamin B12 and Salt with iodine and iron. The Anemia Mukt Bharat (AMB) strategy, India's flagship programme under POSHAN Abhiyan, also encompasses mandatory food fortification as one of the main intervention strategies for controlling and preventing anemia.

1.2.7.3. DEWORMING PROGRAMMES

Deworming approaches are an integral component of anemia prevention and control strategies globally. Hookworm infestations are associated with one-third to one-half of anemia cases in African and Southeast Asian countries (Sarkar et al., 2017). India has the highest burden of soil-transmitted helminths (STH) infections globally; approximately 1 in 5 people are infected with STH (Abraham et al., 2018). Deworming strategies are employed to control worm infections, which exacerbate the risk of anemia. The government of India launched one of the world's largest school-based deworming programs in 2015, aiming to deworm all preschool and school-aged children between 1 to 19 years of age twice yearly on the National Deworming Days (MoHFW, 2018). As part of deworming strategy, an antihelminthic drug is administered to target groups for preventive and therapeutic effects on the anemia (WHO, 2017).

1.2.7.4 BEHAVIOURAL CHANGE COMMUNICATION STRATEGIES (BCCS)

BCCS is used to bring the desired change in the behaviour of the individuals using multiple approaches such as educational activities, training, and communication. Three behaviours under the BCCS strategy are broadly targeted (MoHFW, 2018).

i) compliance and adherence to Iron folic supplementation and deworming programmes
ii) appropriate IYCF
iii) adequate intake of diversified food, including iron, proteins and vitamin-rich food and promotion of delayed cord clamping in all health facilities deliveries followed by early breastfeeding initiation (within one hour of birth).

1.2.7.5. SOCIAL AND COMMUNITY INTERVENTIONS

Integrated public health interventions directed at improving the socioeconomic status, mother's education, food insecurity, water, sanitation and hygiene (WASH) programmes are associated with improving maternal and child nutrition, including anemia (Nguyen et al., 2018). In India, the Integrated child development scheme (ICDS) and mid-day meal (MDM) are the two broad-based policies linked to anemia. ICDS, through a network of Anganwadi workers, is a delivery platform for preschool education, supplementary nutrition, health and nutrition education, immunisation, health check-ups and referral services to children under the age of six years (Saxena & Srivastava, 2009). At the same time, Mid-day Meal (MDM) scheme envisages the adequate supply of macronutrients (energy and proteins) and micronutrients, including iron, to the target beneficiary through hot-cooked meals served to children aged 6-23 months and school-going children in the school (MoHFW, 2013). Aside from ICDS and MDM, there are few broad-based policy efforts addressing anemia in India. The social interventions aim to target the population-level determinants. However, little is known about the use of such interventions for anemia.

1.2.8. SUMMARY

The introductory chapter reviewed the historical construction of chlorosis and showed how the changing social and technological narratives around gender, technology, and disease shaped chlorosis identity. The chlorosis identity changed from the 'disease of virgins' that required social and moral management to 'iron deficiency anemia' that can be rectified by iron supplements. The evolution of the disease construct from 'chlorosis' to 'iron deficiency anemia' encompasses the multiple, diverse, and contested narratives of the illness. There is no one theory about the causation and management of the disease. With the rise of modern medicine, particularly the haematological diagnostic techniques and therapeutic iron as a powerful tool, 'iron deficiency anemia' emerged as the dominant pathological entity characterised by iron deficiency and low haemoglobin levels by the mid-twentieth century.

In the last decades, significant breakthroughs in haematology and iron science, particularly in iron metabolism, have been achieved. Anemia was established primarily as a condition arising from iron deficiency. The role of other nutritional factors (vitamin A, vitamin B12 and folate), including diets and non-nutritional factors (infections, inflammations, and genetic disorders)

associated with anemia, was subsequently recognised. In the present knowledge system, anemia is recognised as a multifactorial problem caused due to numerous nutritional and non-nutritional factors. Iron supplementation, food-based approaches, deworming programmes, and behavioural change interventions are used to address these causal factors. The scientific advancements and plethora of programmes have not yielded desired results. Anemia prevalence continues to be high in children and women in developing countries, including India.

CHAPTER 2

"There are people in the world so hungry, that God cannot appear to them except in the form of bread"

Mahatma Gandhi

CHAPTER 2. RESEARCH METHODOLOGY

2.1. CONCEPTUAL FRAMEWORK

The conceptual framework (Fig:2.1), which is used as a guideline for this thesis, depicts the complex dynamics of social, economic, environmental, and biological factors that determine the risk of developing anemia is derived after the literature review.

2.1.1. DOMINANT FRAMEWORKS OF HEALTH

Raphael suggests that health can be viewed within three general frameworks or paradigms: biomedical, lifestyle behaviours and socio-ecological/socioenvironmental (Raphael, 2006). The biomedical approach emphasises the high-risk groups and incorporates a linear view of single or multiple micronutrient deficiencies and their impacts on health. This traditional approach links singular causes with singular outcomes (e.g., insufficient folate intake and neural tube defects) without considering context or other factors affecting these relationships. The lifestyle approach goes wider, considering multifunctional nonlinear relationships between behaviour and food and dietary patterns. The behavioural approach focuses on high-risk attitudes and behaviours and develops programs that educate and support individuals to change behaviours. The socio-ecological paradigm incorporates health and nutrition within social and ecological contexts. The biomedical and behavioural are the dominant paradigms, while socio-ecological is underemphasised. The concept of 'social determinants of health' resides in the socio-ecological category (WHO, 2008).

Traditional questions on health and nutrition have focused on identifying individual biomedical and behavioural risk factors associated with the disease. Individually oriented approaches focus on individual characteristics such as income, educational level, occupational classification, individual control, and empowerment and how they relate to health and nutrition.

The most significant contribution to understanding the role of social determinants of health comes from social epidemiologists, who have expanded the unit of analysis to broader concerns with social conditions, environments, and occasionally the political context within which environments get created and sustained (Raphael, 2006). Within these frameworks, the focus is on the nature of environmental structures and the pathways that influence health. These

structural approaches concern how societal structures mediate the relationship between social determinants of health and health. Social determinants of health and health both are influenced by horizontal and vertical structures. Horizontal structures are the more immediate structures that shape health and wellbeing, such as class, gender, and race stratification, representing the models of hierarchy that shape the access to economic resources (income, housing, food, employment, and education), influence and power. The vertical structures such as political, economic, and social forces influence and determine the quality of horizontal structures (Raphael, 2006).

2.1.2. MODELS OF SOCIAL DETERMINANTS OF HEALTH

The term "social determinants of health" has emerged due to a search by researchers to identify the specific mechanisms by which individuals of different socioeconomic groups come to experience varying degrees of health and illness. Various approaches to the social determinants of health exist, all concerned with the distribution and organisation of social and economic resources. In 1986 Ottawa Charter for Health promotion identified peace, shelter, education, food, income, a stable ecosystem, sustainable resources, social justice, and equity as prerequisites for health. In 1992, Dahlgren and Whitehead postulated the 'rainbow model' to capture the interrelationship between individual behaviour, social, environmental, and economic determinants of health (Dahlgren & Whitehead, 2007). The Canadian Institute of Advanced Research, British Working group and United States centres for disease control developed models for analysing determinants of health at the population level. A synthesis of these models identified 11 key social determinants of health: Aboriginal status, early life, education, employment and working conditions, food security, health care services, housing, income and its distribution, social safety net, social exclusion, and unemployment and employment security (Raphael, 2006).

A major failing of earlier theories on social determinants of health was that they did not answer the question of the quality of determinants shaped by political, economic, and social forces. This gap was addressed by the WHO's commission on social determinants of health (CSDH), which emphasises the role of the socio-political context under which structural, intermediary and immediate determinants of health operate. CSDH sets out key areas – of daily living conditions and the underlying structural drivers that influence them (Solar & Irwin, 2010).

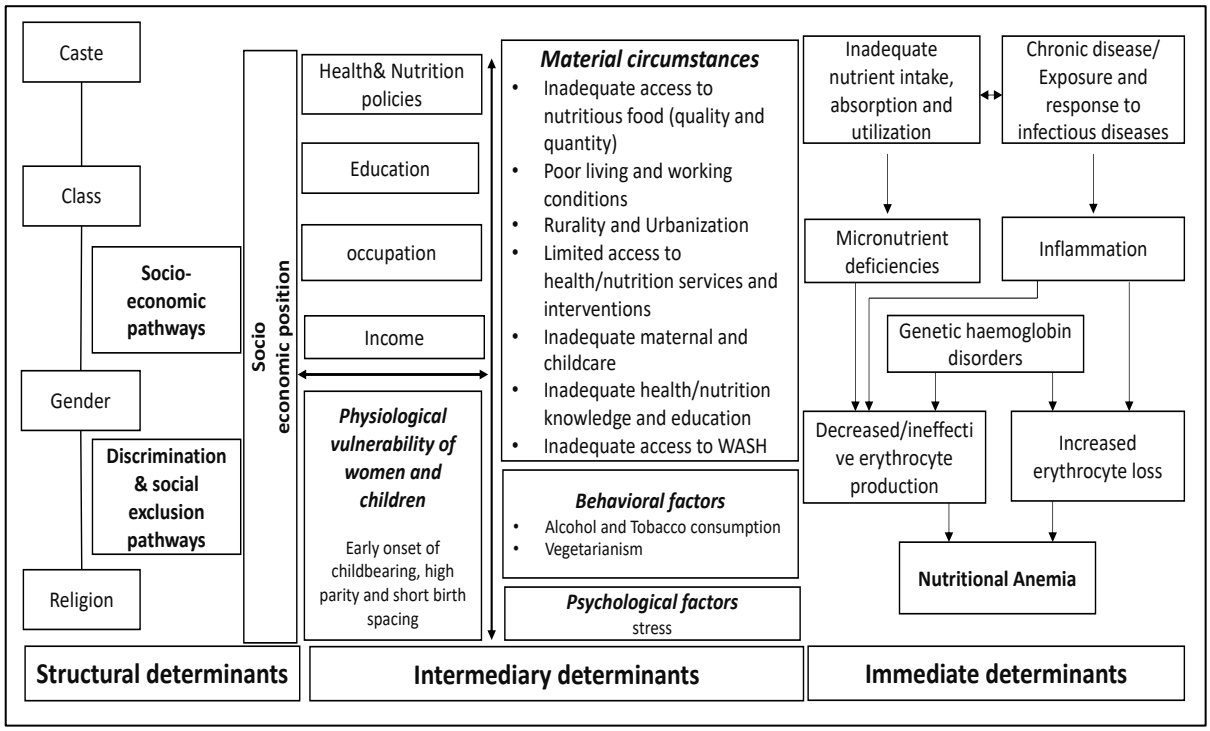
2.1.3. CONCEPTUAL FRAMEWORK OF DETERMINANTS OF ANEMIA

In the last decade, five major conceptual models for determinants of anemia have been proposed. The models (Y. Balarajan et al., 2011) and (S. Pasricha et al., 2013) were developed in low-income and middle-income countries. Another model (Namaste et al., 2017) was developed based on data from 14 countries. Chaparro and Suchdev's conceptual model (Chaparro & Suchdev, 2019) for the etiology of anemia is a syncretic conceptual model adapted from the earlier frameworks (Balarajan, Pasricha and Namaste's model). USAID anemia task force 2013 proposed a framework for understanding anemia's underlying and direct causes (USAID, 2013).

Most conceptual models have reaffirmed the findings of earlier frameworks on health and nutrition. These frameworks identified poverty, the standard of living, education, wealth, access to health services, nutritious food, water, sanitation, and hygiene as determinants of anemia. Despite an agreement on the linkages between anemia and social factors, the approach to social determinants of anemia remains individualised and behavioural. A structural orientation is lacking.

To deepen and extend this analysis, this study uses key components of WHO's commission on social determinants of Health (CSDH) framework to identify the underlying determinants and map the causal pathways of anemia. CSDH defines social determinants of health as "the conditions in which people are born, grow, live, work and age". The distribution of money, power and other resources shape these conditions at global, national, and local levels. The CSDH framework comprises three elements: socioeconomic and political context, structural determinants, and intermediary determinants. Structural determinants operate through a series of intermediary social factors. Structural factors impart differential social position in a stratified social system and have a differential impact on the incidence and prevalence of diseases, including anemia. The differential exposure, vulnerability, and risks due to one's social position lead to a differential disease pattern, including anemia (WHO, 2008).

Figure 2:1 Conceptual framework of the study



Source: Author's adaptation from (Solar & Irwin, 2010) & (Chaparro & Suchdev, 2019)

2.2. STATEMENT OF THE PROBLEM AND RATIONALE OF THE STUDY

Recognising anemia as one of the most pressing public health challenges, worldwide concerted efforts are going on to control and prevent anemia. The world health assembly (WHA) in 2012 set the target to reduce anemia prevalence among women of reproductive age (WRA) by 50 % between 2012 and 2025. National Nutrition Mission (NNM) of India set the target to reduce the prevalence of anemia by three percentage points per year among children, adolescents, and women in the reproductive age group (15–49 years), between 2018 and 2022. India is most likely to fall short of the targets set by WHA and NNM. The latest National family health survey (NFHS-5) reported an increase in anemia prevalence in women and children compared to the last round (IIPS, 2020). Males (15-49 years), a largely ignored population group for anemia control and prevention strategies, have moderate anemia prevalence. Anemia prevalence continues to be high across social groups.

In India, Iron supplementation, food-based strategies (dietary diversification/modification, fortification of food with iron and other micronutrients), nutrition and health education to promote food-based strategies, exclusive breastfeeding and complementary feeding to

children) and parasitic and disease control measures, including deworming, have been part of anemia control strategies for decades (Kapur et al., 2002). Decades of programmes and policies targeted at anemia children and women at global and national levels have minimal impact on reducing anemia.

One of the main reasons for the persistently high prevalence of anemia in India is attributed to low coverage and compliance of programmes at the national level. Regions where coverage is relatively better also have high anemia prevalence. Recently coverage of IFA supplementation and other programmes associated with anemia has improved, but that has not translated into proportionate anemia reduction. The success of control trials in addressing anemia is variable, but there is a commonality among most of them, i.e., they only reduce a fraction of anemia. Why control trials did not address the remaining part remains unexplained. Therefore, the notion that poor coverage and implementation of programmes as the main reasons for high prevalence appears to be flawed as it does not explain why anemia occurs or develops in an individual or a population in the first place. Therefore, it is necessary to understand why prevalence rates of anemia continue to be high in India and what epidemiologically important fundamental factors remain unaddressed by current policy approaches.

There is an abstract understanding of what constitutes anemia, limited knowledge of etiological factors, and their respective contribution to anemia in the population. From the programmatic side, little is known about the reasons for the failure of programmes and policies to control and prevent anemia. Therefore, the thesis seeks to advance the understanding of the nature, causation, and programmatic approaches to address anemia. The thesis focused on the breadth of the published literature and reports and triangulated the information derived from key informants to answer the research question using a narrative review approach.

2.3. OBJECTIVES OF THE RESEARCH

The study has three mutually inclusive objectives, which are as follows:

1. to review the nature and scope of nutritional anemia
2. to explore and analyse the biological and social determinants of anemia.
3. to explore and analyse the programmatic responses to nutritional anemia.

2.4. RESEARCH QUESTIONS

The study has one primary research question

Why does nutritional anemia persist as a major public health problem in India, and why have intervention strategies failed to control and prevent nutritional anemia?

2.5. METHODS

The study is descriptive and qualitative. It used systematic narrative review methods that applied several approaches to synthesise the diverse findings and collectively answer the research questions. The narrative review is a text-based qualitative synthesis that adopts a narrative approach to research synthesis and seeks to generate new insights and recommendations by going beyond the summary of findings from different studies (Snilstveit et al., 2012). The strength of narrative review lies in its unstructured approach to systematically reviewing a large volume of literature to synthesise and synchronise the data. The primary purpose of such a review is to provide a comprehensive background and broad perspective on the topic to understand the nature of the problem or its management and highlight the research gaps (Green et al., 2006; Paré & Kitsiou, 2017). The study used four research approaches to collect and interpret the data and synthesise the findings (Table:2.1).

Table 2:1 Approaches for data collection and synthesis

Subsection	Approaches	Methods used
1	Secondary review of published literature	Narrative review
2	Policy documents as the primary data source	Narrative review & Qualitative content analysis
3	Key informants' interview (KII)	Open-ended, semi-structured interview schedule
4	Triangulation and synthesis	

2.5.1. SOURCES OF DATA

The study used primary and secondary data.

2.5.1.1. PRIMARY DATA

Primary data was derived from key informants' interviews, policy documents and reports from national and international organisations such as WHO, UNICEF, Micronutrient Initiative (MI), Food Fortification Initiative (FFI), and Global Alliance for Improved Nutrition (GAIN). Indian government policy documents from various ministries were also used. In-depth interviews were held with researchers and scientific experts using a semi-structured interview schedule. The different digital platforms such as WHO's e-Library of evidence for nutrition action (eLENA), Institutional repository for information sharing (IRIS), Global health observatory database and world bank health database were used.

2.5.1.2 SECONDARY DATA

Secondary data was retrieved from peer-reviewed literature published online and various national and international data sources such as the National family health survey (NFHS), comprehensive national nutrition survey (CNNS), Global Burden of Disease (GBD), National sample survey office (NSSO), Global Nutrition report and India Health Report on Nutrition.

2.5.2. THE SEARCH STRATEGY

A comprehensive systematic search of peer-reviewed, published literature using carefully devised 'keywords' was undertaken to retrieve the relevant literature using three electronic databases, i.e., Scopus, Web of Science and PubMed, under each theme. WHO's online portals, such as the global health repository, WHO e-Library of Evidence for Nutrition Actions (eLENA), WHO's global database, and World Bank's database, were also searched separately for relevant policy documents. The study also used the snowballing technique of finding important references from published literature.

2.5.2.1. SEARCH TERMS

The study built the search query on three layers with relevant search terms.

1. The first layer referred to "nutritional anemia", "iron deficiency anemia", "iron deficiency", "anemia".

2. The second layer included equity, including possible categories of disadvantaged populations such as residence, race/ethnicity, occupation, gender, religion, education, socioeconomic status, age, causes, classification, etiology, risk factors, assessment, iron deficiency, vitamin A deficiency, folate deficiency, B12 deficiency, riboflavin deficiency, malaria, infection, infectious disease, schistosomiasis, hookworm, intestinal helminths, HIV, tuberculosis, anemia of inflammation; anemia of chronic disease; thalassemia, α-thalassemia, β-thalassemia; sickle cell disease; sickle cell disorders; hemoglobinopathies; haemoglobin disorders; hepcidin; 'Iron supplementation', 'food fortification', deworming, behavioural, nutrition-sensitive, and nutrition-specific interventions.

3. In the third layer, search terms were narrowed down to only include articles on India. The search terms of three layers were combined using Boolean operators' OR' and 'AND'. Search queries were modified to meet the specific requirements of the three databases.

Search Strategy = #1 AND #2 AND #3

2.5.2.1. SCREENING OF LITERATURE

A preliminary screening of literature was done based on the title and abstracts. The literature found not relevant to the objectives of the study was excluded. In those articles where it was impossible to determine the article's relevance based on the abstract, the whole article was obtained and manually read to assess the applicability. Since a wide array of literature was found after the search, literature that did not give any new insights or was found repetitive was excluded.

2.5.3. ANALYSIS AND SYNTHESIS OF WORK

The selected documents were sorted for themes and subthemes, and the findings were presented descriptively.

2.5.3.1. NARRATIVE SYNTHESIS OF PUBLISHED LITERATURE

The various themes, subthemes and their linkages were coherently explained using the narrative synthesis method. Narrative synthesis is better suited to addressing the broad philosophical perspectives and theory in a balanced manner to unpack the inherent controversies and inconsistencies in theories on the constitution, causation, and intervention approaches for anemia (Ferrari, 2016).

2.5.3.2. THEMATIC CONTENT ANALYSIS

Thematic content analysis has been defined as "a research method for the subjective interpretation of the content of text data through the systematic classification process of coding and identifying themes or patterns" (Braun & Clarke, 2006). The thematic content analysis goes beyond merely counting words or extracting objective content from texts to examine meanings, themes and patterns that may manifest or be latent in a particular text. It allows us to understand social reality in a subjective but scientific manner.

The thematic content analysis involves condensing raw data into categories or themes based on valid inference and interpretation. This process uses inductive reasoning, by which themes and categories emerge from the data through the researcher's careful examination and constant comparison. But this method does not need to exclude deductive reasoning (Zhang & Wildemuth, 2009). This study has used an inductive and deductive thematic content analysis approach to explore the pattern of themes or categories that define the epidemiology of anemia in the literature. NVIVO 12 software was used to screen the information obtained from each article/document.

2.5.3.3. KEY INFORMANTS' INTERVIEW (KII)

KII is only a tiny fraction of the whole data collection exercise. KII aimed to gain detailed insights and highlight the knowledge gap into the nature of the problem, causes and approaches

to control and prevent anemia, which can help formulate recommendations to improve the program's performance. The criteria for selecting the key informants were their proven expertise, specialised knowledge, and unique perspectives to reflect on the anemia within health and nutrition discourse. The noted and experienced academicians, researchers or professionals associated with the government and non-government organisations engaged in providing policy inputs in the anemia, health and nutrition domain were selected for interview. A number of 4-6 key informant interviews are recommended for policymakers[4]. Six key informants were finally chosen for the interview. The details of the selected key informants are below (Table:2.2).

Table 2:2 Details of the key informants

Name of Key Informant	**Organisation/ Expertise**
Prof. Anura Kurpad	Former Head of the Department of Physiology at St John's Medical College and Division of Nutrition at St. John's Research Institute, Bangalore. He is the Chairman of the ICMR Expert Committee on Nutrient Requirements of Indians, Nutrition and Fortification Scientific Panel of the FSSAI, and a member of the Technical Board of Nutrition at NITI Aayog.
Dr Rajiv Tandon	Director, Health, RTI International. He is a leader in various areas like reproductive, maternal, newborn, child health and nutrition, neglected tropical diseases, malaria, and health systems strengthening. He is engaged in global, regional, national, and subnational health policy reforms.
Prof. Rajesh Kumar	Retd. Professor, Department of community medicine and school of public health PGIMER, Chandigarh. He is a technical advisor to Health Systems Transformation Platform
Prof. H.P.S Sachdev	Senior Pediatrician and Clinical Epidemiologist, Sitaram Bhartiya Institute of Science & Research, New Delhi
Prof. Dipa Sinha	Professor at Ambedkar University, New Delhi She has worked on issues related to food rights, nutrition and public health.
Ms Ruchika Sachdeva	Nutrition lead, India country office, Bill & Melinda Gates foundation

[4]https://www.atsdr.cdc.gov/communications-toolkit/documents/07b_stakeholder-interview-guide_policymakers-final-101315_508.pdf accessed on 01/04/2022

2.5.3.3.1. ANALYTICAL STRATEGY FOR KII

KII was done (telephonic or video conferencing) using a semi-structured interview schedule containing seven open-ended questions. The main questions were followed by probing questions for in-depth enquiry (Annexure I). The audio and videos were recorded with prior consent, and additional notes for the emerging impressions of the conversation were jotted down. The whole data was transcribed into a single word document, categorised according to the interview questions to have a document of all interviewees' discussions organised under each question. A combination of content analysis and descriptive coding was used to analyse the interviews for common themes and subthemes across open-ended questions. Themes and subthemes for coding were developed after the interview was developed based on the relevance of the interview text. The qualitative software NVIVO 12 was used to generate code and analyse the data systematically. Results were analysed based on the most common themes that emerged throughout the interviews and differences in responses among informants, if any. The results from KII's were used; to substantiate or contradict the findings from three major themes that emerged from the narrative review of the literature and to identify the knowledge gap in the existing literature.

2.5.4. TRIANGULATION AND SYNTHESIS

Triangulation refers to using multiple methods or data sources in qualitative research to develop a comprehensive understanding of phenomena. Triangulation also has been viewed as a qualitative research strategy to test validity through the convergence of information from different sources (Nancy Carter et al., 2014). In the present study, three different sources of data collection, namely secondary sources, primary data from policy documents and key informant interviews, were used to answer the research questions and validate the findings of the enquiry of the study. Two different triangulation approaches were used to understand and map the epidemiology and intervention approaches to anemia in India.

2.5.4.1. METHOD TRIANGULATION

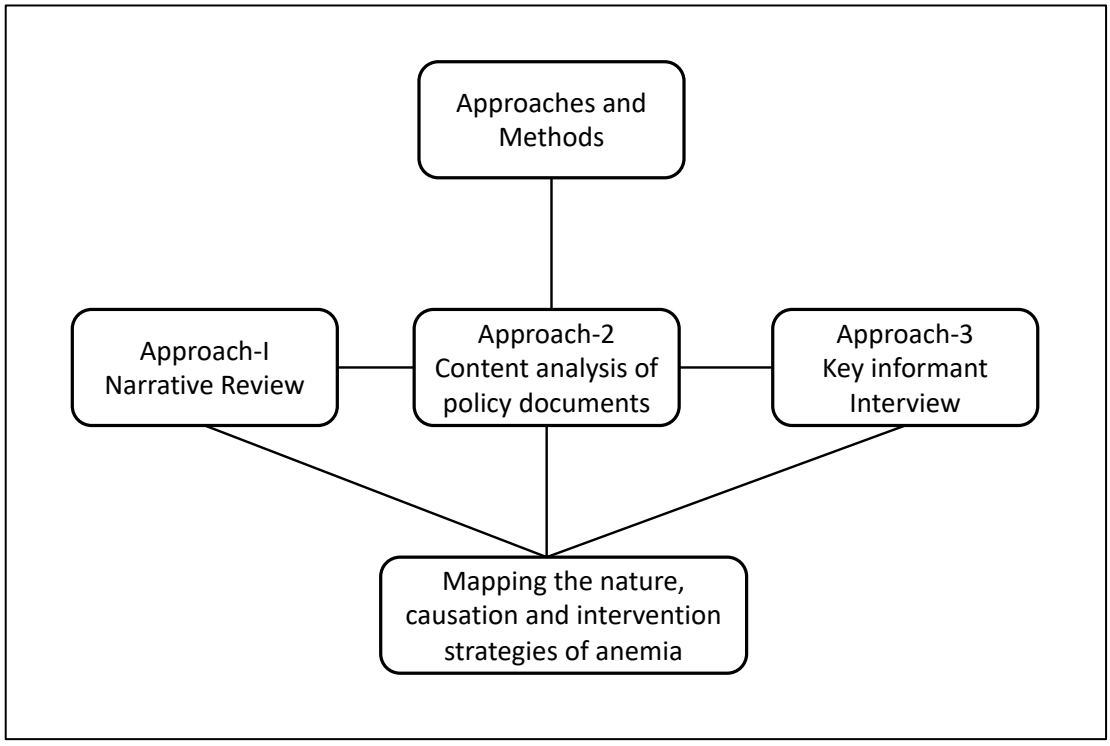
One method is not sufficient to explain the layered complexity of anemia. Using three methods to collect the data is beneficial for a nuanced understanding of the research problem. Three sources complement and supplement each other. For example, the secondary literature review

was inadequate in providing information on the evolution and shifts in programmatic approaches. Therefore, content analysis of policy documents was important. A review of secondary literature filled the inadequacies and limitations of the policy documents to provide relevant information on the alternate discourse of anemia. National and international survey reports and policy documents provided factual information on the prevalence and distribution of anemia and its determinants. Key informants' interviews highlighted in-depth technical, conceptual and programmatic issues. Amidst the conflicting theories and lack of consensus, Key informant interviews confirmed the findings by the other two methods and provided different perspectives, thus adding breadth to the enquiry. Further, the narrative review method helped interwove and synchronise the results coherently. The synthesis and understanding of various themes under the study helped map the knowledge on the nature and causation of anemia and highlight the gap between knowledge and programme practice.

2.5.4.2. THEORY TRIANGULATION

Theory triangulation involves different theories to analyse and interpret the data to help synthesise existing approaches. It aids in describing an appropriate structure for the enquiry

Figure 2:2 Approaches and methods of the study



2.6 STRUCTURE OF THESIS

This thesis provides a detailed overview of nature, causation, and programmatic approaches to anemia. It addresses the gaps in scientific understanding to assess the problem of anemia. There are a total of 10 chapters in this thesis.

The first chapter is Introductory and has two components. The first component gave a historical analysis of the construction and remedies of anemia. The second component introduced the definition, prevalence at the global and national (Indian) level, health consequences, causal factors, and the most commonly used intervention strategies to address anemia.

Chapter two discussed the study's conceptual framework, the problem statement, rationale, and the research methods, followed by a chapterisation of the thesis.

Chapter three reviewed the contradictions within the discourse of anemia to understand the gaps and limitations of defining anemia from a biomedical perspective. The chapter answered the following questions: what is the nature and scope of nutritional anemia? What is anemia/or what constitutes anemia? What are the implications of defining anemia based on haemoglobin thresholds? What frameworks are used to describe anemia? Is there a popular discourse on anemia? What are the alternative discourses of anemia? What contradictions arise within the popular narrative of anemia?

The fourth chapter analysed the epidemiological trends and patterns of anemia and iron deficiency. It further investigated the linkages and contribution of different etiological factors to anemia in India. The chapter addressed the following questions: Is there a linkage between anemia, iron deficiency and other micronutrient deficiency? What etiological factors contribute to anemia development in India? What is the percentage contribution of various etiological factors to anemia in India?

The fifth chapter explored nutritional and non-nutritional etiologies of anemia, their linkages with anemia and mechanisms of causation. The chapter addressed the following questions: What nutritional and non-nutritional factors are associated with anemia? What is the mechanism of interaction between various nutritional and non-nutritional factors?

The sixth chapter discussed the interactions of iron metabolism with dietary factors. The chapter answers the following questions: What is the role of carbohydrates, proteins, and

energy in iron metabolism? What are the linkages between dietary patterns, dietary iron intake and anemia in India? Can diets alone address anemia?

The seventh chapter explored the underlying social, economic, demographic, and environmental factors and traced the underlying pathways that could affect the development of anemia in different social groups. The chapter addressed the two questions: What are the social determinants of anemia? What are the underlying pathways that lead to anemia?

The eight-chapter explored and critically analysed the programmatic approaches to anemia for their public health relevance. The chapter addresses the following research questions. Why have programmes and policies failed to reduce anemia prevalence? What is the evidence of the effectiveness of major programmes and policies? What fundamental factors remain unaddressed by the current intervention approaches?

Chapter nine explored the evolution of India's anemia control and prevention strategies and analysed the programmatic shifts and its implication. The chapter critically analysed the public health relevance of the anemia control programmes with reference to the social determinants framework. The chapter addresses the following question: are the current intervention strategies adequate to address anemia? What elements remain unaddressed in the anemia control strategies in India?

Chapter ten discussed, summarised and concluded the findings of the thesis research. The chapter at the end suggested detailed policy recommendations for India's anemia prevention and control strategies.

CHAPTER 3

"When India achieved independence, more than70 years ago, the people of the country were much afflicted by endemic hunger. They still are"

Amartya Sen

CHAPTER 3. CONTENTIOUS NATURE AND DISCOURSES OF ANEMIA

3.1. INTRODUCTION

The definition of anemia is a determinant of its causation and treatment approaches. The way anemia is defined has implications for public health programs and clinical decision-making. An ambiguous definition of anemia has contributed to the conflicting opinions on the nature and causation of anemia. From a public health perspective, an improved definition has scope for a more accurate assessment of the burden and to make informed decisions regarding allocating resources to address anemia.

The chapter aims to explore the biomedical and alternate discourse of anemia to broaden the scope of understanding of nature and causation. The chapter locates anemia within a broader societal context. It uses the concept of 'adaptation', 'accommodation' and 'structural violence' to describe how social conditions are incorporated within the biologically of anemia. Identifying biological mechanisms may help identify a broader set of intervention opportunities and guide more effective and targeted interventions to break the links between social adversity and poor health. The chapter highlights the inherent contradictions within the definition, classification, and overall understanding of anemia to highlight the gaps and needs for further research.

3.2. DEFINITION OF ANEMIA

The term 'anemia' is derived from the Greek word *'anaimi',* which means 'without blood'. In the literature, there are many definitions for anemia. The book "a comprehensive guide to anemia" by the Iron disorders institute lists 25 definitions of anemia (Garrison, 2009, pp. 23–24), as shown in (Table:3.1).

Although anemia is defined variably, there are areas of agreement. Almost all definitions include a decreased capacity of blood to carry oxygen (O_2) from lungs to body tissues or, more literally, "no blood" and abnormally low levels of haemoglobin in the blood. The most pervasive definition of anemia, as given by WHO, is "*a condition characterised by the reduced number of circulating RBCs below 'normal' or the number of RBCs is insufficient to meet the physiological needs*" (WHO, 2011b). Therefore, WHO defines anemia in terms of statistical

thresholds of haemoglobin levels considered ‘normal’. The individuals with a haemoglobin concentration below this “normal" are considered anemic, whereas those with a haemoglobin concentration above normal are identified as non-anemic. Thus, haemoglobin variability and the construct of ‘normal’ are important to understand the dynamics of anemia.

Table 3:1 Definition of anemia

- a condition in which the number of red blood cells is below normal
- a reduction in total circulating red blood cell mass, diagnosed by a decrease in haemoglobin concentration
- a haemoglobin level below 12 g/dl in women or 13 g/dl in men
- any condition resulting from a significant reduction in the total body erythrocyte mass
- a decrease in the circulating red blood cell mass and a corresponding reduction in the oxygen-carrying capacity of the blood
- decreased ability of the red blood cells to provide adequate oxygen supplies to body tissues
- reduction in the haemoglobin concentration to below 13.5 g per deciliter in an adult male and below 11.5 g/ dl in an adult female
- any condition characterised by an abnormal decrease in the body’s total red blood cell mass
- when either red blood cells or the amount of haemoglobin (an oxygen-carrying protein) in the red blood cells is low
- a condition where a person has inadequate amounts of iron to meet body demands
- a decrease in the number of red cells in the blood caused by having too little iron
- having less than the normal number of red blood cells or less haemoglobin than normal in the blood
- decreases in numbers of red blood cells or haemoglobin content caused by blood loss, deficient erythropoiesis, excessive hemolysis, or a combination of these changes
- a blood disorder that results from a shortage of haemoglobin in the red blood cells, the disk-shaped cells that carry oxygen to all parts of the body
- an abnormal reduction in red blood cells
- when the amount of red blood cells or haemoglobin (oxygen-carrying protein in the blood) becomes low, causing the tissues of the body to be deprived of oxygen-rich blood
- a reduction in the number of red blood cells in the body
- a condition in which the blood is low on healthy red blood cells
- a blood problem
- the reduction of circulating red blood cells per cubic millimetre, the amount of haemoglobin per 100 ml, or the volume of packed red cells per 100 ml of blood
- when haemoglobin levels are too low to provide for the oxygen demands of the body
- decreased or absent iron stores; decreased serum ferritin; low serum iron; low transferrin saturation; increased iron-binding capacity of hypochromic, microcytic, erythrocytes
- a reduced amount of haemoglobin in the blood
- a reduction in haemoglobin
- below-normal haemoglobin

Source: (Garrison, 2009, pp. 23–24).

All the stated definitions of anemia are correct to some extent; none of them presents a complete description. A study in rural Uttarakhand of India found that the definition of anemia varies among governmental organizations, health workers, and mothers; concurrently, the understanding of and response to anemia varied among such groups. The applied definition of anemia in governmental organizations was relatively narrow. National rural health Mission (NRHM) standards dictated the classification and treatment of anemia. NRHM seemed to restrict the categorization of anemia to WHO's range for severe anemia. The term anemic is often reserved for severe cases (Bash, 2013).

3.2.1. TECHNICAL AND METHODOLOGICAL REDUCTIONISM OF WHO'S DEFINITION

Even WHO's definition has limits. The WHO's definition is too general to be applied to every population in every nation, particularly if one considers the wide range of factors that may influence haemoglobin. Multiple health conditions including inadequate iron intake such as malaria, HIV, inflammation, gastrointestinal bleeding (e.g., intestinal parasites or peptic ulcer disease), nonmodifiable genetic blood disorders and hemoglobinopathies, multiple micronutrient deficiencies, Behavioural and environmental factors (altitude and smoking) and physiologic state (e.g., age, sex, pregnancy and menstruation) influence haemoglobin concentration (Williams et al., 2019). Therefore, interpreting the causes of variations in haemoglobin values is crucial to defining anemia. Applying one definition to a multifactorial problem is practically impossible and reduces the scope of understanding the nature and causation of the anemia.

At the population or clinical level, haemoglobin concentration is the most common haematological assessment method and an indicator used to define anemia. Anemia can be diagnosed by clinical signs (such as pallor and conjunctivitis) and medical history, but they are limited in their ability to detect anemia (Karakochuk et al., 2019). Many issues are pertinent to raise while defining anemia based on haemoglobin assessment.

Firstly, measuring haemoglobin values is essential but not a sufficient criterion to define anemia, given the multitude of factors that affect haemoglobin concentration. Haemoglobin

concentration is frequently used as a proxy indicator of determining iron deficiency and iron-deficiency anaemia. The terms iron deficiency, Iron deficiency anemia and anemia are frequently and incorrectly used interchangeably. Haemoglobin as a proxy for iron deficiency, and IDA is a flawed approach and not a suitable indicator for assessing iron status or IDA for two reasons. First, because of the overlap of haemoglobin concentrations in normal and iron-deficient individuals (WHO, 2017). Second, this approach masks the effect of many factors that influence haemoglobin concentration and reduces it to seemingly appear as a problem of Iron deficiency or IDA. It is important to note that iron deficiency is just one of the many causes of anemia. Haemoglobin and iron status are mutually affected. Various confounding factors such as other micronutrients and infections influence both. Therefore, technically, it is challenging to distinguish if anemia is caused by iron deficiency, other micronutrients, or other confounding factors. No single biomarker is enough to characterize all the causes of anemia, including iron deficiency, as each available indicator is vulnerable to one or more sources of misclassification (Wander et al., 2009). Additional biomarkers and tests are required to determine the etiology of anemia (Karakochuk et al., 2019).

The second problem associated with the definition of anemia is the introduction of cut-off values to determine what 'normal' is. In conditions such as anemia of chronic disease (ACD), it is usual for haemoglobin to be slightly lowered. Therefore, for people with ACD to have naturally reduced haemoglobin is perfectly 'normal' in the given situation. Further, the 'normal' range for haemoglobin varies between laboratory and laboratory and healthcare providers and policymakers. Many studies have suggested different cut-off points to diagnose anemia (means have set different values to call it "normal') (Beutler & Waalen, 2006). Some studies consider a person anemic when the haemoglobin value falls below 12.0 g/dl or 13 g/dl for women and men. These levels, however, are perfectly normal for some people. Some studies consider that a female with the haemoglobin values of 11.0 g/dl is not anemic, but at 10.9 g/dl, she is. Some females can function fine with haemoglobin values at 10.9 g/dl and even lower. On the other hand, Males might have symptoms of anemia when their haemoglobin levels drop 2 or 3 points below what they are accustomed to yet still be within a "normal" range (Garrison, 2009, p. 25).

Third, there are concerns that current thresholds may not appropriately define anemia in all populations to which they have been applied, for example, in individuals of African or Asian populations, young children and older persons, and at different stages of pregnancy. Though

widely implemented and cited, these cutoffs are based on qualitative expert opinion, not a systematic appraisal of published work. The current WHO anemia cutoffs were established by 1968 WHO guidance (WHO, 1968) and were derived from mainly white adults of Europe and Canada and later validated using a United States (US) population. The threshold values in the 1968 document were achieved from surveys of a relatively small number of subjects, without documentation of methodology, and without removing anemic patients in calculating values. The whole exercise was convenient yet an oversimplification for population studies that produced unreliable results (Beutler & Waalen, 2006). The near-universal acceptance of WHO criteria for defining anemia is now subject to intense scrutiny and debate, and its reliability has been questioned.

The fourth problem is uncertainties concerning optimal testing methods for haemoglobin concentration, including the type of blood and methods used to diagnose anemia. Venous blood assessed by automated haematology analyzers is considered the gold standard for anemia diagnosis. However, currently, the most common approach to evaluate haemoglobin in field settings uses capillary blood obtained via finger prick, assessed on Hemocue because of resource constraints (technical, financial and time) as well as barriers to acceptability and feasibility of venous blood collection (Neufeld et al., 2019). The key issue emerging from the recent epidemiological studies is the divergence in capillary and venous haemoglobin measurements. In a study among Bangladeshi women and children, Capillary measures resulted in significantly lower haemoglobin concentrations and higher anemia prevalence estimates than venous blood samples, thus likely overestimating the prevalence of anemia in the population (Wendt et al., 2020). Similar results were obtained from India. A study among non-pregnant women living in Uttar Pradesh (UP) revealed that Haemoglobin concentrations from venous samples were consistently higher than from capillary samples resulting in a mean difference of 0.9 g/dL. Prevalence of anemia was significantly higher using capillary samples than venous samples (59.2% versus 35.2%), with no variability in this relationship among iron deficient and iron sufficient women (Neufeld et al., 2019). A study using comprehensive national nutrition survey data (which used a venous blood sample) found that cutoffs to diagnose anemia across age and sex were lower by usually 1-2 g/dl than existing WHO cutoffs. The anemia prevalence was 19.2 percentage points lower than WHO cutoffs (Sachdev et al., 2021). Recent studies have called for a downward revision of the Hb cutoffs by approximately 1.0 g/dL for various reasons (Addo et al., 2021). These discrepancies raise the possibility that

current estimates of the global and Indian prevalence of anemia are overestimated as most population-based estimates used capillary measures of haemoglobin.

Fifth, anemia is defined based on haemoglobin cutoffs, derived statistically rather than from functional health outcomes (Sachdev et al., 2021). Haemoglobin thresholds that appropriately indicate a detrimental health outcome or underlying symptoms remain undefined (Garcia-Casal et al., 2019). Moreover, a consensus on the need to define factors that affect the etiology of anemia is lacking despite evidence of linkages of anemia with nutritional, infectious, and genetic causes. The technical meeting on "Use and interpretation of haemoglobin concentrations for assessing anemia status in individuals and populations," convened by WHO in Geneva in 2017, emphasized the need to standardize the definition and include factors affecting the etiology of anemia when establishing haemoglobin thresholds. Addressing ethnicity in the definition of anemia and its role in influencing thresholds was proposed (Garcia-Casal et al., 2019).

Even within the framework of the WHO definition, there are conflicting opinions. Gillespie and colleagues termed anemia a statistical construct rather than a physiological one linked to meaningful health outcomes (Gillespie et al., 1998; WHO, 2001). Sachdev et al. (Sachdev et al., 2021) state that "*although anaemia is defined functionally, its diagnosis is presently based on a haemoglobin cut-off that is statistically derived rather than on functional or health outcomes, which would be ideal"*.

Anura Kurpad, a leading researcher at St John's Research Institute, Bangalore, states that *"WHO itself is unsure about what anemia really is"* (Kurpad. A, personal communication, Feb 4, 2021)

In the current form, the definition of anemia is premised on statistical calculations and methodological and technological assumptions and is not linked to functional consequences. The confusion over what is anemia has real implications for estimating the prevalence and distribution of public health problems and how we design intervention programs. The prevalence of anemia in a population group is subject to change depending on the haemoglobin thresholds and the concepts applied to define anemia. A slight error in statistical calculations would result in a misjudgement of the magnitude of the actual prevalence of anemia.

"If we define the problem in terms of functional consequences rather than normative indicator distributions, our advocacy to the international health community may be more effective. If we set goals and evaluate programs based on concepts and biological processes that are clear and measurable, we might find that our interventions are more successful than we have documented in the past" (Stoltzfus, 2001).

The present haemoglobin cutoffs for anemia derived 50 years ago need reassessment to enhance the evaluation of determinants, burden quantification, and anaemia management at the individual and population levels (Sachdev et al., 2021).

3.2.2. IRON DEFICIENCY/IRON DEFICIENCY ANEMIA /ANEMIA

"Anemia was unfortunately used synonymously with iron deficiency, and we still have not gotten over that. It is still very synonymous and we still think you have to throw iron at people to cure them " (Anura, K, personal communication, 02/02/2021)

The ambiguity over what constitutes anemia is also evident in the interchangeable use of three overlapping yet epidemiologically distinct terms in literature. There appears to be a mistaken notion that these concepts are the same; therefore, they can be used synonymously. The three concepts are not fully recognized as a disorder distinct from each other. Historical insight into these terms' confusing use, application, and evolution in influential policy documents is perplexing.

In the first international meeting of the "WHO study group on 'Iron Deficiency anemia'" convened in 1958 in Geneva, the term 'iron deficiency anemia' was used. In the report, IDA was also referred to as the "iron-deficient type of anemia" to define anemia developed primarily by iron deficiency in the body and responds to treatment with iron (WHO, 1959).

International Nutritional Anemia Consultative Group (INACG) in 1968 used the term 'Nutritional anemia' for the first time to refer to a *"condition in which the haemoglobin content of blood is lower than 'normal' as a result of a deficiency of one or more essential nutrients,*

regardless of the cause of such deficiency" (WHO, 1968). Iron deficiency was considered a major cause of nutritional anemia

Iron deficiency, the single most crucial factor for nutritional anemia, was reinstated in 1978 WHO report on 'Nutritional anemia: a major controllable public health problem' (Baker, 1978). In a landmark paper published by DeMaeyer & Adiels-Tegman in 1985, nutritional anemia was considered a large component of global anemia prevalence. Iron deficiency was the most common cause of nutritional anemia (E. DeMaeyer & Adiels-Tegman, 1985).

In the next major shift, the concept 'nutritional anemia' (of which iron deficiency anemia is one crucial part) was replaced by 'iron deficiency anemia'. Iron deficiency was considered a significant cause and a subset of iron deficiency anemia (E. M. DeMaeyer, 1989). This was evident in the title of the 1989 WHO monograph, "Preventing and controlling Iron Deficiency Anaemia through primary health care". The Monograph stated.

> *"Iron deficiency anaemia is the most prevalent nutritional disorder in the world today. Iron deficiency is by far the commonest nutritional cause of anaemia; it may be associated with a folate deficiency, especially during pregnancy. Other nutrient deficiencies, such as vitamin B-12, pyridoxine (PN) and copper are of little public health significance because of their infrequency"* (E. M. DeMaeyer, 1989).

In 1993, a joint consultative committee of WHO, United Nations International Children's Emergency Fund (UNICEF) and United Nations University (UNU) made the next major shift in thinking from 'iron deficiency anemia to 'iron deficiency' as the principal problem**.** In the report of the meeting, anemia was considered an indicator of iron deficiency rather than iron deficiency being considered a contributing cause of anemia. Anemia was assumed as a component of Iron deficiency. This is reflected in the writings of the report.

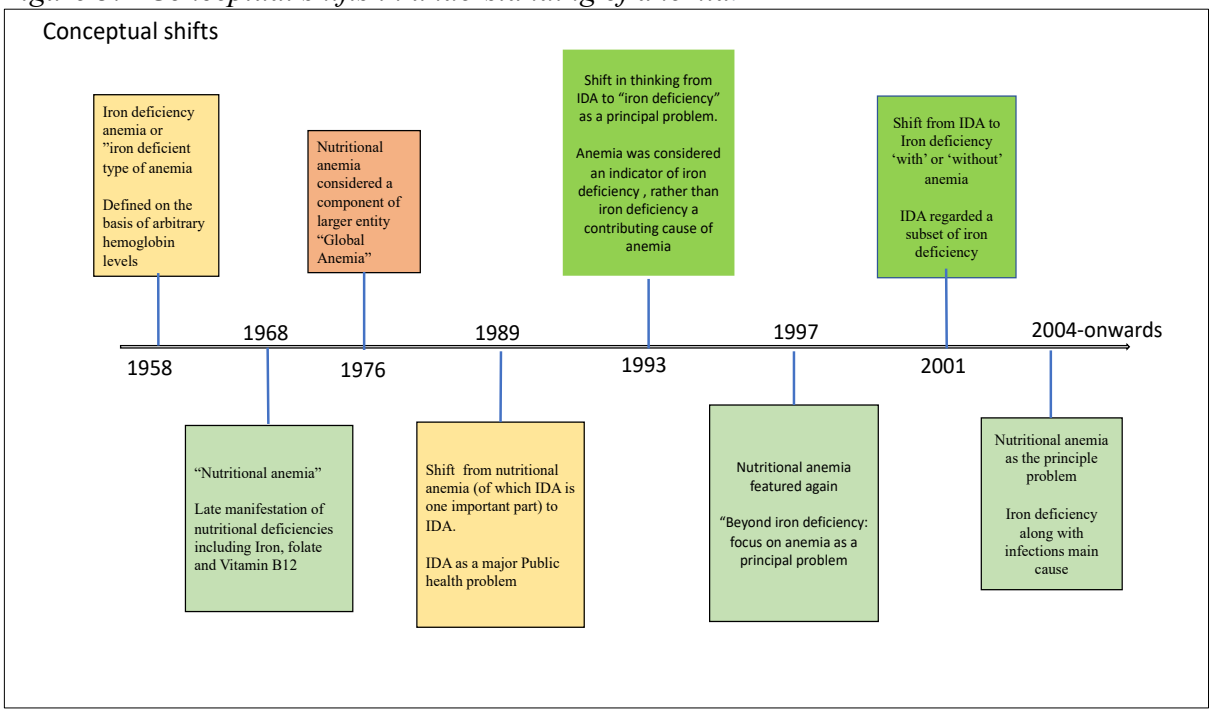
> *"Because anaemia is the most common indicator used to screen for iron deficiency, the terms anaemia, iron deficiency, and iron deficiency anaemia are sometimes used interchangeably. There are, however, mild-to-moderate forms of iron deficiency in which, although anaemia is absent, tissues are still functionally impaired*" (mentioned in (Stoltzfus, 2001).

In 1997, 'Nutritional anemia' as a concept featured again in the "expert consultation on Anemia determinants and Interventions" meeting held in Ottawa, Canada, completing a full circle of events. The consensus was to look beyond iron deficiency and focus on anemia as the principal problem. The proceedings of the meeting stated.

> *"The outcome of concern was not specifically iron-deficiency anemia, but anemia due to all causes. Although it is impossible to define a haemoglobin cut-off with respect to functional impairment, it is nevertheless well understood that anemia has more serious consequences than nonanemic iron deficiency and should thus be given priority attention"* (Gillespie et al., 1998).

The terms anemia, iron deficiency anemia, and iron deficiency with or without anemia kept appearing in reports. 2001 WHO report conceptualized iron deficiency as a principal problem and IDA as a subset of ID (WHO, 2001). A joint statement by WHO and UNICEF in 2004 considered 'anemia' as a public health problem and IDA a form of anemia that results from an extreme form of iron deficiency(WHO & UNICEF, 2004) and in a 2007 WHO report of technical consultation the concept Iron deficiency with or without anemia' reappeared (WHO, 2007). In recent times, the consensus on the need to have a clear definition is growing. There is an ongoing attempt to conceptualize anemia as the principal problem having multifactorial etiology, with iron deficiency being the principal cause (WHO, 2008), (WHO, 2010), (WHO, 2016). The nutritional anemia, recognized as a multidimensional health problem in 1968 WHO report, was reduced to a problem of iron deficiency in the subsequent years. Not only the nature and epidemiology of the iron deficiency and iron deficiency anemia and anemia has perplexed the scientific communities, but confusing use of language in different pieces of literature, shifts in their terminologies and conceptualization have compounded the problem. The shift in conceptual understanding of anemia is shown in Fig:3.1.

Figure 3:1 Conceptual shifts in understanding of anemia.



Source: compiled from WHO technical reports on anemia.

3.2.2.1 THE IMPLICATIONS OF INTERCHANGEABLE USE OF CONCEPTS

The interchangeable use of terminologies reflects the confusion regarding the basic understanding of the nature of the problem. It has major implications for designing intervention programs and evaluating their success. The interchangeable use of these terminologies has a profound effect on accurately estimating the problem, accurately framing and investing the nature of the problem, and analysing the prevalence and distribution of determinants of anemia, particularly iron deficiency in the population. Using iron deficiency in place of IDA or IDA in place of nutritional anemia or vice versa might lead us to misleading diagnoses, invisibilizing the exact nature of the problem and inappropriate design of the programmes. Stoltzfus claims such an approach to defining a serious public health problem as anemia has resulted in exaggerated and unreliable prevalence estimates of anemia and the programmes built to control iron deficiency rather than anemia (Stoltzfus, 2001b).

3.3. THE LINKAGES BETWEEN ID, IDA, AND NUTRITIONAL ANEMIA

Defining these concept boundaries may clarify some confusion surrounding what constitutes anemia and the linkages between ID, IDA, and anemia. We need to differentiate between iron

deficiency, anemia, and iron deficiency anemia to put each of them in their proper perspective. Anemia and iron deficiency, IDA and anemia are distinct yet overlapping entities.

Iron deficiency is defined as a condition characterized by the absence of iron stores, combined with defective erythropoiesis, implying a compromised supply of iron to various tissues appears (WHO, 2001). Iron status is considered a continuum from normal iron status to iron deficiency with no anemia to iron deficiency with anemia.

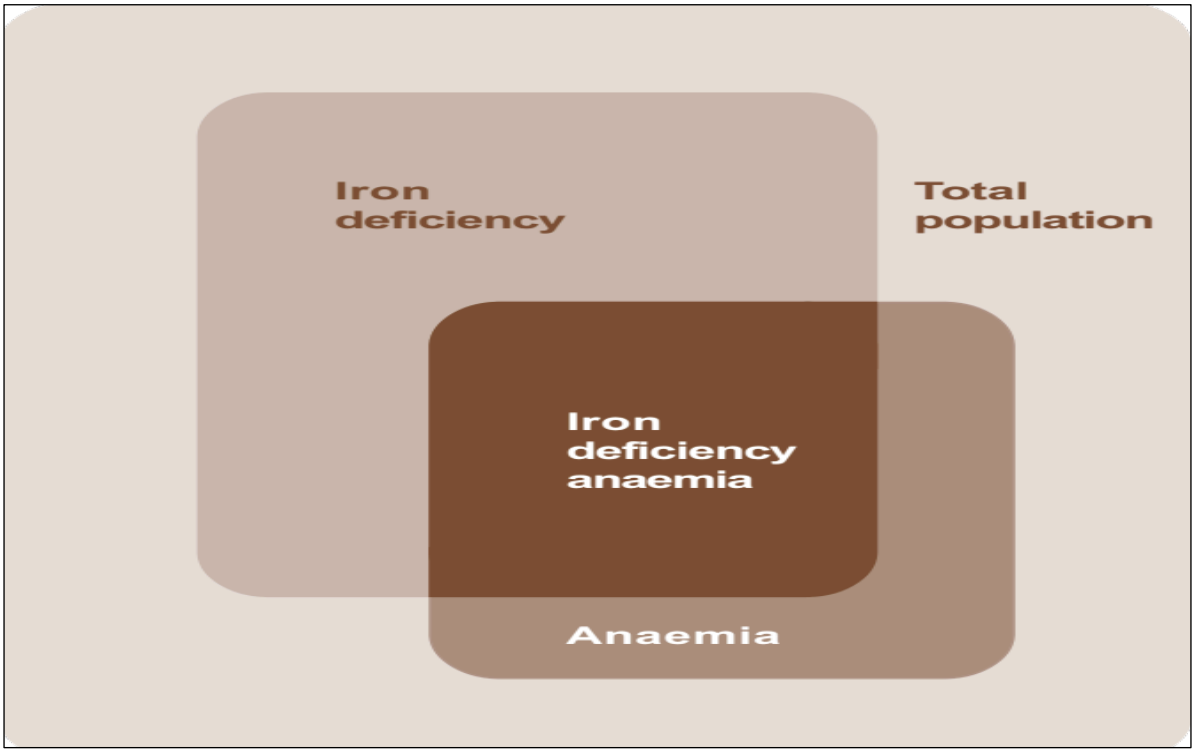
The more severe stages of iron deficiency are associated with anemia. Iron deficiency anemia (IDA) is considered the extreme form of iron deficiency or depleted iron stores where haemoglobin production and other functions related to iron are compromised. Thus, IDA represents the extreme low end of the spectrum of iron status. IDA is absent in mild to moderate forms of iron deficiency. Tissues are, however, functionally impaired even in mild to moderate forms of iron deficiency (Coad & Pedley, 2014). IDA is the most common cause of anemia when an inadequate amount of red blood cells is caused due to a lack of iron. IDA is rather a vague concept and has no immediate physiologic meaning (Thompson, 2007, p. 339).
Nutritional anemia is a condition in which blood haemoglobin content is lower than normal due to a deficiency of one or more essential nutrients (Thompson, 2007, p. 339). There are circumstances where ID is not accompanied by anemia. In this case, an iron deficiency exists as major pathology. In other circumstances, anemia may exist without ID (anemia of other than iron deficiency). In the third case scenario, there could be a population where anemia and ID both exist. ID and IDA represent different levels of iron in the body, and the two terms do not cover the same reality. Finally, IDA is a subset of anemia. Anemia broadly refers to a condition caused by multiple factors, including iron deficiency, other micronutrient deficiencies, infections, inflammations, and haemoglobinopathies (Stoltzfus, 2001b). Anemia due to iron deficiency (IDA) is one of many anemia forms. 2001 WHO report states that IDA should be regarded as a subset of iron deficiency (WHO, 2001). The linkages between ID, IDA and anemia in a hypothetical population are shown in Fig:3.2

Because of the differential need for iron, food habits, differential health and sanitation facilities in various parts of the world based on demography, race, the culture of the population group, the extent of overlap between iron deficiency and iron deficiency anemia and between IDA and anemia may vary considerably among different population groups and according to gender and age groups. The greatest overlap occurs in populations with low dietary iron absorbability, or blood loss is common due to hookworm infestation (WHO, 2001).

The confusion regarding the interchangeable use of ID, IDA and anemia arises because anemia is used as an indicator for iron deficiency; based on cut-off values of haemoglobin, iron deficiency prevalence is characterized. In many cases, iron deficiency is used as a proxy indicator of anemia. Both the approaches are flawed for several reasons. First, haemoglobin assessment is not an adequate method to measure iron deficiency. There is a significant overlap in the distribution of haemoglobin values in healthy (iron-sufficient individuals) and iron-deficient populations (WHO, 2004, p. 258). Second, The haemoglobin measurements in healthy population groups are further diminished by the need to make adjustments to the thresholds for individuals who live at high altitudes or smoke regularly, for seasonal variations or during the menstrual cycle due to haemoglobin variations under these conditions (WHO, 2007, p. 25). Third, iron deficiency is among many known and unknown factors that contribute to anemia; thus, iron deficiency as a proxy for anemia undermines the role of other factors (Chaparro & Suchdev, 2019).

Differentiating anemia from IDA is a vital first step toward effective public health programming. Still, it cannot be done if haemoglobin is measured without a more sensitive and specific measure of iron status (Williams et al., 2019).

Figure 3:2 A conceptual diagram of ID, IDA, and anemia in a population



Source: (WHO, 2001)

3.4. CLASSIFICATION OF ANEMIA: CONDITION, SYMPTOMS, DISEASE, OR ILLNESS

> *"I am not sure, if anemia is a disease or a condition. Do health insurance companies cover anemia? if they do, they consider it as a disease. Also, we need to look at international classification of disease. I have never thought it "* (Anura, K, personal communication, 02/02/2021)

Anemia is one of the most ubiquitous health issues, which is believed not to have its own etiology, shape, and pathology. It is considered a manifestation of a cluster of disorders. Due to the lack of distinct identity, the consensus is divided on whether anemia is classified as a disease, illness, condition, or symptoms. WHO defines it as a 'condition' (WHO, 2017). Iron disorders Institute defines it as a symptom of some underlying condition (Garrison, 2009, p. 26). Anemia is considered an easily treatable "condition" and sometimes "symptoms" in clinical medicine". This is arguably because of complex etiology that requires multiple considerations to find solutions (Ramakrishnan, 2001). Anemia is an associated feature of many pathological conditions resulting from poor diets, chronic inflammation, pregnancy, blood loss or other related disease processes. Therefore anemia is not specific; it can present a widely varied picture, containing elements of any underlying pathologies (Jackson, 2007, p. 216). Rarely it is classified as a non-infectious disease of its own. Generally, such classification (symptom or condition) appears when the whole cause of anemia is reduced either to nutritional (iron, folate, and other nutritional deficiencies) or heredity (sickle cell anemia) or chronic infections and inflammations. Western biomedicine operates within a positivist construct, in which disease causation is isolated to a single origin. This singular approach is focal and transverses across all dimensions of medicine, such as classification, quantification, qualification, treatment, and legitimacy, to exclude contextual dimensions that deviate from the pathological model (Kreiger, 1994). Western Biomedicine works on a singular cause of the condition and a diagnosis. Globally, the singular cause of anemia is a dietary deficiency of iron. Iron is a significant contributor to anemia, but there is little to support that iron deficiency is ever a singular cause. Iron-centric approaches are the best strategies for anemia prevention and control.

The difference between disease and symptom is ambiguous and mostly semantic. The medical definition of a disease often begins by stating that it is a condition. Conversely, the definitions

of condition frequently start by stating that it is a disease or medical pathology. Herynk and Janzen, in their thesis, note that condition or symptom, both the classifications are tenuous. Defining it as a condition may inadvertently shift treatment to single causes. The authors described anemia as (Herynk & Janzen, 2014, p. 31).

> *"Anemia is much more than a condition or symptom; it is a life set dangerously close to the tipping point of disease, particularly in communities where it is endemic and chronic"* (Herynk & Janzen, 2014, p. 31).

3.5. NAVIGATING ANEMIA THROUGH ETIOLOGY

Anemia is frequently classified according to its cause. For example, IDA caused due to iron deficiency, haemolytic anemia due to destruction or lysis of red blood cells and anemia of inflammation due to inflammation. In most cases, the anaemia is of mixed and multifactorial etiological origin. Multifactorial nature is the evidence that this illness has multiple horizons not strictly limited to nutrition. Its etiological basis can broadly be categorized into dietary-induced, disease-induced, or a combination of both (K. M. Nair & Iyengar, 2009). The deficiency or deprivation of numerous factors synergistically can lead to haemoglobin abnormalities resulting in various classifications of anemia. Individuals living in poverty and food-insecure regions are generally deficient in all the hematopoietic nutrients (Iron, folate, vitamins B12, B6, C and A, among others). The different nutritional deficiencies are associated with specific haemoglobin abnormalities (WHO, 2017). Diets are considered inadequate to meet the bioavailable haematopoietic nutrients required for haemoglobin and red blood cell formation (Stuart-Macadam & Kent, 1992) mainly when physiological demands of iron in the body are high such as during infancy, pregnancy, menstruation and infections. Chronic infections and inflammations cause haematological disruptions and exacerbate anemia through different pathways (Camaschella et al., 2020). Infections may aggravate a spiral of chronic illness and undernutrition (Viana, 2011). While anemia is detrimental to health, it may also develop in response to defence against infections and inflammations. The complex dynamics of human physiology in relation to nutritional deficiencies and chronic infections are not well understood. We know little about the etiology of anemia. The etiology of anemia is complex and multidimensional, not strictly limited to dietary deficiencies and infections

In some cases, anemia can also be characterized by the red blood cells' size, shape, and colour. There are different kinds of anemia: microcytic anemia, normocytic anemia, macrocytic anemia, hypochromic anemia, and haemolytic anemia. Most anemias have a characteristic morphological appearance, which provides insights into the diagnosis of anemia (WHO, 2017). There are multiple causes of anemia; haematological manifestation of different causes can also be similar and lead to similar RBC morphology. The numerous confounding factors make it further challenging to distinguish one form of anemia from others and their underlying causes. For example, in both iron deficiency and microcytic anemia, cells are morphologically smaller, and the haemoglobin content in RBC is lower than usual. Iron deficiency-induced microcytic anemia may mask the Macrocytic anemia characterized by vitamin B12 or folate deficiency (Chaparro & Suchdev, 2019). IDA and b-thalassemia both cause microcytosis and hypochromia (WHO, 2017).

Anemia, the term we generally refer to in academic parlance, is an ‘aggregate of anemias’. Each anemia is characterized by distinct cellular abnormality, each having its own etiology and pathology. However, in clinical settings, a multitude of anemias are simply clubbed into one, predominantly as an ‘iron deficiency anemia’. The symptomatic patterns of all red blood cell abnormalities are consistent enough to be simply referred to as ‘anemia’, only in clinical contexts that specific physiologic causes of anemia are isolated from the contextual causes. Most types of anemias have very similar symptoms; however, their causes are so variable that simplistic classifications are nearly impossible.

3.6. ANEMIA IS NOT A STATIC CONCEPT

The etiology of anemia is ambiguous and may vary in the same individual across a life span. The apparent cause of anemia can change over years, months and even days. It is not uncommon to have a high prevalence of anemia coupled with iron and vitamin B12 deficiencies, visible signs of protein deficiency and parasitic infection with internal bleeding during summer and rainy seasons than in winters (Baranwal et al., 2014). The severity, timing and sequence of nutritional deficiencies and other illnesses vary in each person over the course of development; these factors contribute to the holistic experience of anemia (Herynk & Janzen, 2014).

Anemia is a condition or aggregate of symptoms emanating from diverse pathological conditions (such as nutritional deficiencies and infections). The underlying causes of those

pathological conditions, the patterns and distribution of the factors influencing the pathological conditions are in continuous flux. Anemia is a dynamic and fluid concept; its etiology and constitution may change over time and space. Therefore, anemia is not confined to a set discourse. If seen from western biomedicine, anemia in males is seen as a rare anomaly. In contrast, a study reported 89 % anemia prevalence among males (5-20 years) in Punjab, India. Some indigenous communities in Guatemala have a higher anemia prevalence among males (Herynk & Janzen, 2014). This phenomenon highlights a problematic contradiction, where global health intervention strategies decontextualize and narrowly frame anemia as an individual symptom. Outside the developed countries, poverty and inequalities lead to unique demographic trends in anemia. Anemia has become an endemic illness experienced by the majority of the population. Also, the biology of anemia within diverse demographic and cultural settings suggests that it cannot be easily formulated into controlled studies. The intraindividual, interindividual, and intergroup differences moderate the effects of IDA. Different stages of iron deficiency in individuals affect the body's physiology differently, affecting psychobiological domains. There are biological, social, physical, and psychological factors that determine the trajectory of different psychobiological domains due to prolonged stress and living conditions. Thus living conditions, stress, hardships, deprivation, psychobiological domains, and contextual factors become more relevant to defining anemia (Pollitt, 2001).

3.7. SYMPTOMS OF ANEMIA

Clinical medicine uses haemoglobin measurement and clinical diagnostic techniques to identify anemia; it diagnoses morphological, anatomical, biochemical, and physiological changes within cells to construct an identity. In addition to the laboratory, there is a traditional way that, rather than technical accuracy, relies on the experience of medical professionals to diagnose anemia, called the clinical method. In the clinical method, the pink appearance of eyelids, gums and nailbeds is considered normal, and if they are pale, the patient is diagnosed as anemic. The early signs of anemia include weakness, fatigue, palpitations, skin pallor, shortness of breath (dyspnea) with exertion, light-headedness, dizziness, enlarged liver, spleen, and jaundice. The advanced signs of anemia may include fast heartbeat (tachycardia), marked shortness of breath, inability to swallow, poor appetite (anorexia), diarrhoea, depression, mood swings, irritability, angina (chest pain from ischemia in the heart muscle tissue), difficulty

walking, indigestion, and sweating (Herynk & Janzen, 2014). A detailed list of symptoms is presented in Table:3.2

Table 3:2 Symptoms of anemia

Physical Symptoms	**Psychological Symptoms**
tingling in the hands and feet	chest pain, often accompanied by a choking sensation that provokes severe anxiety
damage to the spinal cord	fearfulness
shortness of breath	irritability
faintness or dizziness	confusion, depression, and memory loss
pasty, sallow, and pallid skin, palms, gums, nails, and eyelids	inability to concentrate, memory loss
tingling in the legs	does not want to work
stand-on-end-hair	cannot walk
inflammation of the mouth or tongue	does not want to bathe
irregular or rapid heartbeat	headache
loss of appetite	insomnia
nails that are dry, brittle, or ridged	problems with movement or balance
rapid breathing	weakness, fatigue, and listlessness
sores in the mouth, throat, or rectum	cravings for ice, paint, or dirt (pica)
sweating	see stars
swelling of the hands and feet	poor vision
thirst	ringing in the ears
unexplained bleeding or bruising	
problems with movement or balance	
Source: adapted from (Herynk & Janzen, 2014, p. 33)	

Anemia is often accompanied by other diseases and illnesses, which can blur the line in distinguishing the effects of anemia from the effects of compounding disease and illness. Beyond the commonly identified symptoms associated with anemia, there are neurological, cognitive, behavioural, developmental and socioemotional symptoms (Agrawal, Kumar, et al., 2019). The research shows severe anemia, and tissue iron deficiency results in permanent

cognitive and developmental effects (Stoltzfus, 2001a). The cognitive and neurological impacts are likely due to the decreased oxygen-carrying capacity of the blood linked to anemia. Reduced oxygen supply may lead to a chronic reduction of cerebral oxygenation and reduced oxygen supply to brain areas that can cause ischemic strokes (lesions in the brain) and lead to chronic episodic seizures. Ischema is a common occurrence with anemia (Herynk & Janzen, 2014). Anemia is associated with poor cognitive development, decreased exploratory behaviour, and orientation engagement in children and women. Anemic children exhibited more body contact with their mothers and took fewer breaks in close contact, while mothers spent less time away from their children. These associated behaviours were linked to increased unhappiness, fatigue, inactivity, wariness, hesitance and increased fearfulness (Lozoff et al., 1986).

What is conspicuously missing in the medical texts and an otherwise large body of literature is the narrations and subjectivities of anemia from the perspectives of patients or population groups who are anemic. The limited literature on how communities across the globe perceive and associate themselves with anemia shows an alternate construction of anemia, not necessarily fitting into the narration of the western biomedicine framework. In an alternative qualitative discourse, where people and their subjective narrations become centre stage, the terminology ‘anemia’ and statistical construct relying on haemoglobin thresholds take a backseat. The use of the term ‘anemia’ is often non-existent or rarely heard or used in many communities, which signifies the gap between western construct and local discourses of anemia.

3.7.1. PERCEPTIONS OF ANEMIA

Despite the various clinical symptoms identified by western medicine, very few studies have documented the community's perception and attitude towards anemia. In a study in Uttarakhand, rural Indian women seemed to lack an understanding of anemia altogether, and many health workers had a limited understanding. Less than half of the mothers interviewed in the study recognized the term ‘anemia’, even though the majority reported feeling weak indicates the limits of the definition of anemia (Bash, 2013). A technical working paper published by Bentley and Parekh used various qualitative techniques to examine perceptions and health-seeking practices of pregnant women from four Indian states Haryana, Gujarat, Tamil Nadu, and Karnataka. The study found that women in all four sites largely unrecognized

the term ‘anemia’ and the clinical terms for anemia. Women often used local terms and language to describe anemia. Local words describing frequent symptoms such as weakness, dizziness and blood loss were reported. In rural Tamil Nadu, the clinical term for anemia, "iratha sohai," was unknown to many respondents. Still, many women reported pale skin pallor and weakness as common symptoms they experienced. Likewise, in Baroda, the Gujarati term for anemia, "pandurog", was unknown to any female respondents. The most common causes of anemia perceived across all four sites were poor dietary intake, including low-quality diet, eating last and leftover food, poverty and inability to access foods, repeated pregnancies and dietary restrictions (P. Bentley & Parekh, 1998).

Galloway et al. examined women’s perceptions about anemia in eight developing countries, including India. They reported that anemia is recognized by its symptoms rather than by a specific clinical name or as a specific disease in all but one country. In all the countries, women give the most common descriptions of anemia, including dizziness, headache, paleness, yellowness, decayed blood, thin blood, low blood, loss of appetite and fainting. The most frequent reasons attributed to symptoms were poor quality diet and lack of food due to poverty in all the countries. Women in India specifically mentioned dietary restrictions and ‘‘eating last’’ or ‘‘eating whatever is leftover’’ as reasons for their inadequate diet. In Pakistan and Indonesia, some of the common causes mentioned were: lack of available meat, nutritious food and green vegetables, hard work or working in the sun (*‘sun saps physical strength and drinks blood’*, water loss and blood loss associated with diarrhoea, frequent births, malaria, HIV/AIDS, worms, eating dirt and soap (Galloway et al., 2002).

A qualitative study of anaemia-related perceptions in pregnant women in Mumbai reported that ‘lack of blood in the body’ (*shareer mein Khoon ki kami*) was the respondents' most common description of anemia. Anemia mainly was described by its symptoms such as weakness, dizziness, lack of strength, swelling in the feet and white lines on fingernails (Chatterjee & Fernandes, 2014). A compilation of commonly used terms to describe anemia is shown in Table:3.3

Table 3:3 Terminologies related to anemia across the region

Region	Commonly used terms	Symptoms
North Haryana	Kamzori	Weakness
	Khoon ki Kami	Less blood in the body
	Dholi ho gai hai	Colour becomes white
Urban Gujarat	Kamjori/ashakti	Weakness
	Occhu lohi	Less blood
	Phikkash	Paleness
	Bhook nahi lagti	Loss of appetite/anorexia
	Lohi nu paani thai jay chhe	Blood turns into water
Rural Karnataka	Susthu	Weakness/fatigue
	Thalaisuthu	Giddiness
	Raktha heenathe	Less blood
Rural Tamilnadu	Iratham Kuraivaga ullathu	Low blood
	Udambil iratham illai	No blood in the body
	Iratham sundipochuthu Udampu veluppu	Less blood
	Vellai kaamalai	Paleness in the body
	Varattu kaamalai	Whiteness/paleness
	Kaikaal veluppu	Dryness in the body Paleness in the hands/legs
Mumbai	Shareer mein khoon ki kami	Lack of blood in the body
	Kamzori OR Kum Shakti	Weakness
	Chakkar aana	Dizziness
	Taakat kam hona	Lack of strength
	Pair mein sujan	Swelling in the foot
	Naakhun pe safed reshi	White lines on fingernails
Source: (P. Bentley & Parekh, 1998; Chatterjee & Fernandes, 2014)		

3.7.2. ANEMIA GETS NORMALIZED

The common finding in all the studies exploring perceptions of anemia is the routine presence of fatigue, weakness, dizziness, headaches, pale skin, and faintness. Fatigue and weakness is the primary manifestation of anemia; however, women may not readily associate fatigue with illness. Women consider it quite "normal" to feel weak, particularly during pregnancy. Women assume that weakness is an essential part of physiological changes in their bodies due to pregnancy. Bentley and Parekh, in their study, recount that women respondents admitted openly that;

> *"weakness and giddiness associated with anemia is normal and an accepted part of pregnancy, anemia should not be taken seriously"*(P. Bentley & Parekh, 1998).

The perpetual prevalence of anemia amongst almost every pregnant woman in their social network reinforces a sense of normalcy. Mothers, sisters, in-laws, and neighbours all endure similar experiences (Chatterjee & Fernandes, 2014). The symptoms are engrained so much in people's everyday life that they accept them as usual and do not complain about them to the doctor or seek medical treatment unless the symptoms become severe. Chatterjee and Fernandes reported the narration of some of the respondents in their study:

> *''When the illness increased, and I could not get up, then I went to a doctor in the* village''(Chatterjee & Fernandes, 2014).

Poverty and societal structures further accentuate normalcy. In many cases, Poverty hinders them from seeking treatment, and sometimes, husbands or other family members discourage them from going to the clinic.

> *''When I inform my husband about the problem, it goes into one ear and out the other; he says this problem will be all right on its own'' (Chatterjee & Fernandes, 2014).*

Sometimes, people do complain, but the specificities do not come across. Patients often complain about a set of symptoms associated with anemia, but the symptoms are hardly considered part of their reality (P. Bentley & Parekh, 1998).

3.8. EMBODIMENT OF ANEMIA

Amid normalcy of the vague symptoms, anemic subjects are aware of the inherent dangers of ignoring particular signs and symptoms that drive them to consult a doctor. There is a clear hierarchy of symptoms in which weakness and fatigue are considered normal. In contrast, abdominal pain, vaginal bleeding, and genital discharge, among others, in a woman are considered serious symptoms that require medical attention (Chatterjee & Fernandes, 2014). The women explain their situation in broader societal contexts such as poverty, lack of food and money, eating last and leftovers, and lack of woman agency in household decisions. That is the testimony of their experienced hardships in day to day lives. Despite several hardships (weakness, dizziness, headaches, and others), women carry on their daily chores that represent the resilience to the experience of anemia through a process of adaptation and accommodation, a part of adaptative physiological responses to chronic stress. Therefore, understanding adaptation and accommodation is vital for understanding resilience and recovery and how normalized accommodation is embodied in the context of social adversity.

The notion of the ‘embodiment’ refers to the idea that adverse experiences, social adversity, social exposures or ‘stress’ outside the body get under the skin to influence biological processes from the cellular level through to organ-level function and ultimately lead to manifest disease. In simpler terms, embodiment means the literal incorporation of social and ecological realities into the organism's biology to influence physical health and disease (Krieger, 2005).

The external environment gives rise to circumstances or events characterized as demands or stressors. Social adversity, such as structured social roles, can lead to exposure to stressors such as traumatic experiences and lack of food (Kubzansky et al., 2014, p. 515). Chronic stress is a causal factor leading to poor health, including anemia. Social adversity can influence health through three broad categories: toxic environments (social or physical), health-related behaviours, and psychosocial stress and related cognitive/affective processes. Irrespective of the type of stressor, a biological response to stress is triggered when individuals experience external events (stressors). The stressors may cause physical and psychological stress, leading to behavioural or physiological changes(Kubzansky et al., 2014, p. 512).

Further complicating the issue is the notion of biological embedding. The research shows that childhood exposure to adversity may lead to alterations in brain architecture, which can alter behaviour; changes in corticolimbic circuits that process stress could lead to mistrust of others,

greater vigilance for threats, and poor self-regulation of appetite behaviours. These behaviours may, in turn, exacerbate proinflammatory processes implicated in a range of disease outcomes (cardiovascular diseases and respiratory disease).

3.8.1. POVERTY, DEPRIVATION, AND STRUCTURAL VIOLENCE

Structural violence can be embodied and accommodated across generations. There is a complex relationship between anemia and structural violence. Structural violence is institutionalized social, economic, and political marginalization through a historical dialectic of hegemonic human organization (Farmer et al., 2006). It deprives people of options, power, and resources, leading to the normalization of maladies. The distress endured by individuals in a community produces an experience of social suffering. It is not because of anemia that people suffer; instead, structural violence and poverty create conditions of stress that exacerbate the suffering. The experience of stress and illness is normalized and accommodated in society's worldview across generations, leaving the structural violence unchallenged and anemia untreated (Herynk & Janzen, 2014, p. 7). An entire population may experience life-altering trauma, lasting a generation or more. The population, most at risk has experienced systematic marginalization and deprivation. Communities share their subjective suffering through narration which varies with interpersonal relationships, age, sex, and degree of anemia. Narration is a form of language to describe the common sequence of symptoms used to recognize and describe anemia (Herynk & Janzen, 2014, p. 139). Anemia is a condition that produces pathologies of speech and communication that impact the ability to express and narrate personally meaningful stories. The years of subjugation and deprivation are accommodated and embodied, ultimately expressed through the language identifiable in discourse to describe anemia. Anemia is thus embodied through the process of collective suffering over generations; the subjective experience of that suffering will be complex and multivocal.

3.8.2. ADAPTATION AND ACCOMMODATION OF STRESS

Stress is defined variably and sometimes antagonistically. It may be defined as an external force on the person. However, from a biological perspective, stress is defined as an internal defensive process and "Physical responses of the body to environmental demands that threaten an individual's wellbeing". Stress is the experience of disturbance in homeostasis from both

the physical and social environment to which the human body responds with "hormonal, neurological, and immune system defences (Kubzansky et al., 2014, p. 516).

The decline in metabolic functions, reduced need for oxygen and energy and subsequent reduction in circulating red cell mass are considered normal adaptive responses to endure the stress. The term adaptation implies the functional change, not the momentary dysfunctional changes in an organism under extreme sociostructurally pressures; adaptations may be beneficial in the short term but have undesirable consequences in the long run or in other contexts (Kubzansky et al., 2014, p. 517). However, such fatalistic construction of 'adaptation'dismisses the negative consequences of anemia in exchange for stories of advantages of adaptation required to face environmental, biological, or psychological adversity. Biomedicine misinterprets the biological notion of 'adaptation' and misunderstands how anemia impacts daily life. (Kubzansky et al., 2014, p. 516). Such misconstrued application of the concept of adaptation to define anemia discounts the social, political and economic structures that promote and perpetuate anemia in an endemic and chronic fashion(Herynk & Janzen, 2014, p. 43).

Accommodation is a term used to describe physiological changes in the body under the conditions of deprivation or unusual demands on the body, as in pregnancy in response to a stressor that may enhance the survival (what may be confused with the concept of adaptation) entails some loss in functioning. Anemia symbolises the bodily physiological alterations that accommodate stress as a defence strategy. Physiological alterations are symbolic of change rather than resisting the change in response to stress. Paradoxically, a prolonged defence against perceived stress can compromise the immune system and increase disease risk. Consequently, bodily defence against crisis can become detrimental to the human body (Herynk & Janzen, 2014, p. 43). An example of this dilemma is iron supplementation for a mildly anemic pregnant woman infected with parasites thriving on iron. The treatment may positively affect the individual in one etiological model and a negative in another etiological model.

Unlike the biomedical interpretation of stress, which posits stress as a harmful or detrimental isolated phenomenon, stress is seen as negative, positive, and historically adaptive in other disciplines, such as medical anthropology. The body's response to environmental insults such as poor diet, stress, and infectious disease results in anemia. Stuart-Macadam argues that anemia might be thought of as a disease and a defence against parasitic infections which thrive

on iron in the body (Stuart-Macadam, 2006). Mild anemia may be beneficial as a natural defence response to harsh environmental conditions (Denic & Agarwal, 2007). There is convincing evidence that iron deficiency may confer resistance against many infectious diseases such as malaria, tuberculosis, and plague as part of an evolutionary defence mechanism. The iron deficiency phenotype is considered to have culturally evolved as a part of natural selection against epidemic infections (Denic & Agarwal, 2007). Denic and Agarwal draw a parallel between social norms, customs and acquired skills to genes and calls them 'cultural genes which mutate, undergo selection, and transmitted in a way analogous to gene transmission. The customs such as vegetarianism and habitual consumption of tea and coffee, which are known to cause iron deficiency, and anemia, are some of the cultural traits that may have emerged and spread due to their adaptive response for better survival in the epidemics (Denic & Agarwal, 2007). The ambiguity of whether anemia is disease or defence is, in fact, often echoed in local discourses that normalize illness.

3.8.3. COMPENSATION FOR ANEMIA

The human body accords a high priority to maintaining red cell mass as an essential function. In anemic conditions, metabolic demands fall, oxygen and energy are reduced, and the red cell mass and count required to deliver oxygen to tissues declines (Jackson, 2007, p. 219).

The body adopts several compensatory and coordinated adaptive physiological mechanisms to maintain oxygen supply and limit consumption. There are four mechanisms the body uses to compensate for anemia. First, the volume of blood pumped through the heart increases due to decreased blood viscosity and vascular tone. Second, more blood flows into specific organs such as the heart and brain and away from other areas such as skin and kidneys. Blood flows quickly because lesser volume travels towards the peripheral tissues. Third, certain organs such as the heart and brain increase oxygen extraction from blood. Fourth, only seen in the case of chronic anemia, the affinity between oxygen and haemoglobin is decreased so that more oxygen is available for utilization. Ultimately, these physiological changes result from increased breathing and circulation involuntarily controlled by the central nervous system (Zarychanski et al., 2012).

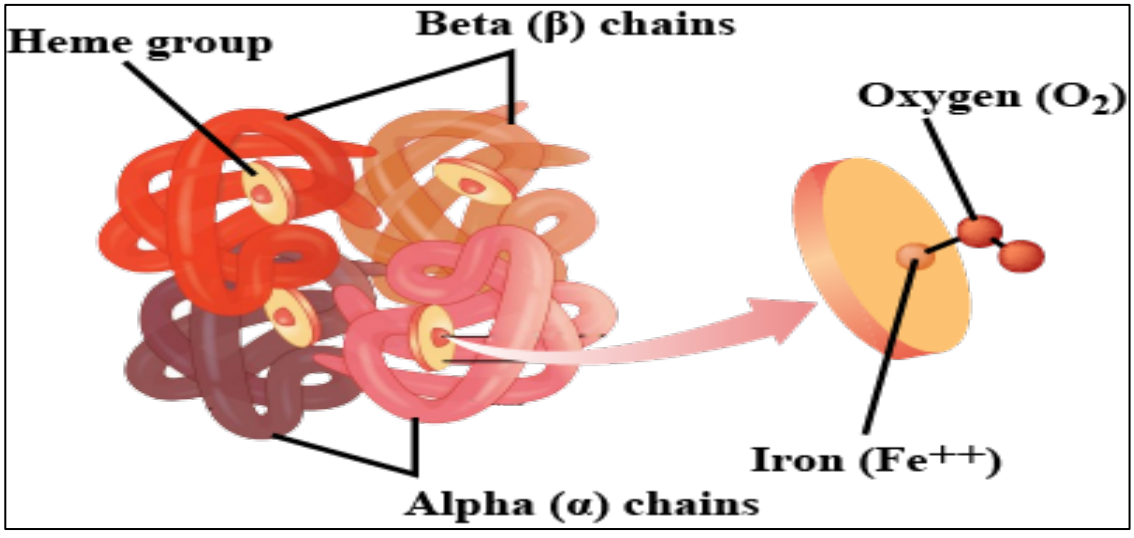
3.8.4. ANEMIA EXPERIENCED AS PROCESSES IN THE BIOLOGICAL MATRIX

The symptoms of anemia are not simply an itemized list of complaints; they are contextualized in stories of people's daily lives. Anemia is about blood and the distribution of oxygen to cells. Cells are the most basic unit of life to generate energy through biochemical reactions. Oxygen in the human body is involved continually to maintain a balance between life and death through cellular respiration (shown in the equation below). The purpose of cellular respiration is to generate energy from nutrients for the cell to function. Typical cellular respiration involves a chemical reaction between glucose (nutrients) and oxygen to produce carbon dioxide, water, and energy. Therefore, oxygen is a vital cog in the wheel for the biochemical reactions that produce energy that is the force behind all bodily functions, body movement, growth, and development.

Cellular Respiration: $C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O$ **+ Chemical Energy**

Blood primarily consists of red blood cells (RBCs) suspended in blood plasma. RBCs carry oxygen from the lungs to the tissues. Inside RBCs, millions of haemoglobins (Hb) molecules, a protein, are present. Haemoglobin constitutes about a third of the content of RBC and provides the blood with its distinctive red colour. Each haemoglobin molecule consists of four heme groups. Each heme group stores one atom of iron. Oxygen binds to iron ions at the centre of all four heme groups Shown in Fig:3.3.

Figure 3:3 Haemoglobin complex with iron and oxygen



Source: (Coad & Pedley, 2014)

Oxygen inhaled through respiration goes into blood circulation, binds with the Hb molecule, and is distributed to tissues throughout the body where the oxygen pressure is low. Thus, oxygen moves from high pressure to low pressure in the body. This oxygen circulation and pressure balance process supply oxygen to all cells to sustain energy metabolism. Although it appears elementary, arguably, it is the most crucial function in the human body. However, this elementary biological function of the body varies among individuals and populations.

The availability of iron thus becomes fundamental to oxygen transport in the body. Iron deficiency varies significantly according to host factors: age, gender, physiological, pathological, environmental, and socioeconomic conditions (WHO, 2017). If Iron content in the tissues is lower or depleted (for example, in anemia individuals) than optimum for normal physiological functioning of the body, the oxygen-binding capacity of the Hb molecule is severely restricted. That means the elementary function of the blood, i.e., to distribute oxygen to tissues, is compromised. The energy produced through cellular respiration gets adversely impacted by limited oxygen availability. Inadequate iron implies insufficient oxygen and low energy availability to cells. Cells are strained to acquire more oxygen; muscles stressed to function without sufficient blood flow become progressively weaker and eventually may begin to spasm. Oxygen-deprived organs cannot function properly and may fail if deprived of oxygen-rich blood for a prolonged time.

The symptoms of anemia are numerous and complex. Poor diet, disease, injury, and physical and mental stress cause anemia to worsen. Severe anemia increases the susceptibility to other diseases such as respiratory and kidney disease. Untreated anemia can develop into acute or chronic anaemia with any added insult to the mind or body. Physical, mental, and general well-being can all be affected. Chronic and severe anemic individuals feel fatigued, faint, and have impaired abilities to work, walk, lift, sleep, eat and focus. They appear pale, sallow, disoriented, cognitively slowed, have visions of floating lights, and suffer constant headaches. Those afflicted with anemia are visibly irritable, fearful and can be easily startled. Anemic individuals are typically reserved and withdrawn. Anemia can be a temporary stressor if left untreated and can cause irreversible damage. Ultimately, the development and function of the mind and body are compromised due to a lack of oxygen (Herynk & Janzen, 2014, p. 5).

3.9. THE CONFLICTING EXPRESSIONS OF ANEMIA

The ambiguity is not limited to the definition and conceptualization of anemia but transcends its classification and other biological processes. The ambiguity is reflected in contradictory manifestations of anemia at biological, physiologic, and social levels.

> *"In our hospital (St. John's Medical College and hospital, Bangalore), many women come walking; their haemoglobin levels are 3g/dl; how are they surviving when in ideal terms, they should be dead" (Kurpad. A, personal communication, 04/02/2021)*

Some women walking around are so anemic that they should be dead, the walking dead. The 'walking dead' metaphor characterizes the medical community's many contradictions. In many cases, individuals are simply too anemic for surgery. In such cases, life defies the perceived logic of death. An anemic individual's fate hangs in a strained balance between life and death. The contradictions stem from the biomedical construct of anemia in which anemia and survivability of even severe cases is not an errand.

Second, from public health perspective manifestation of anemia appears to vary from one community to another. It is chronic, endemic, and life-threatening in one community, while it is generally easily treatable in wealthy communities. It is merely perceived as a risk of pregnancy in one community, whereas in others, it is a chronic illness of childhood and adulthood, not merely of pregnancy.

The third paradox arises from the taxonomy of anemia in biomedicine. Anemia is simply considered a symptom or condition of underlying factors but not an illness or disease. This implies that anemia itself is not categorized as a direct object of study. It is linearly associated with dietary deficiency of iron or infectious diseases as a symptom or condition. Therefore, the scope to define anemia as a social problem caused due to multiple factors rooted in societal structures such as poverty is reduced to singular etiologies.

Fourth, the role of anemia as a harmful disease or defence mechanism raises contradictions. Evidence shows that anemia helps to fight infections in some instances. Thus, while being a harmful disease, it is also a defence mechanism at the same time. It is this contradictory nature that has been overlooked in biomedical discourse.

Fifth, there is a possibility that many people are anemic but are either unaware or unconcerned of their symptoms; they keep carrying on their daily lives as usual. Concerns are being raised about the biomedical construction of 'normal' and its thresholds which neither captures the reality of illness nor reduces disease. For millions, anemia or the anemic conditions set up as early in utero persists through infancy, childhood and during the hardships of adult life onto death. Classifying anemia as a simple pathology, an aberration from normal, is challenging. It is a phenomenon that keeps changing its form and severity throughout the human life cycle. On the global and local scale, anemia may be considered a norm. Still, a non-anemic person in their lifetime may experience repeated cycles of mild, moderate, or severe forms of anemia, albeit unaware. The statistical methods have failed to capture the accounts of generations of lived experiences of anemic patients, which has reinforced anemia to be considered 'normal' in dominant discourse.

Sixth, gender and demographic variability in anemia are rarely considered. Across the world, women are generally more anaemic than men. However, anemia among men has also been high enough to be treated as a public health issue in developing countries, including India. There is evidence of a higher incidence of anemia among males in some indigenous communities of Guatemala. Such phenomena point to a problematic contradiction global health strategies to anemia are facing. Existing studies, policies and programs focus on women and children, ignoring men in policymaking. Anemia among males is considered a rare anomaly.

Seventh, a narrow etiologic focus where iron deficiency is generally considered a primary cause of anemia is another principal contradiction in anemia. Stuart-Macadam and Kent argue that local diets in most cultures are usually sufficient to provide the dietary needs of iron, and diets alone can never be the sole cause of iron deficiency (Stuart-Macadam & Kent, 1992). Also, iron deficiency alone could rarely lead to severe anemia in most cases (Stoltzfus, 2001a).

Eighth, contradictions lie in how anemic people perceive themselves and how others see them. The range of symptoms associated with anemia affects how a community sees themselves and others see them. These symptoms may appear stereotypically abnormal or unhealthy to outsiders, and practitioners of western biomedicine may blame the local communities for their ignorance to maintain good health. The perception of one community against others ranked lower in the dominant construct of social order leads to contradictory perceptions. Most studies attribute unawareness and ignorance about the symptoms and health-seeking behaviour as one of the causes of anemia. Contrary to it, the findings of the qualitative studies point out that the

indigenous communities are not ignorant. They situate the subtle symptoms of anemia amid the suffering of daily life hardships. The illness becomes so much internalized and normalized as a part of their life that they barely focus on the seriousness of the illness.

The range of contradictions (life/death, symptom/illness, disease/defence, normal/abnormal, iron sufficient/deficient) in the discourse of anemia highlight the gap between what is known about anemia in western biomedicine and what is experienced by communities where it is a chronic and endemic problem. Focus on local discourse can help bridge the gap between biomedical narratives and the local discourse of anemia. Also, situating the biology of anemia within the broader social, economic, and political contexts can help broaden the western biomedical models of illness.

3.10. SUMMARY

Anemia is an ambiguous health problem. Its ambiguity is derived not only from the vague symptoms that characterize anemia but also from its very constitution. On a broader scale, a nuanced understanding of what constitutes anemia or what it implies when we use the term 'anemia' is lacking. Anemia may mean different things to different people, communities, and disciplines. Anemia defined is defined in the dominant biomedical discourse based on haemoglobin thresholds. However, the voices have emerged against the appropriateness of this approach even within biomedicine. Beyond the positivist biomedical paradigm, alternate realities exist. The alternate discourses situate anemia within people's narration of daily life struggles, social adversities, and hardships. The people and context, i.e. poverty and deprivation, assume a central place in defining anemia. Anemia is a manifestation of the biological embodiment of social adversities. There are inherent contradictions over the nature and causation of anemia. These contradictions arise from the epistemological differences between western biomedicine and local alternate discourses.

CHAPTER 4

The most startling aspect of the nutrition situation in India is that it is notmuch of an issue in public debates and electoral politics"

Jean Dreze

CHAPTER 4. EPIDEMIOLOGY OF ANEMIA IN INDIA

4.1. INTRODUCTION

The chapter analyses the trends and patterns of anemia and iron deficiency prevalence in India. It explores the etiology, their respective contribution to anemia, and the relationship between iron deficiency and anemia.

4.1. ANEMIA PREVALENCE IN INDIA

India reportedly has one of the highest prevalence of anemia in the world. Different national surveys report variable prevalence estimates; therefore, the exact prevalence of anemia is disputed. According to the latest round of NFHS, anemia prevalence among children (6-59 months), all women (15-49 years), non-pregnant women (15-49 years), pregnant women (15-59 years), all women (15-19 years), males (15-49 years) and males (15-19 years) is 67 %, 57 % and 25 % respectively (IIPS, 2020). In contrast to NFHS, the comprehensive national nutrition survey (CNNS), which provides data for children and adolescents in the age group 1-19 years, reported a prevalence of 41 %, 24 % and 28 % among preschool children (1-4 years), school-age children (5–9 years) and adolescents (10–19 years) respectively (MOHFW & UNICEF, 2019). NFHS-4 (2015-16) and CNNS (2016-18) provide prevalence estimates for the roughly same period. The two surveys report differential anemia prevalence. Anemia prevalence in children (6-59 months) according to NFHS-4 is 58.6 %, whereas, in a comparable age group (1-4 years), the reported prevalence by CNNS is 41 %, as shown in Table:4.1.

The difference in reported anemia prevalence between NFHS and CNNS is due to different methodologies used to calculate the anemia prevalence (MOHFW & UNICEF, 2019). NFHS uses capillary blood, whereas CNNS uses venous blood. The use of capillary blood is believed to show higher prevalence estimates; that is why NFHS surveys report higher anemia prevalence among all age and population groups compared to the CNNS survey. Due to methodological differences in assessing haemoglobin levels, the prevalence estimates in NFHS and CNNS cannot be compared (Sachdev et al., 2021).

A consensus regarding the exact prevalence of anemia in India is lacking. A recent study using CNNS data shows that the prevalence of anemia is much lower than what NFHS data reported.

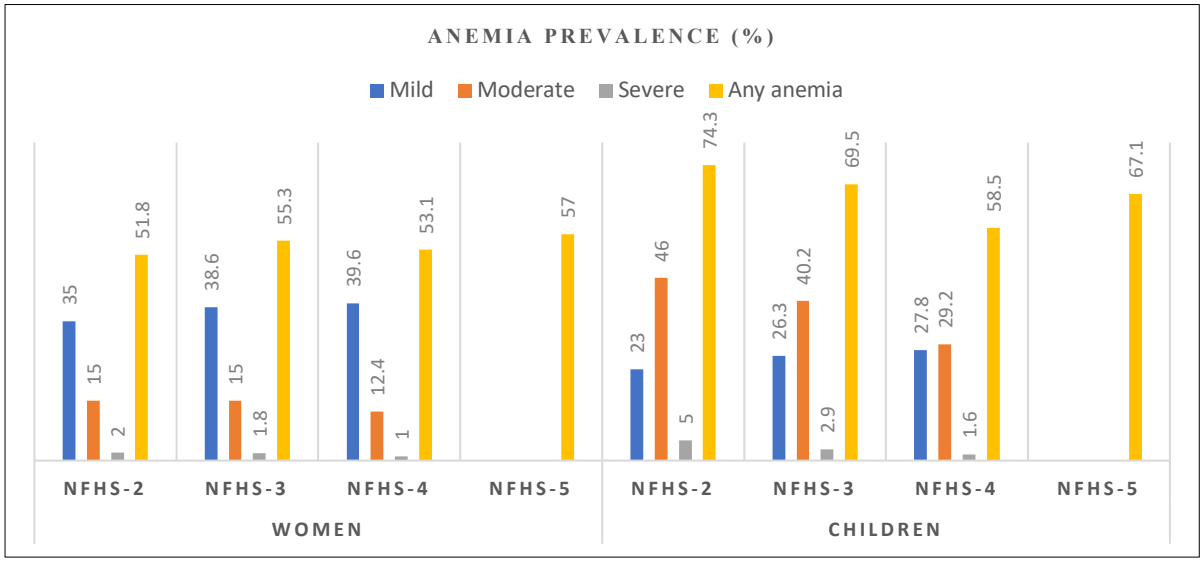
CNNS uses venous blood, which is considered a gold standard for haemoglobin measurement (Sachdev et al., 2021). According to CNNS, anemia was a moderate to severe public health problem among preschoolers in 27 states, among school-age children in 15 states, and among adolescents in 20 states (MOHFW & UNICEF, 2019)

4.1.2. TRENDS OF MILD, MODERATE AND SEVERE ANEMIA

> *"Eventually do you see mild anemia as a big deal or is it just a natural fluctuation of Hb around a set point. Unfortunately cut off point is same as cut-off for mild anemia. At some point you will find hundreds of people are anemic, they may be shifted other side of threshold, therefore there will not be anemia. For severe or moderate anemia ambiguity does not exist but for mild, it does. Public health is so far not making this distinction. They club all anemias as one. They are painting country as bad or good based on that which is utterly wrong"* (Anura, K, personal communication, 02/02/2021).

In a span of approximately 20 years (period from NFHS-2 to NFHS-5), anemia prevalence has decreased marginally (from 74.3 % to 67 %) among children (6-59 months), whereas it increased (51.8 % to 57 %) among women (15-49 years). Overall, anemia prevalence remains high among all population groups, including children and women. Anemia intervention strategies appear to be rendered almost ineffective (Fig:4.1).

Figure 4:1 Trends of mild, moderate, and severe anemia in women and children



Source: Compiled from various rounds of NFHS

Among mild, moderate, and severe forms of anemia, mild anemia constitutes the largest share in children and women, followed by moderate and severe anemia. Also, mild anemia is the most and severe anemia is the least prevalent form of anemia[5]. Mild anemia among women increased (from 35% to 39.6 %), whereas moderate and severe anemia decreased (from 15% to 12.4% and 2% to 1%, respectively) from NFHS-2 to NFHS-4 period. In the same period, mild anemia experienced a rise (23 % to 27.8 %), whereas moderate anemia (46 % to 29.2 %) and severe anemia (5 % to 1.6%) declined in children. Severe anemia decreased significantly from 2% to 1 % (100 % decline) and from 5 % to 1.6 % (212.5 % decline) women and children respectively (Fig:4.1). Overall, the prevalence of mild anemia among children and women has increased, whereas moderate and severe anemia decreased during this period. The rise in mild anemia is due to the shifts in the population's distribution from severe to moderate to mild.

[5] Anemia is classified as mild, moderate, or severe based on the concentrations of haemoglobin in the blood. Mild anemia corresponds to a level of haemoglobin concentration of 10.0-10.9 g/dl for pregnant women and children under age 5 and 10.0-11.9 g/dl for nonpregnant women. Moderate anemia corresponds to a level of 7.0-9.9 g/dl, while severe anemia corresponds to a level less than 7.0 g/dl.

*Data on mild, moderate, and severe anemia for NFHS-5 was not available on the time of writing this thesis.

4.2. INTERSTATE VARIATIONS IN ANEMIA PREVALENCE

The averages could be misleading as they often mask the interstate variations in anemia prevalence. In a geographically vast and culturally diverse country like India, huge interstate differences exist in anemia prevalence among children and women. There are states with reasonably less prevalence than others and vice versa.

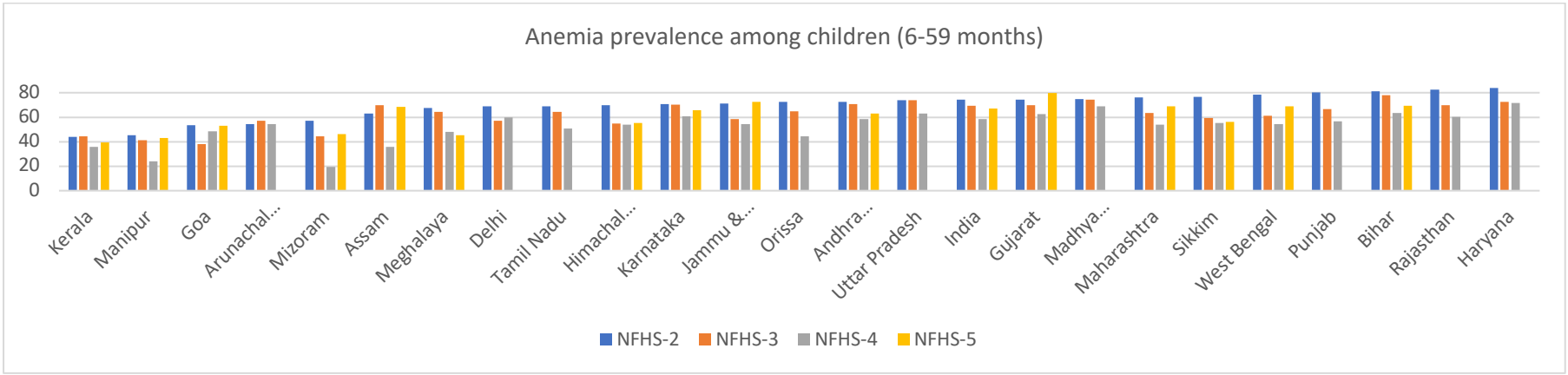
According to NFHS-5, the state of Kerala (39.4 %), Manipur (42.8 %), Meghalaya (45.1 %), Mizoram (46.4 %) were among the least affected, whereas Gujarat (79.7%), Jammu & Kashmir (72.7 %), Maharashtra (68.9 %), West Bengal (69 %) and Punjab (69.4 %) were among the worst anemia affected states for children aged 6-59 months. For women aged 15-49 years, Manipur (29.4%), Kerala (36.3 %), Mizoram (34.8%) and Goa (39 %) were among the least affected, while West Bengal (71.4 %), Jammu & Kashmir (65.9 %), Assam (65.9 %) and Bihar (63.5 %) were among the most affected states. Anemia among children and women in many states increased. Assam, Mizoram, Manipur, Jammu & Kashmir, Gujarat, and West Bengal were among the states which experienced a maximum rise in prevalence among children and women from NFHS-4 to NFHS-5 period (Fig:4.2). As many as 13 out of 22 states for which the first phase of NFHS-5 data was released reported an increase in prevalence (IIPS, 2020).

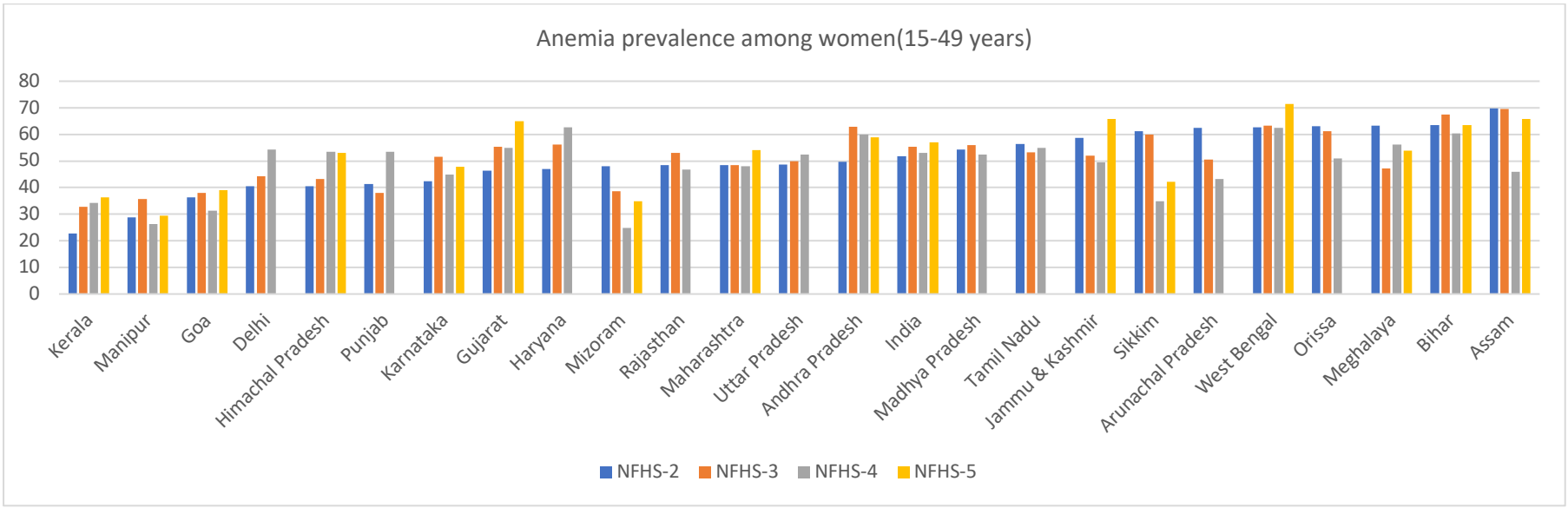
Table 4:1 A comparative analysis of anemia prevalence estimates of NFHS and CNNS

	NFHS-5 (2019-21)	***NFHS-4 (2015-16)***			***CNNS (2016-18)***			
Children (6-59 months)	67.1	58.6	Mild	27.8	Preschool children (1-4 years)	41	Mild	21.5
			Moderate	29.2				
			Severe	1.6			Moderate	17.7
							Severe	1.2
Non-pregnant women (15-49 years)	57.2	53.2			School-age children (5-9 years)	24	Mild	10.2
							Moderate	12.6
							Severe	0.7
Pregnant women (15-49 years)	52.2	50.4			Adolescents (10-19 years)	28	Mild	17.4
							Moderate	10.1
							Severe	0.9
All women (15-49 years)	57.0	53.1	Mild	39.6				
			Moderate	12.4				
			Severe	1				
All women (15-19 years)	59.1	54.1						
Men (15-49 years)	25.0	22.7						
Men (15-19 years)	31.1	29.2						

Source: Compiled from various rounds of NFHS and CNNS

Figure 4:2 trends of interstate variations in anemia prevalence among children and women





4.3. ANEMIA PREVALENCE ACROSS THE SOCIAL GRADIENT

Anemia is socially patterned. According to NFHS, anemia prevalence varies with the type of residence, years of education, caste status, religion, occupation/work status, and wealth quintiles are associated with anemia in children and women. The disparity according to the place of residence (urban (56 %) vs rural (60 %)), levels of education (uneducated (64.5%) vs educated (52%)), Caste (schedule caste (SC) (61 %) vs Schedule Tribe (ST) (63%) vs Other backward castes (OBC) (59 %) vs others (54 %)), Religion (Hindu (59 %), Muslim (60 %), Christian (45 %), Sikh (56 %), Jain 53 %), Buddhist (57 %)), and standard of living and wealth index (lowest (64 %), Middle (59 %), and highest (52%)) are visible. Children eating vegetarian food have a higher anemia prevalence (43.2%) than those taking non-vegetarian food (37.5%). The prevalence of anemia declined with an increase in the wealth index (IIPS, 2020)

Irrespective of the socio-demographic characteristics, the evidence points towards a common direction, i.e., first, there is a differential rate of anemia. The second prevalence is high across states and background characteristics such as irrespective of place of living and wealth quintiles, education, occupation, and caste**.**

4.4. ETIOLOGY OF ANEMIA

Biologically anemia is caused when erythrocyte loss exceeds erythrocyte production. This physiological phenomenon can occur through three main mechanisms: (i) due to ineffective or deficient erythropoiesis (when the body makes fewer red blood cells than the normal) (ii) haemolysis and destruction of red blood cells) and (iii) excessive loss of erythrocytes or blood loss. Ineffective erythropoiesis generally occurs from nutritional deficiencies, inflammation and genetic Hb disorders, while loss of erythrocytes arises from haemolysis, blood loss, or both (WHO, 2017).

4.4.1. CLASSIFICATION AND BIOLOGICAL MECHANISM

Anemia is also frequently classified based on the biological mechanism of causation, such as IDA caused due to iron deficiency, haemolytic anemia due to destruction or lysis of red blood cells and anemia of inflammation due to inflammation (Table:4.2). There are multiple causes of anemia, and the haematological manifestation of different causes can also be similar and, in some cases, be masked by other causes. The numerous interrelated confounding factors make distinguishing one form of anemia from the other difficult.

Broadly, there are two types of anemia based on their etiological origins. The first is nutritional anemia caused due to nutritional deficiencies; the second, which has gained attention with recent scientific discoveries, is anemia caused by chronic inflammation and infections (WHO, 2017). There is a complex bidirectional relationship between nutritional anemia and anemia due to infections. Nutritional deficiencies may exacerbate the risk of infections and inflammation, which may further have a deleterious impact on the nutritional status by adversely affecting the absorption. In developing and low-income countries, where the livelihood resources of most people are limited, and health is compromised, opportunistic infectious diseases such as pneumonia, a parasitic infection or tuberculosis further dampen the ability of the body to metabolise nutrients and repair the body (Viana, 2011). In places where anemia is endemic and chronic, there is a likelihood of nutritional anemia and anemia of inflammation occurring together.

Nutritional anemia may arise due to inadequate intake or bioavailability of hematopoietic nutrients. Hematopoietic nutrients are more in demand due to enhanced requirements during excessive blood loss or early red blood cell destruction. The most common hematopoietic nutrients are iron, folate, vitamin B12 and vitamin B6. The most common causes of nutrient deficiency are inadequate dietary intake, increased nutrient loss (due to menstrual blood loss, blood loss due to infections, or haemorrhage associated with childbirth), impaired absorption (e.g., high intake of phytate or *Helicobacter pylori* infection that hamper iron absorption, or lack of intrinsic factors that helps vitamin B12 absorption), or altered nutrient metabolism (e.g. vitamin A deficiency or riboflavin deficiency adversely impact the mobilisation of iron stores). The bioabsorption of nutrients depends on multiple confounding factors. Therefore, the effect of different nutrient supplement preparations could vary. The reduced bioavailability and absorption of nutrients limit the impact of nutrient supplementation programmes (Ramakrishnan, 2001).

Table 4:2 Causes, classification, and biological mechanisms of anemias

Increased RBC loss/destruction				**Deficient/defective erythropoiesis**		
Blood loss		Excessive hemolysis				
Acute	Chronic	Acquired	Hereditary	Microcytic	Normocytic	Macrocytic
Postpartum haemorrhage	Heavy menstrual bleeding Gastrointestinal blood loss (Hookworm infection, ulcers, schistosomiasis) Urinary blood loss (schistosomiasis)	Immune-mediated Microangiopathic Infection (malaria) Hypersplenism	Haemoglobin disorders (sickle cell disorders and thalassemia) Enzymopathies (G6PD deficiency)	Iron deficiency Anemia of inflammation (chronic disease) Thalassemia Vitamin A deficiency	Anemia of inflammation (chronic disease) Renal disease Bone marrow failure (aplastic anemia, leukaemia)	Folate deficiency Vitamin B12 deficiency
Source: adapted from (Chaparro & Suchdev, 2019)						

4.4.2. MULTIFACTORIAL ETIOLOGY

Anemia has a multifactorial etiology. Dietary iron deficiency is considered the most common cause of anemia, which is true but misleading (Kinyoki et al., 2021). It is important to recognise that not all causes of anemia are due to iron deficiency. However, much of the public health literature failed to make this distinction in the past. It is generally estimated that half of the anemia burden worldwide is due to nutritional iron deficiency(WHO, 2011b). Other factors that contribute to the etiology of anemia are mineral and essential element deficiencies such as folate, vitamin B12, Vitamin A, Vitamin B 6, Vitamin, Vitamin D and Vitamin E, folate, riboflavin and copper, genetic haemoglobin disorders, and infectious diseases (WHO, 2017). Iron deficiency, haemoglobinopathies and malaria are considered the top three causes of anemia globally (Kassebaum, 2016). GBD 2019 estimated iron deficiency, followed by thalassaemia; sickle cell trait; menstrual disorders; endocrine, metabolic, and immune disorders; and malaria as the top-ranked global causes of anemic. The contribution of these factors varies by age, sex, geography, population groups, and environmental settings (Kinyoki et al., 2021). In developing countries, including India, the etiology of anemia is largely unknown. However, rapid advancement in this regard has happened recently. Some of the recent studies have explored a range of etiological factors. A paper published in 2013 identified 17 etiologies using data from the global burden of disease (GBD) 2010 study (Kassebaum et al., 2013). Another study in 2016 identified 23 distinct etiologies (Kassebaum, 2016) and 35 underlying causes in 2020 (Gardner & Kassebaum, 2020). The cause-specific etiologies are shown in Table: 4.3.

Table 4:3 Cause-specific etiology of anemia

• Iron deficiency anemia	• Chronic Kidney disease owing to other causes
• Thalassemia trait	• Schistosomiasis
• Malaria	• Other gynecologic females only
• Gastritis and duodenitis	• Chronic kidney disease due to hypertension
• Other neglected tropical diseases	• Chronic kidney disease owing to glomerulonephritis
• Other haemoglobinopathies and haemolytic anemias	• Chronic kidney disease owing to diabetes mellitus
• Other infectious diseases	• Sickle cell disorder
• Endocrine, metabolic, blood, and immune disorders	• G6PD deficiency trait (females Only)

• Sickle cell trait	• Maternal haemorrhage (females only)
• Uterine fibroids (females only)	• G6PD deficiency
• Hookworm disease	• Thalassemias
• Peptic Ulcer disease	
Source: (Kassebaum, 2016)	

4.4.3. CONTRIBUTION OF IRON DEFICIENCY TO NUTRITIONAL ANEMIA

The knowledge of the extent of anemia caused by the iron deficiency may provide insights on the percentage of anemia that can be amenable by improving iron status. The evidence suggests that the proportion of anemia attributable to ID varies by population group, geographical settings, infectious disease burden and the prevalence of other confounding factors causing anemia. The representative data on iron status is scarce for most developing countries. In the past several decades, several approximations of the proportion of anemia due to ID have been made. WHO facilitated a series of studies on pregnant women across the different regions of the globe (Israel, Poland, Delhi, Vellore, Mexico, and Venezuela) to determine the extent of the contribution of various nutritional deficiencies to anemia. The earlier studies found that 40-90% of pregnant women are iron deficient. Iron deficiency was considered responsible for a significant proportion of anemia. However, the prevalence of iron deficiency and anaemia in different population groups was not apparent (WHO, 1968).

The first systematic attempt to quantify the proportion of anemia caused by ID was made in 1985 in a landmark paper titled: 'The prevalence of anemia in the world' (DeMaeyer & Adiels-Tegman, 1985). Based on the assumption that iron deficiency does not contribute to anemia in the adult male, the paper tentatively estimated that approximately 50 % of anemia in children and women was attributable to iron deficiency (Stoltzfus, 2001b). This finding formed a consensus that iron deficiency contributes to half of the total causes of anemia, later reinstated by WHO (WHO, 2001).

A systematic analysis of global anemia data from 188 countries calculated the cause-specific attribution of 23 distinct etiologies related to anemia. The Study showed that ID is the dominant cause of anemia in all global regions contributing to 62.6 % of the global burden of anemia (Kassebaum & GBD 2013 Anemia Collaborators, 2016). Another study involving systematic analysis of representative data on 'change in haemoglobin concentration from iron

supplementation studies' from 107 countries found that the proportion of all anemia amenable to iron 'was 50% among non-pregnant and pregnant women and 42 % in children (Stevens et al., 2013). The studies on Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) project found that ID, along with age and malaria, was one of the most consistent factors leading to anemia; and IDA among children and women varied with infectious disease burden (Engle-Stone et al., 2017; Wirth et al., 2017). A systematic review of nationally representative data from 23 countries with varying rankings on the Human development index on iron deficiency, IDA, and anemia among preschool children (PSC) and women of reproductive age (WRA) showed that approximately a quarter to a third of anemia was associated with ID. The contribution of ID was much smaller in countries where the prevalence of anemia was higher than 40 % and in countries where inflammation rates were higher (Petry et al., 2016).

Further, in many countries, including African countries high prevalence of anemia was not attributed to iron deficiency; instead, infections were the primary etiology (Kassebaum & GBD 2013 Anemia Collaborators, 2016). A study found that any anemia amenable to iron was about 50 % in non-pregnant and pregnant women and 42 % in children. At the same time, the proportion of severe anemia amenable to anemia was higher (more than 50 % for children and non-pregnant women and more than 60 % for pregnant women) (Stevens et al., 2013).

Though ID is the primary cause in many settings, the proportion of anemic individuals with ID varies by contextual factors; poor iron nutrition cannot be assumed to be the primary cause in all cases. Even in cases where ID is the primary cause, other nutritional and non-nutritional factors contribute to anemia development. The etiology factors of anemia, including iron and other nutrition and non-nutritional factors, vary greatly by age, sex, geographical regions, and other contextual factors. Their specific etiology and contribution are unknown in the case of developing countries. There is considerable heterogeneity in the proportion of anemia associated with ID between countries in the same region. The proportion of anemia associated with ID may vary from one country to another, even from one place to another in the same country (Stevens, 2013).

In many cases, nearly half of anemia cases are not caused by iron deficiency, nor they can be corrected by providing additional iron (WHO, 2017). Despite this, iron interventions (e.g., iron supplementation, fortification, and food-based approaches) are central to the anemia control programs, and WHO currently has 17 guidelines on iron supplementation. The extent to which

iron interventions alone can decrease anemia prevalence is lower than previously believed. The relative impact of iron interventions may be smaller in populations with a high burden of anemia and inflammation exposure. The proportion of anemia associated with ID tends to be relatively low, and iron absorption is restricted in the presence of inflammation (Petry et al., 2016). In such populations, more context-specific combinations of programmatic approaches to reduce the anemia may be needed

Petry and colleagues argue that the estimate of 50 % of anemia attributable to ID is too high for preschool, children and WRA in countries with a low, medium, and high human development index (HDI) ranking. The current practice of assuming 50 % of anemia attributable to anemia ID should no longer be used. Also, estimating the proportion of anemia attributable to the ID using a fixed proportion (based on data from another country or haemoglobin shifts observed by supplementation studies) is inappropriate. Where possible, national surveys should measure ID and IDA prevalence so that program planners and national stakeholders can better understand the etiology of anemia in their country (Petry et al., 2016).

4.5. ETIOLOGY OF ANEMIA IN INDIA

Iron deficiency is the most common cause of anemia in India. In the absence of nationally representative data, iron deficiency is generally assumed to contribute to 50 % of anemia in India (WHO, 2016). Iron deficiency and its contribution to anemia vary from one context to another. A study setup in Bangalore found 39 % of women to be anemic and 62 % to be iron deficient, and 95 % anemic women were iron deficient (Thankachan et al., 2007). The prevalence of ID among four and five months old, predominantly breastfed, term infants of Chandigarh was 21.4% and 36.4%, respectively (Krishnaswamy et al., 2017). A recent study using CNNS data reported that 32 % of children (1-4 years), 30.4 % of adolescent girls and 11-15 % of adolescent boys and children (5-9 years) were iron deficient. ID was higher in urban than rural areas and richer quintiles than poorer quintiles (Kulkarni et al., 2021).

A landmark paper published in Lancet recently, using CNNS data, revealed that iron deficiency anemia contributed to 36.5 %, 15.6 % and 21.3 % of total causes of anemia in 1-4 years, 5-9 years and 10-19 years old children and adolescents. Folate or vitamin B12 deficiency also contributed significantly (18.9 %, 24.6 %, and 25.6 %) in the three age groups. The share of dimorphic anemia (anemia caused by iron deficiency, folate, or vitamin B12 deficiency) was

13.5 %, 5.1 %, and 18.2 % in the three age groups. Therefore, 69 % of anemia in children 1-4 years, 51 % of anemia in 5-9 years, and 65 % of anemia in children and adolescents aged 10-19 years was caused due to nutritional causes. Anemia of Inflammation did play a fair part in anemia, contributing a share of 6.5 %, 5.4 % and 3.4 % of total anemia in 1-4 years, 5-9 years and 10-19 years children and adolescents, respectively. Interestingly, etiological factors of a large share of anemia were unknown. Approximately the causes of 25 %, 44 %, and 31 % of anemia in 1-4 years, 5-9, and 10-19 years children and adolescents remained undiagnosed (Table:4.4).

Iron deficiency anemia was the most common form of anemia among younger children (1-4 Years); folate or vitamin B12 deficiency anemia and dimorphic anemia were most common among children and adolescents aged 10-19 years. Anemia of other causes was most prevalent in children aged 5-9 years (Sarna et al., 2020). The Study by Sarna et al. (2020) was the first to use a large-scale nationally representative data source (CNNS) to characterise the types and contribution of anemia among children and adolescents in India.

The inadequate and inconsistent data regarding the prevalence and distribution of nutritional and non-nutritional factors affecting anemia is notwithstanding; also conspicuously lacking is information on 'unknown' factors. Sachdev et al. (2020) describe that lack of physical exercise and fitness among the Indian population may partly explain the 30-48 % of anemia of unknown causes. The paper argued that improved physical activities elevate haemoglobin concentration and that only 17 % of children and 38 % of adolescents in India achieve the recommended physical activity levels in India (Sachdev et al., 2021).

4.5. PREVALENCE OF IRON DEFICIENCY

Overall, 32 % of children aged 1-4 years, 17 % of children aged 5-10 years and 22 % of adolescents aged 10-19 years had iron deficiency. The prevalence of iron deficiency followed a similar pattern to anemia in both boys and girls, with the highest prevalence among children under two years of age and a steady decline to 10 years of age. Overall, gender, religion, caste, and wealth differential were observed among adolescents. The prevalence of iron deficiency among girls is almost three times that of adolescent boys.

The prevalence of iron deficiency among children and adolescents belonging to the Sikh religion was much higher than in other religions. Iron deficiency among adolescents in

schedule castes (27 %) was higher than in other castes (21%). The children and adolescents living in urban areas reported higher iron deficiency than their rural counterparts. Surprisingly, iron deficiency among wealthier households across all three age groups was higher. The iron deficiency in richest vs lowest wealth quintiles among preschoolers, school-age and adolescents were 43 %vs 20%, 27 % vs 12 % and 27 % vs 15 %, respectively (MOHFW & UNICEF, 2019, p. 166).

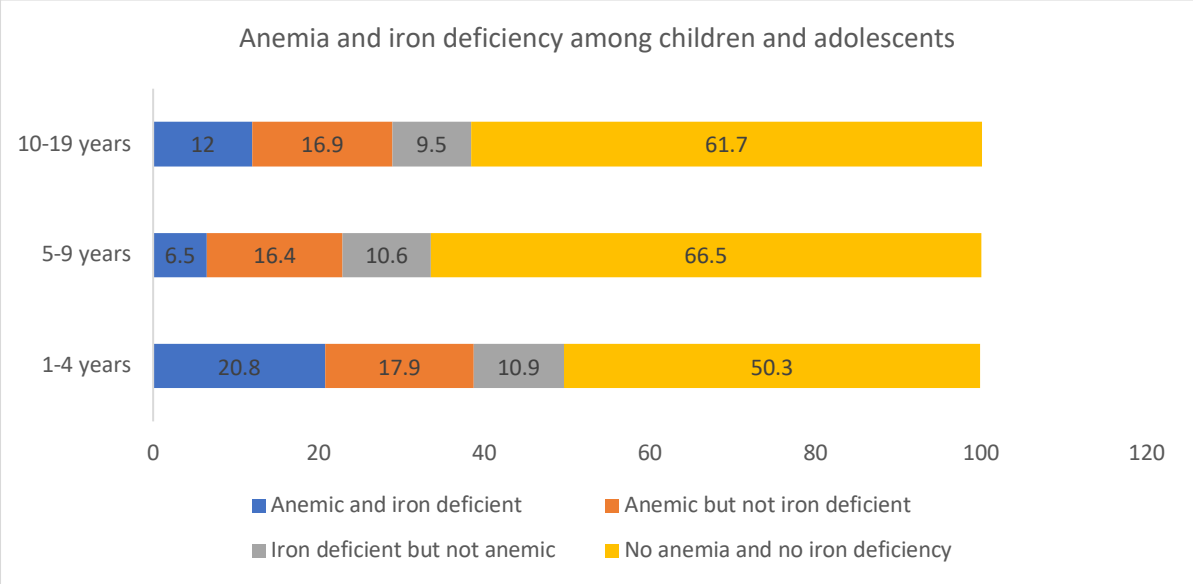
4.5.1. ANEMIA AND IRON DEFICIENCY TOGETHER IN THE POPULATION

Overall, among children aged 1-4 years, almost 21 % were both anemic and iron deficient, 18 % were anemic but not iron deficient, 11 % were iron deficient but not anemic, and more than 50 % were neither anemic nor iron deficient. Among children aged 5-9 years, 6.5 % were both anemic and iron deficient, 16 % were anemic but not iron deficient, 10.6 % were iron deficient but not anemic, and 66.5 % were non anemic and noniron deficient. Among adolescents aged 10-19 years of age, 12 % population had both anemia and iron deficiency, 17 % had anemia but not an iron deficiency, 10 % were iron deficient but not anemic, and more than 60 % were non-anemic noniron deficient (Fig:4.3).

Table 4:4 Etiology and their respective percentage contribution to total anemia in children and adolescents (1-19 years)

	Anemia due to nutritional causes						
Age group	Iron deficiency anemia (IDA)	Folate or vit B12 deficiency anemia	Dimorphic anemia (IDA + folate and Vit B 12 deficiency)	Share of nutritional causes	Anemia of Inflammation	Anemia of other causes	Total Anemia
1-4 years	36.5	18.9	13.5	68.9	6.5	24.5	100
5-9 years	15.6	24.6	10.7	50.9	5.4	43.6	100
10-19 years	21.3	25.6	18.2	65.1	3.4	31.4	100
Source: (Sarna et al., 2020)							

Figure 4:3 Anemia and iron deficiency among children and adolescents



Source:(MOHFW & UNICEF, 2019)

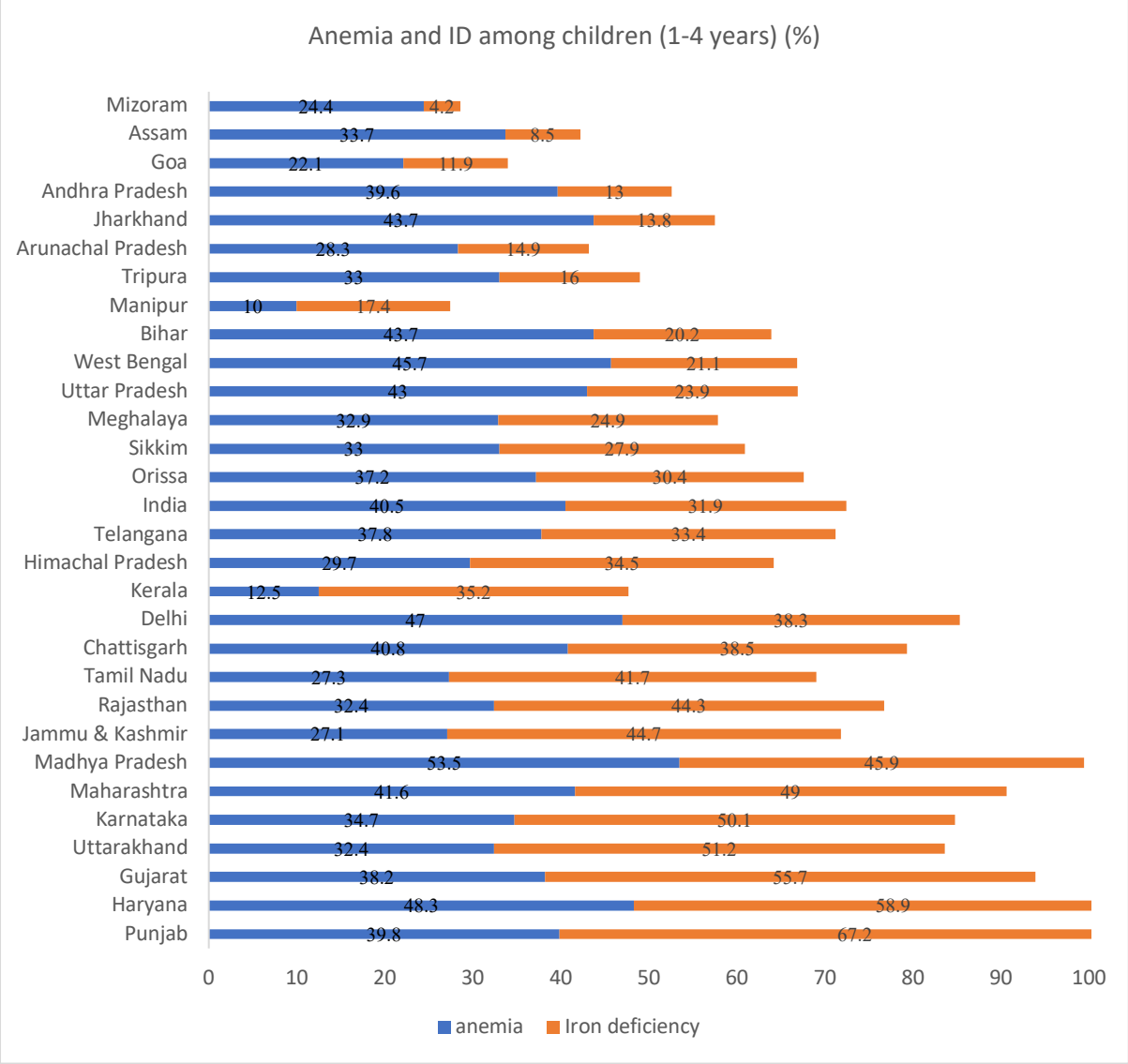
4.5.2. IRON DEFICIENCY AND ANEMIA ACROSS STATES

According to WHO, the estimated prevalence of iron deficiency in a population is much higher (2-5 times) than anemia prevalence(WHO, 2001). Using the same calculations, ID prevalence in a population was calculated worldwide. However, this hypothetical relationship was achieved in the second round of the National Health and Nutrition Survey (NHANES II), not from a randomised sample from different population groups. Contrary to the earlier hypothesis, a linear relationship between anemia and iron deficiency prevalence does not exist. The prevalence of anemia and iron deficiency in a population is a composite function of various factors that vary according to age, sex, geography, and other socioeconomic variables. Even fewer data on iron deficiency than on anemia illustrate a defined relationship between anemia and iron deficiency.

CNNS data shows huge interstate variations in anemia and iron deficiency prevalence. Also, iron prevalence and contribution of iron to anemia across states vary. A non-uniform relationship between iron deficiency and anemia in the Indian population dispels some earlier assumptions. The first assumption is that the more the iron deficiency, the more the anemia prevalence in a population and vice-versa. Second, iron deficiency is more prevalent than anemia (ID is 2-5 times more prevalent than anemia). CNNS survey reveals a nonlinear relationship between anemia and iron deficiency prevalence. On a national scale, anemia is

more prevalent (41%) than ID (32 %) nationally. However, in states such as Mizoram, Assam, Goa, Andhra Pradesh, Jharkhand, Arunachal Pradesh, Tripura, Uttar Pradesh, Bihar, Meghalaya, Sikkim, Orissa, Telangana, West Bengal, and Delhi, anemia prevalence is higher than iron deficiency. Iron deficiency is higher than anemia prevalence in Punjab, Haryana, Uttarakhand, Karnataka, Maharashtra, Jammu & Kashmir, Rajasthan, Tamilnadu, Kerala and Himachal Pradesh. Fig:4.4 shows the relationship between anemia and iron deficiency prevalence in children aged 1-4 years across states. The dynamics of anemia and iron deficiency can be interpreted in many ways, as shown in Table:4.5.

Figure 4:4 Anemia and ID prevalence among children (1-4 years)



Source:(MOHFW & UNICEF, 2019)

Table 4:5 The relationship between anemia and iron deficiency prevalence across states

Several logical conclusions can be drawn from anemia and iron deficiency patterns in states

- A nonlinear pattern between anemia and iron deficiency in the Indian population testifies that anemia and iron deficiency have an overlapping yet distinct mechanism of causation
- The extent of overlapping may vary between states and contexts
- contribution of iron deficiency to anemia varies from state to state
- Anemia may exist without iron deficiency, i.e., not all anemic populations are iron deficient
- Iron deficiency may exist without anemia, i.e., not all iron-deficient populations are anemic
- Some people are anemic and iron deficient both
- In an anemic population, where iron deficiency is less, the contribution of other factors (nutritional and non-nutritional) to anemia are more and vice -versa
- With the change in contexts, the prevalence and percentage contribution of factors leading to anemia may vary

4.6. EPIDEMIOLOGY OF UNKNOWN FACTORS

The knowledge of the etiology of anemia is far from adequate to make a coherent understanding of the factors and in what proportion they contribute to anemia. Nutritional deficiencies (iron, folate and Vit B12) contribute close to 60 % of anemia, and non-nutritional factors, including infections, contribute to the rest 40 % of anemia. Of the total nutritional deficiencies, iron supplementation and dietary iron fortification can reduce up to 25 %, and folate and vitamin B12 supplementation can reduce average anemia prevalence by 23 %. In addition to folate or vitamin B12, iron can reduce an average of 12 % of dimorphic anemia among children and adolescents aged 1-19 years. However, this can happen only in settings where the effect of other confounding factors is controlled.

Such a generalised understanding of etiology may lead to misleading conclusions in real-life settings. There could be a possibility that some population groups may be iron deficient, some folate and vitamin B12 deficient, and some have other nutritional deficiencies such as vitamin

A. Several permutations and combinations may exist. For example, the iron-deficient population may not have other nutritional deficiencies. A population group may be deficient in nutritional deficiencies but iron. Similarly, bringing a range of infections and nutritional deficiencies compounds the problem. The non-nutritional factors operate in tandem or conjunction with nutritional deficiencies. In the complex social and demographic setting of the Indian population, seldom does iron deficiency or folate or vitamin B12 or vitamin A or other nutritional deficiencies occur in isolation. Iron deficiency in such a context often occurs in conjunction with other nutritional deficiencies and infections. Several possibilities need consideration, and the exact prevalence and the contribution of those nutritional deficiencies occurring either singly or in combination are unknown in diverse population groups at regional and national scales. We have, as of now, a generalised understanding, i.e., close to 50 % of anemia is caused by iron deficiency. A large proportion of the population in India are neither iron, folate, or vitamin B12 deficient nor have hemoglobinopathies or infections and inflammations, and they still have anemia. Therefore, the unknown factors that influence anemia, their patterns and distribution in various population groups, and the specific contribution of those unknown factors and their mechanisms that cause anemia are unknown.

4.7. MOVING BEYOND IRON DEFICIENCY

On a global scale, dietary iron deficiency was the singular cause of anemia in low and middle-income countries. WHO predicted half of the anemia is caused by iron deficiency (WHO, 2011b). While iron deficiency is a significant contributor to anemia, there is little evidence to suggest that iron deficiency is ever actually a singular cause. Other nutritional deficiencies - vitamins A, B6, B12, C, D and E, folate, riboflavin, and copper play an important role in anemia development. With current advances in knowledge, the earlier estimation that 50 % of anemia is attributed to iron is increasingly being questioned. A systematic analysis of nationally representative surveys on the prevalence of iron-deficiency anaemia showed that the contribution of iron deficiency to anemia varies by geographical region, inflammation exposure and urban/rural setting. Using data from 25 surveys, a study reported that 25% and 37% of anemia is associated with iron deficiency in preschool children and WRA, respectively. The Study further concluded that anemia prevalence associated with iron deficiency is much lower than previously assumed (Petry et al., 2016). The findings by Sarna et al. (2020) in the Indian context are consistent with some studies suggesting that the percentage contribution of iron deficiency to anemia is overestimated and is based on assumptions.

A multicounty analysis showed that the percentage share of iron to anemia was smallest in regions where other factors contribute to anemia (e.g., <45% in children and non-pregnant women in different parts of sub-Saharan Africa and South Asia. The iron-amenable share of anaemia was largest where fewer other causes of anaemia exist (e.g., >55% in pregnant women and children in east and southeast Asia and southern and tropical Latin America, and roughly 70% in the same groups in high-income regions)(Stevens, 2013). This finding has implications for analysing the role of iron deficiency in contexts where other confounding nutritional and non-nutritional factors are also present. It is well established that besides iron deficiency, other nutritional deficiencies and non-nutritional factors play a vital role in the development of anemia. However, the etiologies and their respective contribution to anemia are not well known in the Indian context.

Several factors are associated with the development of anemia. Poor dietary intake (quantity and quality) is often the primary cause of micronutrient malnutrition, including anemia (Thompson, 2007). Inadequate dietary intake of haematopoietic nutrients (iron, vitamin B12, folate, and vitamin A) required to produce haemoglobin, and red blood cells is the primary pathway that leads to anemia (WHO, 2017). While diets poor in iron are the primary cause of anemia, diets deficient in one micronutrient are also likely to lack other micronutrients that may contribute to anaemia development (Thompson, 2007). In low-and middle-income countries, the diets of a large section of the population are characterised by poor in micronutrients, low in dietary diversity (monotonous diets), and high in antinutrient components such as Phytates and phenols, which inhibit the absorption of nutrients, including iron (K. M. Nair & Iyengar, 2009).

Besides limited access to diversified nutritious food, micronutrient deficiencies may be due to limited access to knowledge, adequate health care, hygiene, and sanitation (Kothari et al., 2019). Poor sanitation exacerbates bacterial and parasitic infections (malaria) and infestations with soil parasites (hookworms). At the household level, the physiological vulnerability of women due to early onset of pregnancy, multiparity and inadequate spacing results in the increased risk of maternal and childhood nutritional anemia (Chaparro & Suchdev, 2019). The above factors are influenced at the proximal level by broad underlying factors affecting food access, health care access, sanitation, agricultural practices, and anemia control policies; finally, the prevailing social, economic, political and environmental landscape (Y. Balarajan et al., 2011). The anemia prevalence varies greatly across states, and so does the prevalence of

nutritional deficiencies and non-nutritional factors associated with anemia. Likely, the contribution of various factors to anemia might also vary across states.

4.8. SUMMARY

The chapter discussed the trends, patterns and distribution of anemia and its etiological factors. The exact prevalence of anemia is a prerequisite criterion to deliberate on actions and design interventions. However, an estimated prevalence of anemia is disputed owing to variable methodologies and diagnostic techniques used to estimate the prevalence. NFHS and CNNS, the two national surveys, reported anemia prevalence, which differed considerably among comparable age groups. NFHS survey reported 67 % anemia among children and 57 % among women (15-49 years). CNNS reported 41 % anemia prevalence among children (1-4) years and 24 % among 5-9 years, and 28% among 10-19 years, which is less than NFHS estimated prevalence by huge margins. The difference in prevalence between the two surveys is mainly attributed to the type of blood (capillary versus venous) to assess haemoglobin concentrations. Despite the controversial prevalence, there is consensus that anemia prevalence is high across population groups. Moreover, many states have reported an increase in prevalence, thus raising questions about the ineffectiveness of existing programmes. A closer examination of trends and patterns reveals that mild and moderate anemia, which constitutes a larger share of anemia, has increased significantly, whereas severe anemia has reduced substantially.

Anemia was once thought to be caused primarily by iron deficiency. The recent findings, including in India, suggest that though iron deficiency is the primary etiology, its contribution is much lower than previously believed. Moreover, the contribution of iron is not uniform; rather, it varies from one state to another, suggesting a nonlinear relationship between anemia and iron deficiency. The other factors might contribute significantly to an anemic population, where iron deficiency is low. A range of factors, broadly categorised into nutritional deficiencies and infections, affect the haemoglobin concentrations. The patterns and distribution of many of these factors are unknown at the community level, including in India. The only Study that provides information on the contribution of iron deficiency, vitamin B12, folate and inflammations using nationally representative data suggests that approximately the etiology of 60 % of anemia is known. In contrast, the etiology of the rest of the factors is unknown. Therefore, we need to identify the factors that cause anemia in the Indian context.

CHAPTER 5

"Of all the forms of inequality, injustice in health care is the most shocking and inhumane."

Martin Luther King Jr.

CHAPTER 5. ANEMIA OF MICRONUTRIENT DEFICIENCIES AND INFLAMMATIONS

5.1. INTRODUCTION

Seldom does iron deficiency exist in isolation. Iron deficiency co-occurs with other micronutrient deficiencies such as Vitamin A, B12, folic acid, and riboflavin. In poor and food-insecure regions, inadequate intake of nutritious food may result in simultaneous multiple micronutrient deficiencies. In poor settings, the rate of infections is generally high. The parasitic infections due to hookworm or malarial infections can cause simultaneous malabsorption of iron, retinol, folic acid and vitamin B12 (L. H. Allen, 2000b). The chapter explores the nutritional deficiencies other than iron and the role of infections and other diseases in the causation of anemia.

5.1.1.1. INTERLINKAGES OF VITAMIN A DEFICIENCY AND ANEMIA

Evidence from geographical regions and population groups highlights a close association between VAD and anemia. Vitamin A has been shown to improve haemoglobin concentration and other iron indices even without iron supplementation (Zimmermann, 2007). A meta-analysis of 23 clinical trials further reveals that vitamin A supplementation reduced the risk of anemia by 26 % and raised haemoglobin and ferritin levels, indicating that vitamin A supplementation alone may reduce the risk of anemia by improving haemoglobin and ferritin levels (Cunha et al., 2019). Another study analysing the data from 12 countries in Asia, America and Africa observed a reduction in the number of anemic individuals with improved vitamin A status (Semba & Bloem, 2002). The simultaneous use of iron and vitamin A supplements seems to be more effective in preventing anaemia than using either micronutrient alone, which emphasises the need for studies on the interaction between these micronutrients, especially regarding iron absorption and erythropoiesis modulation (Michelazzo et al., 2013). Supplementation of iron and VA appears to increase the haematological response synergistically. In India, a cohort of pregnant women receiving iron in addition to vitamin A supplementation had higher haemoglobin levels at 26-28 weeks than the groups that received only iron alone (Panth et al., 1990). The combined administration of vitamin A and iron yielded

a better haematological response than the administration of only vitamin A and Fe alone. Vitamin A improves the haematological condition and Fe metabolism (Mejía & Chew, 1988). In a study done in Guatemala, a positive correlation between serum vitamin A and blood haemoglobin levels was found in children having adequate iron intake but not among the children with inadequate intakes. The author found that vitamin A deficiency promotes iron storage, and Vitamin A supplementation induces the transferrin synthesis that facilitates the availability of iron for hematopoiesis (Majia et al., 1977). A study in India among vitamin A-deficient children reported a significant increase in haemoglobin, haematocrit and serum iron levels when administered a daily supplementation of 8 mg retinyl palmitate for two weeks (Mohanram et al., 1977). VAD is also related to anemia, probably through its role in the mobilisation and transport of iron(West Jr et al., 2007).

In low-income countries, anemia and VAD co-exist in the same population (Bailey et al., 2015; Mejia, 1993). BRINDA analyses showed that VAD was associated with anemia in close to half of the surveys (5 out of 12) and across the levels of infectious disease burden in PSC. Among WRA, VAD and ID were associated in all surveys (5/5) in both high and low infection burden groups (Engle-Stone et al., 2017; Wirth et al., 2017). Despite the proven efficacy of vitamin A, most epidemiological studies did not identify the proportion of subjects with concurrent vitamin A deficiency and anemia. Like iron, vitamin A status is also affected by inflammation, making it challenging to assess the anemia due to VAD in settings where infectious disease is prevalent (Chaparro & Suchdev, 2019).

Some food sources are rich in iron and VA and provide joint protection against anemia and VAD, such as green vegetables and liver, but not all foods are a good source of both iron and VA. Therefore, it is reasonable to believe that anemia and VAD may overlap in some population groups, while in others, it may not (Bailey et al., 2015). In food-insecure low, low-income countries, the likelihood of anemia and VA occurring together is higher (Mejia, 1993).

Unlike IDA, which is characterised by depletion of iron stores, anemia due to VAD increases iron stores in the liver and spleen and increases serum ferritin concentrations (Michelazzo et al., 2013). The anemia of VAD is also known as hypochromic or microcytic anemia. Still, multiple confounding factors, including other nutritional deficiencies and infections, may cause inconsistencies in RBC parameters (Semba & Bloem, 2002).

5.1.2. MECHANISM OF IRON AND VITAMIN A INTERACTION

The mechanism by which Vitamin A affects anemia remains unclear. Several mechanisms may define the effect of VA status on anemia. 1) decreased resistance to infection in VAD and, hence, an increase in the anemia of infection; 2) effects on iron absorption and metabolism; and 3) direct modulation of erythropoiesis (Zimmermann, 2007, p. 202). There could be a possible overlap between pathways, as iron metabolism and erythropoiesis are modulated by infection (Cañete et al., 2017).

Vitamin A appears to interfere at several stages of iron metabolism (Fig:5.1). First, Vitamin A is an important factor of hematopoiesis that requires large amounts of iron for heme synthesis and subsequent incorporation into the haemoglobin molecules. Second, vitamin A has a regulatory role in the expression of genes involved in iron metabolism. During Vitamin A deficiency, iron is trapped in the liver and spleen and not effectively released for erythropoiesis by bone marrow; Iron absorption appears to increase, and bone marrow uptake of iron is impaired. Control of erythropoiesis is regulated by erythropoietin. Vitamin A deficiency downregulates the renal erythropoietin expression and interferes with effective erythropoiesis, resulting in erythrocyte malformation and higher phagocytosis of undifferentiated erythrocytes in liver and spleen cells (M. S. da Cunha et al., 2014). VAD is also associated with low iron binding capacity and a lower percentage of transferrin saturation (Mejia, 1993)

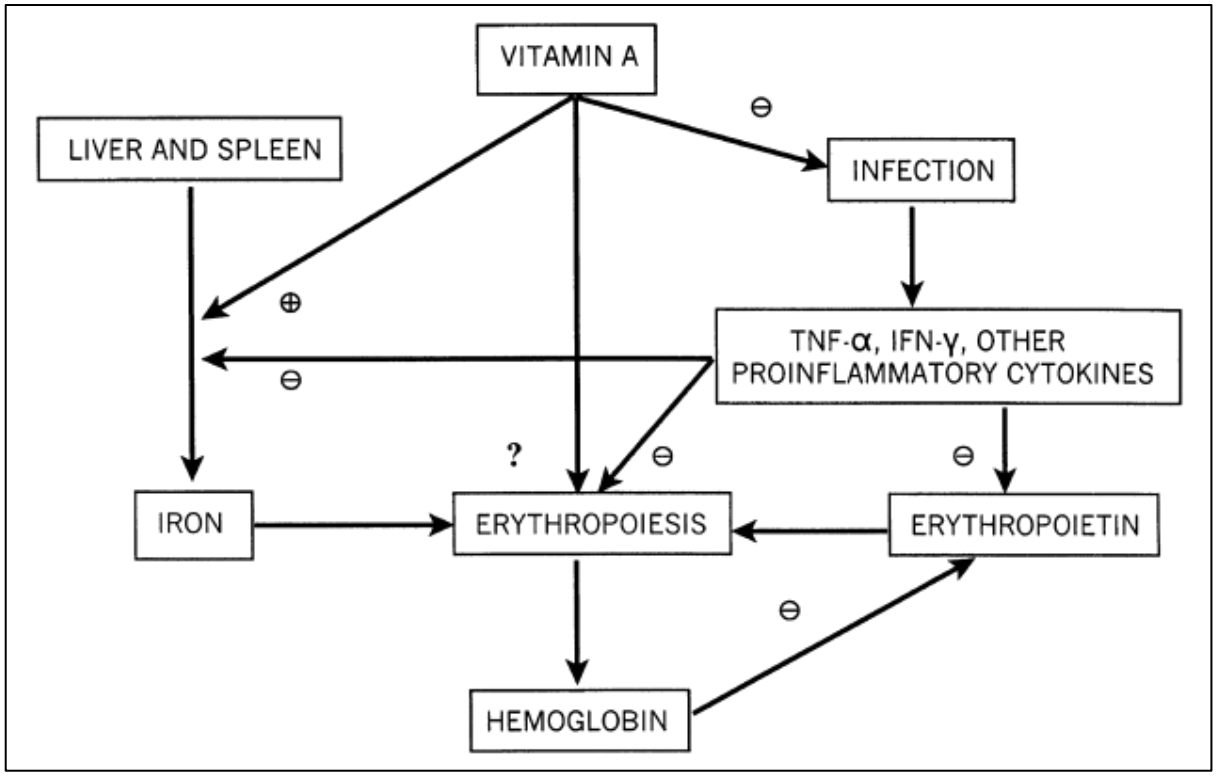
Vit A supplementation promotes an anti-inflammatory response, upregulates the erythropoietin expression, and mobilises the iron stores for erythropoiesis resulting in improved haemoglobin levels (Wiseman et al., 2017).

Recent evidence suggests that Vitamin A modulates the expression of the HAMP gene, which encodes the ‘hepcidin’ hormone, an antimicrobial peptide produced primarily in the liver and regulates iron homeostasis. Hepcidin binds to an iron exporter protein ‘ferroportin’ (FPN1), to cause lysosomal degradation and prevent iron release from splenic macrophages and enterocytes. Thus, hepcidin regulates iron homeostasis by reducing intestinal iron absorption and iron recycling from senescent red blood cells in the reticuloendothelial cells. Hepcidin also negatively modulate Duodenal divalent metal transporter 1(Dmt1)(M. S. da Cunha et al., 2014). The iron status, erythropoiesis, and inflammatory processes modulate the hepcidin expression. The pro-inflammatory cytokines IL-6, IL-1β, Tumor necrosis factor (TFN), and

IFN-Y modulate hepcidin expression through phosphorylation and activating the transcription of RBC (Semba & Bloem, 2002).

The retinoic acid (RA), a precursor of vitamin A plays a crucial role in erythropoiesis, modulation of erythropoietin and homeostasis of the immune system (Semba & Bloem, 2002). RA induces differentiation of T cells into T helper cells, which helps mount an anti-inflammatory response in the body. Thus, vitamin A helps to protect against infections and strengthens the immune system and vitamin A deficiency leads to an increase in the levels of pro-inflammatory cytokines, such as interleukins IL-6 and IL-1β and tumour necrosis factor-α (TNF-α) (Wiseman et al., 2017).

Figure 5:1 The conceptual model of vitamin A interaction with anemia



Source:(Semba & Bloem, 2002)

5.2. DEFICIENCY OF B VITAMINS (B12, RIBOFLAVIN AND FOLATE)

Many B vitamins, including Riboflavin (B2), cobalamin (B12), and folate, are involved in the Hb synthesis or iron metabolism. The deficiency of these nutrients may contribute to the development of anemia. The extent to which deficiency of B vitamins contributes to the global prevalence of anemia is variable and, in many cases, not identified.

5.2.1. VITAMIN B12 DEFICIENCY

Vitamin B12 deficiency is more prevalent in poorer populations worldwide but is common in developed countries, particularly among the elderly, starting early in life and persisting throughout life. However, a review study of the magnitude of the global prevalence of folate and vitamin B12 found no clear correlation between vitamin B12 prevalence and geographical distribution, population groups or level of development. The global data on the distribution of B12 are inadequate to analyse the magnitude of these deficiencies (McLean et al., 2008). The reported prevalence of vitamin B12 deficiency was 5% or higher in five out of seven countries (McLean et al., 2008). In the BRINDA project of WRA, 4 out of 10 surveys measured vitamin B12 status. Vitamin B12 deficiency was found to be low (<3 %)in Mexico and the United States and higher (approximately 15 %) in Côte d'Ivoire and Colombia (Wirth et al., 2017). In India, 14% of pre-school children (1-4 years), 17% of school-age children (5–9 years), and 31% of adolescents (10–19 years) had vitamin B12 deficiency. The prevalence of vitamin B12 deficiency ranged from 2% in West Bengal to 29% in Gujarat among children aged 1–4 years, from 0% in Nagaland and 1% in Kerala to 31% in Uttar Pradesh and 32% in Punjab among children aged 5–9 years, and from 2% in Kerala and Nagaland to 48% in Gujarat among adolescents aged 10–19 years (MOHFW & UNICEF, 2019). A review study found considerable variations in vitamin B12 deficiency across states. The deficiency ranged from 16 % among elderlies in Karnataka to 74 % in Delhi (Gonmei & Toteja, 2018).

The prevalence of vitamin B12 deficiency was underestimated for several reasons. The erroneous belief that Vitamin B12 is found only in animal-based foods and the deficiency is unlikely except in people following strict vegetarian diet regimes or persons with pernicious anemia(J. M. Scott, 2007, p. 124). Contrary to popular belief, the deficiency is not only prevalent in strict vegetarians or vegans but a broad spectrum of populations (L. H. Allen, 2009). There are two leading causes of vitamin B12 deficiency. First, inadequate dietary intake and second, malabsorption of vitamins from food, particularly in the elderly, with gastric atrophy common (McLean et al., 2008). The risk of vitamin B12 is highest when impaired absorption and low intakes co-exist (Ramakrishnan, 2001). It is believed that most diets have more vitamin B12 than RDA. The widespread vitamin B12 deficiency in the population is attributed to hypochlorhydria (low levels of stomach acid) in large proportions of all populations. This is due to gastric atrophy, with the absence of acid preventing the liberation of vitamin B12 from the bound form present in foods. High levels of malabsorption in

developing countries render vitamin B 12 unavailable for absorption. (J. M. Scott, 2007, p. 124).

5.2.3. FOLATE DEFICIENCY

In India, 23% of children aged 1–4 years, 28% of children aged 5-9 years and 37% of adolescents aged 10-19 years had folate deficiency. Folate deficiency was more common in children (5-9 years) from the wealthiest quintile (30 %) than poorest households (21 %). Among children aged 10-19 years, folate deficiency was 43 % in the richest households compared to 28 % in the poorest households.

Folate deficiency is more common among population groups that consume low amounts of green leafy vegetables and legumes and rely more on unfortified wheat or rice as a staple food (Gillespie & UNICEF, 1998). The high-risk population groups of folate deficiency are pregnant women, preterm birth babies, and individuals inhabiting malaria-endemic regions (as folate promotes malarial parasite growth). During pregnancy and lactation, the demand for folate increases several times. At the start of pregnancy, poor folate status can lead to megaloblastic anemia, further exacerbated by the additional need for folate during lactation. Folate deficiency may cause a reduced erythrocyte life span (Bailey et al., 2015). Contrary to vitamin B12, folate in its natural form is unstable, has significantly reduced bioavailability and is not abundant in almost any diet, even in affluent countries (J. M. Scott, 2007, p. 124).

The contribution of vitamin B12 and folate deficiency to the global prevalence of anemia is minimal (WHO, 2017) and, in many cases, unknown (Chaparro & Suchdev, 2019). The limited evidence suggests that a high prevalence of vitamin B12 or folate deficiency did not necessarily correlate with a high prevalence of anemia except in women and their children consuming vitamin B12 deficient vegetarian diets. BRINDA project also supported this theory and did not show a significant association between anemia and vitamin B12 and folate deficiencies (Wirth et al., 2017). Several intervention trials have used vitamin B12 combined with folic acid with or without iron, almost without exception. Vitamin B12 or folic acid on its own do not produce a benefit. Folate and vitamin B12 are interdependent; one needs another to function optimally. Vitamin B12 and folate deficiency compromises the cell's ability to divide properly, thus reducing erythropoiesis (J. M. Scott, 2007, p. 127).

5.2.4. RIBOFLAVIN (VITAMIN B2)

Low intake of riboflavin is associated with an increased risk of anemia. Riboflavin deficiency is prevalent across many population groups. It is common among pregnant and lactating women, preschool and school-aged children, adolescent girls, and the elderly in developed and developing countries. Riboflavin is abundant in most diets as long as they have a component of meat, fish, milk, milk products, vegetables and fruits. Therefore, riboflavin deficiency is associated with a low intake of meat and milk/dairy products (Powers, 2003).

Riboflavin is an essential component (as a cofactor) of a range of enzymes involved in oxidation and reduction reactions; therefore, riboflavin deficiency could have a wide range of effects. (J. M. Scott, 2007, p. 127). Riboflavin deficiency may contribute to the reduced mobilisation of iron stores, reduced iron absorption, the release of iron from ferritin and increased iron losses (Wirth et al., 2017).

The evidence of Riboflavin deficiency as a primary contributor to anemia is unclear. However, riboflavin, along with iron supplements, has been shown to improve Hb levels more than iron supplements alone in pregnant women and children in some studies, if not all (Rohner et al., 2007). In a survey among adults in China, inadequate riboflavin was associated with an increased risk of anemia (Z. Shi et al., 2014). Riboflavin supplementation increased haemoglobin status among women aged 19-25 years in the United Kingdom (Powers et al., 2011). Other studies have also reported the effect of riboflavin on enhancing the haematological response to iron (J. M. Scott, 2007, p. 127).

5.2.5. VITAMINS C, D AND E

A study reported that 74 % of adults in North India and 46 % of adults in South India are deficient in vitamin C. Vitamin C deficiency was associated with dietary deficiency of vitamin C (Rowe & Carr, 2020). Vitamin C affects iron metabolism in many ways. It enhances non-haem iron absorption and increases iron mobilisation from stores. Vitamin C acts as an antioxidant that protects the erythrocytes from oxidative damage, haemolysis and blood loss. Pregnant women, the elderly, smokers, and infants fed exclusively with cow's milk are at risk of vitamin C. The studies show that vitamin C supplementation leads to increased haemoglobin

concentration and serum ferritin among non-pregnant women and children (Fishman et al., 2000).

In India14 % of preschool children aged 1–4 years, 18% of school-age children aged 5–9 years and 24% of adolescents aged 10–19 years were reported to have vitamin D deficiency (MOHFW & UNICEF, 2019, p. 186). Sikhs have the highest and scheduled tribes lowest prevalence of vitamin D deficiency. Vitamin D has been associated with anemia in different population groups. However, the strength of association may likely vary between race and ethnic groups. Vitamin D is known to inhibit pro-inflammatory cytokines and hepcidin-regulated transcription. Evidence suggests that vitamin D may impart protection against anemia by supporting erythropoiesis. Other calciotropic hormones, parathyroid hormones and fibroblast growth factors are associated with iron homeostasis and erythropoiesis (E. M. Smith & Tangpricha, 2015). A recent systematic review and metanalysis of 14 randomised controlled trials (RCT) on the effect of vitamin D on haemoglobin levels among 17.5-68 years old adults found that vitamin D supplementation leads to a non-significant reduction in haemoglobin levels. However, it positively affected transferrin saturation and iron status (Arabi et al., 2020). The exact mechanism and the extent to which vitamin D contributes to the development of anemia are poorly understood.

Vitamin E is an antioxidant that protects the polyunsaturated fatty acids in RBC membranes and other fat-soluble parts such as low-density lipoprotein (bad cholesterol) from oxidative damage and prevents hemolysis of RBCs. Vitamin E deficiency can cause hemolytic anemia. The clinical trials have indicated that vitamin E supplementation improves the blood haemoglobin and hematocrit levels in some the anemic subjects, including low birth weight, premature infants, chronic renal failure patients or patients suffering from inherited hemolytic anemia (Jilani & Iqbal, 2011). HOWEVER, Vitamin E deficiency is considered limited to premature and low birth weight infants and individuals with pathological malabsorption syndromes. Vitamin E is routinely used among premature/low birth weight infants in high-income countries to prevent the anemia of prematurity (Fishman et al., 2000).

5.2.6. COPPER AND ZINC

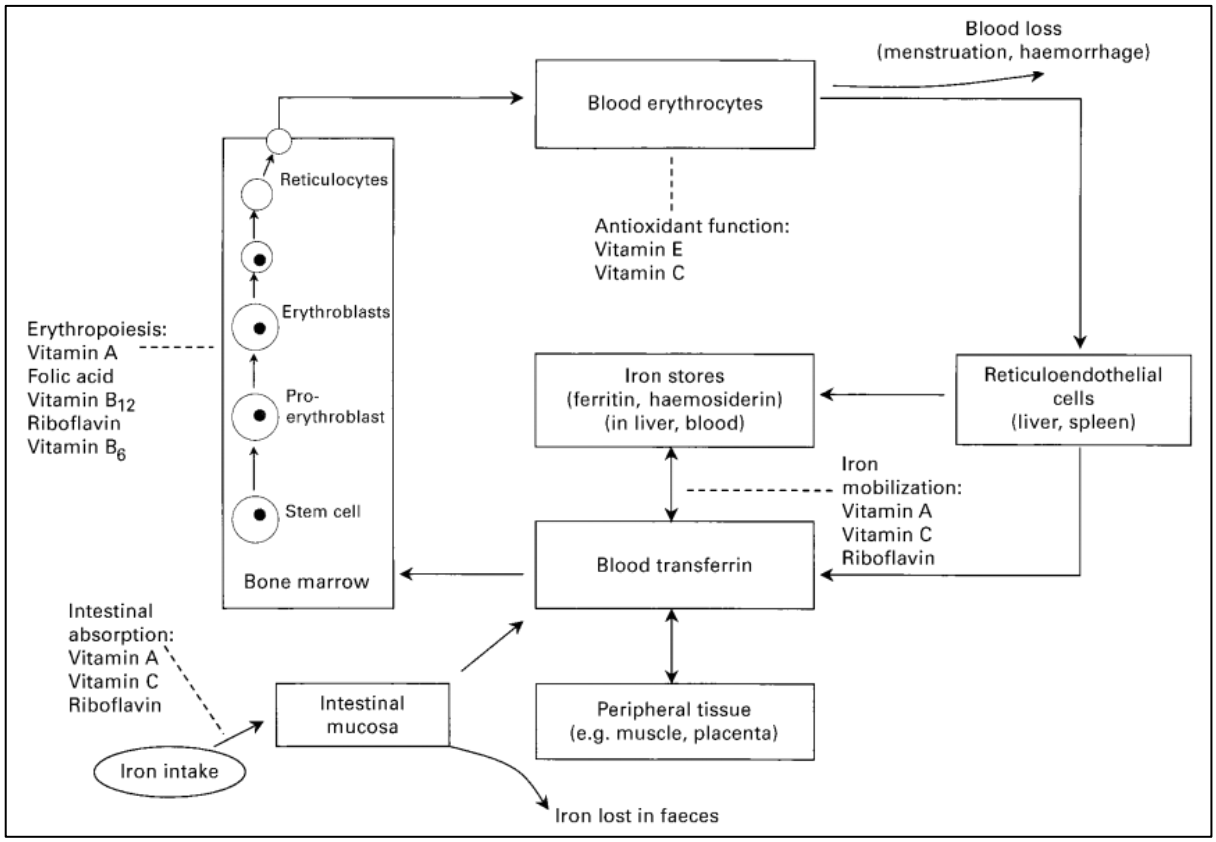
Copper is among many micronutrients humans need for proper organ function and metabolic processes such as haemoglobin synthesis and iron oxidation (Myint et al., 2018). Copper

facilitates several enzymes required for iron metabolism to perform their normal function, such as oxidation of ferrous iron and transfer of iron from storage to haemoglobin synthesis sites, thus is essential for the normal functioning of iron metabolism and erythropoiesis. Copper deficiency is uncommon; many cases have been reported in the past. The high-risk groups include premature and low birth weight, exclusively breastfed infants, individuals receiving parenteral nutrition for a prolonged duration, infants with prolonged diarrhoea and individuals with malabsorption syndromes. High intakes of zinc or iron can interfere with copper absorption. High intake of divalent metals such as copper, calcium, zinc, and manganese share the same transporter as iron, interfere with iron absorption, and lead to iron deficiency (Knovich et al., 2008).

Zinc is a trace element found in the structure of enzymes that catalyse or coordinate iron metabolism. There is evidence that indicates an association between IDA and Zinc deficiency. A recent study demonstrated that a person with IDA was more likely to have zinc deficiency; the study also recommended adding zinc with iron supplementation for IDA patients (Kelkitli et al., 2016).

In addition to iron and vitamin A, several dietary factors influence the haemoglobin concentration via various mechanisms (Fig: 5.2). Table:5.1 illustrate some of the basic features and mechanisms of iron metabolism and erythropoiesis, emphasising how specific vitamins may influence iron deficiency and anemia.

Figure 5:2 role of micronutrients in iron metabolism and erythropoiesis



Source: (Fishman et al., 2000)

5.3. ASSOCIATION OF ANEMIA WITH OTHER FORMS OF UNDERNUTRITION

Anemia is associated with stunting, wasting and being underweight in some studies but not all (Engle-Stone et al., 2017; Gosdin et al., 2018). In the BRINDA project, anemia among PSCs was associated with stunting, wasting and underweight in more than half of the surveys (9/15, 5/15 and 10/15). Stunting, wasting, and underweight due to similar causal factors such as inadequate nutrition, poor environment, and sanitation are associated with anemia (Engle-Stone et al., 2017).

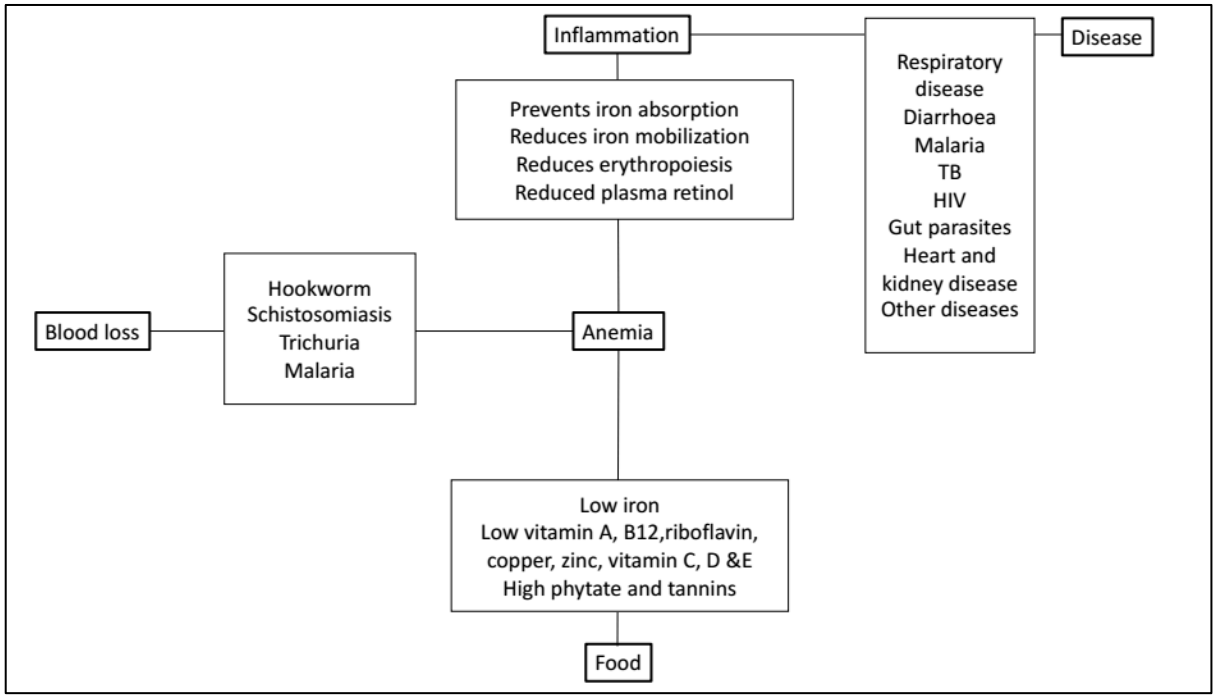
Table 5:1 illustrates the mechanisms by which vitamin deficiencies can play roles in the development of anemia

Vitamin deficiency	Mechanism by which vitamin deficiency affect iron metabolism
Vitamin A	Impaired mobilisation of iron stores
	Impaired erythropoiesis
	Increased susceptibility to infection
Folic acid	Impaired DNA synthesis, leading to ineffective erythropoiesis
Vitamin B12	Impaired metabolism of folate, leading to ineffective erythropoiesis
Riboflavin	impaired iron mobilisation
	Impaired globin production, leading to impaired erythropoiesis
	Reduced intestinal absorptive capacity
Vitamin C	Reduced absorption of iron
	Reduced mobilisation of iron from stores
	Impaired folate metabolism
	Oxidant damage to erythrocytes, leading to haemolysis
	Capillary haemorrhaging, leading to blood loss
Vitamin E	Oxidant damage to erythrocytes, leading to haemolysis
Vitamin B6	Impaired haem synthesis, leading to impaired erythropoiesis
Calcium	Inhibits absorption of both heme and non-heme iron, Inhibition of iron transport
Copper	Impaired oxidation and reduction of iron affecting absorption, transport, storage and mobilisation
Iodine	Iron is better absorbed when used with mixture of iodine, precise mechanism is not known (Sattarzadeh & Zlotkin, 1999)
Zinc	Impaired coordination between enzymes helpful in iron absorption
Manganese and Phosphate	Inhibit iron absorption
Source: adapted from (Fishman et al., 2000; Gillespie & UNICEF, 1998; Jackson, 2007)	

5.4. ANEMIA OF INFLAMMATION AND PRIMARY DISEASES

Infections can contribute to anemia via multiple mechanisms, including blood loss, hemolysis, and reduced erythropoiesis. A systematic analysis of the global burden of anemia between 1990 and 2010 identified three primary causes of anemia, i.e. hookworm, schistosomiasis, and malaria (Kassebaum & GBD 2013 Anemia Collaborators, 2016). Infections are now widely recognised as an important cause of anemia. The contribution of infections is higher than previously thought. Anemia results from a synergy of inflammation and insufficient bioavailable dietary iron to meet iron requirements. Figure:3 provides a conceptual map of causes of anemia (disease, blood loss, and diet) and illustrates the central role of inflammation in all three. Solving the problem of anemia, especially in developing countries, including India, will require understanding the causes of diseases and how inflammation impairs the adequate absorption and utilisation of iron.

Figure 5:3 Factors contributing to anemia



Source: adapted from (Thurnham & Northrop-Clewes, 2007, p. 232).

5.4.1. INFLAMMATION

Anemia of chronic disease or anemia of Infections (AI) is the second most common cause of anemia after IDA (Weiss & Goodnough, 2005). In settings where infections are high, anemia

due to infections is the primary etiology (Kassebaum, 2013). AI varies by disease burden and environment; however, despite being one of the top causes, the global proportion of anemia due to infections and inflammation is unknown. Inflammation was significantly associated with anemia among WRA in high and low infection burden countries. The odds of anemia among WRA with inflammation were 90 % and 50 % higher in countries with high and low infection burdens than in WRA without inflammation (Merrill et al., 2017). BRINDA project found that in PSC, the inflammation was associated with anemia across countries; 9 out of 10 surveys showed a marked association between inflammation and anemia. However, a pooled analysis of countries by disease burden revealed an association between inflammation and anemia in very high and high infection burden groups but not in low and moderate infection groups. The rate of inflammation among PSC with anemia was 9.1 %, 13.7 %, 37. 4% and 70. 3% in countries with low, moderate, and very high burden of infection. The role of inflammation in the development of anemia is likely to be higher in countries with higher infectious disease burdens and vice versa (Engle-Stone et al., 2017).

Anemia of Infection alters the iron metabolism by inducing the release of pro-inflammatory cytokines (IL-6 and other cytokines) as a host defence mechanism against infection. The cytokines stimulate the sequestration of iron inside the reticuloendothelial system (liver and spleen) and enterocytes, resulting in reduced life span and production of RBC (Nairz et al., 2016; Weiss & Goodnough, 2005). Hepcidin plays a crucial role in mediating the iron metabolism in anemia of infections. In response to infection, inflammatory cytokines allow the increased production of hepcidin. Hepcidin downregulates the ferroportin expression inside enterocytes, macrophages and hepatocytes to reduce or block the iron absorption and interferes with the mobilisation of iron stores into circulation (Nairz et al., 2016). Anemia of infection also affects iron metabolism through a different mechanism using inflammatory cytokines. Inflammatory cytokines released in response to infection; activate the macrophages, leading to the reduced life span of RBC, impairing the normal functioning and production of erythropoietin(EPO) and inhibiting the normal proliferation and differentiation of erythroid progenitor cell (Weiss & Goodnough, 2005).

5.4.2. HELMINTH INFECTIONS

In a systematic analysis of the global burden of anemia in 2010, hookworm infections were ranked third and fourth most prevalent causes of anemia among males and females, respectively (Kassebaum et al., 2013). Hookworms are most common in low-income southeast

Asia and sub-Saharan African countries with poverty and poor access to water, sanitation, hygiene and health infrastructure (Anand et al., 2014). Anemia associated with hookworm infection was the predominant cause of anemia in East Asia and Oceania (Kassebaum et al., 2013). Hookworm feeds on the intestinal mucosa blood (and iron) and can cause severe depletion of iron levels leading to IDA (WHO, 1994). Several factors, such as intensity of infection (i. e the number of hookworms carried by an individual), the species of hookworms, and coinfection with multiple parasites, determine the severity of blood loss and subsequent anemia caused due to hookworm infection. Hookworms of moderate to heavy infection were associated with lower Hb in schoolchildren whereas, in adults, any level of infection was associated with lower Hb. Children born with poor iron status are severely affected even with mild hookworm infections (J. L. Smith & Brooker, 2010). Infection afflicted by *A.duodenale* is more severe, causing fivefold more blood loss and increased risk of ID and anemia than *N.americanus.* Both the species of hookworms are endemic to many areas and often exist together in a geographic region (Albonjco et al., 1998). Geographical regions infested with multiple parasites such as *Schistosoma* sp., *Ascaris lumbricoides* (roundworm), *Trichuris trichiura* (whipworm), or *plasmodium* pose a more significant risk of anemia than an independent parasitic infection would do because of synergistic effect (Ezeamama et al., 2008).

5.4.3. SCHISTOSOMIASIS

Schistosomiasis, similar to hookworm, has been associated with blood loss and subsequent IDA, particularly if the intensity of infection is high. Schistosome infection may cause splenic sequestration of erythrocytes, reduced RBC life span, autoimmune hemolysis and anemia of chronic disease (Ezeamama et al., 2008). Schistosomiasis is a primary cause of anemia in sub-Saharan Africa, particularly in females (Kassebaum & GBD 2013 Anemia Collaborators, 2016).

5.4.4. MALARIA

Malaria caused by *plasmodium* sp. is one of the major causes of anemia globally and is a primary cause of severe anemia (Kassebaum et al., 2013). Malaria is the primary cause of anemia in sub-Saharan African countries, even more than iron deficiency. Approximately half of the world's population is at risk of malaria. However, malaria prevalence is disproportionately concentrated in Africa, accounting for 90 % of malarial cases and 92 % of

malarial deaths in 2015. PSC and pregnant women are the most vulnerable to the risk of malaria (WHO, 2017).

Malaria generally occurs at places where ID is also present. The relationship between malaria and iron deficiency is complex; ID may confer protection against severe malaria while the parasite requires iron for its growth. Malaria-related anemia is multifactorial, and malaria causes anemia through multiple mechanisms. Malaria interferes with iron metabolism and distribution, promoting defective erythropoiesis, hemolysis, and decreased iron absorption (WHO, 1994). The malarial infection induces the hemolysis of infected RBCs but rupturing of non-parasitised RBC during malarial infection is the primary cause of anemia development. Blood loss is rarely a cause of anemia due to malaria. Hepcidin is upregulated during malaria infection, contributing to anemia development (Spottiswoode et al., 2014).

5.4.5. HUMAN IMMUNE VIRUS (HIV)

Anemia is one of the most common haematological abnormalities associated with HIV (Redig & Berliner, 2013). HIV infection causes altered iron metabolism and elevated hepcidin. The opportunistic infections and nutritional deficiencies in HIV increase the risk of anemia among HIV patients. HIV directly affect the hematopoietic progenitor cells and decreases responsiveness to EPO. Anemia prevalence among HIV-positive individuals increases with the progression of HIV, and the degree of anemia is correlated with the severity of HIV (Redig & Berliner, 2013).

5.4.6. TUBERCULOSIS

Anemia is a common condition associated with Tuberculosis and is more common among those coinfected with TB and HIV (Papathakis & Piwoz, 2008). In Indonesia, 60 % of TB patients were found anemic. In Uganda, 71 % of patients coinfected with TB/HIV were anemic. Anemia in TB is caused mainly due to chronic infections, increased blood loss (blood in sputum), decreased RBC production, poor appetite, and low food intake that leads to poor nutritional status, including iron (Chaparro & Suchdev, 2019).

5.4.7. GENETIC HAEMOGLOBIN DISORDERS

Sickle cell disease (SCD) and Thalassemias are inherited genetic haemoglobin disorders that are among the top causes of anemia globally. Sickle cell disease is the most common genetic disease associated with hemolytic anemia in sub-Saharan Africa. Children with SCD are at more risk of malnutrition and infection, leading to increased hemolysis and severe acute anemia (Ansong et al., 2013).

Thalassemias are a group of inherited disorders in which there are defects in the synthesis of one or more of the globin chains that constitute Hb. Thalassemias are primarily found in Southeast Asia; are characterised by hemolytic anemia and impaired erythropoiesis (Muncie Jr & Campbell, 2009).

Because of the complex mechanism of iron metabolism, different nutrients and infections have distinct mechanisms to affect iron metabolism. Often nutrients act in tandem, deficiency of one nutrient affects the physiology and functioning of other nutrients. Infections may lead to nutritional deficiencies, which in turn exacerbate infections. Identifying various nutritional factors and infections and their mechanisms of action concerning iron metabolism is key to addressing anemia.

5.5. SUMMARY

A range of nutritional deficiencies such as vitamin A, B12, C and D and infections and inflammations affect the different domains of iron metabolism and contribute to anemia. Anemia is a distinct epidemiological entity when envisioned in the context of multiple micronutrient deficiencies, infections and diseases acting in tandem in a population. The literature in the past has focused on iron deficiency. The recent advances highlighted the role of other micronutrients and infectious diseases in developing anemia. Anemia due to iron deficiency, other micronutrient deficiencies and infectious diseases are still seen as separate and disjointed phenomena. Rarely in the literature the role of multiple micronutrient deficiencies, the concurrent infections, and their cumulative, synergistic impact on the development of anemia is recognised.

CHAPTER 6

"Helath care is vital to all of us some of the time, but public health is vital to all of us all of the time"

C. Everet Koop

CHAPTER 6. IRON METABOLISM AND DIETARY FACTORS

6.1. INTRODUCTION

An improved understanding of iron metabolism has profoundly changed the approach to anemia in the last two decades. There was hardly any serious discussion on anemia beyond iron deficiency. Anemia still is largely unexplored, but one dimension that needs reflection to locate anemia within the broader biological realm is iron metabolism. An examination of iron metabolism uncovers the linkages of anemia with a wide range of nutritional and non-nutritional factors. Therefore, iron metabolism offers opportunities to understand anemia from biological systems perspective involving various enzymes, proteins, dietary factors, and organs. The chapter reviews the current understanding of iron metabolism, particularly the role of hepcidin in maintaining iron homeostasis and its function in the manifestation of several iron-related disorders. It also discusses the role of diets in anemia causation.

6.1.1. PHYSIOLOGY OF IRON

The body's iron requirements vary with age, gender, and physiological status, including pregnancy and menstruation. Iron is utilised for the growth and maintenance of tissues and to carry out a range of physiological processes. In contrast, iron is lost through urine, skin, and faeces in the basal processes. The total median iron need in the body is the aggregate sum of the requirements for growth, basal losses, and menstrual losses. The iron required for growth, basal metabolism, and menstruation vary according to age, gender, and physiological status. (Ramakrishnan, 2001). The Iron requirement may differ between seemingly similar individuals. The iron requirement is a function of three factors, i.e., absorption (intake and bioavailability of iron), iron losses and stored iron. Not all dietary iron is available for absorption; only a tiny fraction of it is ingested in the duodenum. The proportion of dietary iron absorbed determines the body's iron levels. During Infancy, pregnancy and menstruation, iron needs are higher.

6.1.1.1. INFANCY

Infancy is characterised by rapid growth and a high requirement for iron. The newborn term infant contains approximately 250-300 mg (75mg/kg body weight) (WHO, 2004, pp-247). The

haemoglobin concentration in the first two months of life falls because of the improved oxygen situation in the newborn infant compared to the intrauterine fetus. This results in a significant redistribution of iron from catabolised erythrocytes to iron stores. The redistribution of iron maintains the total body iron during the first four months of life constant. A substantial proportion of this stored iron is utilised for haemoglobin synthesis, and it covers the need of the term infant during 4-6 months of life. That is why human milk that contains very little iron can meet the demand during this period. The iron requirements of infants increase significantly after 4-6 months for body size and energy intake, which cannot be supplied by breast milk alone (WHO, 2004, p. 247). Breast milk does not contain enough iron; neither the iron in breast milk is absorbed efficiently (WHO, 2010). In the weaning period (transitional phase in an infant's diet when the mother gradually begins to introduce foods other than breast milk or formula), the iron demands of the body in relation to energy intake are highest of the lifespan except for the last trimester of pregnancy when iron requirements are majorly met from the mother's iron stores. Infants have no iron stores at this phase and rely on dietary iron alone. High anemia prevalence among children persists in many population groups in developing countries because iron depletion in early years rarely gets compensated due to delayed complementary feeding beyond six months, lack of diversified nutritious food, and accompanying parasitic infections (Ramakrishnan, 2001; WHO, 2017).

6.1.1.2. MENSTRUATION

Menstruation is the one reason why iron requirements of women are almost twice that of men, and iron deficiency is much more prevalent among women than men. Menstrual iron loss accounts for about half of the total iron requirement (WHO, 2017). The frequency distribution of physiological menstrual blood loss is highly skewed, i.e. some women lose iron lesser than others and vice versa (WHO, 2004, pp-250). The evidence suggests that the differential rate of menstrual blood loss and associated iron loss in geographically separated populations (China, Burma, Canada, Egypt, England, and Sweden) is genetically controlled by the fibrinolytic activators in uterine mucosa. These findings suggest that the variable iron status across different population groups is not associated with the variation in iron requirements but with differential absorption rates from the diets (WHO, 2004, pp-250). Women who menstruate heavily are more likely to develop anemia (Ramakrishnan, 2001).

6.1.1.3. PREGNANCY

During pregnancy, more iron is required for increased haemoglobin synthesis in women and to transfer iron to the fetus. There is increased demand for oxygen in pregnancy. The body undergoes physiologically adaption to increase haemoglobin mass to meet oxygen demand. The iron requirements over the entire pregnancy period are not uniform; iron absorption also varies across the length of pregnancy. Besides the amount of iron in the diet and the bioavailability of iron (meal composition), the stage of pregnancy also determines the overall iron absorption during pregnancy. There is a paradoxical reduction in iron requirements in the first trimester compared to nonpregnant women, decreasing iron absorption. The iron absorption during the second trimester increases by 50 %, and in the last trimester, it may increase up to four times than usual. Despite high iron absorption, pregnant women can't meet high iron requirements from diets alone, even if the diet's iron content and bioavailability are very high. The pregnant women of most developing countries are at increased risk of falling short of meeting the ideal iron quota. Even in developed countries, women experience a deficit of 400-500 mg in the amount of iron absorbed versus what is required during pregnancy (WHO, 2004, pp-265). An adequate iron balance can only be maintained if iron stores of 500 mg are available during the second and third trimesters. However, it is rare to have iron stores of this size during pregnancy; therefore, all pregnant women are recommended iron supplements (WHO, 2004, pp-265).

Multiple pregnancies and short intervals (less than two years) between pregnancies may cause frequent depletion of iron stores. The iron stores in late pregnancy decide postpartum iron status in women (L. H. Allen, 2000a). The risk of anemia immediately after postpartum is lower unless severe blood loss occurs during delivery. After 2-3 months postpartum, the iron stores and the additional haemoglobin synthesised during pregnancy start to fall, increasing the risk of anemia reappearing (L. H. Allen, 2000a).

6.2. IRON METABOLISM

Iron is an essential component of blood, oxygen transport, energy production, cellular respiration, and DNA synthesis. For example, iron constitutes an integral component of haemoglobin, transporting oxygen from the lungs to the peripheral tissues and carrying carbon dioxide back to the lungs. Most of the iron is present in erythrocytes as haemoglobin. Myoglobin, an oxygen storage protein that provides oxygen to muscle cells, contains iron

(Chifman et al., 2014). Several enzymes have iron as an essential constituent to perform normal metabolic functions in the body. For example, enzyme cytochromes act as electron carriers to facilitate the oxidative metabolism to transfer energy within the cell, particularly in mitochondria (WHO, 2004, pp-246). Iron-containing enzymes such as cytochrome P450 are involved in synthesising steroid hormones and bile acids, regulating the signal from neurotransmitters, such as serotonin and dopamine in the brain, and detoxifying foreign substances in the liver (WHO, 2004,pp-246). However, excess iron can also be toxic because of the ability of iron to exist in various oxidation states and facilitate the formation of hydroxyl or lipid radicals, which can damage proteins, lipids, and DNA. Human beings have developed a tightly regulated iron intake, storage, utilisation, and recycling machinery to maintain iron homeostasis at systemic and cellular levels. A disruption of the homeostatic mechanism because of the poorly functional iron metabolism caused either due to nutritional deficiencies, infections, or other diseases either singly or synergistically can impair iron metabolism. Dysregulation of tightly controlled iron metabolism is crucial in several disorders, including micronutrient deficiencies, HIV, TB, and Malaria.

Iron metabolism involves a range of body organs, proteins, and enzymes ranging from organ to cellular level, each closely intertwined at different scales (Coad & Pedley, 2014). Iron is involved in several biologically essential reactions. Iron is an integral component of several haemoproteins, heme-containing enzymes and many non-heme iron proteins that catalyse a wide range of reactions and play a central role in oxygen sensing (Tandara & Salamunic, 2012). A recent study has identified that iron homeostasis consists of an extensive network of 151 chemical species, 107 reactions, and transport steps (Ganz, 2011).

Iron homeostasis is a tightly regulated and controlled affair at the levels of iron absorption, uptake, release from recycling macrophages and hepatocytes, utilisation and storage in the body (Camaschella et al., 2020). Physiological malfunctions in any of these organelles, cells, proteins, and enzymes could lead to abnormalities in iron metabolism and affect haemoglobin's oxygen-carrying capacity. In this context, it is essential to highlight the critical multiscale control mechanism of iron regulation and the associated factors directly or indirectly in iron metabolism that contribute to developing anemic conditions.

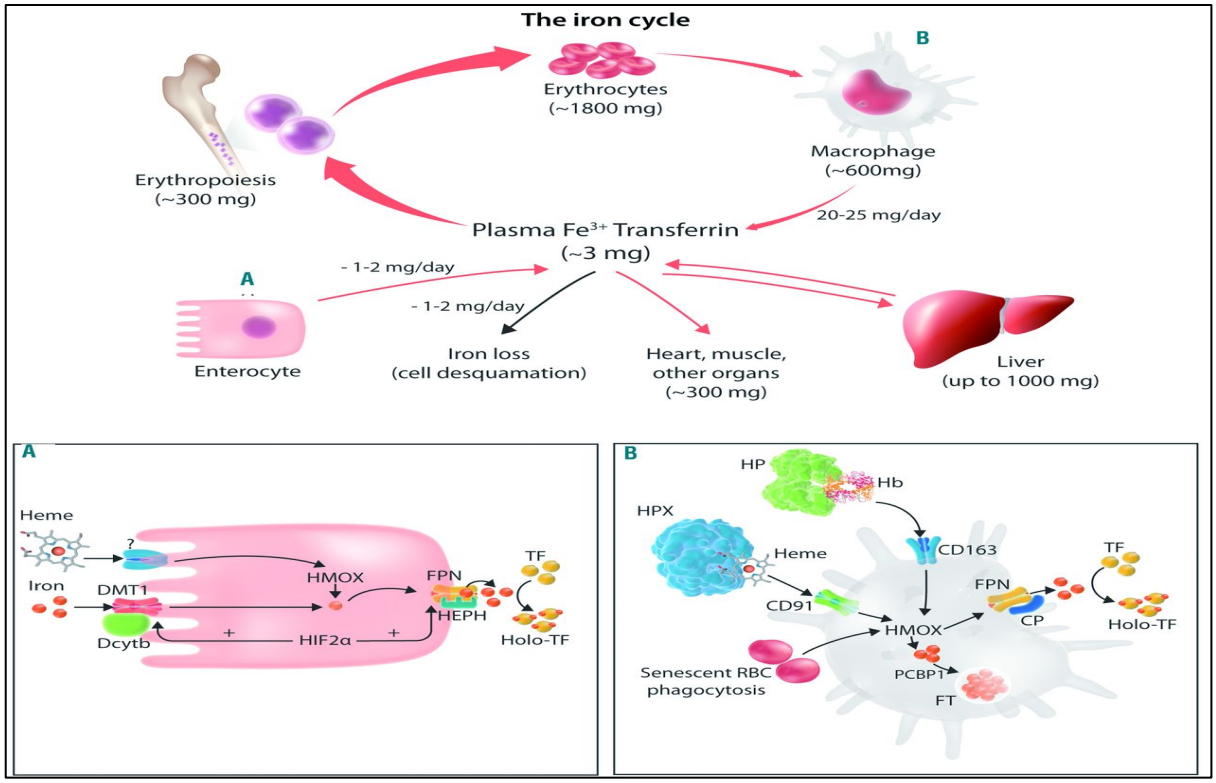
Generally, a well-nourished adult contains approximately 3-5 g (~55 mg/ kg for men and ~45 mg/kg for women). Most of the body's iron (~60-70 %) is incorporated into the haemoglobin of circulating erythrocytes used for oxygen transfer to tissues, 10 % in myoglobin and the rest

(20-30%) is stored within ferritin in the liver and hemosiderin in reticuloendothelial macrophages (Tandara & Salamunic, 2012). Only a tiny fraction of iron (2-4 mg) circulates in the bloodstream attached to the plasma iron carrier, transferrin, central to iron trafficking (Katsarou & Pantopoulos, 2020). The amount of transferrin bound iron (~3 mg) constitutes less than 1% of the total body iron (3-5 g) in adults. The circulating pool of transferrin bound iron turns over every few hours (full ten rounds/day) to meet the daily requirement of iron for erythropoiesis and other body needs (25-30 mg/day) (Dev & Babitt, 2017; Katsarou & Pantopoulos, 2020). Transferrin binds to its ubiquitous receptor TFR1 and delivers iron to cells through the endosomal cycle (Fig:1). The reticuloendothelial macrophages phagocytise the senescent and damaged erythrocytes, recover iron from heme and utilise, conserve, or recycle the iron. To a lesser extent, duodenal enterocytes maintain the iron supply to the circulating transferrin (Katsarou & Pantopoulos, 2020). The iron reserve (~1 g in adults) stored in tissue stores can be mobilised to meet the unmet metabolic needs of iron.

There is no known mechanism of iron excretion. Approximately 1-2 mg of iron is lost through nonspecific and non-regulated mechanisms such as blood loss, sweat, sloughing of intestinal epithelial cells and desquamation. The gut absorbs 1-2 mg of dietary iron daily to compensate for this loss. However, haemoglobin synthesis alone requires 20-25 mg of iron daily. Macrophages recycle iron upon phagocytosis of erythrocytes to continue the haemoglobin synthesis and other metabolic processes. The non-heme iron uptake takes place in the duodenum. The apical divalent metal transporter (DMT 1) protein imports the non-heme iron from the lumen into enterocytes after reduction from ferric to ferrous iron by duodenal cytochrome B reductase (DCYTB). Absorption of heme is higher than non-heme iron, though the precise mechanism is obscure. In enterocytes, non-utilised iron is stored in ferritin and either lost to mucosal shedding or exported to plasma by basolateral membrane ferroportin according to the body's needs. A detailed schematic presentation of the iron cycle is shown in Fig: 6.1[6].

[6] **The iron cycle:** Iron (Fe) circulates bound to transferrin to be released to all organs/tissues through transferrin receptor 1. Most iron (20-25 mg) recycled by macrophages, which phagocytise senescent red blood cells (RBC), is supplied to the bone marrow for RBC production. The daily uptake of dietary iron by duodenal enterocytes is 1-2 mg; the exact amount is lost through cell desquamation and blood loss. Excess iron is stored in the liver and macrophages as a reserve.
(A) Focus on intestinal iron absorption. The metal transporter DMT1 takes up ferrous iron, reduced by DCYTB, on the luminal side of the enterocyte. Iron not used inside the cell is either stored in ferritin (FT) or exported to circulating transferrin (TF) by ferroportin (FPN) after ferrous iron is oxidised to ferric iron by hephaestin (HEPH). Hypoxia-inducible factor (HIF)-2α, stabilised by local hypoxia, stimulates the expression of the apical (DMT1) and basolateral (FPN) transporters. After entering the cell through an unknown mechanism, Heme is converted to iron by heme oxygenase.

Figure 6:1 The iron cycle: systemic iron homeostasis and body iron distribution



Source:(Camaschella et al., 2020)

6.2.1. ROLE OF HEPCIDIN IN IRON ABSORPTION

Hepcidin is one vital cog in the iron homeostatic mechanism, regulating iron movement across the gut and cells. Hepcidin is a master regulatory hormone released from the liver that governs the availability of iron for biological functions. It is a negative regulator of iron metabolism. As a part of the homeostatic mechanism, hepcidin concentrations are reduced in iron deficiency anemia or iron-replete individuals to enhance iron absorption to replenish the iron stores. However, hepcidin production in the liver increases in iron overload to suppress iron absorption and maintain normal iron levels (Ganz, 2011).

There are at least four major pathways of hepcidin regulation: regulation by iron status, dietary iron and iron stores; regulation by inflammation; regulation by hypoxia/anemia; and regulation by erythroid factors (Tandara & Salamunic, 2012). In response to inflammation, the

(B) Focus on the iron recycling process. Macrophages recover iron from phagocytised RBC after heme is degraded by heme oxygenase. They also recover heme from haemoglobin (Hb)-haptoglobin (HP) or heme-hemopexin (HPX) complexes. Iron not used inside the cells is either stored in FT or exported to the circulation by FPN with the cooperation of ceruloplasmin (CP). The latter is the preferential route in normal conditions.

inflammatory cytokines interleukin-6 (IL-6) are activated, stimulating hepcidin production in hepatocytes (Andrews, 2000).

6.2.1.1. DIETARY ENERGY AND IRON ABSORPTION

> *"The micronutrient deficiencies and protein & calorie deficiencies are kind of conceptualized separately. Micronutrient deficiencies are seen as specific deficiencies which can be treated by giving vitamins and minerals and mass prophylaxis. At the broadest sense, micronutrient deficiencies are the lack of protein, energy, and calories. This medicalized approach of tackling this problem without considering underlying factors such as balanced diets is problematic"* (Rajesh, K, personal communication, o6/02/2022)

Diet is the energy source to carry out all physical and physiological processes. Low energy availability, either due to low energy intake, excessive energy expenditure, or a combination of both, is known to impair physiological processes that undermine health and performance, including iron absorption (McKay et al., 2020). The body physiology appears to have a complex cyclical relationship between energy availability and iron absorption or iron stores. In the case of iron deficiency, low iron stores may contribute to energy deficiency or its clinical manifestations. Energy deficiency may lead to low iron status (Pasiakos et al., 2016). High energy expenditures can also accompany low energy availability during strenuous work, which can induce iron losses through sweating, hemolysis, gastrointestinal bleeding, inflammation and hepcidin elevations. This imbalance between iron uptake and losses could partially explain the high prevalence rate of IDA observed among athletes, manual labourers, and agricultural farm workers with low energy intake (McKay et al., 2020).

The duration of physical activity is a crucial determinant of inflammation levels. Further, intensity and modality of the physical activities have a bearing on IL-6 response, with higher intensity workouts and more strenuous physical activities invoke higher cytokine levels (McKay et al., 2020; Peeling et al., 2008). A study investigating the link between exercise, IL-6 and hepcidin demonstrated that the 60 min of treadmill running was associated with a 7-fold increase in IL-6 and a more than 5-fold rise in hepcidin levels post-exercise. This was the first

study to establish that exercise-induced inflammatory response increases hepcidin levels and impairs iron absorption (Peeling et al., 2009).

Hepcidin mediates iron absorption during low energy availability. A study showed that hepcidin expression was linked to the energy content, independent of the effect of the inflammatory stimulus on hepcidin levels (Pasiakos et al., 2016). The exact mechanism driving the alterations in the hepcidin levels due to energy deficiency is not well understood. One pathway could be the regulation of hepcidin by gluconeogenic signalling. An individual with low dietary intake working under physically demanding conditions may experience periods of acute energy deficit due to increased energy expenditure. Food deprivation has been reported to significantly increase transcription of the hepcidin gene and hepcidin concentrations. The ability of hepcidin to stimulate gluconeogenesis during starvation leads to the synthesis of glucose from non-glucose precursors and subsequent depletion of stored glycogen stores. Glycogen depletion can activate hepcidin production (Hennigar et al., 2021; McKay et al., 2020). Alternatively, nutrient availability regulates the erythroferrone (ERFE), a key regulator of iron metabolism. ERFE acts on hepatocytes to suppress hepcidin production. The starvation and energy deficiency in the body leads to a reduction in ERFE production, increasing hepcidin concentrations.

Irrespective of the lack of knowledge on exact mechanisms, the link between hepcidin and energy availability is evident. This has led to the belief that hepcidin is a valuable biomarker for the early identification of energy deficiency. While most of the literature has explored the mechanisms through which energy deficiency can augment hepcidin levels and subsequent iron deficiency, the evidence of a bidirectional relationship in which low iron stores contribute to energy deficit also exists. For example, in cases where iron stores are compromised, the body becomes metabolically inefficient and shifts from oxidative phosphorylation to the anaerobic mode of adenosine triphosphate (ATP) production. This metabolic shift renders the body use more energy for a given task, reducing the energy availability.

Iron provides immunity against invading pathogens, and its deficiency could severely compromise immune response, increasing susceptibility to infections. There are population groups in which iron deficiency and energy deficiency may co-occur and are more vulnerable to risks of IDA because of the severely compromised immune system. Iron deficiency can be an early indicator of energy deficiency in the body.

6.2.1.2. CARBOHYDRATE AVAILABILITY AND IRON REGULATION

Though high-intensity physical activities can stimulate increased production of IL-6 and hepcidin, which could negatively impact iron absorption, a regular carbohydrate intake can reduce the effects of elevated levels of IL-6 (Hennigar et al., 2021). During high-intensity physical work, the carbohydrates can maintain blood glucose concentrations and safeguard the muscle glycogen stores from depletion. Therefore, promoting carbohydrate availability may help limit the adverse impact of physically challenging conditions on iron absorption by attenuating inflammation and minimising hepcidin levels. However, the quantity and timing of carbohydrates are vital factors in regulating iron absorption (McKay et al., 2020). The limited evidence suggests that a nutritional intervention to control IL-6 response to heavy physical activities may provide a mechanism to increase iron absorption.

6.2.1.3. DIETARY PROTEIN INTAKE AND IRON METABOLISM

For several decades, the linkage between dietary proteins and iron bioavailability has been known. Dietary protein is needed irrespective of the dietary iron to maintain normal haemoglobin levels. The experimental results demonstrate that different protein sources affect iron availability and absorption (Miski & Kratzer, 1977). Unlike energy and carbohydrate sources, which generally enhance iron absorption by keeping the hepcidin production at low levels, many dietary proteins, including milk and egg proteins, inhibit iron absorption. In contrast, meat protein has been shown to increase iron bioavailability (Thomas et al., 2013). The diets adequate in iron but deficient in protein reported a noticeable reduction in growth, erythropoiesis, and iron absorption. Meat is known to influence iron bioavailability for absorption from food. The studies have shown that an unknown factor in meats (meat factor) improve non-heme iron absorption in human.

6.2.1.3.1. MILK PROTEIN AND IRON ABSORPTION

Milk proteins, unlike meat proteins, are generally believed to inhibit iron absorption. A study reported a ~71 % and ~62 % decline in iron absorption in humans when beef was replaced by milk and cheese, respectively (Cook & Monsen, 1976). However, recent findings suggest that the hydrolysis of bovine milk proteins (whey and casein) into smaller peptides and amino acids before ingestion may improve iron absorption and bioavailability. Therefore, recent data

highlights that milk proteins (casein and whey) influence bioavailability depending on whether the milk proteins are intact or hydrolysed. This finding has public health importance because casein and whey are primary protein sources of commercial infant formula.

There are conflicting studies depicting the impact of protein on iron absorption; however, general trends predict that plant, milk, and egg proteins suppress non-heme iron intake relative to meats or protein-free meals. While different proteins may affect iron absorption variably, possible confounding factors may affect the interaction of proteins with iron metabolism. First, the inclusion of other non-proteins such as calcium and phosphorus present in milk products rather than milk proteins, per se, could inhibit iron absorption. Second, it is challenging to distinguish protein effects versus the effect of the chemical form of iron when using proteins such as egg or soy, which contain a high concentration of iron. Overall, the bulk of evidence suggests that protein per se does affect iron absorption variably (Berner & Miller, 1985).

6.3. EFFECTS OF DIETARY COMPONENTS ON IRON ABSORPTION

At the macro level, intestinal iron absorption is physiologically controlled by energy levels, protein levels, hormones including hepcidin, iron status and overall health status (infections and inflammations). Iron absorption can also be affected by four dietary characteristics: dietary iron content, a physicochemical form of the food, other dietary constituents, dietary factors and the chemical nature of diets (Gillespie & UNICEF, 1998, pp-33).

6.3.1. IRON CONTENT IN DIETS

The quantity of iron habitually ingested in a diet is constant and difficult to modify, but some diets are inherently denser in iron than others. The dietary iron density (amount of iron ingested per unit of energy consumed) is generally inversely related to bioavailability, i.e., the higher the iron level, the lower the relative efficiency to which iron is absorbed in the intestine. (Gillespie & UNICEF, 1998, pp-33). Dietary Iron density is higher in developing countries than in developed countries. However, the advantage of high iron density in developing countries is offset by the low bioavailability of iron because of inadequate total energy consumption. Given that iron is in assimilable form, the amount absorbed rises progressively with increased dietary intake. Therefore, the most straightforward way to increase the amount of iron absorbed is to increase the total energy intake (E. M. DeMaeyer, 1989).

6.3.2. PHYSICOCHEMICAL FORM OF THE FOOD

The factor just as important as the dietary iron density is the bioavailability of iron. How much the body effectively absorbs iron varies considerably depending on several factors, including the physicochemical nature of the food. There are two kinds of dietary iron concerning the mechanism of iron absorption: heme iron and non-heme iron. In the human diet, primary sources of heme iron are haemoglobin and myoglobin in animal source foods such as meat, poultry, and fish. In contrast, non-heme iron is derived from plant and animal-based foods such as cereals, pulses, legumes, milk, fruits, and vegetables. The two forms of iron are absorbed in fundamentally different pathways and with varying degrees of efficiency (Gillespie & UNICEF, 1998, pp-34).

Heme iron is readily available and is estimated to contribute 10-15 % of the total iron intake in meat-eating populations (R. Hurrell & Egli, 2010). Another study reported that 30—70 % of the iron in non-vegetarian food is in heme form, of which 15-35 % is absorbed. This likely explains why non-vegetarians are less prone to the iron deficiency than vegetarians (Zimmermann & Hurrell, 2007). The bioavailability of heme iron is little affected by the nature and composition of a given meal (E. M. DeMaeyer, 1989). In western countries, heme iron from meat and meat products contributes to the bulk of dietary iron. Besides being readily absorbed, heme iron in meat, fish, and seafood also promotes the absorption of non-heme iron by forming complexes with amino acids such as cysteine or peptides. Meat enhances the absorption of heme iron and non-heme iron to about the same extent. Therefore, meat provides nutrition in two ways: first, it provides readily absorbed heme iron and second, it promotes the absorption of both heme and non-heme iron.

In developing countries, a significant proportion of dietary iron is in the non-heme form derived from cereal-based diets (Gillespie & UNICEF, 1998, pp-34). Non-heme iron constitutes 90-95 % of the total daily iron in Indian diets (K. M. Nair & Iyengar, 2009). In contrast to heme iron, the absorption of non-heme iron is highly variable. It is influenced not only by the iron content of the meal but also by food composition consisting of factors that promote and inhibit iron absorption (WHO, 2004, pp-255). In developed countries, the daily iron intake ranges from 8 to 18 mg in adults across socioeconomic groups. At the same time, the average iron intake in non-industrialised developing countries is often higher (15 to 30 mg), especially where cereals and legumes are the staple diets. The plant-based diets in many developing countries, such as cereals and legumes, majorly contain non-heme iron, with less bioavailability of 2-5 % (K. M.

Nair & Iyengar, 2009). Despite high iron intake, a more iron-deficient population is likely because of the relatively low bioabsorption of iron in developing countries. Non-heme iron absorption among individuals of comparable iron status may vary between 1-40 % depending on the balance of dietary constituents (Gillespie & UNICEF, 1998, pp-34).

One-third of the total iron in cereals and pulses is believed to be a contaminant. The in-vitro studies on the bioavailability of contaminant iron suggest that it is essentially unabsorbable (K. M. Nair & Iyengar, 2009). Table:6.1 depicts the dietary sources of iron.

Table 6:1 Sources of dietary iron

Chemical form and type of iron	Source
Heme iron	o Meat, Fish, poultry, and blood products o Accounts for 10-15 % of iron intakes in developed countries o Less than 10 % of total intake (often negligible) in developing countries o High bioavailability: absorption range: 20-30 %
Non-heme iron	o Mainly found in cereals, vegetables, tubers, and pulses. o Bioavailability is determined by a complex matrix of inhibiting and enhancing factors in the same meal.
Contamination iron	o Soil, dust, water, iron pots etc. o Bioavailability is usually low. o May be present in large quantities, and nutritional contribution is generally significant.

Source: Adapted from (DeMaeyer, 1989, pp-15)

6.3.3. OTHER DIETARY CONSTITUENTS

The presence of Inhibitors and enhancers greatly influence the absorption of dietary iron in the meal. The various enhancers and inhibitors and their food sources are listed in Table: 6.2

Table 6:2 dietary enhancers and inhibitors of iron absorption

Active substance	**Food examples**
Absorption enhancers	
Ascorbic acid and citric acids	Orange, lemon, lime, pear, apple, pineapple, papaya, plums, guava, banana, mango, pear, cauliflower, pawpaw, and cantaloupe
Malic and tartaric acid	Tomato, potato, carrots, pumpkin, broccoli, cabbage, turnip, and beetroot
Cysteine containing peptides	Chicken, beef, pork, lamb, liver, and fish
Ethanol	White wine and beer
Fermentation products	Soy sauce and sauerkraut
Absorption inhibitors	
Phytate	Wheat bran, rice, maise, soy protein, nuts, legumes, milk, and chocolates
Polyphenols	Tea, coffee, spinach, nuts, legumes, spinach, and red wine
Calcium and phosphate	Milk and cheese
Source: Adapted from (Gillespie & UNICEF, 1998, pp-35)	

6.3.3.1. ENHANCEMENT OF IRON ABSORPTION

Ascorbic acid is the most potent enhancer of non-heme iron absorption. The synthetic vitamin C is also as efficient as native ascorbic acid in fruits, juices, and vegetables. Ascorbic acid form soluble complexes with iron, thereby preventing polymerisation and precipitation. It also reduces ferric iron to ferrous iron, which is better absorbed in the duodenum and small intestine (WHO, 2004, pp-254).

6.3.3.2. INHIBITION OF IRON ABSORPTION

Phytates, polyphenolic compounds, calcium and phosphate, are essential ingredients of many food items such as Bran, rice, and maise. Phytates and polyphenols, including tannins, are complexed with essential proteins and minerals, forming large insoluble and biologically unavailable polymers under physiological conditions, thus decreasing iron solubility in the

meal (L. Allen & Ahluwalia, 1997). Phytates strongly inhibit iron absorption dose-dependent; even small amounts of phytates have a marked effect (WHO, 2004, pp-252). Tea, coffee, and cocoa contain high content of polyphenols. In contrast, many vegetables, especially green leafy vegetables such as spinach, herbs, and spices (e.g., oregano), contain galloyl groups, which inhibit iron absorption. Beetle leaves used commonly in Asian countries have marked adverse effects on iron absorption (WHO, 2004, pp- 253). Calcium, an essential component of salt or dairy products, interferes with heme and non-heme iron absorption. Since calcium is an essential nutrient, it cannot be considered an iron absorption inhibitor in the same way as phytates or phenolic compounds.

6.4. IRON BIOAVAILABILITY

Absorption of iron from a meal depends not only on iron content but also to a marked degree on the meal's composition (including balance of all inhibitory and enhancing factors within a meal). Meals with similar iron contents, energy, protein, and fat can have 10-fold variations in bioavailability depending on the iron absorption enhancers and inhibitors factors. Adding tea or certain spices (e.g., oregano) reduces the iron bioavailability by one-half or more. Whereas vegetables or fruits containing ascorbic acid may double or even triple iron absorption depending on the amount of ascorbic acid and other dietary factors present in the meal (WHO, 2004, pp-255).

The bioavailability of iron in different meals is linked to energy content (i.e., bioavailable nutrient density). The bioavailability of iron varies with food composition across geographical regions. In more developed countries, the bioavailability of iron in the diet is higher because of a higher intake of meat and ascorbic acid with meals, a low intake of phytate-rich cereals, and no coffee or tea within two hours of the main meals. A western diet comprising servings of meat, fish, and vegetables has 10-15 % bioavailability. In developing countries such as India, the reported bioavailability was 1.7-1.8 % for millet-based diets, 3.5-4.0 % for wheat-based diets, and 8.3-10.3 % for rice-based diets (WHO, 2004, pp-269).

FAO and WHO keeping in view the variations in iron absorption from different diets, especially in vulnerable groups, FAO and WHO in 1980 proposed three bioavailability levels, 5 %, 10 % and 15 %, for didactic reasons to calculate recommended intakes. Because of low iron bioavailability from diets in developing countries, the 5 % and 10 % bioavailability figures were considered more realistic. For population groups consuming western diets, two levels, i.e. 12% and 15 %, are deemed appropriate, depending mainly on meat intake (FAO/WHO, 1988).

The recommended nutrient intakes (RNI) for varying dietary iron bioavailability are shown in Table 6.3. The RNI is based on the 95th percentile of the absorbed iron requirements.

Table 6:3 RNI for dietary iron by bioavailability

Requirements for absorbed iron (mg/day)				**Recommended nutrient intake (mg/day) for a dietary iron by bioavailability**			
Group and age[7] (years)	Mean body weight (kg)	RNI 95th percentile (mg/day)	Median requirement	15 %	12%	10%	5%
Infants and children							
0.5-1	9	0.93	0.72	6.2[a]	7.7 [a]	9.3[a]	18.6[a]
1-3	13	0.58	0.46	3.9	4.8	5.8	11.6
4-6	19	0.63	0.50	4.2	5.3	6.3	12.6
7-10	28	0.89	0.71	5.9	7.4	8.9	17.8
Males							
11-14	45	1.46	1.17	9.7	12.2	14.6	29.2
15-17	64	1.88	1.50	12.5	15.7	18.8	37.6
18+	75	1.37	1.05	9.1	11.4	13.7	27.4
Females							
11-14 (premenarche)	46	1.40	1.20	9.3	11.7	14.0	28.0
11–14 (after menarche)	46	3.27	1.68	21.8	27.7	32.7	65.4
15-17	56	3.10	1.62	20.7	25.8	31.0	62.0
18+	62	2.94	1.46	19.6	24.5	29.4	58.8
Postmenopausal	62	1.13	0.87	7.5	9.4	11.3	22.6
lactating	62	1.50	1.15	10.0	12.5	15.0	30.0

Source: adapted from (WHO, 2004, pp-271)

The extent to which diets can provide iron nutrition depends on the bioavailability of iron and energy status. Since dietary iron is closely linked to energy intake, assuming a supply of 7mg iron/1000 kcal, the FAO/WHO (1988) calculated the iron intake derived from cereal-based diets depending on median energy requirement. The energy requirement among children aged

[7] No figures in the table are given for dietary requirements of iron in pregnant women because iron balance in pregnancy depends not only on the properties of the diet but also mainly on the amounts of stored iron.

1-2 years, children 2-6 years, Men and women were estimated to be 1140 kcal, 1450kcal, 3100 kcal and 2200 kcal, respectively. Therefore, iron derived from dietary intake was 8 mg, 10.2 mg, 21.7 mg, and 15.4 mg for children aged 1-2 years, 2-6 years, and women, respectively, as shown in Table:6.4.

Table 6:4 Relationship between daily iron requirement and dietary iron supply on a cereal-based diet

	Children		Adults	
	1-2 years	2-6 years	Men	Women
Mean weight(kg)	11	16	65	55
Median energy requirement and assumed food intake (kcal)	1,140	1450	3100	2200
Derived iron intake (mg)	8	10.2	21.7	15.4
Median requirement for absorbed iron (mg)	0.49	0.56	0.91	1.25
Necessary absorption (%)	6.1	5.5	4.2	8.1

Source: adapted from (Gillespie & UNICEF, 1998, pp-37).

The high variability in bioabsorption among different diets raises an important question, i.e., what proportion of iron requirement can be compensated by diets? Again, this question requires highlighting a close relationship between iron intake and energy intake and the accurate information on iron bioavailability from different diets. FAO/WHO (1988) has estimated the bioavailability of various diets as presented in Table:6.5.

Table 6:5 Diets with estimated overall bioavailability

Typical diet	Bioavailability of iron (%)	
Cereal-based, roots, or tubers, and legumes with negligible meat, fish, or ascorbic acid-rich foods.	Low	5%
Cereal-based, roots or tubers with negligible quantities of food of animal origin or containing ascorbic acid (albeit higher than for the "low" diet) or a diet with still higher levels of animal source foods or ascorbic acid but also large amounts of tea or coffee consumed with meals.	Intermediate	10%
Diversified diet containing generous quantities of meat, poultry, and fish or foods containing high amounts of ascorbic acid.	High	15%

Source: (FAO/WHO, 1988).

For adult men with calorie intake and high energy needs, a 4.2 % absorption rate is sufficient to meet the median requirement of 0.91 mg for absorbed iron. Women, having more increased iron need and conventionally lower energy intake, need to absorb about 8 % of the iron in the diet, while preschool children aged 1-2 years need to absorb 6.1 % and 2-6 years at 5.5% (Gillespie & UNICEF, 1998, pp-38).

Assuming 5% absorption from cereal-based diets, the adult men would have an ample supply of iron, the preschool children would fall marginally short of the required median requirement of absorbed iron, and adult women would be critically iron deficient and at risk of anemia. (Gillespie & UNICEF, 1998, pp-38). Though this model is a rudimentary tool to estimate the iron requirement from the diverse types of foods (as the ranges within categories are wide), it illustrates the type and size of changes in bioavailability that may be expected through certain dietary modifications.

6.5. HEME/NON-HEME COMPOSITION OF INDIAN DIETS

Generally, iron deficiency is more prevalent in developing countries despite high dietary iron density. This is because of poor iron absorption from the diets. There are two forms of iron, i.e., heme or non-heme, found in food. Heme iron, which constitutes 40 % of the iron in meat, fish, and poultry, is well absorbed. Rest 60 % of the iron in animal-based food, and all the iron in plant-based foods (cereals, pulses, fruits, vegetables, and nuts) is non-heme iron and is relatively poorly absorbed. In western countries and the countries where meat and meat products are extensively consumed, heme iron accounts for the bulk of dietary iron and the US dietary reference intakes are calculated on an assumption of 75% heme iron absorption. Non-heme iron contributes about 90-95 % of the total daily iron in Indian diets. Heme iron intake is minimal in India due to economic and cultural constraints, with most Indians obtaining non-heme iron from plant-based foods. Indian diet is plagued by low iron content and poor iron absorption (K. M. Nair & Iyengar, 2009). Non-heme iron remains the primary source of dietary iron for most people worldwide. However, heme contribution to iron can rise to 50 % where non-vegetarian foods are primarily consumed (L. Allen & Ahluwalia, 1997). The daily dietary intake of iron was about 25 mg among nonpregnant, nonlactating women, more than 80 % of RDA of 30 mg of iron for Indian women. Based on this analysis, Thankachan et al.; argued that the cause of the iron deficiency and anemia among Indian women may not be the inadequate iron intake. The poor bioavailability of nonheme iron in local diets that are primarily

plant-based, and high in phytic acid and fibre could inhibit iron absorption and is likely to be an important factor in the development of anemia and iron deficiency (Thankachan et al., 2007).

6.6. FOOD CONSUMPTION PATTERN AND ENERGY REQUIREMENTS

According to the NNMB survey carried out across 9 states, rice, wheat, millets, ragi and sorghum were widely consumed staples in various regions of India. Different cereals together form the bulk of the food basket for most Indians (NNMB, 2012). The consumption pattern of cereals is diverse as rice, wheat and maize are consumed in varying quantities across different states. An annual survey of NIN estimating the food composition in the major regions of India found that distinct regional differences in the consumption of the type of major staples exist. Bajra (Pearl Millet) was a staple food of West (Gujarat) and rice among Southern states. Rice and wheat were more common in Northern states, but less rice was consumed than wheat. Urban and rural households had a distinct food consumption pattern as cereal consumption was significantly higher in rural while vegetables, fruits and milk consumption was higher in urban households (NIN Annual Report, 2005).

For most Indians, a significantly higher share of daily energy requirement is derived from cereal-based foods. A recent ICMR-NIN report titled 'what India Eats' reveals that the percentage of energy intake contributed by Cereals and Millets is 65.2 % for rural India and 51.4 % for Urban India. The contribution of other food sources, including pulses, legumes, meat, poultry, milk and other dairy products, vegetables and fruits together is less than 50 % of the total energy derived from foods (Table:6.6)**.** Moreover, the contribution of cereals to total energy requirements varies across states. NNMB data shows that the contribution of cereals to total energy requirement varied across states from 42 % (Punjab) to 70 % (Odisha) in the rural regions and from 39 % (Haryana) to 60 % (Odisha and Bihar) in the Urban areas (NNMB, 2012).

Table 6:6 Energy from various food groups in Urban and Rural India (Pooled) in adults (%)

	Urban India (%)	Rural India (%)
Cereals and Millets	51.4	65.2
Pulses and legumes	6.1	6.9
Meat, poultry, and fish	5.4	4.5
Milk and milk products	5.1	4.2
Vegetables and GLVs	1.5	1.4

Fruits	1.1	1
Roots and Tubers	2.7	3
Nuts and Oilseeds	2	2.9
Visible fats and oils	13.7	7
Others	11.1	4.1
Source: *What India Eats, ICMR-NIN report*		

The average intake of cereals and millets across 9 states was 368 gm as against a recommended intake of 460 g, providing about 30-82 % of total dietary non-haem iron. The average Intake of pulses was 33 g against RDI of 40 g, which contributed 5-10 % of dietary intake of iron, while the share of green leafy vegetables was reported to be only 2-5 % (K. M. Nair & Iyengar, 2009). A recent paper using the model diet and food composition table calculated that cereals contributed 60 %, Pulses 18 %, vegetables 12 %, fruits 6 % and Meat only 4 % of daily iron intake in a typical Indian diet (Table:6.7). Therefore, dominantly plant-based cereals and, to a lesser extent, pulses and vegetables contribute most of the dietary iron in Indian households. The share of flesh foods is minimum (~5 %) (M. K. Nair et al., 2016)**.**

Table 6:7 Percent contribution of iron from various food sources

Food sources	% Contribution
Cereals	60
Pulses	18
vegetables	12
Fruits	6
Meat	4
Source: Nair et al., 2016	

6.6.1. DIETARY CONTRIBUTION OF IRON

The contribution to energy and the relative contribution of foodstuffs to total iron intake also varies widely across states. The reported iron intake in Gujarat was 23 mg, Kerala 12 mg, Karnataka 12 mg, Andhra Pradesh 8 mg and Tamilnadu 10 mg. Andhra Pradesh's diet with rice as the staple had the lowest (1.02 mg/100 g), and Gujarat, with Bajra (6.4 mg Fe/100g) as the staple diet, had the highest iron content (NIN Annual Report, 2005). Bajra, ragi, rice flakes (poha) and jowar have higher iron content than maize and rice. Rice has the lowest iron content. The iron content of cereals and grains commonly consumed in India is shown in Table:6.8.

Table 6:8 The iron content in various food items

Name of cereals	Iron (per 100mg)
Bajra	6.4
Ragi	4.6
Rice flakes	4.5
Whole Wheat flour (atta)	4.1
Jowar	3.9
Maize, dry	2.5
Rice, raw brown	1.02
Rice, raw milled	0.65
Source: (Longvah et al., 2017)	

The interstate differences in iron intake and anemia prevalence highlight the complex relationship between iron deficiency and anemia. For example, in Odisha, anemia prevalence was high despite high cereal intakes, whereas in Kerala, anemia prevalence was lowest despite the lower cereal intake**.** Among regional differences, one common factor for most states was a grossly inadequate dietary iron intake, meeting less than 50 % of RDA. The reported deficit was highest in Andhra Pradesh (72 %) and lowest in Gujarat (23 %). The difference in iron takes across states are due to regional differences in the food consumption pattern. Wheat and rice are the staple food among Northern states, rice among southern and coarse cereals such as Bajra and Ragi among western states and rice among northeastern states.

Nair and Iyengar showed that iron intake and the relative contribution of each food item to total iron intake varies across states (K. M. Nair & Iyengar, 2009). There were differences in absolute amounts of iron intake across states due to different food consumption patterns. Andhra Pradesh, where rice is a staple diet, had the lowest (8.5 mg/day), while Gujarat, where bajra is the staple diet, had the highest iron intake (23 mg/day) (NNMB, 2012). In Gujarat, the dietary intake of iron was highest because of the consumption of bajra (highest iron density) as the major staple diet.

There are marked variations in anemia prevalence and iron density (Table:6.9). However, the magnitude of anemia prevalence is not correlated with the current iron intake, with Kerala reporting only 33 % of anemia prevalence upon 11 mg/d iron intake. Gujarat reported a 55 % anemia prevalence upon 23 mg/d iron intake (Longvah et al., 2017). A similar situation of no

correlation between iron density and anemia prevalence exists. The data suggests that the average iron density of an Indian diet is not more than 8.5 mg/1000 Kcal, with the lowest density of 4.3 in Andhra Pradesh and the highest of 15.6 mg/1000 in Gujarat (K. M. Nair & Iyengar, 2009). Despite a lower iron density of 7.1 mg/1000 Kcal, the Prevalence of anemia in Kerala is distinctly lower than in other states. Rice is the major staple diet in most southern states, but this cannot account for the observed differences. Tamilnadu and Andhra Pradesh have anemia prevalence above 50 %, comparable to Gujarat, where wheat and millets are the main staples.

Table 6:9 Iron density, iron intake and anemia prevalence in rural males and females

Region	Iron density(mg/1000) Kcal	Males		Females	
		Iron intake* (mg/d)	Anemia prevalence** (%)	Iron intake* (mg/d)	Anemia prevalence** (%)
Kerala	7.1	13.7	11.7	11.0	34.3
Tamilnadu	8.2	12.1	20.4	9.6	55.0
Karnataka	7.7	15.9	18.2	13.0	44.8
Andhra Pradesh	4.3	9.4	26.9	8.4	60.0
Maharashtra	10.4	18.8	17.6	15.3	48.0
Gujarat	15.6	28.2	21.7	23.0	54.9
Madhya Pradesh	9.0	17.5	25.5	16.9	52.5
Odisha	8.5	17.4	28.4	14.3	51.0
West Bengal	7.1	16.2	30.3	13.7	62.5
India	8.5	16.8	22.7	13.6	53.1
* Iron intake among males and females 16 years and above (NNMB-2012) ** Prevalence of anemia in males and females of age15-49 years (NFHS-4)					
Source: (IIPS & ICF, 2017; NNMB, 2012)					

Higher iron density and higher iron intake are not uniformly and strongly related to lower anemia prevalence or vice-versa. Also, the variable iron intake does not explain the observed interstate differences in anemia prevalence. A recent study evaluating the relationship between dietary iron intake and anemia in WRA with respect to iron fortification in India concluded that dietary iron intake and anemia are weakly associated (Swaminathan et al., 2019). Iron deficiency and anemia prevalence are modulated by other micronutrient deficiencies such as vitamin B12, folate and vitamin C and other non-nutritional causes such as poverty, parasites, infections, hemoglobinopathies and blood loss, thus necessitating the identification of other factors (Thankachan et al., 2007).

The food matrix plays a vital role in influencing non-heme iron solubility. A study evaluating the various dietary components in non-heme iron solubility from typical Indian composite diets in Andhra Pradesh, West Bengal, Madhya Pradesh and Gujarat found a significant correlation between iron content and iron density, phytate and phytate density (NIN Annual Report, 2005). The study found that Phytate content and density were negatively associated with iron availability. The in-vitro analysis showed that the iron solubility decreased as the phytate content increased. Further, diets with low iron and phytate (Rice) had better bioavailability than those with high iron and phytate (Bajra). That is why coarse cereals have less bioavailability despite having high iron density, and the states having coarse grains as staples, such as Gujarat, have a higher anemia prevalence. The adequate iron availability can be optimised by minimising inhibitors (phytates and tannins) and enhancing promoters (ascorbic acid, meat, and fish).

Ascorbic acid increases dietary non-heme iron; however, intake is deficient in Indian dietaries. Because of the thermally unstable nature, much of the ascorbic acid in uncooked food is destroyed upon cooking, leaving a negligible content. Thus, one of the plausible explanations for the lower Prevalence of anemia in Kerala is increased intake of fish, nuts and oilseeds, which could have contributed to increased iron solubility, resulting in lower anemia prevalence. Inadequate consumption of animal-based foods and green leafy vegetables and fruits have relatively higher bioabsorbable iron content. It can lead to deficient intake of other hematopoietic nutrients, vitamin A, beta carotene (nuts and oilseeds), riboflavin, and folic acid, further exacerbating the risk of anemia(K. M. Nair & Iyengar, 2009).

Most dietary non-heme iron enters the gastrointestinal tract in an insoluble ferric form which is not readily absorbed. An acidic pH is required to convert ferric iron into soluble ferrous iron,

which is absorbed into the intestine. It is known that basal acid output (gastric secretion) in Indians is significantly lower (~pH 3.4) than in the western population (~pH 2.5). This difference in basal acid output may account for compromised non-heme iron solubility and accessibility in Indians and therefore be considered in the etiology of high anemia prevalence. Possibly cereal-based nature of diet habits of most Indians has led to an adaptation of decreased acid secretion as acid secretion is determined by the type of proteins (plant vs animal origin) in the food (K. M. Nair & Iyengar, 2009).

6.6.2. LINKAGES BETWEEN IRON INTAKE, IRON DENSITY AND ANEMIA

Anemia is widely perceived to be caused mainly by dietary iron deficiency. In developed countries, a typical diet contains about 6 mg iron per 1000 Kcal (equivalent to daily consumption of 8 to 18 mg iron by most adults) with slight variation from meal to meal for the person from different socioeconomic status. In contrast, the daily iron intake in many developing countries is generally considered higher, ranging from 15 to 30 mg; a large portion is an insoluble iron (L. Allen & Ahluwalia, 1997).

The diets should provide an average of 14.2 mg of iron /1000 kcal. The mean Iron density (amount of iron per 1000 kcal) in Indian diets is 8.5 mg/1000 kcal based on diet surveys and 9 mg/1000 kcal based on chemical analysis. The dietary iron density of Indian foods is ~25 % lower[8] than the recommended adequate dietary iron density of 14.2 mg/1000 kcal because 30 % iron is present as a contaminant that is barely absorbed (S. Ghosh, Sinha, Thomas, et al., 2019). This range of iron density would require more than 3000 kcal/day intake to meet the iron requirements. If the iron density of ~9 mg/1000 Kcal is assumed for all socioeconomic groups, age, and gender categories, very few Indians would satisfy RDAs for iron and energy with current food consumption patterns. The present considerations make it impossible for the Indian population to meet the iron requirements through regular diets alone. Therefore, efforts are being made to increase iron intake through supplementation and fortification (S. Ghosh, Sinha, Thomas, et al., 2019; S. Ghosh, Sinha, Shivakumar, et al., 2019; ICMR, 2010).

India's per capita median daily iron intake is 14 mg/day, with interstate variations ranging from 7 to 21 mg/day. The risk of inadequate iron intake among the Indian population is higher

[8] The earlier estimated figures of iron density (amount of iron per 1000 kcal) for Indian diets were 14 mg/1000. However, iron density for Indian diets has been revised based on revised iron values from nutritive value of Indian foods. According to latest ICMR's guidelines on RDA, Indian diet contains 7-9 mg iron /1000 kcal.

because intake is much lower than what has been recommended for all age and sex groups by ICMR (S. Ghosh, Sinha, Thomas, et al., 2019). Moreover, the recommendations for dietary iron for Indians are the highest in the world. The RDA for pregnant women and boys aged 13-15 years is as high as 35 mg/d and 32 mg/d. The recommended dietary iron is at least two to three times higher than in developed countries such as the United States and Canada and much higher than those suggested for Asian countries. (ICMR, 2010). Nair and Iyengar found that Indian RDA is 2-3 times higher than United states recommendations. The lower RDA in the US is due to higher iron bioavailability in the US diets primarily because of higher heme iron content and ascorbic acid consumption. Conversely, the high RDAs in India are due to the poor bioavailability of Indian diets (K. M. Nair & Iyengar, 2009).

6.6.3. IRON BIOAVAILABILITY OF INDIAN DIETS

The earlier studies found that the bioabsorption of iron from Indian diets varied from 7-20 %. Apte and Iyengar using the chemical balance method, demonstrated that iron absorption during pregnancy increased significantly from a mean of 7 % to 33 %, and up to 58 % of dietary iron ingested per day could be absorbed by an iron-deficient full-term pregnant woman. There was reportedly a considerable difference in iron absorption between pregnant and nonpregnant women (Apte & Iyengar, 1970).

In 1983, a study on the estimation of iron absorption from habitual Indian diets involving a single staple (wheat, rice, ragi or sorghum) in adult men found mean iron absorption to be 0.8 to 4.5 %, depending on the type of staple used. The absorption was lowest (0.8-0.9 %) with millet-based diets, intermediate (1.7- 1.9 %) in wheat-based diets and highest (4-5 %) in rice-based diets (N. Rao et al., 1983). Also, the staple diets, i.e. cereals and pulses, contain about 1/3rd of iron in contamination, which are essentially unabsorbable (K. M. Nair & Iyengar, 2009). Based on the studies done in adult men, a uniform 3% absorption of iron from a mixed cereal pulse vegetarian diet was considered for deriving the iron RDA for Indian men and 5 % for Indian women. More recent studies on iron absorption reveal that the iron absorption in Indian diets is not as poor as was reported in the early studies. Thankachan et al. showed that the mean Iron absorption in young Indian women is 17.5 % (Thankachan et al., 2007). Mean iron absorption of 8-10% was reported in women and adolescent girls aged 18-35 years (S. Ghosh, Sinha, Thomas, et al., 2019). RDA of Iron suggested earlier appeared unrealistic given the recent findings.

Indians have reduced iron stores compared to the people in the developed world. Iron absorption is inversely related to body iron stores. A realistic estimate of iron absorption was calculated as 5 % for adult males and 10 % for adult females, which was in agreement with the recommendations of WHO/FAO, which for didactic reasons listed three bioavailability levels, i.e. 5 %, 10 % and 15 % (K. M. Nair & Iyengar, 2009). In the Indian context, absorption from the cereal-pulse diet is considered 5 % in adult males and a conservative figure of 8 % for women (expected to have better absorption due to iron-deficient stores). While in infants aged 6-12 months, an absorption of 15 % is derived (ICMR, 2010).

6.7. VEGETARIANISM AND IRON DEFICIENCY

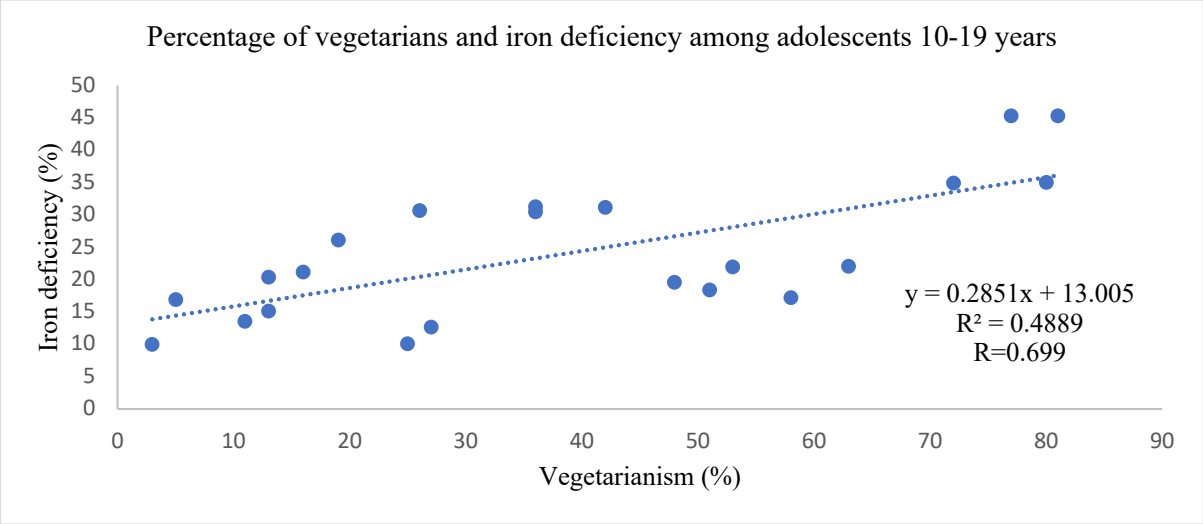
India has more vegetarians than the rest of the world combined. Various surveys show that the estimated percentage of the vegetarian population is between 23 % and 37 %, whereas a large proportion of the population identifies themselves as non-vegetarian[9]. According to the National sample survey office (NSSO), 62.3 % of Indian households consumed non-vegetarian food in 2011-12, 56.7 % in 1993-94, and 58.2 % in 2004-05. However, the Sample Registration system baseline survey 2014 reports that 71 % of the Indians (population above 15) are non-vegetarians.

A statewide analysis shows that seven states in the Northeast had the highest proportion (97%) of non-vegetarians in 2011-12, followed by West Bengal (95 %) and Kerala (92 %). On the other hand, Haryana has the lowest non-vegetarian population (19 %), followed by Rajasthan (20 %), Punjab (23 %) and Gujarat (28 %). The CNNS data on the Prevalence of iron deficiency and NSSO's data on the percentage of non-vegetarian/vegetarian population across states provide an interesting insight on plausible linkages between iron deficiency and the extent of vegetarianism. The iron deficiency among children 1-9 years and adolescents aged 10-19 is generally more prevalent in the western states of Rajasthan, Haryana, Gujarat, and Punjab, which have the highest percentage of vegetarianism population. Also, Northeastern states, West Bengal, Goa, Odisha, and Andhra Pradesh, which have the highest rates of the non-vegetarian population, are among the least iron-deficient states. A scatter plot of change in iron deficiency prevalence versus the percentage of vegetarianism shows a strong correlation (0.69) between vegetarianism and iron deficiency (Fig:6.2). Regression analysis also indicates that

[9] Non vegetarian population is defined as those consuming eggs or fish or meat or any combination of these.

the correlation strength is strong in half of the cases (0.488). For the other half cases, this model does not explain the correlation.

Figure 6:2 percentage of Vegetarianism versus Iron deficiency in Indian states



Source: plotted using CNNS and NSSO data

Vegetarianism is associated with iron deficiency in many states. However, the strength of association between anemia and vegetarianism is weak. Thus, vegetarianism might explain the occurrence of iron deficiency to an extent, but there is no robust evidence to suggest that high anemia prevalence in India is linked to vegetarianism.

6.7.1. FOOD COMPOSITION MATRIX AND ANEMIA

Overall, non-vegetarianism in India has increased, attributed to rising incomes and increased diversification of diets with high protein intake[10]. The surveys identify India as a predominantly non-vegetarian country, but the daily and weekly eating habits of most Indians are counterintuitive to being called a dominantly non-vegetarian. According to the National family health survey, not more than 6% of the Indian population consumes fish, chicken, or meat daily, nearly 40 % every week, and less than 30 % any form of non-vegetarian food only occasionally (IIPS & ICF, 2017). Overall meat consumption in India is 3.3 kg/capita, much lower than the world average of 34.3kg/capita (Bhatnagar & Padilla-Zakour, 2021). Not only meat, chicken or fish, but only 4.5 % of the population also consume eggs daily, about 35 % weekly and 30 % occasionally. Among vegetarian diets, close to 47 % population consume Green leafy

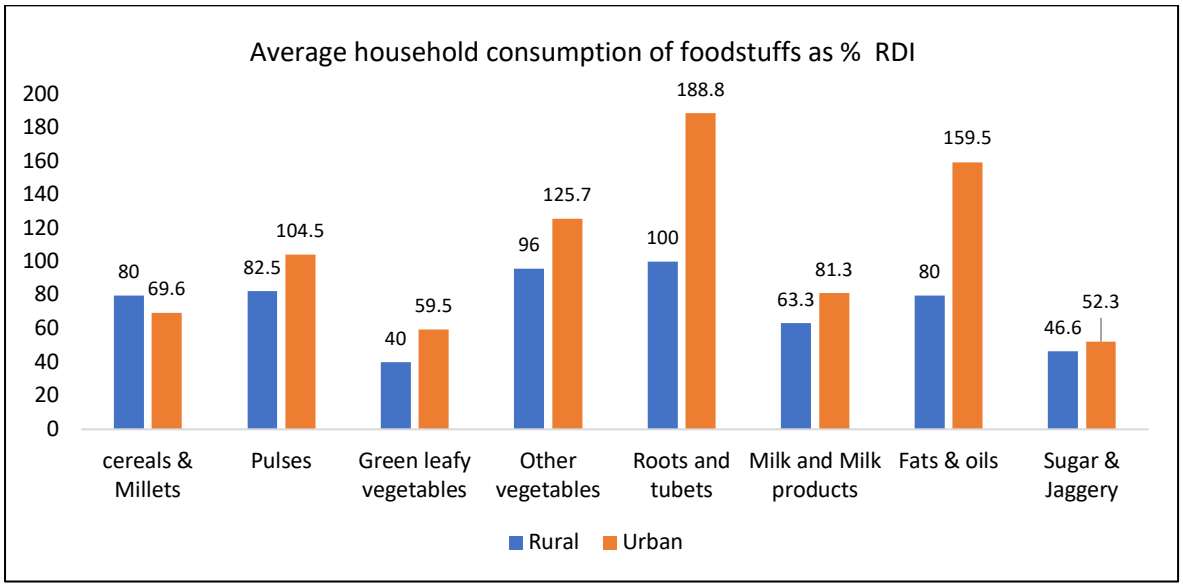
[10] https://indianexpress.com/article/opinion/columns/india-diet-indian-palate-non-vegetarian-vegetarianism-3099363/accessed on 8/12/2021

vegetables, which are a rich source of iron daily, 40 % weekly and 12 % occasionally. About 45 % of the population consume Milk or curd daily, 26 % weekly and 25 % sometimes. Approximately 45 % consume Pulses or beans daily, 45 % weekly and 9 % occasionally. Overall, the frequency of essential food items required to maintain the recommended macronutrient and micronutrient levels, including iron and other hematopoietic nutrients, is inadequate for a large proportion of the population.

The inadequate frequency of various dietary items is reflected in lower than recommended intake of many foodstuffs, which ultimately translates into the insufficient intake of essential macronutrients and micronutrients. According to the NNMB rural survey, which collected data from 10 major states, and the NNMB urban survey collected data from 16 states, the average intake of cereals and millets was 375 g/CU/day, which was lower than recommended daily intake (RDI) of 460 g. The intake of pulses and legumes was 31g/CU/day against the RDI of 40 g, while the intake of green leafy vegetables was 18g/CU/day against the RDI of 40 g. The intake of roots and tubers was 63 g/CU/day, on par with the suggested level of ICMR's RDI of 50 g. The daily intake of fruits was 26g/CU/day against RDI of 55 g, while milk and milk products intake was 85g/CU/day against RDI of 150g (NNMB, 2012), (NNMB, 2017).

In a similar pattern, the average intake of most foodstuffs is lower than RDI in urban India too. Except for the intake of roots and tubers, and fats and oils, urban Indians were reported to consume much lower foodstuffs than suggested levels of ICMR RDI. The consumption of cereals and millets, the primary source of energy for most Indians, and other foodstuffs such as Pulses, green leafy vegetables, milk, and milk products were lower than recommended and inadequate (Fig:6.3)**.** **N**on-vegetarian food items are good sources of bioabsorbable iron, but their consumption was grossly insufficient. Under these circumstances, a large population is not only at risk of iron deficiency but also several other macronutrients and micronutrients. Several micronutrient and micronutrient deficiencies may coexist in a population, as reflected in NNMB rural and urban surveys.

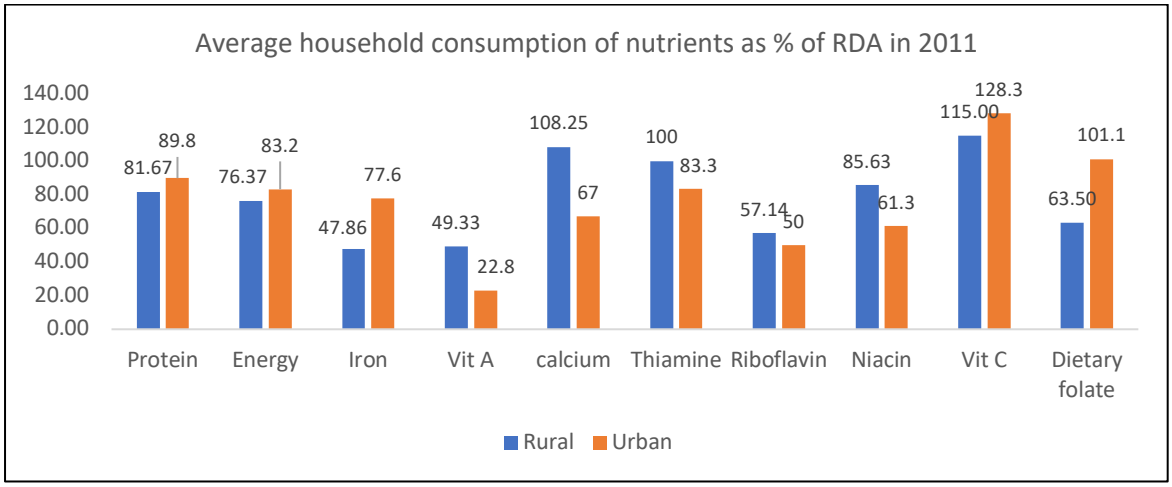
Figure 6:3 Average household consumption of foodstuffs as % of RDI in the rural and urban areas



Source: Compiled from (NNMB, 2012) & (NNMB, 2017)

NNMB rural and urban surveys reveal that Indians consume macronutrients (proteins and energy) and micronutrients (iron, vitamin A, calcium, thiamine, riboflavin, niacin, and folate) at lower than recommended values. The protein intake was 81 % in the rural area and close to 90 % of RDA in the urban area against the percentage of RDA. The energy consumption is approximately 80 % in both rural and urban areas. Against RDA, iron intake in rural areas was 48 % and 77.6 % in urban areas, vitamin A consumption was 49 % in rural and 23 % in urban and Riboflavin intake was 57 % in rural and 50 % in urban areas. The overall intake of calcium, thiamine, niacin and dietary folate was also deficient when rural and urban combined. At the same time, vitamin C consumption was higher than RDA in rural and urban areas, as shown in Fig:6.4 (NNMB, 2012) & (NNMB, 2017).

Figure 6:4 Average household consumption of nutrients as % of RDA in 2011-12



Source: Compiled from (NNMB, 2012) & (NNMB, 2017)

6.7.2. TO WHAT EXTENT CAN THE DIET ADDRESS ANEMIA AND IRON DEFICIENCY

The evidence suggests that Indians have low iron stores. The average iron intake in India is much lower than recommended, aided by the low iron density and low iron bioavailability of Indian diets. It is logical to infer that most of the burden of anemia (`~50 %) is due to iron deficiency. Therefore, intervention strategies are targeted toward alleviating dietary iron deficiency. However, the evidence supporting that iron deficiency is linked to anemia is limited at the national level. Recent evidence highlights the weak association of dietary iron deficiency with anemia (Swaminathan et al., 2019).

Sarna et al. show that approximately 60 % of cases of anemia are due to nutritional deficiencies, including iron deficiency. Therefore, 60 % of anemia in controlled settings can be amenable to diets and supplementation. However, in natural life settings, where a range of factors, including nutritional and non-nutritional factors, determine the outcome of anemia, it is hard to evaluate precisely how much anemia can be addressed by diets alone. To predict, we need more consistent data on dietary patterns, nutrient contents in the diet, and the contribution of those nutrients to anemia.

6.8. SUMMARY

The chapter discussed the heightened iron need during infancy, menstruation, and pregnancy. The body has a tightly regulated mechanism of iron metabolism that keeps a homeostatic balance between iron intake, absorption, and excretion via hepcidin. In the case of excess iron, hepcidin expression is activated, which restricts iron absorption, whereas, in iron deficiency, hepcidin allows to absorb more iron. Thus, hepcidin maintains the iron balance in the body. Hepcidin concentration is influenced not only by iron deficiency but inflammations, availability of energy, carbohydrates, and proteins. Thus, hepcidin is the primary molecule that mediates iron absorption amid iron deficiency, inflammations, carbohydrate, energy, and protein deficiencies. Research shows that iron absorption is restricted in the absence of other nutritional deficiencies such as vitamin A, vitamin B12, folate, vitamin C, D and E and other minerals. The adequate availability of carbohydrates, energy, and proteins is also essential in iron absorption, thus could help reduce anemia.

Food is central to addressing anemia. The composition of the food matrix determines anemia prevalence. The available evidence shows no direct correlation between iron intake, the iron density of food and anemia. High iron intake and high iron-dense food do not guarantee lower anemia prevalence in a particular setting. For example, in Gujarat, anemia prevalence is higher despite high the iron intake and iron density in food than in Kerala. Iron intake and iron absorption are also essential factors that influence anemia prevalence. Iron absorption is affected by a range of dietary and inflammations. Indian food is characterised by both low iron intake and low iron bioavailability. Low iron intake is because of inadequate intake and poor access to diversified food. Low bioavailability is due to cultural, economic, and social reasons such as vegetarianism and lack of access to diversified food. It is believed that diets alone cannot address anemia, particularly in vulnerable groups such as infants, menstruating and pregnant women, because of the low hematopoietic nutrient intake and absorption. A diversified diet is an essential but not a sufficient criterion to address anemia. The impact of a diversified diet can be rendered ineffective due to poor absorption of nutrients due to endemic infections because of the absence of water, sanitation, and hygiene.

CHAPTER 7

"We have to put health inequalities at the centre of public health strategy and that will require action of social determinants of health"

Michael Marmot

CHAPTER 7. SOCIAL DETERMINANTS OF ANEMIA

7.1. INTRODUCTION

A large body of literature assigns primacy to immediate biological determinants of anemia. Anemia is primarily seen as a biological phenomenon caused due to nutritional deficiencies and infections; therefore, programmatic approaches are designed to address the iron deficiency and infections. Focusing on the immediate biological determinants is necessary but not a sufficient condition to holistically understand the nature and causation of nutritional anemia. Social, economic, demographic, and environmental factors influence biological processes. Therefore, more immediate biological risk factors are contingent on upstream underlying determinants. Social determinants of anemia have received less attention in the academic and policy discourse. There is limited evidence on the linkages between anemia and social, economic, and environmental factors in the Indian context. Therefore, the chapter explored the breadth of the literature to identify the social determinants and causal pathways of anemia in India. The chapter used key components ('structural' and 'intermediary' determinants) of WHO's commission on social determinants of Health (CSDH) framework (Solar & Irwin, 2010) to identify the determinants and explain the possible causes of inequalities and disparities in the prevalence of anemia. 'Social determinants' refer to determinants of health and inequalities in health and consider both the social factors influencing health and the social processes shaping their social distribution.

7.1.1. MODELS OF SOCIAL DETERMINANTS OF HEALTH

In the last decades, several models for determinants of health and nutrition have emerged that advanced our understanding of the linkages of health and nutrition with a range of social factors. UNICEF's conceptual model for malnutrition (UNICEF, 1990), Bronfenbrenner's human ecological model (Bronfenbrenner & Evans, 2000), Dahlgren and Whitehead's social determinants of health model (Dahlgren & Whitehead, 2007), Lancet's framework for achieving optimum nutrition (Black et al., 2013) and CSDH framework (Solar & Irwin, 2010) revealed that poverty, the standard of living, education, wealth, access to health services,

nutritious food, water, sanitation and hygiene influence health and nutritional status of the population.

7.1.1.1. MODELS OF SOCIAL DETERMINANTS OF ANEMIA

The focus on anemia gained momentum in the last decade. Six conceptual models for anemia were proposed to provide a framework for understanding various determinants and their interlinkages. They are 'Conceptual framework of anemia' in 2013 by USAID anemia Taskforce (USAID, 2013), Balarajan et al. (2011) and Pasricha et al. (2013) model for low-income and middle-income countries, Biomarker's reflecting Inflammation and nutritional determinants of anemia (BRINDA) Project's conceptual Framework (Namaste et al., 2017), Chaparro and Suchdev's conceptual model (Chaparro & Suchdev, 2019) and Nguyen et al. (2018). Chaparro and Suchdev's conceptual model is a syncretic model adapted and advanced from the earlier three frameworks discussed above.

These models generally described three levels of determinants: proximal, intermediate, and fundamental/underlying. The proximal level determinants are micronutrient deficiencies and Inflammation. Food insecurity, inadequate maternal and childcare, limited access to health/nutrition services and interventions, inadequate health/nutrition knowledge and education, and inadequate access to WASH were identified as intermediate-level determinants. Underlying determinants constituted the physiological vulnerability of women and children and early onset of childbearing, high parity, and short birth spacing. Political economy, ecology, climate, and geography were conceptualized as fundamental determinants of anemia. These frameworks adapted the UNICEF framework on causes of malnutrition as an analytical tool to explain the underlying, intermediate, and proximal determinants of anemia. UNICEF's conceptual framework for malnutrition is an established tool for understanding how the social, political, economic, and household factors cause malnutrition; however, it fails to explain how different population groups are impacted differentially due to their differential social position in a stratified social system. Therefore, the thesis has used the CSDH framework to identify and unpack structural and intermediate factors and their hidden mechanisms that create conditions for the development of anemia in the population.

7.2. STRUCTURAL DETERMINANTS OF ANEMIA

Structural determinants refer to the root causes of health inequities because they determine the quality of the social determinants of health experienced by the people. Structural determinants include social, political, and economic contexts that create a stratified society (WHO, 2008). The structural determinants operate through a series of intermediary determinants, including material circumstances such as housing quality and physical environment, psychosocial circumstances such as stressful living conditions, social support, and behavioural and biological factors such as lifestyle and genetic factors. A complex interplay of structural and intermediate determinants influences the population's prevalence and distribution of the immediate biological risk factors (WHO, 2008). The findings of this thesis reveal that in the Indian social system, poor socioeconomic status, caste, gender, and religion are the major structural determinants.

7.2.1. POVERTY, SOCIAL CLASS, AND DEPRIVATION

Poverty is used as a proxy for socioeconomic position (Nayar, 2007). The concepts 'social class', 'socioeconomic status' (SES) and 'socioeconomic position' (Krieger, 2005) are often interchangeably used, thereby lacking a consensus. Socioeconomic status/ position (SES) is generally measured by poverty, level of income, occupation, education, size of landholding, ownership of livestock, source of drinking water, type of cooking fuel and durable household assets such as television, fridge and toilet facilities or a composite of these indicators (Subramanian et al., 2008).

Household poverty was identified as an important factor associated with a high prevalence of anemia among women and children in low and middle-income countries, including India (Yang et al., 2018). Several studies from India demonstrated a strong relationship between poverty and the risk of anemia (M. E. Bentley & Griffiths, 2003; S. R. Pasricha et al., 2010). Household poverty characterised by poor living conditions such as the use of biofuels by pregnant women (Nguyen et al., 2019; Page et al., 2015), no latrine and electricity facility (Arlappa et al., 2010; Laxmaiah et al., 2013), non-concrete houses and passive smoking (Baranwal et al., 2014) was associated with the adverse outcome on haemoglobin levels.

The large size of landholdings was shown to have a significant positive impact on haemoglobin concentration in pregnant women at the community level in Assam (P. Dutta & Sengupta, 2017) and among women working in the farming system in the Chandrapur district of

Maharashtra (Gupta et al., 2019). The study showed that the primary source of income for people of large landholdings was cultivation. In contrast, for landless or with little land ownership, the primary source of income was casual labour in the non-agriculture sector (Gupta et al., 2019). This showed a logical link between landholding, the type of occupation, source of income and anemia. Evidence shows that the size of landholding is related to income, food security and nutrition (Yadu, C. R., & Satheesha, B, 2016).

Landholding was also associated with women's autonomy and empowerment and increased access to food, including green leafy vegetables (rich in iron), consequently affecting iron status (Gupta et al., 2019). Livestock ownership was associated with a reduced risk of moderate anemia among women aged more than 20 years in rural Tamil Nadu. Livestock such as meat and fish is an excellent source of bioavailable iron that can improve haemoglobin concentration (Little et al., 2018).

Lower wealth and food insecurity (S. R. Pasricha et al., 2010), poor sanitation and less bargaining power (Nguyen et al., 2019), reduced purchasing power and working as daily wage labourers (Vijaya Bhaskar et al., 2017), uncertain availability of casual wage employment among poor urban women was associated with increased risk of anemia (M. E. Bentley & Griffiths, 2003). Limited access to adequate and nutritionally diverse diet food among poor Santal tribes of West Bengal (Stiller et al., 2020) was linked with higher risks of anemia.

7.2.2. CASTE

Several cross-sectional studies demonstrated caste as an important factor associated with anemia status. Schedule Caste (SC), Schedule Tribe (ST), and other backward castes (OBC) had a higher prevalence than other caste groups (S. Bharati, Pal, Sen, et al., 2019). The markers of wealth, living standards and living conditions that include material assets, landholding, housing quality, quality of drinking water and sanitation practices are distributed differentially across the caste groups, which possibly explains the differential rates of anemia among different social groups (A. Dutta et al., 2020). Women and children from disadvantaged caste groups are less educated, have lower purchasing power, have limited access to nutritious food and health services, including IFA supplementation programs, and are more prone to work-related psychological stress. These factors might affect haemoglobin levels differentially (Vart et al., 2015). In one study, caste was independently associated with household hunger, dietary

diversity and increased risks of anemia among children in Bihar (Gosdin et al., 2018). This study was consistent with the findings of another study, establishing a strong link between low caste and higher prevalence of anemia even after controlling for other socioeconomic factors such as wealth and education (Y. S. Balarajan et al., 2013; Vart et al., 2015). Caste, Poverty and Social Exclusion were reported as the leading cause of differential rates of anemia among different social groups (Nayar, 2007). Caste-based discrimination was associated with poor mental health and stress; stress is linked to an increased risk of iron deficiency (Vart et al., 2015). A few studies show caste as a robust and independent variable that affects anemia status even after controlling wealth and education, i.e., lower caste population groups, in comparison to other caste groups, are more vulnerable to anemia even if they have relatively a good access to economic and educational resources (Gosdin et al., 2018; Sabharwal & Sonalkar, 2015; Stiller et al., 2020). This finding suggests that there could be two possible pathways leading to differential rates of anemia among women and children of different social groups: i) Socioeconomic pathways and ii) social exclusion and discrimination pathways.

7.2.3. GENDER

The deeply rooted gender discrimination and lower status of women are among the most important causes of the higher prevalence of anemia among women in India (S. Rao et al., 2011). Women's autonomy in household decision-making and access to and control of resources such as finance, education, food and health are constrained (Chandran & Kirby, 2021). Women with little control over cooking preferences get an unequal share and less diversified food. Lesser autonomy in Maternal and reproductive health decisions, including family planning and early age at marriage, was associated with lower iron stores in women (S. Ghosh, 2009; Paul et al., 2019). Female literacy, education, and economic status are linked to decision-making power that affects health and nutrition, including anemia. Women from a lower caste are more vulnerable to anemia because of their caste and gender identity (Anne et al., 2013).

Women living in households with little control over household financial decisions and food preferences were at higher risk of anemia in Mysore city in Karnataka (Krupp et al., 2018). Using NFHS data, Chakrabarti et al. (2018) showed that pregnant women (15-49 years) have less diverse and lower meal intake than their male counterparts. Women had to make dietary sacrifices for children and male members, who often ate last (Chakrabarti et al., 2018). Social discrimination and lack of control over intrahousehold resources were found to limit women’s

autonomy in purchasing and cooking nutritious food in Oraon tribes of North 24 Parganas, West Bengal (Chowdhury & Roy, 2019), pregnant women in Chandigarh (Diamond-Smith et al., 2016) and access to healthcare in Andhra Pradesh. The intake of green leafy vegetables (GLV), a rich source of iron, was low among women in Pune city, Maharashtra. Inadequate intake of GLV was associated with the husband's dislike for GLV, and the purchase of vegetables from the market was the domain of duties of male members (S. Rao et al., 2011). A husband's control over family planning practices was associated with a high prevalence of anemia among women. A lack of family planning might lead to unintended pregnancy, unsafe abortion, and shorter birth intervals exacerbating the risk of nutrient loss and anemia among children and women (Rana & Goli, 2017). Living with a mother-in-law significantly reduced anemia. It increased women's chances of receiving iron supplements. However, the beneficial effects of coresidence waned with both parents-in-law (Varghese & Roy, 2019). In a study spanning 26 Indian states, women aged 15-49 years old subjected to domestic violence were at higher risk of anemia because of withholding food from abusive members and increased psychosocial stress (Ackerson & Subramanian, 2008). Young age at marriage and early and often repeated pregnancy decreased iron storage in women (S. Ghosh, 2009). Further, early married women were controlled by their husbands and in-laws, which limited their decision-making power (Paul et al., 2019).

7.2.4. RELIGION

Hindu and Muslim children (6-59 months) were at a much higher risk of being anemic than Christians (S. Bharati et al., 2020). Hindus were at higher risk of anemia than Muslims (S. Bharati, Pal, Sen, et al., 2019; S. Bharati et al., 2020). In another study on tribal women in Maharashtra, Muslim women were 4 %, and Christian women were 9 % more likely to have anemia than Hindu women (Rokade et al., 2020).

The role of religion in determining anemia status is ambiguous. The differences in anemia mainly were attributed to cultural dietary patterns or socioeconomic conditions that vary with religion. The low prevalence of anemia in the northeastern region was associated with a high standard of living among Christian Scheduled tribes of the Northeastern region. In contrast, high prevalence in Jharkhand was attributed to the high concentration of non-Christian Scheduled Tribes (P. Bharati et al., 2009). A few studies have established the association between religion and anemia, though research examining a detailed relationship is missing.

7.3. INTERMEDIATE DETERMINANTS OF ANEMIA

The main intermediate determinants are education, occupation, access and utilization of health services, water, sanitation, and hygiene.

7.3.1. EDUCATION AND AWARENESS

A reverse relationship between levels of education and anemia severity exists. Women of Chandigarh belonging to lower socioeconomic status with less education had little health and nutrition awareness, less autonomy, and bargaining power in the households (Diamond-Smith et al., 2016). Mothers without exposure to mass media were significantly at higher risk than those exposed to media (A. Dutta et al., 2020). Women exposed to mass media acquired knowledge on safe health practices, eating nutritious diets (S. Ghosh, 2009) and contraceptive use (Perumal, 2014). A summary of four qualitative studies showed that many women did not know the importance of iron supplements or the link between anemia and Iron-folic acid tablets (IFA) (P. Bentley et al., 1998). Less literate women were misinformed about the benefits of iron supplementation, ICDS, and midday meal programmes (Sedlander et al., 2020).

Lack of awareness about health-promoting behaviours such as knowledge about the symptoms of anemia or its adverse effects on mother or child, nutritious food, use and benefits of IFA, lack of information on free services and meals provided through Anganwadi centres, inadequate knowledge on health, hygiene and sanitation was shown as risk factors of anemia among women in Pune, Maharashtra (S. Rao et al., 2011). One study concluded that maternal education could be more important than household wealth in determining the intake of various food items (Agrawal, Kim, et al., 2019). Lack of awareness of contraception use was associated with anemia (Kavitha, 2011). Maternal education was associated with increased intake of green leafy vegetables, legumes and nuts and higher iron and vitamin A-rich foods (Agrawal, Kim, et al., 2019).

7.3.2. OCCUPATION

The occupation is linked to anemia through complex pathways. Studies have shown that people working in physically challenging and strenuous conditions are more susceptible to anemia (McKay et al., 2020). The tea pluckers and tea garden labourers in Doors, West Bengal,

reported lower haemoglobin levels than those in other professions (Kundu et al., 2013). Tea garden workers in Assam were more likely to be anemic because of less access to diversified food due to land and geographical bottlenecks. They had low wages, lived in huts or temporary accommodation and were reported to be discriminated against access to ration cards and other public provisioning services such as hospitals, housing and other amenities (P. Dutta & Sengupta, 2017). Oraon females of North 24 Parganas working as agricultural labour or maid were anemic irrespective of their income and socioeconomic status. Low animal protein intake in the study population was the primary risk factor for anemia (Chowdhury & Roy, 2019). A study on adult women of two ethnic groups living in a peri-urban area of Kolkata city found that heavy workload and less leisure time among women of Munda tribes contributed to lower haemoglobin levels. They needed to work hard for long hours with a meagre income that constrained access to quality foods (R. Ghosh & Bharati, 2003). Business ownership among adults of rural Tamil Nadu was positively associated with blood haemoglobin concentration in women (Little et al., 2018). In a subsistence farming community of Pune, Maharashtra, poverty and an overall lower intake of diversified food, including non-vegetarian foods, was the main reason for the high prevalence of anemia (S. Rao et al., 2011). Women engaged in farming had a greater risk of anemia than women working in government or non-government jobs in rural Andhra Pradesh. The occupation of farming was shown to be a risk factor for anemia (Subasinghe et al., 2014). Anemia was higher among textile workers than in comparative groups in Rajasthan. A higher prevalence of anemia was attributed to comorbidities associated with education, income, environmental factors, housing conditions and WASH (Singh et al., 2005). A study attributed high anemia prevalence among agricultural workers to infestation with hookworms and other kinds of worms and parasites in farm fields (S. Bharati et al., 2015). These findings highlighted that occupation derived from one's social position could affect anemia in numerous ways.

7.3.3. FOOD SECURITY

The studies have found inadequate intake of bioavailable dietary iron as the most common cause of anemia (Y. S. Balarajan et al., 2013; Little et al., 2018). The studies among women in Bangalore (Thankachan et al., 2007) and Tamilnadu (Little et al., 2018) found a positive correlation between haemoglobin levels and improved dietary intake of meat and fish, egg, milk, pulses and GLV that contained a diversity of nutrients including iron. The low intake of fruits, vegetables and meat products among socially disadvantaged santal tribes (Stiller et al.,

2020), high intake of cereal-based foods (DeFries et al., 2018), selling of the agricultural produce to the market instead of self-consumption among Khasi tribe of Northeast region (Chyne et al., 2017), husband's control over the choice of food cooked in the household (S. Rao et al., 2011), rising food prices (DeFries et al., 2018) was associated with anemia. Using NFHS-4 data, a study concluded that regular consumption of fruit was the most effective way to reduce anemia among women (S. Bharati, Pal, Sen, et al., 2019). The subsistence agricultural activities among small farmers of rural Tamilnadu involved in the cultivation of iron-rich coarse cereals and animal husbandry were protective factors against anemia (Little et al., 2018). Various factors such as agricultural policies, food distribution policies, women empowerment, and income generation are linked to food security and anemia.

7.3.4. WATER, SANITATION, AND HYGIENE

Studies have reported open defecation, absence or inadequate toilet facilities, lack of periodic deworming, and lack of safe drinking water as leading causes of anemia (DeFries et al., 2018; Karlsson et al., 2020). Mean haemoglobin level was significantly associated with intake of treated water for drinking and cooking among adolescent girls in Punjab (Dhillon et al., 2021).

Open defecation, inadequate sanitary latrines, lack of access to piped water and poor sanitation were the risk factors for anemia among children (Arlappa et al., 2010) and urban poor women (Chakrabarti et al., 2018). A recent study using 47 nationally representative demographic and health surveys showed that anemia prevalence among children and women was higher for those living in households using unimproved or surface water and open sanitation facilities (Kothari et al., 2019). A meta-analysis of multiple indicator surveys showed that community-level sanitation access reduced the odds of anemia prevalence in children irrespective of individual household sanitation access (Larsen et al., 2017). A study showed reproductive health infections as a strong risk factor for maternal anemia (Onyeneho et al., 2020). Haemoglobin levels among adolescent girls in Punjab increased with the frequency of changing sanitary pads (Dhillon et al., 2021). Pregnant women who used biomass fuels compared to clean fuels were at higher risk of anemia in rural settings of Nagpur (Page et al., 2015). A study using NFHS-4 data showed that the use of biofuels in poor households was associated with the adverse outcome on haemoglobin levels (Nguyen et al., 2019). Biomass smoke triggers systemic inflammation that causes anemia (Page et al., 2015).

The contaminated water, poor hygienic conditions and low sanitation may cause diarrhoea and aggravate iron deficiency (S. Bharati, Pal, Sen, et al., 2019). Recurrent infections with intestinal parasites such as hookworm and schistosomal infections, malarial infections, Tuberculosis and HIV/AIDS are reported as major causes of blood loss and iron deficiency, resulting in anemia in many cases (Y. S. Balarajan et al., 2013). In a study, women from Assam were at a significantly higher risk of anemia than women from Bihar and Jharkhand because of the higher possibility of hookworm infections and malaria incidence attributed to local agro-climatic conditions such as humidity and high rainfall for most of the year in Assam (S. Ghosh, 2009).

7.3.5. ACCESS AND UTILIZATION OF HEALTH SERVICES

Mothers having access to good health care, such as antenatal care and routine blood and urine checkups, were less likely to develop anemia during pregnancy (Onyeneho et al., 2020). Improvement and access to health and nutrition interventions were recognized as the most vital driver of anemia reduction (Nguyen et al., 2019). The use of family planning methods such as contraception use was reported as a protective factor for anemia. Contraceptive use helps delay birth intervals and avoid unintended pregnancy and unsafe abortion, which would otherwise cause nutrient depletion and exaggerate the risk of undernutrition and anemia (Rana & Goli, 2017).

Pregnant women in lower socioeconomic positions in rural areas may not attend the regular antenatal checkups (ANC) at the primary health centre because of transportation costs, lack of transport services and long waiting times at health centres (Perumal, 2014). Low coverage of IFA was associated with an increased risk of anemia. The coverage of IFA supplementation among rural preschool children of West Bengal was almost nil (Arlappa et al., 2010). Irregular supply and poor quality medicines, lack of understanding about IFA programmes, and cultural beliefs among healthcare workers were associated with low coverage and noncompliance with IFA among women (DeFries et al., 2018). Inadequate coverage of nutrition and health interventions (NHI) among pregnant women and children across the continuum of care was reported as a barrier to reducing the high prevalence of anemia (S. Rao et al., 2014).

7.3.6. PLACE OF RESIDENCE

In a study, poor urban women in Andhra Pradesh were more likely to be anemic than poor rural women (M. E. Bentley & Griffiths, 2003). Similarly, urban women were at more risk of anemia than rural counterparts in studies done in east, central, north and south India (Chakrabarti et al., 2018) and eastern states of India (S. Ghosh, 2009). Increased rurality was shown to increase blood haemoglobin and decrease the odds of severe anemia in women and men, possibly because of intake of iron-rich coarse cereals and dependence on livestock, which are part of the subsistence farming practices (Little et al., 2018). There was no marked difference in anemia prevalence between urban and rural areas (S. Bharati, Pal, & Bharati, 2019). In another study, anemia among women aged 15-49 was positively related to rural residence and negatively associated with the urban (S. Bharati, Pal, Sen, et al., 2019). The place of living did not significantly affect anemia prevalence among children aged 6-59 years old in Madhya Pradesh (Chandran & Kirby, 2021). Therefore, the linkages between the place of residence and anemia are complex. Other confounding variables in the region may explain anemia prevalence.

7.4. WHO ARE ANEMIC?

India is home to a maximum number of poor people in the world who face extreme poverty and face multiple deprivations in the form of undernourishment, unemployment, illiteracy, landlessness, poor housing conditions, unavailability of safe drinking water, sanitation and type of fuel used for cooking purposes (Ansary & Das, 2018)**,** (Khan et al., 2014)**.** Indian poverty is closely linked to social identity. A report, 'Mind the Gap: the state of Employment in India 2019', stresses that India's poor are most likely to be Dalits, other lower castes, tribal people and Muslims (McCullagh, 2016). A majority of these population groups (88 % of the SC and ST and (80 % of the OBCs) are reported to be extremely poor, with an average consumption of less than Rs 20 a day (~ one-third of a dollar), most of them are landless, manual casual labours and cultivators, often engaged in what were traditionally considered to be a ritually polluting environment (Subramanian et al., 2008). SC, ST and OBCs comprise more than 70 % of the Indian population, and their deprivation is reflected in low educational, income and occupational levels. Women and children in these caste groups are more vulnerable (Sengupta et al., 2008). The differential rates of prevalence of anemia and overall health utilization patterns among such groups indicate their social exclusion and its linkages with anemia.

7.5. THE PARADIGMS OF ANEMIA

Three interesting findings emerge from the review on social determinants of anemia. First is the hegemony of natural and allied sciences into the foray of nutritional sciences and anemia research, which gives primacy to immediate biological causes (Hayes-conroy & Colleges, 2015). The share of research papers from social science disciplines is meagre. Second, disciplinary bias from within the social sciences discipline is evident, as most of the body of literature is produced from the field of demography, focused primarily on the strength of association of risk factors with anemia. Third, many of the studies in the recent past do choose the population as the subject of the study, but the analysis is done on the individual level. For example, an analysis of haemoglobin levels among individuals of a particular social group merely explains whether the person is anemic or not; it does not reflect why the particular social group is at more or less risk of anemia.

A large body of literature does highlight the importance of economic, demographic, cultural and social factors. However, these factors are narrowly conceptualized and framed in isolation, devoid of the context under which the risks emerge. These findings exemplify the dominant discourse of Biomedical and Lifestyle approaches to modern epidemiological studies rooted in the 'risk factor' paradigm, characterized by analyzing decontextualized individual risk factors rather than studying population factors in their social and historical context (Pearce, 1997). Social concepts are reduced to a mere quantifiable risk factor. For example, caste, class, and gender are merely seen as risk factors. As a result, discriminatory and social exclusion pathways are ignored while explaining anemia.

Two main approaches can be used to best define anemia, i.e., Biomedical and Lifestyle paradigms. The biomedical and Lifestyle approaches are the dominant approaches to epidemiologic theorizing, including the 'atheoretical' stance. The hallmark of the two methods is

i) The disease arises because of Biophysical agents, genes, and 'risk factors, and their exposure is primarily a consequence of individual characteristics and behaviours.

ii) The causes of disease in individuals are sufficient to explain the population rates of disease, and

iii) Theorizing disease occurrence is equivalent to theorizing about biological disease causation about mechanisms occurring within biological organisms, which means population-level theorizing is largely irrelevant (Krieger, 2011, p. 126).

The biomedical and lifestyle discourse started with a singular focus on iron deficiency as the leading cause and advanced to multiple micronutrient deficiency theory, infections and inflammations. Iron is the main protagonist; while other nutritional deficiencies and diseases are considered complementary, their presence or absence may exacerbate or reduce iron deficiency.

7.5.1. BIOMEDICAL PARADIGM

Three factors identify the characteristic features of biomedical perspectives in anemia research:

- the domain of anemia and its causes are restricted to solely biological, chemical, and physical phenomena, as is evident in the diagnosis of definition, classification and causes of anemia. Anemia is defined and classified based on haemoglobin, ferritin, and other laboratory-based biochemical markers. The causes are identified based on the biological response to chemical and physical characteristics.
- The characteristic of many natural sciences, i.e., the emphasis on laboratory research, use of biochemical tests and methods, and discounting of research questions that cannot be studied by popularly used biomedical methods such as randomized control trials and experimental research.
- Anemia is characterized by biological reductionism, a philosophical and methodological worldview that views the properties of their parts best explain that phenomenon. According to this view, the focus on discrete variables or factors such as nutritional deficiencies and infections would be sufficient to explain the population rates of anemia. That causal features of anemia can be fully explained by genetics and molecular biology studied experimentally, preferable in laboratories. The premise of this reductionist worldview holds that properties of phenomena at a ‘higher level’ can be reduced to and hence be solely determined and explained by phenomena at a ‘lower level’ and that lower levels are not only essential but also sufficient to explain the phenomenon at higher levels (Kreiger, 1994).

In simpler terms, within this reductionist premise, genetics and molecular biology can explain the features of a biological organism, and it is possible to alter and disrupt the disease mechanism at the biological level to find a cure.

7.5.2. LIFESTYLE PARADIGM

The premise of Lifestyle approaches is that personal habits are discrete and independently modifiable and that individuals can voluntarily choose to alter such behaviours. (Krieger, 2011, p. 148). Lifestyle approaches chose discourses of individual empowerment and responsibility over collective action and structural reform (K. E. Smith et al., 2009). This discourse in public health focuses on individual behaviours, such as dietary habits, tea, coffee, smoking, alcohol, drugs and exercise. It tends to moralize 'healthy lifestyle' as individualized matters and blame the victim. This policy trend is called 'lifestyle drift'. This term evokes a situation whereby governments start with a commitment to address broader social determinants of health but ends up instigating narrow lifestyle interventions on individual behaviours (Hunter et al., 2010). The promotion of lifestyle interventions for anemia reduction is part of this discourse.

At the core of the issue are inadequate intake of a diversified diet and poor public provisioning of health, hygiene, and sanitation. The systematic reasons why a population cannot access nutritious diversified food or hygienic life conditions are ignored. Not consuming an adequate diet is assumed as a subject of personal choice and ignorance, leading to anemia. The current discussion on lifestyle and health largely ignores systemic factors and focuses almost exclusively on individual responsibility.

7.5.3. BIOMEDICAL AND LIFESTYLE PARADIGMS CONJOINED: A SPIDER LESS WEB OF CAUSATION

The modern epidemiologic thoughts are best represented by the confluence of biomedical and lifestyle approaches. This epidemiologic thought is a popular approach to address the complexities of 'multiple causations'. The focus is not only on advancing the idea that multiple factors can cause disease but also on identifying probabilistic, not deterministic, orientation to understanding risk. This approach relies on identifying new exposures that increase risk. However, these exposures are neither necessary nor sufficient to cause disease occurrence. The 'multiple causation' theory with 'risk factor' approach is the dominant paradigm within the

discourse of anemia. A large body of literature with multifactorial hypotheses carries out multivariate analyses to establish the link between a range of factors and the risk of anemia. Kreiger calls it a 'web of causation' that evokes an image of a spider's web, a linked network of delicate strands, the multiple intersections representing risk factors or outcomes, and the strands symbolizing diverse causal pathways (Kreiger, 1994).

The biomedical and lifestyle orientation identifying the nutritional and non-nutritional risk factors of anemia symbolizes the 'spider less' web characterized by a constellation of risk factors, ignoring dimensions of both societal and historical context and time and place in the lives of individuals and populations. The risk factors offer no ability to distinguish between factors that determine the occurrence of anemic cases versus determined population rates of anemia. Despite a range of identified risk factors, the larger question of why anemia prevalence differs by social group and changes over time remains unanswered.

A web of multicausal theory is a marked shift from singular causation theory. Unlike previous paradigms, this new epidemiologic paradigm somewhat espouses a holistic view of disease, focuses on the multicausal theory and the need for a multicausal approach (social, biologic and statistical), and specifies the population group as a unit of study; however, the unit of analysis remains at the individual level (Susser, 1985).

The competing explanations for anemia causations (iron deficiency at individual level vs socioeconomic factors in populations) require different analysis levels. Just as anemia within a population can be studied at various levels, including people, individuals, organs, tissue, cells and molecules, the causes can also be looked at different levels, including socioeconomic factors, lifestyle, and individual levels. Although a specific risk factor may appear to operate at the individual level, exposure and susceptibility may occur due to social, political and economic factors (Pearce, 1997).

7.5. SUMMARY

The influence of biomedical and lifestyle approaches to health and nutrition, including nutritional anemia, has resulted in a myopic understanding of the nature and causation of anemia. Anemia is primarily considered a biological condition which can be cured by biological interventions. Biology is seen disjointed from the structures of society and the complex social processes. Therefore, the context, i.e., social, political, economic, and

environmental milieu which promotes the biological manifestation of anemia, remains ignored and unaddressed. The evidence shows that the structures of society such as caste, class, gender, and religion exert influence and determine the rate of anemia prevalence in a population. The structures of society bestow a socioeconomic position to an individual or a community, which in turn provides differential access to intermediate determinants such as education, income, occupation, public provisioning services such as housing conditions, safe drinking water, sanitary toilets, access to health services, and access to nutritious food. The biological matrix of anemia is entangled in the complexity of the structural and intermediate determinants.

Poverty, deprivation, and social exclusion are linked to anemia. People from poor and disadvantaged sections are most likely to be anemic. The inadequate dietary intake, less education, and poor housing conditions among the poor and underprivileged are manifestations of poverty and deprivation. Caste is a strong predictor of anemia; people from lower caste are at increased risk because of economic and discriminatory pathways. In a patriarchal society such as India, discriminatory and exclusionary gender norms are a strong determinant of anemia in women. The lack of women's autonomy in household decisions such as finances, cooking, and health-seeking behaviour results from women's subordinate position in the hierarchy. The intersectionality of caste, class, gender, and religion may produce a synergistic effect on the outcome of anemia. Anemia is not a technical or biological problem; it is a social problem. However, little is known about the social processes and how they manifest anemia.

CHAPTER 8

We need to move beyond treating our patients to preventing diseases in the first place

Anonymous

CHAPTER 8. GLOBAL POLICY RESPONSES TO ANEMIA

8.1. INTRODUCTION

Discourses are embedded either visibly or invisibly within the language, the way language is used in policy documents and transmitted textually. In this context, discourses can be thought of as a series of statements that address a given topic. Through a process called intertextuality, which means the texts or policies that organisations produce are linked to other texts both in the present and past, some discourses become dominant, often allowing those with the most power to shape the discussion. Discourses are not only linked to power and knowledge but also to social practices and the actors that influence these social practices. Wherever there is power, there is the possibility for resistance and change from actors with less power. Resistance can manifest textually as gaps, inconsistencies, and contradictions in the statements of these actors. It can also manifest as an active denial of, or passive disregard for, a given text or policy (Evans-Agnew et al., 2016).

In this context, this chapter critically analyses the international policy documents (WHO, FAO, and UNICEF) and examines the approaches and discourse meant to address nutritional anemia. Critical discourse analysis (CDA) is used to unpack the existing programmes and policies recommended by international agencies and their influence in shaping the health and nutrition policies in developing countries, including India. This approach of analysis is a valuable tool to explore why anemia control programmes have minimal impact on anemia reduction and identify the gaps in knowledge and practice.

8.2. NUTRITIONAL ANEMIA PREVENTION AND CONTROL STRATEGIES

In 1958, the first-ever "WHO study group on Iron Deficiency Anaemia" constituted to discuss the etiology, evaluation, and prevention of IDA focused on several approaches, including:

a) Overall, focus on increasing the access and availability of iron-rich foods: such as pulses and vegetables, by reducing their price and increasing their production.

b) The improvement in dietary habits and behavioural changes through nutritional educational programmes

c) control of parasitism associated with blood loss by preventing the transmission of parasites by improved environmental sanitation and the effective therapy of infected persons.
d) The use of prophylactic iron, especially for vulnerable groups in cases where natural food was insufficient to supply the required iron.
e) Fortification of food with iron where IDA was prevalent.

In 1968, a WHO technical report of a group of experts on nutritional anemia underlined the importance of improved living standards, good sanitation measures, and health and nutrition awareness programmes besides access and affordability of foods as the 'long-term approaches'. At the same time, iron supplementation and iron-fortified foods were suggested as immediate measures. The report underlined the urgent need to fortify foods and called it a 'best approach that could potentially be effective for iron deficiency in the long term (WHO, 1968).

Food fortification was reinstated as the best method to combat anemia in the following group of experts meeting on nutritional anemia in 1972. The report reads:

> *"The most practical method of eliminating iron deficiency in a community is probably the fortification of food with iron" (WHO, 1972).*

The strategies to control anemia started with a somewhat broader vision of ensuring increased access and affordability to iron-rich foods. The contention that the natural food in tropical areas was insufficient to address anemia prompted the recommendation of iron supplementation and food fortification strategies as the most appropriate strategies. There was a paradigm shift in thinking from ensuring access and affordability of food to prevent and control anemia to primarily iron-centric approaches, including supplementation and fortification. A component of behavioural interventions to improve dietary habits was considered an integral part of the control strategies. The confluence of biomedical and lifestyle paradigms was evident in recommendations, including supplementation, fortification, and behavioural changes to improve dietary habits since the early years of prevention and control strategies of anemia.

A 1978 bulletin of WHO, titled "Nutritional anemia – a major controllable disease", emphasised the need to educate common people, doctors, nurses, paramedical workers, health planners and politicians regarding the importance of diets, social norms, and parasitic infections to bring behavioural change. Thus putting the onus of health on individual responsibility (Baker, 1978). The bulleting reads:

> *"Because numerous conditions such as types of diet, social customs, extent of parasitism, etc., are likely to vary from country to country, and even within regions in one country, it cannot be assumed even that "giving iron pills" or "adding iron to the diet" will deal with the situation". Experience to date indicates that in regions where there is a high prevalence of anaemia, there is unlikely to be any simple public health solution to the problem. To achieve success, it will probably be necessary to develop and combine a number of different approaches" (Baker, 1978; Baker & DeMaeyer, 1979).*

The notion that natural diets alone cannot address anemia paved the way for iron-centric approaches. Subsequently, the idea that even iron-centric approaches would be inadequate to reduce anemia shifted the focus on raising awareness about the risks (diet, social norms, and parasitic infections) to bring a behavioural change among individuals.

A fallacy in conceptual understanding of anemia and intervention approaches was evident; more than an issue rooted in societal factors, anemia was seen as a regular occurrence that can be controlled by broadening the coverage and implementing supplementation programmes. The WHO report on "Preventing and controlling anaemia through primary health care" recommended bringing the Primary health care approach into practice to treat assumably what it called a 'simple problem' whose treatment was simple. Still, the prevention was considered complex (E. M. DeMaeyer, 1989). The prevailing assumption was that the poor coverage and implementation of iron supplementation programmes was the main reason for anemia, and anemia can be cured by increasing the coverage by administering iron pills through primary health care. While bringing the anemia control strategies into Primary health care was a positive step, this was done to increase the coverage of iron supplementation programmes, not to converge and integrate different programmes. The report reads:

> *"The treatment of iron deficiency anaemia is technically quite simple, requiring only the administration of medicinal iron, although millions of sufferers are currently left untreated for various reasons. Prevention is somewhat more complex. Fortunately, there are a number of simple control measures available that can be applied through primary health care" (E. M. DeMaeyer, 1989).*

1993 WHO technical working group report on "prevention and management of severe anaemia in Pregnancy" emphasised the programme's coverage, planning, and management aspects. It was amply clear from the report that the working group had this erroneous understanding that they knew enough about the epidemiology of anemia, and all it needed was to put this knowledge into practice (WHO, 1993)—the report states.

> *"Although the epidemiology of anemia and the knowledge and technical means of preventing and controlling it are well known, there as yet few MCH (maternal and child health) programmes that successfully apply this knowledge to the development and implementation of comprehensive control strategies in developing countries" (WHO, 1993).*

The epidemiology of anemia, particularly in developing countries, including India, is largely unknown. The primary etiological factors in local contexts are not adequately defined, and the causal mechanism remains unexplained. The claims that epidemiology was well known back in the 1990s highlight the narrow framework within which anemia was seen, defined, and devised intervention strategies. The dominant paradigm in that era was iron deficiency. The data on iron deficiency in a different context is still lacking to map an epidemiological path of iron deficiency. The conceptual flaws in the understanding of anemia have translated into the design of intervention strategies.

There was a paradigm shift from identifying causes of anemia to more focus on coverage, planning, and implementation of anemia control programmes. The focus shifted from 'disease' to expanding the coverage of the 'programme'. Thus, it marked a shift from prevention and control to curative aspects of anemia control.

In a joint statement issued by WHO &UNICEF (2004) and the report of the WHO global database on the worldwide prevalence of anemia (WHO, 2008), the scope of integrating anemia prevention and control strategies into the 'primary health care' system was broadened. Maternal and child health, adolescent health, safe pregnancy, safe motherhood, roll back malaria, deworming, routine anthelminthic control measures, and 'stop tuberculosis' were recommended to integrate into primary health care as part of anemia prevention and control strategies.

> *"Strategies should be built into the primary health care system and existing programmes such as maternal and child health, integrated management of*

> *childhood illness, adolescent health, making pregnancy safer/safe motherhood, roll-back malaria, deworming (including routine anthelminthic control measures) and stop-tuberculosis. Furthermore, strategies should be evidence-based, tailored to local conditions and take into account the specific etiology and prevalence of anaemia in a given setting and population group"* (WHO & UNICEF, 2004), (WHO, 2008).

Gillespie et al. *(1998),* in an 'expert consultation on Anemia determinants and interventions', introduced the "Life cycle perspective" to examine the role and pattern of determinants at different stages of life in a different age, sex, and physiologic groups. This approach helped prepare a matrix of assessment tools and the interventions that would be efficacious in dealing with such determinants (Gillespie et al., 1998).

The report on a joint statement by WHO & UNICEF (2004) recommended the 'targeted' interventions to provide iron supplements to vulnerable segments of the population, particularly women. The targeted interventions shifted the focus from population to individual-level intervention strategies. The report also recommended 'Food-based approaches' to increase iron intake through food fortification, dietary diversification, and improved food consumption. Food-based approaches were proposed to increase dietary iron intake, not to increase the uptake of the diversified matrix of micronutrients and macronutrients.

In a significant shift, the expert group consultation on strategies to prevent anaemia in 2016, the issue of availability and accessibility of iron/micronutrient-rich foods and the role of agriculture and education sectors were flagged. The expert group emphasised the linkages between micronutrients and food production, preservation, processing, marketing, and food preparation. Counselling and behaviour change communication were also considered important components of improving diets. The focus was on improving complementary feeding and exclusive breastfeeding to infants up to 6 months of age. The expert group strongly emphasised the possible linkages between water, sanitation, and hygiene (WASH) and anemia prevention. The importance of multisectoral interventions such as social safety support, livelihood approaches, women's empowerment, the education sector, and their convergence into anemia prevention was recommended.

> *"Improvement and enhancement of supportive interventions; social safety support, livelihood approaches, women's empowerment and education*

> *positively impact anaemia and overall nutritional status in several ways and need more focus and priority. These will cause improved dietary diversity, food security, delayed pregnancies, birth spacing and health-seeking behaviours. Different sectors would need to focus on specific areas in the prevention of anaemia"* (WHO, 2016).

To effectively address anemia at the country or regional level and recognise the need for intersectoral strategies, the recent WHO document "Nutritional Anaemias -Tools for effective prevention" frames anemia intervention strategies into nutrition-specific and nutrition-sensitive interventions (WHO, 2017).

i) Nutrition-specific interventions address the immediate causes of anemia, such as poor dietary intake of hematopoietic nutrients, including iron or vitamin A, infant feeding practices, and access to fortified foods.

ii) Nutrition-sensitive interventions tackle underlying causes of anemia involving various sectors, including disease control (e.g., malaria, intestinal helminths), water, sanitation, and hygiene and strategies that address root causes such as poverty and social and gender norms.

Significant progress has been achieved in understanding iron physiology and metabolism and increasing iron bioavailability as it evolved as the main point of contention for policymakers. Besides iron and, to an extent, folate and vitamin B12, other nutritional factors, including vitamin A have received disproportionately less attention in programmatic approaches. The conceptual knowledge gap on anemia and myopic understanding of anemia as the problem of iron deficiency or, in extreme cases, iron deficiency anemia has probably led to a focus on iron-centric approaches at the expense of other nutritional and non-nutritional factors. The programmes and policies at large have evolved within the narrow framework of 'Iron deficiency or Iron deficiency anemia' rather than the broader health framework.

Historically, anemia has been assumed to predominantly be a problem of iron deficiency; therefore, public health control strategies have evolved to supply the deficient iron. With the advancement of knowledge, more nutrients such as folate and vitamin B12 and parasitic control strategies were integrated into the programmes and policies. Mainly, three intervention techniques are employed:

I) Therapeutic supplementation with the hemopoietic nutrients, mainly iron.

II) Fortification of the diet with nutrients, including iron.

III) Reducing nutrient losses by parasitic control, e.g., hookworm and malaria eradication.

8.3. NUTRIENT SUPPLEMENTATION

Iron supplementation is the most common strategy established as early as the 1960s to prevent and control nutritional anemia. The current approach of nutrient supplementation relies on differential doses of iron and folic acid treatment to age and population groups for a specified period (Table:8.1).

8.3.1. CHANGES IN SUPPLEMENTATION REGIMEN

The variable doses of elemental iron have been advised for different age and sex groups. The limited knowledge of the amount of iron and its subsequent impact on the haemoglobin concentration and functional outcomes have made it challenging to choose which Dose of iron to be recommended. As the understanding evolved of the effects of iron on haemoglobin response, the dose recommendations have been revised and progressively lowered (Table:8.1) Initial policy responses started with supplementation in pregnant women. It was estimated that 1000 mg of additional iron was needed during the second and third trimesters; therefore, an average of 6 mg of iron per day should be absorbed from the diet. The average iron bioavailability in developing countries' diets was considered 5 %. A dose of 120 mg of iron would be required for 6 mg of iron to be absorbed at 5 % absorption. Several supplementation trials during that era tested 120 mg of iron and multiples of it (60 mg and 240 mg) to assess the change in haemoglobin concentration. Much interest in iron supplementation trials was generated, and a monograph was also published with detailed instructions on the design and analyses of iron supplementation studies. It may be that by using the bioavailability of iron in the diet and the amount of extra iron required daily for pregnant women, the practice of iron supplementation in multiples of 120 mg started.

1958, the WHO study group recommended 63 mg of elemental iron or the equivalent of another iron compound once daily throughout pregnancy and the first six months of lactation (WHO, 1959). In 1968, ferrous salt containing 60 mg of elemental iron daily during the second and

third trimesters of pregnancy and the first six months of lactation was recommended. The importance of folate and vitamin B12 for nutritional anemia was also acknowledged, but no specific recommendation was made on their doses (WHO, 1968). In 1972, 30-60 mg of iron and 500 µg folic acid per day for population groups with iron stores and 120-240 mg of iron and 500 µg folic acid per day for groups severely deficient in iron were recommended (WHO, 1972). In 1977, for the first time, the prevalence of anemia was chosen as a parameter to decide the doses rather than iron stores as the criteria to determine the iron doses (INACG, 1977).

In 1997, the International Nutritional Anaemia Consultative Group (INACG) identified five population groups, namely pregnant women, children aged 6-24 months, children aged 2-5 years, children aged 6-11 years and adolescents and adults for iron/folate supplementation and complementary parasitic control measures. These guidelines covered all age groups, and recommendations for young children and adolescents were made for the first time. Bringing new age groups and variable duration for variable anemia prevalence among pregnant women and children aged 6-24 months was a significant shift from earlier guidelines and recommendations (Stoltzfus & Dreyfuss, 1998).

In 2001, more age groups were added (low birth weight infants, women of childbearing age and lactating women) within the realm of iron supplementation strategy. 2001 WHO guidelines recommended the same iron doses for respective age groups but brought marked changes in the duration of the supplementation regimen in comparison to preceding guidelines. Also, in contrast to the 1997 guidelines, which suggested variable doses for pregnant women according to anemia prevalence, the 2001 guidelines recommended universal supplementation of 60 mg/day of iron and 400 µg/day of folic acid tablets for all pregnant women. Again, for children aged 6-23 months, duration of supplementation from 6 months onwards to completion of 23 months was recommended, unlike the variable duration for variable anemia prevalence in 1997 guidelines. For children aged 24 to 59 months and school-aged children, the recommendation was made to supplement each for three months, which was a shift from the 1997 guideline, which did not specify the duration of supplementation within this age group (WHO, 2001).

8.3.2. CURRENT GUIDELINES ON IRON SUPPLEMENTATION

The current guidelines recommend variable doses of iron and folic acid according to age, sex, and prevalence of anemia in the region. In settings where anemia is a severe public health

problem (≥ 40 %), WHO recommends daily iron supplementation as a public health intervention in all age and population groups. At the same time, intermittent iron supplementation has been suggested among pregnant women and WRA in areas where anemia prevalence is less than 40 % and ≥ 20 % and among pregnant women in settings where anemia prevalence is lower than 20 % (Table:8.1). Current guidelines do not recommend iron and folic acid supplementation for adult males (WHO, 2017). The intermittent iron supplementation approach marked a shift from earlier daily supplementation approaches irrespective of conditions.

The quality of evidence for iron recommendation among infants and young children (6-23 months), preschool-age children (2-5 years), and school-age children (5 years or more) are moderate, very low, and high-quality, respectively. Also, good quality evidence is available to recommend iron supplementation in conjunction with anti-malarial measures in infants and children in malaria-endemic regions with adequate[1.]

8.3.3. CONTROVERSIES OF IRON SUPPLEMENTATION STRATEGIES

Oral iron supplementation is considered the first-line treatment for iron deficiency and IDA among children, women, adolescents, and adults. However, controversies are related to the optimal Dose, frequency, and type of oral iron preparations. The guidelines may vary from one country to another. For example, in the case of women, traditionally, 100-200 mg of iron per day is recommended in three or four divided doses of ferrous salts. Expert guidelines generally recommend 80-200 mg of elemental iron per day. The recent guidelines suggest lower doses, which are claimed as effective and may produce fewer adverse effects. For example, current British guidelines recommend 40-80 mg of elemental iron (ferrous fumarate) every morning (Stoffel, von Siebenthal, et al., 2020).

WHO provides population-based guidelines and has progressively lowered the recommended iron doses. One can question the logic of modifying the doses for individuals based on the change in population prevalence, suggesting that each individual's requirement changes with the number of anemic individuals in society (Ramakrishnan, 2001).

Table 8:1 Changes in Iron and folic acid supplementation regimen in population groups on the timeline

Year	***Pregnant women***	***WRA***	***Infants and Children***	***Adolescents and Adults***
	Recommended Dose, frequency, and duration			
1958	Three grain tablets (180mg) equivalent to 63 mg elemental iron, once daily. Throughout pregnancy & first six months of lactation			
1968	60 mg elemental iron daily, 2nd and 3rd trimester of pregnancy & first six months of lactation			
1972	30-60 mg elemental iron+500 µg folic acid for the population, deriving 25 % calories from animal sources and having iron stores at the beginning of pregnancy. Daily, 2nd and 3rd trimester of pregnancy & first six months of lactation			
	120-240 mg elemental iron+ 500 µg folic acid for the population, deriving less than 10 % calories from animal sources and having no iron stores at pregnancy. 2nd and 3rd trimester of pregnancy & first six months of lactation			
1989	2 Tablets (60 mg elemental iron +250 µg folic acid)		3mg/kg body weight/day	60 mg in case of mild anemia and 120 mg for severe anemia
1991	anemia prevalence <20%- A tablet (60 mg +250 µg folic acid) daily For moderate to severe anemia -2 tablets (60 mg +250 µg folic acid) daily		**For Infants-1** mg/kg body weight/day **For preschool children**: 30 mg elemental iron in tablet or liquid form **School children:** 30-60 mg elemental iron/day	
1993	Severe anemia: 180 mg elemental iron+ 2 mg folic acid			
1997	A.P <40 % - 60 mg iron + 400 µg folic acid 2nd & 3rd trimesters of pregnancy		Children 6–24 months- 12.5 mg iron + 50 µg folic acid A.P <40% - 6–12 months for normal birth weight, daily A. P >40 % - 6–24 months for birth weights <2500 g. daily	Male 60 mg iron Female: 60 mg iron +400 µg folic acid Duration: Not specified
	A.P >40 %- 60 mg iron + 400 µg folic acid		Children 2–5 years-20–30 mg iron	

	2nd & 3rd trimester and three months postpartum			Duration: Not specified	
				Children 6–11 years- 30–60 mg iron Not specified	
2001	Pregnant women: - 60 mg elemental iron + 400 µg F.A, daily to all pregnant women (Universal supplementation) As soon as possible after gestation starts - no later than the 3rd month – and continuing for the rest of the pregnancy		A.P >40 % - 60 mg elemental iron +400 µg F.A Daily, three months	Low birth weight infants Iron: 2 mg/kg body weight/day. Universal supplementation From 2 months to 23 months of age	
	Lactating women (A.P>40 %): 60 mg elemental iron + 400 µg F.A Daily, three months post-partum			A.P >40 % - Children (6-23 months): Iron: 2 mg/kg body weight/day From 6 months to 23 months of age	
				A.P >40 % - Children (24-59) months: Iron: 2 mg/kg body weight/day up to 30 mg 3 months	
				A.P >40 %- School-aged children (above 60 months)- 30 mg elemental iron+ 250 µg F.A, daily 3 months	
Current guidelines	Settings/countries where, A.P <20 % (Non-anemic pregnant women)	**120 mg elemental iron[a] + 2800 µg folic acid** **Frequency: Intermittent supplementation** (One supplement once a week) **Duration:** Throughout pregnancy, supplementation should begin as early as possible	**In settings where A.P ≥ 20 % (20-39%)** 60 mg of elemental iron[c] + 2800 µg F.A **Frequency**: **Intermittent supplementation** (One supplement per week)	Low birth Infants (1.5-2.5 kg) -2 mg/kg body weight per day 2 months to 23 months	A.P ≥40% ***Adolescent Boys-*** 6o mg of elemental iron +400 µg folic acid Daily, 3 months
				(Preschool and school-age children, A.P - ≥20 %) Preschool-age children (24-59 months)- 25 mg of elemental iron[e] (drops/syrups) School-age children (5-12 years) - 45 mg of elemental iron[f]	

			Duration and time interval: 3 months of supplementation followed by 3 months of no supplementation, after which the provision of supplements should restart	**Weekly/Intermittent** (One supplement per week) Three months of supplementation followed by 3 months of no supplementation, after which the provision of supplements should restart	
	As part of routine antenatal care in all settings	**30-60 mg elemental iron[b] + 400 µg folic acid** Frequency: daily Folic acid should be commenced as early as possible (ideally before conception) to prevent neural tube defects	**Settings where A. P ≥40%** **30-60 mg elemental iron[d]** Frequency: daily **Duration:** three consecutive months in a year	**(Infants and young children, A.P ≥40%)** Infants (6-23 months): 10-12.5 mg elemental iron[h] Children (24-59) months: 30 mg elemental iron[g] (Drops/syrup) Children (5-12) years: 30-60 mg elemental iron[g] (tablet/capsules) Frequency: Daily, one supplement per day Duration: Daily, Three consecutive months in a year	
	A.P ≥40%	60 mg elemental iron +400 µg folic acid daily is preferred Throughout pregnancy, supplementation should begin as early as possible			
	Post-Partum women: Oral iron supplementation, either alone or in combination with folic acid supplementation, may be provided to postpartum women for 6–12 weeks following delivery where anemia prevalence is ≥20%				
Source: compilation from WHO documents					

a: 120 mg of elemental iron equals 360 mg of ferrous fumarate, 600 mg of ferrous sulfate heptahydrate, or 1000 mg of ferrous gluconate ; b: 30 mg of elemental iron equals 90 mg of ferrous fumarate, 150 mg of ferrous sulfate heptahydrate or 250 mg of ferrous gluconate ;c: 60 mg of elemental iron equals 180 mg of ferrous fumarate, 300 mg of ferrous sulfate heptahydrate or 500 mg of ferrous gluconate; d: 0–60 mg of elemental iron equals 90–180 mg of ferrous fumarate, 150–300 mg of ferrous sulfate heptahydrate or 250–500 mg of ferrous gluconate; e: 25 mg of elemental iron equals 75 mg of ferrous fumarate, 125 mg of ferrous sulfate heptahydrate or 210 mg of ferrous gluconate; f: 45 mg of elemental iron equals 135 mg of ferrous fumarate, 225 mg of ferrous sulfate heptahydrate or 375 mg of ferrous gluconate; g: 30-60 mg of elemental iron equals 150–300 mg of ferrous fumarate, 90–180 mg of ferrous sulfate heptahydrate or 250–500 mg of ferrous gluconate ;h: 10–12.5 mg of elemental iron equals 50–62.5 mg of ferrous fumarate, 30–37.5 mg of ferrous sulfate heptahydrate or 83.3–104.2 mg of ferrous gluconate.

8.3.4. DAILY VERSUS INTERMITTENT IRON SUPPLEMENTATION

The opinions are divided between daily verses and intermittent iron supplementation. WHO recommends intermittent iron supplementation in women in settings where women experience significant side effects with oral supplementation or daily supplementation is not successful or not possible (WHO, 2017). A multiple micronutrients (MMN) supplementation significantly reduced anemia among children who took daily MMN than those who took it intermittently (Tam et al., 2020). A systematic review of 25 RCTs concluded that intermittent supplementation alone or with other vitamins and minerals produces similar effects to daily supplementation alone or with other vitamins and minerals on anemia. The intermittent iron supplementation had an equal haemoglobin concentration to daily supplementation but was associated with more minor side effects (Fernandez-Gaxiola & De-Regil, 2019). The finding of the study was consistent with an earlier study that demonstrated that daily regimens had similar haematological and pregnancy outcomes to intermittent regimens(Peña-Rosas, De-Regil, Malave, et al., 2015).

The recent evidence suggests that more and frequent iron doses have a little added benefit. Iron supplementation twice daily and thrice daily was not having a better haematological response than supplementation once daily (Moretti et al., 2015). Several studies have shown comparable iron absorption even with alternate day iron dosing. Though results show contradictory results. (Stoffel, von Siebenthal, et al., 2020). Plasma hepcidin follows a circadian rhythm, i. e an increased hepcidin level persists for 24 hours after the iron dose but subsides by 48 hours. Therefore iron absorption from supplements given later on the same or next day is reduced (Stoffel, von Siebenthal, et al., 2020). Iron absorption among women was higher if twice the target daily iron dose was given on alternate days. An alternate day schedule of oral iron supplementation sharply increases iron absorption and may be preferable in anemic women (Stoffel, Zeder, et al., 2020). These studies suggest changing the daily regimen to alternate days schedule and from divided to morning single doses to increase the iron absorption and minimise the side effects (Stoffel, von Siebenthal, et al., 2020). Contrary to this, one study showed that intermittent iron supplementation had no effect on Hb levels and IDA but increased the risk of anemia at or near term and ID and reduced the risk of side effects (da Silva Lopes K, Takemoto Y, Garcia-Casal MN, Ota E et al., 2018). Whether the alternate day iron dose schedule benefits women with IDA is unknown.

8.3.5. TYPES OF IRON PREPARATIONS USED IN IRON SUPPLEMENTATION

The existing policy on iron preparations for the treatment of anemia is highly variable. Two kinds of iron preparations are most common in use. They are (a)oral iron preparations and (b) Parenteral iron preparations. Often a comparison is drawn between the most widely used oral preparations versus intravenous iron sucrose for their effectiveness and safety. There is no clear consensus on the efficacy of different iron preparations (Rogozińska et al., 2021).

8.3.5.1. ORAL IRON PREPARATIONS

Common iron preparations are ferrous fumarate, ferrous sulfate, ferrous gluconate, and the amino acid chelate, ferrous bis-glycinate. Ferrous iron is preferred over ferric iron because of its high bioavailability. In general, the bioavailability of ferrous iron compounds is comparable; however, they vary in elemental iron content (Table:8.2). The iron content, tolerance and cost determine the choice of ferrous salt to be used (Stoffel, von Siebenthal, et al., 2020). The evidence suggests that tolerance to ferrous fumarate is better than ferrous sulfate (Rogozińska et al., 2021).

Table 8:2 Iron content and relative bioavailability (RBV) of Iron salts

Iron salt	Ferrous sulfate	Ferrous sulfate (dried)	Ferrous fumarate	Ferrous gluconate	Amino acid chelates	Carbonyl iron	Sugars(saccharides) usually contain ferric iron
Elemental iron content (%)	20	32.5	33	12	20	99	variable
RBV to ferrous sulfate (%)	Reference	100	100	89	100	5-20	variable

The carbonyl iron has high iron content and can be effective in high doses. However, because of low bioavailability, their use is generally not recommended. There is no consistent evidence to support Ferric iron polysaccharide complexes to treat anemia. Many multivitamin/mineral preparations do not contain sufficient doses of iron to correct iron deficiency. Such preparations may also have other minerals (such as Zinc), which may interfere with iron absorption. Some oral iron preparations contain ascorbic acid to enhance iron absorption. Prebiotic galacto-

oligosaccharides are added to Ferrous fumarate to increase iron absorption. However, there is no robust evidence to support that including other nutrients such as vitamin A, or vitamin B complex improves iron bioavailability (Stoffel, von Siebenthal, et al., 2020).

The studies demonstrate a lack of conclusive evidence that one oral iron preparation is superior to the other (Tandon et al., 2018). Clinicians tend to prescribe the most readily available oral iron preparations, which might not be the most effective (Rogozińska et al., 2021). Oral iron doses produce gastrointestinal (GI) side effects such as nausea, constipation, diarrhoea, indigestion, and metallic taste, leading to reduced adherence to the iron regimen. Measures such as taking the iron with meals, reducing the content and frequency of oral iron or changing to alternate preparations are generally employed to minimise GI side effects (Tandon et al., 2018).

8.3.5.2. PARENTERAL IRON THERAPY

Intravenous (IV) iron and Intramuscular (IM) iron are primary parenteral iron therapy methods. The IV route replaces the IM method because of inconvenience caused by the painful injection, risk of arthritis, and hypersensitivity at most centres. Intravenous iron produces fewer side effects and has high bioavailability than oral iron. Iron dextran, iron isomaltose, iron carboxymaltose and iron sucrose are commonly used in Intravenous iron.

A meta-analysis of 30 RCTs comparing 15 different iron preparations suggested that parenteral iron preparations were more effective than oral preparations at improving the haemoglobin concentrations. The reason why parenteral preparations were more effective could be improved compliance, better bioavailability, and targeted dosing. The study further concluded that intravenous ferric carboxymaltose and intravenous iron sucrose were the most effective interventions for enhancing haemoglobin among WRA four weeks after the treatment (Rogozińska et al., 2021). Other studies have also demonstrated that iron sucrose; is more effective than oral iron therapy for pregnant and post-partum women with IDA in terms of rapid replacement of iron stores and is associated with fewer adverse effects (Radhika et al., 2019; Q. Shi et al., 2015).

Contrary to this, the parenteral preparations are associated with a higher risk of systemic reactions, severe allergic reactions, and thrombosis in a few studies. The gastrointestinal side effects of oral iron preparations may be considered less problematic than the adverse effects of

intravenous and intramuscular iron (Rogozińska et al., 2021). Recent evidence suggests that parenteral iron preparations are more effective, but clinicians often prescribe oral preparations because they are cheap and widely available. The policymakers and clinicians should consider which oral preparation to use as the first line of treatment based on availability and tolerance for each individual rather than their availability (Rogozińska et al., 2021).

8.3.6. EFFECTIVENESS OF IRON AND OTHER NUTRIENTS SUPPLEMENTATION

The systematic reviews evaluating the effectiveness of iron supplementation alone or other nutrients show significant but a variable reduction in risk of anemia and iron deficiency (Table:8.3).

Table 8:3 Review of Efficacy trials

Author	Type of supplementation	Target group	Outcome (reduction in risk)
Pena-Rosas et al. (2015)	daily	Pregnant women	Anemia-70% IDA- 57 %
Fernandez-Gaxiola & De-Regil (2011)	intermittent	Non-pregnant women	27 % reduction in risk of anemia
Low et al. (2013)	daily	Children (5-12 years)	Risk of anemia reduced by 50% and iron deficiency by 79%
Gera (2007)	daily	Children under 6 years	38-62 % reduction in risk of anemia 6-32 % in malarial endemic regions
Pasricha et al. (2013)	daily	Children (4-23 months)	Risk of anemia reduced by 50 %
De-Regil (2011)	Intermittent	Children under 12 years	Risk of anemia reduced by 49 % and iron deficiency by 76%
Das et al. (2019)	daily	6-23 months	21% reduction in anemia

Multiple micronutrient deficiencies like Fe, vitamin A, B12, and Zn co-occur in developing countries. Therefore, supplementation with multiple micronutrients is generally considered an effective solution. However, a systematic review of 25 trials reported that adding multiple micronutrients to iron supplementation might only marginally improve Hb response compared with Iron supplementation alone. Adding other micronutrients may negatively affect (Gera et al., 2009). The basic assumption behind introducing MMN to iron supplementation is that nutrients act synergistically and may produce an added benefit. However, the mechanism of interaction of many of these micronutrients is poorly understood. The possibility of adverse

and unpredictable effects of co-administration of MMN with Iron cannot be ruled out. Micronutrients are often added to supplements without understanding the complex interaction mechanisms that may lead to poorer haemoglobin response than iron supplementation alone (Gera et al., 2009). A systematic review evaluating the comparative effects of iron supplementation and dietary iron fortification showed that iron supplementation had a better impact on haemoglobin recovery in anemic and iron-deficient children. No difference was observed between iron supplementation and dietary iron fortification in treating adolescents and adults (Silva Neto et al., 2019).

8.4. FOOD FORTIFICATION

The fortification of food staples (rice, wheat, salt, or cornflour) is considered an effective approach for improving the nutritional intake of the general population, with little risk of adverse health effects. The number of countries with mandatory food fortification programs rose from 33 in 2004 to 54 in 2007 and 91 in 2021. Of 91, 90 countries mandated fortification of wheat flour alone or other grains. While one country, Papua New Guinea, has the mandate for rice fortification. 64 countries have legislated for wheat flour alone, 17 countries for wheat flour and maize flour, five countries for wheat flour and rice (Nicaragua, Panama, Peru, Philippines, Solomon Islands), two countries for wheat flour, maize flour, and rice (Costa Rica and the United States) and one country for rice alone (Papua New Guinea) [11].

8.4.1. WHO RECOMMENDATIONS ON WHEAT FLOUR FORTIFICATION

WHO recommends that each country must assess the daily iron intake in the groups at risk of iron deficiency, estimate the iron bioavailability from the diet, compare the estimated iron intake and bioavailability (based on dietary iron bioavailability) and calculate the amount of iron lacking in the diet. This amount of iron should then be added to the mean daily flour consumption of the target group (R. Hurrell et al., 2010). WHO recommended adding 15 ppm iron (NaFeEDTA) for >300 g/day, 20 ppm iron for 150-300 g/day flour intake, 40 ppm for 75-149 g/day flour intakes and <75 g/day flour intakes (Table:8.4). The preferred iron fortificants for wheat flour fortification are NaFeEDTA, ferrous sulfate, and ferrous fumarate (WHO et al.,

[11] Food Fortification Initiative. Global Progress. Accessed on 20/ 11/2021.

2009). The ideal choice for iron fortificants for wheat flour is NAFeEDTA, ferrous sulfate and ferrous fumarate, whereas, for fortification of high extraction wheat flour, only NAFeEDTA is recommended (WHO, 2017).

According to Hurrell and colleagues, the WHO approach to developing the current recommendations combines experimental evidence and pragmatism. With these levels of iron fortification, the fortified flour was expected to significantly improve iron status in women and children to reduce the prevalence of IDA and iron deficiency to rates comparable in Western societies (R. Hurrell et al., 2010). Unfortunately, very few countries have the capability to use this procedure (R. Hurrell et al., 2010).

Table 8:4 Required fortification levels and recommended iron fortification levels (ppm) for Wheat flour according to iron compound and daily flour consumption.

			Level of nutrient to be added in parts per million(ppm) by estimated average per capita wheat flour availability (g/d)			
Nutrient	Flour extraction rate	compound	<75g/d	75-149g/d	150-300g/d	>300g/d
Iron	Low	NaFeEDTA	40	40	20	15
		Ferrous sulfate	60	60	30	20
		Ferrous fumarate	60	60	30	20
		Electrolytic iron	NR	NR	60	40
	High	NaFeEDTA	40	40	20	15
Folic acid	Low or high	Folic acid	5.0	2.6	1.3	1.0
Vit B12	Low or high	Cyanocobalamin	0.04	0.02	0.01	0.008
Vit A	Low or high	Vitamin A Palmitate	5.9	3	1.5	1
Zinc	Low	Zinc oxide	95	55	40	30
	High		100	100	80	70

Source:(WHO et al., 2009)

Note: 1. These estimated levels consider only wheat flour as the main fortification vehicle in a public health program. If other mass-fortification programs with other food vehicles are implemented effectively, these would suggest that fortification levels may need to be adjusted downwards as needed.
2. Estimated per capita consumption of <75 g/d does not allow for the addition of sufficient levels of fortificant to cover micronutrient needs for women of childbearing age. Fortification of additional food vehicles and other interventions should be considered.
3. NR (Not recommended)- because the very high levels of electrolytic iron needed could negatively affect sensory properties of fortified flour.
4. These amounts of zinc fortification assume 5 mg of zinc intake and no additional phytate intake from other dietary sources

8.4.2. RICE FORTIFICATION

Nearly half of the world's population consumes rice as a staple food. From a public health perspective, fortifying rice is similar to the fortification of wheat and maise flour. From a technical and practical perspective, fortifying rice differs from fortifying flour. Compared to wheat and maise, there are few options such as ferric pyrophosphate as iron fortificant available for rice fortification because all other compounds colour the rice brown or gray. The data on the effectiveness and the choice of iron compounds suitable for iron fortification is limited. The recommended iron fortification level for both >300 g/day and 150-300 g/day has been set at 7mg/100 g. The recommended levels for 75-149 g/day and <75 g/day are almost twice as high (12 mg/100g). These fortification levels aim to provide the food's estimated average requirement (EAR). The recommended concentrations for folic acid, vitamin B12 and vitamin A are the same as that for wheat and maise flour fortification (Table:8.5)

Table 8:5 Nutrient levels proposed for fortified rice at the moment of consumption (mg/100g)

Nutrient	Compound	<75g/d	75-149g/d	150-300g/d	>300 g/d	EAR
Iron	Micronized ferric pyrophosphate	12	12	7	7	
Folic acid	Folic acid	0.50	0.26	0.13	0.10	0.192
Vitamin B12	Cyanocobalamin	0.004	0.002	0.001	0.0008	0.002
Vitamin A	Vit A palmitate	0.59	0.3	0.15	0.1	0.357
Zinc	Zinc oxide	9.5	8	6	5	8.2
Thiamine	Thiamine mononitrate	2.0	1.0	0.5	0.35	0.9
Niacin	Niacin amide	2.0	1.0	0.5	0.35	0.9
Vitamin B6	Pyridoxine hydrochloride	2.4	1.2	0.6	0.4	1.1
Source: (de Pee, 2014)						

WHO recommends mass or universal fortification[12] of Wheat and Maize flour in regions where the prevalence of iron deficiency and iron-deficiency anemia in women and children is greater than 5 %. And targeted fortification for population groups (such as infants and children aged

[12] Mass or universal fortification comprises addition of one or more micronutrients to food that is commonly consumed by the public (e.g., cereals, condiments, or milk).

two years or people in emergency settings such as displaced/refugees) with high iron needs that cannot be met through universal fortification.

Besides iron, folic acid, vitamin A and B12 are added to wheat and maize flour. Folic acid, vitamin A and vitamin B12 are not added to flour to prevent anemia but prevent the more specific deficiency symptoms linked to a lack of these micronutrients (R. F. Hurrell, 2015). For example, folic acid is added to increase folate intake to prevent neural tube defects and other congenital anomalies (WHO, 2017).

8.4.3. EFFECTIVENESS OF IRON-FORTIFIED FOODS

A meta-analysis of 60 RCTs showed that consuming iron-fortified foods resulted in average reductions of 41% anemia and 52 % iron deficiency among children and adults (Gupta et al., 2019). A large-scale food fortification with iron had no significant effect on haemoglobin levels (Tam et al., 2020). A recent Cochrane systematic review of 43 RCTs showed that food fortification with multiple micronutrients (MMN) might reduce anemia by 32%, IDA by 72%, micronutrient deficiencies (including iron deficiency by 56%, vitamin A deficiency by 58%, vitamin B2 deficiency by 64%, vitamin B6 deficiency by 91% and vitamin B12 deficiency by 58%) (Das et al., 2019).

The countries without or with flour fortification showed that fortification with iron, folic acid, vitamin A and vitamin B12 was associated with a 2.4 % decrease in the odds of anemia prevalence among non-pregnant women in countries that fortify wheat or maize flour with micronutrients. The countries that had never introduced flour fortification programmes reported no decrease in the odds of anemia prevalence over a similar period (Barkley et al., 2015). The countries selected in the study conformed to the WHO recommendations on iron fortification of flour. Based on the outcome of this study Hurrell (2015) stated that if WHO recommendations are followed, the prevalence of IDA can be decreased. The countries that did not follow WHO recommendations on the fortification of flour, and their national flour fortification programmes, may have little or no effect on the iron status or IDA prevalence in their population (R. F. Hurrell, 2015). A systematic review of efficacy trials demonstrated that fortification of rice with iron (alone or in combination with other micronutrients) might make little or no difference in the risk of anemia. Further studies in the systematic review found that rice fortification may reduce the risk of iron deficiency and increase mean haemoglobin concentration. However, all studies provided low certainty evidence (Peña-Rosas et al., 2019).

It is believed that Fortification, though promising, is not an answer to the global widespread nutritional deficiencies. Widespread malabsorption due to high diarrhoea burdens and enteropathy may be a barrier to fortification strategies. Integration of fortification and supplementation strategies together with other mother and child health and prevention programs may be the answer to address the widespread global under-nutrition and ensure sustainable benefits. Community education and promotion campaigns should also be implemented parallel to the primary fortification programs to increase awareness, acceptability, and equity. Fortification is potentially an effective strategy, but evidence from the developing world is scarce, and future programs also need to assess the direct impact of fortification on morbidity and mortality (Das et al., 2013).

8.5. DEWORMING

The world health organisation recommends periodic treatment with an anthelminthic drug (albendazole) for various age groups, as shown in Table:8.6.

Table 8:6 Dose and regimen of Deworming

Target population	***Baseline prevalence of STH***	***Frequency***	***Dose of Deworming***
All children younger than 24 months	≥ 20 %	Annually	Half dose of Albendazole i.e., 200 mg
	>50 %	Biannually	
All Children (1-12 years) and adolescents (12-23 years)	≥ 20 %	Annually	Single dose Albendazole 400 mg or Mebendazole 500 mg
	>50 %	Biannually	
All Non-pregnant and WRA	≥ 20 %	Annually	Single dose Albendazole 400 mg or Mebendazole 500 mg
	>50 %	Biannually	
*All Pregnant women after the first trimester	≥ 20 % and anemia prevalence ≥ 40 %	Annually	Single dose Albendazole 400 mg or Mebendazole 500 mg
	>50 %	Biannually	
Source: (WHO, 2017) Note: In the case of pregnant women, the helminthic drug is recommended for STH and *T. trichiura* infection			

8.5.1. EFFECTIVENESS OF DEWORMING PROGRAMMES

Hookworms are common in tropical and subtropical areas, particularly in sub-Saharan Africa and Southeast Asia. According to one estimate, one-third to one-half of total moderate to severe cases of anemia in pregnant women and children are due to hookworm infestation. Therefore, the Dose of the anthelminthic drug is expected to provide therapeutic and preventive effects on anemia prevalence (WHO, 2017).

A Cochrane systematic review of the effect of large-scale deworming programmes on school children concluded that treating children known to have worm infection with the anthelminthic drug may have some nutritional benefits for the individual. However, mass treatment of children with the anthelminthic drug in endemic areas did not improve average nutritional status, haemoglobin levels, cognitive ability, school performance, or survival (Taylor-Robinson et al., 2012). The review demonstrated a lack of solid scientific evidence to support a deworming programme. The paper's findings contradicted WHO's current recommendations on periodic deworming of all children and women in areas where many people are affected by worm infection, including India, sub-Saharan Africa, East Asia, and the Americas. This finding by Cochrane's systematic review sparked a debate and raised concerns over the significance of deworming programmes.

A recent systematic review on the effect of deworming programmes among pregnant women (R. A. Salam et al., 2021), non-pregnant women and adolescent girls (Tanjong Ghogomu et al., 2018) and among children (Welch et al., 2016) showed results consistent with Taylor-Robinson et al. (Taylor-Robinson et al., 2012). These studies among different age and population groups highlight that mass deworming for soil-transmitted helminths has little to no effect on growth, haemoglobin, cognitive development, and school attendance. The evidence to date is insufficient to recommend the use of antihelminth drugs.

One of the reviews concluded that:

> *"Mass deworming may reduce the prevalence of soil-transmitted helminths infections but have little or no effect on anemia and iron deficiency in non-pregnant women and adolescent girls. We are uncertain about the effect on severe anemia. The results of the paper are limited by sparse data and the moderate to very low quality of evidence" (Tanjong Ghogomu et al., 2018).*

In contrast to these findings, some studies have argued that children treated with deworming medications grow better and have better cognitive performance, reduced stunting and reduced anemia (Lo et al., 2018). Other studies argued that large-scale repeated administration of anthelminthic drugs could reduce the burden of soil-transmitted helminths, potentially reducing morbidity among individuals heavily infected by soil-transmitted helminth infections. These studies raised questions about the methodology of the Taylor-Robinson et al. (2012) study. They distinguished that a lack of evidence to support effectiveness cannot be considered evidence of ineffectiveness (De Silva et al., 2015).

8.6. ISSUES IN INTERPRETING THE RESULTS OF EFFICACY TRIALS

"The Cochrane Collaboration (CC) was created in 1993 to systematically review published research to facilitate the selection of appropriate interventions by health professionals and policymakers. CC systematic reviews focus on a wide range of healthcare interventions and typically consider the evidence only from randomised controlled trials (RCTs). Because they rely on chance to minimise the potential for epidemiological confounding, RCTs are commonly acknowledged as the strongest, least biased source of evidence on particular therapies or medical interventions for clinical practice. Similarly, it is well known that their utility in evaluating public health interventions is not always optimal and, as a consequence, can result in distorted conclusions" (Montresor et al., 2015).

Efficacy trials evaluate the impact of test intervention under ideal circumstances. Most of the efficacy trials assessing the effect of supplementation and fortification have improved the micronutrient status and reduced iron deficiency and IDA. Though the efficacy of clinical trials is well established by now, very few supplementations and fortification programmes have been rigorously evaluated for their impact on iron status and anemia (WHO, 2006). Without an adequate evaluation of the effectiveness of programmes, it is difficult to know whether the changes in nutritional status of the population group are due to the intervention or improvement in socio-economic condition, improved provisioning of public health services, or increased consumption of diversified food (R. F. Hurrell, 2015). The evidence that iron supplementation and food fortification programmes improve nutritional status is derived from either efficacy trials or reports of programme effectiveness. Numerous efficacy trials on iron supplementation

and fortification conducted in controlled feeding situations have documented the impact of supplements and fortified foods on iron deficiency, IDA, or anemia. The evidence of programme effectiveness in comparison to efficacy trials is significantly less. Additionally, as a new understanding of iron biology, the impact of iron administration, supplementation and food fortification strategies emerge, preventing and controlling anemia are increasingly being questioned (R. F. Hurrell, 2015). Also, concerns are being raised over iron overload and its adverse consequences for health.

Though most efficacy trials demonstrate improvements in haematological indices, good quality evidence that these laboratory improvements translate into clinical improvements or improvements in functional health outcomes is lacking. Very few RCTs assess clinical outcomes (Reveiz et al., 2011). There is a lack of evidence to measure the effects of iron supplements and food fortificants on underlying metabolic and hormonal changes that could detect, predict and explain functional responses (L. H. Allen, 2002).

The efficacy trials often do not identify the various causes of anemia (poverty and undernutrition) or the relative contribution of different micronutrient deficiencies, haemoglobinopathies, malaria, worm infestations, and other coexistent infections. There are limited data on how micronutrient interventions affect population groups with variable health status and underlying micronutrient deficiencies and levels of malnutrition. They do not provide information on the objective of the micronutrient intervention (whether they are meant for therapeutic purposes or preventive), nor do they report possible adverse effects of micronutrient interventions (Reveiz et al., 2011).

Many efficacy trials evaluating the iron supplementation and fortification strategies are small and bear significant methodological flaws. Due to variable study questions and research designs, different target population groups, variable doses, frequency and duration of intervention, various forms of iron and variable use of other micronutrients, it becomes challenging to pool and compare the data in a meaningful way. The results of efficacy trials are confusing and conflicting; they produce a low to very low quality of evidence to conclude their impact on anemia outcomes. There is a lack of robust data on the effectiveness of iron supplementation, food fortification and deworming programmes.

Additionally, many of the trials are fully or partially commercially funded. Concerns are being raised against the possible association between commercial funding and more positive findings

of the trials (Das et al., 2019). These factors have made public health scientists question the effectiveness of iron supplementation and food fortification programmes. There is a lack of adequate data to inform the real-life benefits of micronutrient intervention programmes. Including such data and understanding an intervention's biological potential through the synthesis of trial efficacy data will better guide policymaking and inform recommendations of the interventions that are likely to be successful in uncontrolled environments.

8.7. SUMMARY

Anemia control Programmes have evolved and expanded to include all age groups, revised and lowered the iron doses, and changed the frequency and duration of the treatment regimen. The limited understanding of the relationship between iron and folic acid dose and their subsequent effect on haemoglobin concentration and functional outcome have made it difficult to predict the accurate Dose and frequency of iron. Similarly, inadequate information on iron biology has led to an indecisive change in treatment duration.

Anemia prevalence remains high globally, especially in developing countries. One of the most common reasons cited for high prevalence is the poor effectiveness of programmes in terms of coverage, unavailability of IFA tablets, poor adherence to the use of supplements mainly due to its side effects such as nausea, vomiting, colic and diarrhoea, prompting individuals to discontinue the treatment, and thus decreasing effectiveness (Silva Neto et al., 2019). While poor coverage of the programme may limit its effectiveness, it cannot be the sole reason for the high prevalence of anemia. Though efficacy trials under the controlled conditions demonstrate significant improvement in haematological indices, it does not eliminate anemia in study population groups (Sood et al., 1979). The evidence shows that Iron supplementation and food fortification may only be efficacious in preventing anemia if anemia is due to iron deficiency. According to WHO, only 50 % of anemia is amenable to iron-centric interventions (WHO, 2011b). The lower Haemoglobin response to iron and micronutrient supplementation in malaria hyperendemic areas confirms that these micronutrients alone cannot address the problem of anaemia in such settings (Gera & Sachdev, 2002).

The iron supplementation and food fortification strategies look promising for reducing iron deficiency and IDA in the population. Still, the low quality of evidence from efficacy trials

raises questions over their effectiveness in real-life settings. Also, the impact of these interventions on other causes of anemia is not well understood (WHO, 2006).

There is a need to identify evidence-based population-specific etiologies of anemia to design appropriate intervention strategies. For a long time, anemia has been identified as a multifactorial problem requiring integrated intervention strategies besides evidence-informed doses of iron supplements and iron-fortified foods. The current approaches to estimating iron doses, treatment frequency and duration are not backed by sound epidemiological investigations. There is little evidence-based information about the exact amounts of iron, forms and frequency that need to be supplemented. Moreover, because of excessive iron overload, there is a strong possibility that these approaches may have adverse health consequences.

CHAPTER 9

"Imlicit bias is the single most important determinant of health and health care disparities"

Dayna Brown Matthew

CHAPTER 9. ANEMIA PREVENTION AND CONTROL STRATEGIES IN INDIA

9.1. INTRODUCTION

This chapter discusses the evolution and programmatic shifts in anemia control strategies in India and critically analyses the programmatic responses within social determinants of health framework.

9.1.1. NATIONAL NUTRITIONAL ANEMIA PROPHYLAXIS PROGRAMME

India was one of the first countries to initiate a programme in 1970, i.e., the National Nutritional Anemia Prophylaxis Programme (NNAPP), during the fourth five-year plan, in response to global policy actions to contain and prevent anemia. NNAPP was started with only three target beneficiary groups -pregnant women and lactating women, intrauterine device acceptors (IUD), and pre-school children (1-5 years). The recommended doses for Pregnant women, lactation women and IUD acceptors were one large tablet containing 60 mg of elemental iron and 500 µg folic acid daily for 100 days, for severe anemic women (<7g/dl), a large tablet (60mg elemental iron & 500 µg folic acid) twice daily for 100 days. For pre-school children, one small tablet containing 20 mg of elemental Iron and 100 µg folic acid daily for 100 days and for those who could not swallow tablets, liquid syrup containing the same amount of IFA was recommended.

9.1.2. NATIONAL NUTRITIONAL ANEMIA CONTROL PROGRAMME

In 1991, the Ministry of Health and family welfare (MOHFW) revised the guidelines. Under the new guidelines, NNAP was modified to the National Nutritional anemia control Programme (NNACP). Doses of Iron in Pregnant women were increased to 100mg of elemental iron in the form of one large adult tablet. At the same time, doses for lactating women, IUD acceptors and pre-school children remained the same as in NNAPP. For severe anemia, women in the reproductive age group were recommended to take three adult tablets (equivalent to 180mg elemental iron and 1500 µg folic acid) per day for 100 days. Components of Information, education, and communication (IEC) were added to raise awareness and increase the

consumption of iron-rich food. For example, drinking tea was discouraged as it may inhibit the absorption of Iron in the stomach (MOHFW, 1991)[13]. The objectives and programme components did not change much. However, the focus shifted from prevention to control and management of the anemia (Kapil et al., 2019).

9.1.3. NATIONAL NUTRITION POLICY AND INTEGRATION OF NNACP WITH OTHER SCHEMES

In 1993, the National Nutrition Policy, with the objective of operationalising multi-sectoral strategies to address undernutrition/malnutrition, came into being. In 1995, the National plan of action on nutrition was formulated to lay out a sectoral plan of action for 14 ministries and departments of the government of India. The national nutrition mission set up under the Ministry of Women & child development (MWCD) suggested multi-sectoral approaches to address the problem of iron deficiency anemia in India in a mission mode. In 1992, NNACP was made an integral part of the Child Survival and Safe Motherhood Programme (CSSMP). In 1997, the programme was integrated into Reproductive and Child Health (RCH), and in 2005 was merged with National Rural Health Mission (NRHM).

In 2007, NNACP was revised to include the liquid formulation of ferrous sulphate and folic acid, containing 20 mg elemental iron and 100 µg folic acid for children aged 6-60 months and expanded to include school children (6-10 years) and adolescents (11-18 Years). The recommended doses for children aged 6-10 years were 30 mg elemental iron and 250 µg folic acid daily for 100 days in a year. For adolescents, recommended doses and duration remained the same as for adults. Besides Iron and folic acid supplementation, double fortified salts, sparklers, and other micronutrients were suggested as an alternative strategy (MW&CD, 2007).

9.1.4. WEEKLY IRON FOLIC ACID SUPPLEMENTATION (WIFS)

In 2012, weekly iron-folic acid supplementation (WIFS) programme for adolescents (10-19 years) was launched that administered a weekly dose of enteric-coated (EC) 100 mg elemental iron and 500 µg folic acid with biannual deworming to adolescents having poor bioavailability of Iron (MoHFW, 2013). The evidence suggests that enteric-coated tablets release iron in the

[13] https://hetv.org/pdf/anaemia-policy.pdf accessed on 11 Nov,2021.

lower parts of the intestine, having a lower acidic environment, where bioabsorption is low. The absorption of iron from EC tablets was lower than from non-EC tablets. Many countries, including the National Health Services (NHS) of the United Kingdom, do not recommend using modified-release iron formulations (EC) for the treatment of anemia (Kapil et al., 2019).

9.1.5. NATIONAL IRON PLUS INITIATIVE (NIPI)

In 2013 MoHFW initiated the National Iron Plus Initiative, which adopted a life cycle approach comprising age-appropriate Iron and folic acid supplementation for all age groups and treatment protocol for facility-based anemia management. NACP and WIFS were integrated into NIPI. Age-specific doses under NIPI remained the same. NIPI, through the life cycle approach, envisioned establishing a continuum of care through a service of packages for treatment and management of anemia across levels of care. Besides medical interventions, NIPI emphasised the need to bring a behaviour change (dietary habits and compliance) to control anemia (MoHFW, 2013).

9.2. NATIONAL NUTRITION STRATEGY AND POSHAN ABHIYAN

In 2017, National Institution for Transforming India (NITI) aayog laid out the National Nutrition Strategy (NNS) with 'vision 2022- 'Kuposhan Mukt Bharat' (Free from malnutrition, across the life cycle). NNS chalked out strategies to reduce anemia prevalence among young children, adolescent girls and WRA by one-third of NFHS-4 levels by 2022[14]. Most of these strategies were integrated into Prime Minister's Overarching Scheme for Holistic Nutrition (POSHAN), launched in 2018 to address the problems of malnutrition in mission mode. Complying with the targets of POSHAN Abhiyaan and the National Nutrition Strategy set by NITI Aayog, NIPI was changed to Intensified National Iron Plus Initiative (I-NIPI), popularly known as Anemia Mukt Bharat (AMB). AMB aimed to intensify the efforts to reduce anemia prevalence by three percentage points per year among children, adolescents, and women in the reproductive age group (15–49 years) between 2018 and 2022.

[14] https://pib.gov.in/newsite/printrelease.aspx?relid=174442 accessed on 10 January, 2022.

9.2.1. INTENSIFIED NATIONAL IRON PLUS INITIATIVE (NIPI-I)/ ANEMIA MUKT BHARAT (AMB*)*

Under NIPI-I, the recommended doses for children aged 6-59 months are 20 ml elemental iron + 100 µg folic acid biweekly, for children aged 5-9 years, 45 mg elemental iron+ 400 µg folic acid weekly, for adolescents aged 10-19 years, 60 mg elemental iron + 500 µg folic acid weekly, for pregnant women and lactating mothers 60 mg elemental iron + 500 µg folic acid daily and women of reproductive age group a tablet containing 60 mg elemental iron + 500 µg folic acid weekly (MoHFW, 2018). Under AMB scheme, the recommended IFA doses among children aged (6-10 years) were increased to 45 mg elemental iron+ 400 µg folic acid from 30 mg elemental iron+250 µg folic acid. At the same time, in adolescents (10-19 years), pregnant women, lactating women and WRA iron doses were reduced from 100 mg elemental iron+ 250 µg folic acid to 60 mg elemental iron + 250 µg folic acid. The chronological evolution of programmes and shifts in doses, frequency and target groups are illustrated in Table:9.1

Table 9:1 evolution of programmes and intervention strategies

Year	Programme	Target group	Intervention	Highlights
1970	National Nutritional Anaemia Prophylaxis Programme (NNAPP)	Pregnant and Lactating women	60mg iron and 500µg folic acid daily for 100 days	poor coverage, monitoring, compliance, and lack of screening.
		Children 1-5years	20mg iron and 100µg folic acid daily for 100 days	
1990	National Anaemia Control Programme	Pregnant, Lactating women and Children 1-5 years	Dosage changed to 100 mg iron in pregnancy. Anemic person receives 2 tablets	Emphasis on screening of anemia and improving coverage.
2012	Weekly Iron Folic Acid Supplementation Programme	Adolescent girls and boys enrolled in government/government aided/municipal schools from 6th to 12th classes, and Adolescent Girls who are not in school	100mg elemental iron and 500µg folic acid for 52 weeks in a year	Fixed day approach for weekly IFA distribution, Branding of IFA as blue WIFS
2013	National Iron Plus Initiative (NIPI)	Life cycle approach	Targeted approach for anemic persons and mass programme for non-anaemic persons Age-specific doses remained unchanged	Tie-up with NRHM. The colour of the IFA tablet for adolescent girls was changed to blue. Auto dispenser for feeding biweekly iron syrup to children.
2018	Poshan Abhiyaan	Prime Ministers Overarching Scheme for Holistic nutrition for all age groups		Leveraging technology, a targeted approach and convergence (food

				fortification, supplementation, anemia)
2018	Intensified National Iron plus initiative (I-NIPI). (Anemia Mukt Bharat)	6X6X6 strategy	The iron dosage was reduced from 100 mg elemental iron + 500 µg folic acid to 60 mg+500 µg folic acid for adolescents, pregnant women and WRA. Iron dose among children aged 6-10 years increased to 45 mg elemental iron + 400 µg folic acid from 30 mg elemental iron + 250 µg folic acid	Test, Treat and Talk Camp

9.2.1.1. COMPARISON OF INDIAN AND WHO'S GUIDELINES ON IRON SUPPLEMENTATION

A comparative analysis of Indian and WHO guidelines on Iron and folic acid supplementation highlights differences in recommended iron supplementation strategies regarding doses, frequency, and duration. Indian guidelines recommended higher Iron and folic acid doses for pregnant and lactating women than the WHO guidelines. A comparative illustration of recommended iron and folic doses, frequency, and duration between India and WHO for various age groups is shown in Table:9.2.

Table 9:2 Comparative picture of IFA supplementation between India and WHO guidelines

Parameters	***NIPI-I, 2018***	***WHO guidelines***
Infants aged 6-23 months		
Dose of Iron	1 ml IFA syrup containing 20 mg elemental iron and 100 µg folic acid	10-12.5 mg elemental iron/kg
Frequency	Biweekly	Daily
Duration	Throughout the year	Three consecutive months in a year
Children aged 24-59 months		
Dose of Iron	1 ml IFA syrup containing 20 mg elemental iron and 100 µg folic acid	30 mg elemental Iron
Frequency	Biweekly	Daily
Duration	Throughout the year	Three consecutive months in a year
Children aged 5-10 years		
Dose of Iron	1 IFA sugar-coated tablet (Pink colour) containing 45 mg elemental iron and 400 µg folic acid	30-60 elemental Iron
Frequency	weekly	Daily
Duration	Throughout the year	Three consecutive months in a year
Children and adolescents aged 10-19 years		
Dose of Iron	1 IFA sugar-coated tablet (Blue colour) containing 60 mg elemental iron and 500 µg folic acid	30-60 elemental Iron
Frequency	Weekly	Daily
Duration	Throughout the year	Three consecutive months in a year
Pregnant and Lactating women		
Dose of Iron	1 IFA sugar-coated tablet (red colour) containing 60 mg elemental iron and 500 µg folic acid	30-60 elemental iron and 400 µg of folic acid

Frequency	Daily	Daily
Duration	To be started from the second trimester, continued throughout pregnancy (minimum of 180 days) and to be continued for 180 days post-partum	Throughout the pregnancy for pregnant women and 6-12 wk post-partum for lactating women
Women of reproductive age group		
Dose of Iron	1 IFA sugar-coated tablet (Red) containing 60 mg elemental iron and 500 µg folic acid	30-60 mg of elemental Iron and 400 µg of folic acid
Frequency	weekly	Daily
Duration	Throughout the year	Three consecutive months

Source: Compiled from (MoHFW, 2018) and (WHO, 2017)

9.2.2. 6X6X6 STRATEGY OF AMB

Anemia Mukt Bharat encompasses the '6X6X6' strategy that implies six age groups, six interventions and six institutional mechanisms (Table:9.3) (MoHFW, 2018).

Table 9:3 AMB 6X6X6 strategy

Six beneficiaries	***Six interventions***	***Six institutional mechanisms***
Children (6-59 months)	Prophylactic Iron and Folic Acid Supplementation	Inter-ministerial coordination
Children (5-9 years)	Deworming	National AnemiaMukt Bharat Unit
Adolescent girls and boys (10-19 years)	Intensified year-round Behaviour Change Communication (BCC) Campaign and delayed cord clamping	National Centre of Excellence and Advanced research on Anemia Control
Pregnant women	Testing of anaemia using digital methods and point-of-care treatment	Convergence with other ministries
Lactating women	Mandatory provision of Iron and Folic Acid fortified foods in government-funded health programmes	Strengthening supply chain and logistics
Women of Reproductive Age (WRA) group (15-49 years)	Addressing non-nutritional causes of anaemia in endemic pockets with a special focus on malaria hemoglobinopathies and fluorosis	Anemia Mukt Bharat Dashboard and Digital Portal-one-stop-shop for anemia.

Source: (MoHFW, 2018)

9.2.2.1. SIX AGE GROUPS

AMB continues with a life cycle approach of bringing all age groups under the domain of programme strategies. The six beneficiaries identified under AMB programme are children (6-59 months), children (5-9 years), adolescent girls and boys (10-19 years), pregnant women, lactating women, and Women of reproductive age group (15-49 years). Adult males above the age of 19 are not included in the programme.

9.2.2.2. SIX INTERVENTION STRATEGIES

The six intervention strategies under AMB strategies are: i) Prophylactic Iron and Folic Acid Supplementation ii) Deworming iii)Intensified year-round Behaviour Change Communication (BCC) Campaign and delayed cord clamping iv)Testing of anaemia using digital methods and point of care treatment v) Mandatory provision of Iron and Folic Acid fortified foods in government-funded health programmes vi) Addressing non-nutritional causes of anaemia in endemic pockets with special focus on malaria hemoglobinopathies and fluorosis.

9.2.2.2.1. PROPHYLACTIC IRON AND FOLIC SUPPLEMENTATION

This chapter's earlier section on Intensified National Iron Plus Initiative (NIPI-I) includes a detailed description of the regimen of Iron and folic supplementation.

9.2.2.2.2. DEWORMING

India has the highest burden of soil-transmitted helminths globally, with 241 million children (68 % of the children in this age group and approximately 28 % of children estimated to be at risk of STH infections globally) at risk of parasitic worm infections. "Soil-transmitted helminths interfere with nutrient uptake in children; can lead to anemia, malnourishment and impaired mental and physical development" (NDD, 2015). Ministry of Health and family welfare (MoHFW) launched the world's largest national mass deworming program on 10th February 2015 to control soil-transmitted helminths. The programme was started to provide albendazole twice a year to an initial 140 million children aged 1-19 years in 11 states with presumed high levels of soil-transmitted helminths and once a year to 100 million children in other states in schools and pre-schools**.** Under Anemia Mukt Bharat, the age and population groups covered under the program have been expanded to include children, non-pregnant and lactating women, and pregnant women. Children under the age of five years, out-of-school children and adolescents are provided deworming tablets (albendazole) at Anganwadi centres by Anganwadi Worker (AWW).

In contrast, school-going children and adolescents receive deworming treatment through school platforms. Non-pregnant and non-lactating newlywed or married women (20-24 years) are provided biannual deworming during National deworming day. MoHFW organises a National Deworming Day programme biannually on 10th February and 10th August every

year. Under this strategy, pregnant women are given deworming treatment during the second trimester through antenatal care contacts such as Antenatal clinics (ANC) and village health nutrition day (VHND), as shown in Table:9.4.

Table 9:4 Dose and Regime for deworming

Age group	***Dose and Regime***
Children 12–59 months of age	Biannual dose of 400 mg albendazole (½ tablet for children 12–24 months and 1 tablet to children 24–59 months)
Children 5–9 years of age	Biannual dose of 400 mg albendazole (1 tablet)
School-going adolescent girls and boys (10–19 years) and Out-of-school adolescent girls (10–19 years)	Biannual dose of 400 mg albendazole (1 tablet)
Women of reproductive age (20-49 years) (non-pregnant, non-lactating)	Biannual dose of 400 mg albendazole (1 tablet)
Pregnant women	One dose of 400 mg albendazole (1 tablet) after the first trimester, preferably during the second trimester
Source: (MoHFW, 2018)	

WHO recommends biannual deworming for every population group with anthelminthic drugs in areas where the baseline prevalence of STH infections is over 50% (WHO, 2017). The recommendation for deworming in India is consistent with WHO guidelines, assuming helminthic prevalence is high across age, population groups and regions. In the lack of nationally representative data on STH infections, the information on the distribution and prevalence of STH infection in India is scarce and scattered. A systematic search of published literature from 19 states reported lower than 20 % STH infection across most locations and between 20-50 % prevalence in other locations (N. Salam & Azam, 2017).

The efficacy of deworming programmes on improving the nutritional indicators, weight gain, cognitive ability and improved school attendance is highly contentious (Discussed separately in another chapter). A landmark paper published in 2013 concluded that taking albendazole twice a year had little impact on weight gain and mortality after two years of treatment. The study, however, did not rule out the effects of mortality in other populations but concluded that any such effects were likely to be small if any (Awasthi et al., 2013). The document on the operational guideline for national deworming day states that deworming can lead to increased nutritional status and physical and cognitive development due to reduced STH infections

(NDD, 2015). Reacting to the government's launch of India's mass deworming programme, a study published in the *Journal of BMC* quoted the view of *Professor Paul Garner from the Liverpool School of Tropical Medicine. He said:*

> *"Deworming programmes are presented as a panacea, a single solution to multiple problems in low- and middle-income countries. The belief that deworming will substantially impact economic development seems delusional when you look at the results of reliable controlled trials". We are not saying children with worms should not be treated. It is just that there is a particular emphasis on the deworming programme in India. The deworming community says it does not cost very much but talk to India's administration, and it is a massive scale-up. It is the country's money. It is people's resources that are involved. It is not cheap to deliver. There are other things to do in the world" (Mudur, 2015).*

The evidence shows that the prevalence and control of STH infections are linked to socioeconomic, environmental and water quality, sanitation, and hygiene practices in the affected areas. Mass deworming may reduce the infection in areas with heavy STH infection load, but eradication is difficult. Deworming is unlikely to impact areas where STH loads have tapered down (Mudur, 2015). Because of STH's fecoral (faecal-oral route) and penetration via skin transmission, the chances of reinfection remain high among the population living in endemic areas (N. Salam & Azam, 2017). The worm control may be achieved by the targeted use of chemotherapy and improving sanitation, drinking water, and pit latrines. However, the efficacy trials evaluating the outcome of deworming on anemia remain inconclusive and controversial.

9.2.2.2.3. FOOD FORTIFICATION

The history of food fortification in India dates to the 1950s when 'Vanaspati fortification with vitamin A was mandated. In the 1970s, the National Institute of Nutrition created iron-fortified salt[15]. In the same year, voluntary wheat flour fortification standards were notified. Subsequently, many state governments such as West Bengal, Rajasthan, Kerala, Madhya Pradesh, West Bengal, Tamil Nadu, Haryana, Gujarat, Andaman and Nicobar Islands, and

[15] https://ffrc.fssai.gov.in/micronutrient#iron accessed on 03/01/2022

Jammu & Kashmir went ahead with fortified wheat flour in the public health programmes or through market channels. In 1986, a national salt iodisation policy was adopted, and subsequent legislation in 2005 prohibited the sale of non-iodised salt for human consumption, both at the national and state level. National Nutrition Policy of 1993 emphasised fortifying essential food items with iodine and Iron as a short-term direct intervention. Food fortification was also promoted and seen as an instrument to alleviate large-scale malnutrition, including anemia, in India's 10th, 11th, and 12th national five-year plan[16].

India's National Institute of Nutrition (NIN) developed double fortified salt (DFS) with iodine and Iron, a significant breakthrough for tackling iron and iodine deficiency. DFS providing 3.3 mg ferrous fumarate was shown to cause significant improvements in Hb, ferritin, soluble transferrin receptor and body iron among female tea pickers for nine months (Haas et al., 2014). In 2009, the Ministry of health and family welfare endorsed the addition of Iron in DFS at 0.8-1.1 parts per million (PPM) (mg/g of salt) (FFI, 2015). However, under the compositional standards contained in the Food Safety & Standards (Food Products Standards & Food Additives) Regulations, 2011, manufacturers were not obliged to fortify many foods-stuffs – exemptions include margarine and infant formula.

9.2.2.2.3.1. MANDATORY FOOD FORTIFICATION

India's fortification landscape changed with the release of the Food Safety & Standards (fortification) regulation in 2016. This legislation introduced the mandatory fortification of rice, salt, and flour (including Atta, Maida, and Vanaspati), considered a staple for the Indian population. With this legislation, the Government of India introduced the mandatory fortification of salt with iodine and Iron and wheat flour with iron, folic acid, and Vitamin B-12. The social safety-net programs in the country, including the public distribution system, mid-day meal scheme, and the integrated child development services program, are now mandated to use these fortified products to benefit the vulnerable population in society.

Under the food safety & standard regulation, 2016, three food items, Atta, Maida and Rice, were mandated to fortify with Iron, folic acid, and vitamin B12. Food safety & standard regulation, 2016 was revised and updated in 2018 to be called food safety & standard

[16] https://static1.squarespace.com/static/5e1df234eef02705f5446453/t/5f98953f92b51472c1592e8d/1603835236613/India_Journey.pdf accessed on 01/01/2022

(fortification of food) regulation, 2018. The level of fortification per kilogram of iron, folic acid, and vitamin B12 was reduced; new vehicles for iron fortification were also recommended in the latest guidelines (FSSAI, 2018). The recommended level of fortification, the form of vehicle for iron fortification and shift in approaches are shown in Table:9.5

Table 9:5 level of fortification in foodstuff (India vs WHO)

Level of fortification per kg					
			FSSAI, 2016	***FSSAI, 2018***	***WHO (ppm)***
Atta	Iron	Ferrous citrate or Ferrous lactate or Ferrous sulphate or Ferric pyrophosphate or electrolytic Iron or Ferrous fumarate or Ferrous BisGlycinate;		28 - 42.5 mg*	20
		Or Sodium Iron (III) Ethylene diamine tetra Acetate. Trihydrate (Sodium feredetate-Na Fe EDTA	20 mg	14 - 21.25 mg	15
	Folic Acid		1300 µg	75 - 125 µg	1
	Vitamin B12-Cyanocobalamine or Hydroxycobalamine		10 µg	0.75 - 1.25 µg	0.008
Maida	Iron	Ferrous citrate or Ferrous lactate or Ferrous sulphate or Ferric pyrophosphate or electrolytic Iron or Ferrous fumarate or Ferrous BisGlycinate;	60 mg	28 - 42.5 mg*	
		Or Sodium Iron (III) Ethylene diamine tetra Acetate. Trihydrate (Sodium feredetate-Na Fe EDTA		14 -21.25 mg	
	Folic Acid		1300 µg	75 - 125 µg	
	Vitamin B12 - Cyanocobalamine or Hydroxycobalamine		10 µg	0.75 - 1.25 µg	
Rice	Iron	Ferric pyrophosphate	20 mg	28 - 42.5 mg*	7
		Sodium Iron (III) Ethylene diamine tetra Acetate. Trihydrate (Sodium feredetate-Na Fe EDTA		14 - 21.25 mg	NR
	Folic Acid		1300 µg	75 - 125 µg	0.192
	Vitamin B12 - Cyanocobalamine or Hydroxycobalamine		10 µg	0.75 - 1.25 µg	0.002
Note: * - added at a higher level to account for less bioavailability					

Source: Compiled from FSSAI, 2016 & FSSAI, 2018

Studies from India have shown positive effects of food fortification. Fortified wheat flour introduced in Indian social safety net programs such as Midday Meal (MDM) and Public distribution system (PDS) in Gujarat effectively eliminated the deficiencies due to inadequate intakes of iron and Zinc. Insufficient iron intake was reduced by 94 % among PDS beneficiaries (Fiedler et al., 2012). Another study showed that iron fortification of whole wheat flour reduced iron deficiency from 62 % to 21 % and IDA from 18 % to 9 % after seven months of taking fortified flour among school-aged children in Karnataka and Maharashtra (Muthayya et al., 2012). Other efficacy trials evaluating the impact of iron-fortified rice and multiple micronutrients fortified rice among school children in Bangalore decreased IDA from 30 % to

15 % (Moretti et al., 2006) and improved plasma vitamin B 12 and homocysteine concentration, respectively (Thankachan et al., 2012). Most studies investigating the effect of iron fortification used high amounts of iron (above 10 mg/100g). The studies using even low concentrations (3mg/100g) decreased anemia prevalence (Steiger et al., 2014). A study conducted to assess the impact of Rice fortification in the Gadchiroli district of Maharashtra from 2018 to 2020 through the public distribution system (PDS) showed a reduction of 21.4 % in anemia prevalence among women, adolescents, and children. A micronutrient fortified rice provided through Mid-day meal (MDM) for eight months improved mean haemoglobin levels by 0.4g/dl and reduced anemia prevalence by 10 % among school children (Mahapatra et al., 2021).

9.2.2.3.2. COMPARISON BETWEEN INDIAN AND WHO GUIDELINES ON FORTIFICATION

Wheat and rice are the staple food for most Indians. According to National Nutrition Monitoring Bureau (NNMB) survey (2012), the average intake of cereals and millets in India was 375g/CU/day, providing more than 70% of Recommended Dietary Intake (RDI). Based on dietary consumption, wheat, salt, rice, milk, and oil are identified as the appropriate vehicle for fortification in India[17]. There are marked differences between WHO and Indian guidelines for fortifying wheat and rice. The recommended iron levels added to Atta (Wheat flour) and rice according to Indian guidelines are higher than WHO. There is also a difference in recommended levels of folic acid and vitamin B12 fortificants added to wheat and rice by FSSAI and India (Table:5). High levels of iron fortificants suggested by FSSAI are probably because of the lower iron bioavailability of Indian foods.

9.2.2.2.4. BEHAVIOURAL CHANGE COMMUNICATION STRATEGIES

It is generally believed that poor coverage of IFA supplementation programmes, insufficient dietary intake or poor bioavailability of Indian foods, and inappropriate and insufficient feeding practices (including complementary feeding practices) are factors for the high prevalence of nutritional anemia. The knowledge about Iron-rich foods such as spinach, legumes, green leafy vegetables, meat, and fish and the foods that enhance or inhibit the absorption of Iron can have

[17] https://ffrc.fssai.gov.in/commodity?commodity=fortified-wheat-flour accessed on 03/02/2022

a considerable impact on an individual's nutritional status (L. Allen et al., 2001). Nutrition and health awareness can increase the consumption of IFA tablets (Pal et al., 2013), change eating behaviours and improve haemoglobin levels (Shet et al., 2019).

NIPI and NIPI-I emphasise changing or inducing new behaviour among the population through behavioural change communications.

> *"Since anaemia is not just about medical interventions but to a great degree about behaviour change (both in terms of dietary habits and compliance), an extensive communication campaign will be developed" (MoHFW, 2013) .*

Behavioural change communication strategies under AMB seek to bring desired behaviour change among the target population through various activities such as nutrition education, counselling, sensitisation meetings for the school teachers, administration, media, faith leaders, panchayat leaders, village health sanitation and Nutrition Committee (VHSNC) (MoHFW, 2018) with the objective to;

i) increase adherence and compliance to IFA supplementation and deworming
ii) use appropriate Infant and young child feeding (IYCF) practices, including complementary foods for children above six months
iii) Increase the intake of iron-rich, protein-rich and vitamin C rich foods through dietary diversification and food fortification
iv) Promote delayed cord clamping (by at least 3 minutes or until cord pulsation ceases) in all health facility deliveries, followed by early initiation of breastfeeding within one hour of birth.

Behavioural change interventions were an important component of NIPI. AMB plans to use multiple approaches to educate health workers and the general population at risk of anemia through various channels to bring the desired behavioural change. The prevalence of anemia continues to be high despite such intervention strategies.

The evidence supporting that increased knowledge and awareness related to better health and nutrition leads to a change in behaviour is weak. Also, there is less likelihood of achieving a sustained behaviour change through a single activity. The evidence suggests that multiple channels and approaches are more effective than a single approach (Lamstein et al., 2014).

Several specific behaviours and practices contribute to a population's health and nutrition, and complex contextual determinants influence and shape those individual decisions to adopt and sustain a given behaviour or practice.

A systematic review by the Strengthening Partnerships, Results, and Innovations in Nutrition Globally (SPRING) assesses the available evidence on effective approaches to social and behavioural change communication (SBCC) for preventing stunting and anemia. The study concluded that while literature may reflect a bias to publish positive results, SBCC approaches can induce a behavioural change to improve women's dietary practices during pregnancy and lactation, breastfeeding, and complementary feeding practices for children. However, there is a lack of consistency in the detailed description of SBCC interventions (single interventions or combination of interventions, target groups, content, messages, scale, coverage, length, and intensity), dietary practices, breastfeeding and complementary feeding practices are measured. Also, the limited body of literature on the effectiveness of SBCC approaches on this topic is small to draw a conclusion and raises questions about the scalability and sustainability of the approaches used (Lamstein et al., 2014). A recent meta-analysis of a systemic review assessing the healthcare professional training on patient behaviour change reported significant improvement in health delivery in the medium term (6-12 months) and significantly affected patient health behaviour. However, the high risk of bias, noticeable heterogeneity in outcome measures, and the low number of studies in the review raise questions about the quality of the evidence (Hatfield et al., 2020). Another systematic review reported limited evidence on the effectiveness of stage-based interventions in inducing health-related behaviour change (Bridle et al., 2005).

In recent years, behavioural insights have been increasingly used as a lens in policy processes to design techniques meant to influence behaviour. However, critiques have highlighted several problems with behavioural change interventions aimed at improving health and nutritional status. Barnes (2015) argues that current behavioural health change intervention approaches have little evidence of impact, have little or no underlying theory and are poorly evaluated (if they are evaluated at all) (Barnes, 2015). First, behavioural interventions have yielded mixed results, and the effectiveness of these programmes is questionable because of the lack of rigour of the scientific evidence. Second, behaviour interventions address the individual behaviour of users based on evidence from RCTs conducted in laboratory settings, which fails to consider the broader social context in which individual behaviour is embedded. There are doubts over

whether these approaches have the potential to address the more distal and underlying causes of anemia (Ewert, 2020).

Third, behavioural interventions are top-down technocentric approaches because such interventions reflect the behaviour that policymakers want to see rather than engaging citizens to have inputs concerning the content and design in a meaningful way. The top-down approach stems from the individualistic assumptions that people are ignorant of their health risks and that improving how they think about their health can bring behaviour change if they are motivated enough. There are social, structural, environmental, and economic barriers beyond the control of individuals that affect both their current practices and the likelihood that they will change or not change current behaviour and practices. Due to these reasons, current behavioural interventions are considered inappropriate for addressing complex policy problems adequately and are limited in scope and scale (Barnes, 2015).

There is a consensus that the way nutrition interventions are delivered is suboptimal. The World Bank report on improving health service delivery in developing countries reviewed the available evidence on strategies to improve health service delivery in low and middle-income countries (LMIC). It concluded that evidence is weak for claiming the success of any particular health service programme and noted that how a strategy is implemented is as important as the type of strategy implemented (Peters, 2009).

9.3. INTERVENTIONS FOR NON-NUTRITIONAL CAUSES

AMB emphasises screening and treatment and raising awareness of non-nutritional causes, focusing on malaria, haemoglobinopathies and fluorosis. AMB seeks to utilise the existing platforms such as Anganwadi centres (AWCs), sub-centres (SCs), health and Wellness centres and events such as Village Health Nutrition Day (VHND), Nutrition week, Breastfeeding week, Women's Day, World Thalassemia Day to raise awareness, generate dialogue and discussions about non-nutritional causes.

9.3.1. MALARIA TREATMENT AND INTERVENTIONS

Malaria has been identified as one of the main causes of anemia in developing countries, including India. Many states have identified the malaria-endemic districts, blocks/sub-centres, and villages. AMB aims to integrate anemia control strategies with the National vector-borne

disease control program (NVBDCP) in the identified malaria-endemic regions. As per NVBDCP, people who report recent fever and are screened for anemia will also be tested for malaria and vice-versa. The treatment protocol for the management of anemia is the same as described in NIPI-I guidelines (Table: for WHO and Indian guidelines for iron supplementation). For the treatment of malaria in pregnant women, guidelines issued by NVBDCP, including Artemisinin combination Therapy (ART) for the treatment of plasmodium falciparum, are followed. As part of the preventive measures, Indoor residual Spray (IRS) with appropriate insecticides is carried out in school premises and residential areas before and after the monsoon season. AMB seeks to promote Long-lasting Insecticide Nets (LLINs) to all target groups, especially under-five children and pregnant women provided under NVBDCP to prevent Malaria (MoHFW, 2018).

9.3.2. HAEMOGLOBINOPATHIES TREATMENT

Under AMB, screening and appropriate treatment for Haemoglobinopathies are recommended as per the guidelines on Prevention and control of Haemoglobinopathies[18].

9.4.2. FLUOROSIS TREATMENT

AMB aims to integrate the National programme for prevention and control of Fluorosis (NPPCF) with nutritional improvement approaches. AMB recognises the link between fluoride, anemia and malnutrition and recommends a combined approach of safe drinking water and nutritional improvements to treat people affected with anemia due to fluorosis. The focus is on promoting safe drinking water and dietary diversity (vitamin C, calcium and magnesium) by using systemic counselling services in the community at the district level by establishing local protocols for anemia and fluorosis control (MoHFW, 2018).

There is a growing recognition that a range of non-nutritional factors in addition to malaria, worm infestations, haemoglobinopathies and fluorosis play an important role in anemia development. For example, ecological factors may contribute to multiple micronutrient deficiencies; seasonality may limit the year-round access to micronutrient-rich foods. Poverty

[18] National Guidelines on Prevention and Control of Haemoglobinopathies (2016) - http://nhm.gov.in/images/pdf/programmes/RBSK/Resource_Documents/Guidelines_on_Hemoglobinopathies_in%20India.pdf accessed on 21/01/2022

limits food access and choice, leading to micronutrient deficiencies and chronic malnutrition. A lower rise in Hb levels in stunted children upon Iron and multiple micronutrients reflects the role of food insecurity and chronic deprivation in the high prevalence of anemia. Other underlying factors such as women's autonomy, household income, education, the standard of living, and WASH are also associated with anemia (Gera et al., 2009).

However, AMB's policy document mentioned only three non-nutritional causes: malaria, haemoglobinopathies, and fluorosis. AMB strategy remains silent on the role of other factors in anemia causation and how to address those factors (MoHFW, 2018). There is a lack of data on detailed etiologies and their respective contribution to anemia at the national level. It is unclear how well the work on non-nutritional causes of anemia is moving. The data on non-nutritional causes is inadequate for geographically nuanced diagnosis. There is a need to identify the local etiologies of anemia and the underlying causes.

9.4. SIX INSTITUTIONAL MECHANISMS

AMB charted out six institutional mechanisms for the effective implementation of intervention strategies. The six institutional mechanisms are as follows: i) Intra ministerial coordination, ii) National Anemia Mukt Bharat Unit, iii) National Centre of Excellence and Advanced Research on Anemia Control, iv) Convergence with other ministries, v) Strengthening supply chain and logistics vi) Anemia Mukt Bharat Dashboard and Digital portal.

The institutional mechanisms under AMB strategy are guided mainly by two core approaches: i) convergence and inter-ministerial coordination as the core strategy and ii) technical and logistic support for monitoring.

9.4.1. INTRA MINISTERIAL COORDINATION AND CONVERGENCE

Complying with the targets and objectives of POSHAN Abhiyaan, AMB strategy envisaged the convergence of a broad range of programmes for wider reach and efficiency. These include programmes such as the Pradhan Mantri Matri Vandana Yojana (PMMVY), Anganwadi services, Scheme for Adolescent Girls of Ministry of Women & Child Development (MoWCD), Janani Suraksha Yojana (JSY), National Health Mission (NHM), Anemia Mukt Bharat (AMB), Indradhanush of MoHFW; Swachh Bharat Mission of Ministry of Drinking water & Sanitation (MoDWS), Public Distribution System (PDS) of Ministry of Consumer Affairs, Food & Public Distribution; Mahatma Gandhi national rural employment guarantee

scheme (MGNREGS) of Ministry of Rural Development; Drinking water & Toilets with Ministry of Panchayati Raj (MoPR) and Urban Local bodies through Ministry of Housing & Urban Affairs[19].

As effective as the convergence approach sounds in theory, it is a multi-sectoral governance challenge that faces several Political and technical barriers. Political barriers include the difference in levels of participation by the different political actors, which often work in silos. POSHAN Abhiyaan document is silent on this aspect of governance (Dasgupta et al., 2020). The convergence process has run into technical and practice-based roadblocks. A recent study assessing the convergence under POSHAN Abhiyaan in the Banswara district of Rajasthan pointed out several key challenges. There was little or no orientation for staff to convergence planning; the orientation was limited to filling up the templates; the officials arbitrarily set targets at different levels, and actions and Interventions were generic and unimaginative. The convergent action plans (CAP) at district and block levels did not lay out a specific roadmap of how to carry out the issues related to convergence, and budgetary provisions were not specified (Dasgupta et al., 2020). Under the guidelines, States, Districts, and Blocks are mandated to conduct quarterly review meetings; however, the discussions are often generic and fruitless at grassroots levels of Blocks and Districts.

These integrated programmes have existed for a long time but have little or no evidence of impact on anemia. The Integrated Child Development Services (ICDS) is a case in point. Under the ICDS, supplementary nutrition is provided to pregnant and lactating women at Rs. 5 per day, providing 600 Kcal and 18–20 grams of protein. Children aged 0–6 years receive supplementary nutrition, immunisation, and pre-school education. (MoHFW, 2013). ICDS has been operational for more than 45 years, integrating health, educational and nutritional interventions through the network of Anganwadi centres but offers little for children except the Take Home Ration (THR). ICDS is plagued by institutional weaknesses and other barriers, including inadequate training of frontline health workers, high workload, staff shortage for supportive supervision, and dissatisfaction with remuneration. ICDS, in its siloed form, shall continue to be ill-equipped to deliver a multi-dimensional package of interventions (Dasgupta et al., 2020). For the success of such complex programmes, it is important to align the

[19] Convergent Action Plan Guidelines for effective implementation under POSHAN Abhiyaan http://icds-wcd.nic.in/nnm/NNM-Web-Contents/LEFT-MENU/Guidelines/Operational-Guidelines-for-Convergent-Action-Plan-02-11-2018.pdf accessed on 03/01/2022.

departments to focus on the relative roles of each department for the commitment and motivation, funding, administration, organisation and service delivery (Dasgupta et al., 2020).

9.4.2. MONITORING AND TESTING OF ANEMIA

Anaemia Mukt Bharat emphasises the failure of previous approaches and seeks to address them by introducing critical monitoring to ensure IFA supplementation for each child, pregnant woman, and adolescent girl across states through strengthening supply chain mechanism and filling the implementation gaps. AMB dashboard has been created for more robust monitoring of IFA across different groups. The dashboard provides data on anemia prevalence, targets, beneficiaries, interventions, and institutional mechanisms. While dashboards are helpful to visualise data, it is not clear how the dashboards are being used, who is looking at them and what actions are being taken. The output indicators used in AMB dashboard for assessing the state of nutrition do not provide sufficient information to take action. Program input indicators (e.g., Iron and folic acid tablets supply) and program coverage indicators (e.g., percentage of children who were ever weighed in the last 12 months) are critical to identifying steps to improve outcomes. Unfortunately, the dashboard is reporting on a limited number of input indicators. Likewise, the AMB dashboard has few coverage indicators, especially for adolescents and newborn care programs [20].

9.4.3. TEST-TREAT-TALK CAMPS (T3)

T3 anemia camp is a key strategy to generate demand and mobilise people. These camps use a digital hemoglobinometer to test for anaemia, give IFA tablets to treat, and counsel beneficiaries on lifestyle measures to increase iron levels and foods rich in iron, protein, and vitamin C. A digital hemoglobinometer allows instant haemoglobin testing, thus improving testing and compliance.

9.5. SUMMARY

Global policy responses to anemia have greatly influenced the Indian policy landscape. Indian programmes and policies experienced shifts in their programmatic components consistent with

[20] https://poshan.ifpri.info/2020/06/05/how-are-nutrition-data-visualization-tools-dvts-in-india-supporting-decision-makers/ accessed on 07/01/2022

global programmatic shifts. Anemia control strategies in India have evolved significantly since its inception in 1972. The main strategies have revolved around four intervention approaches, iron supplementation, food fortification, deworming, and behavioural change. Iron supplementation and mandatory food fortification have been shown to improve iron deficiency and IDA under controlled trials; however, they showed a little demonstratable effect on anemia reduction in the population. Similarly, the evidence of deworming and behavioural change programmes to improve anemia is weak. These findings, however, do not mean that these nutrition-specific strategies, including iron supplementation and fortification, are not required in India. The nutrition-specific interventions could significantly reduce anemia; however, they may not be sufficient to address anemia alone. Nutrition specific in combination with nutrition-sensitive interventions has enormous potential to enhance the effectiveness of nutritional interventions. Nutrition-sensitive interventions integrated with can serve as a delivery platform for nutrition-specific interventions

CHAPTER 10

"Leave your drugs in the chemist's pot if you can heal the patient with food"

Hippocrates

CHAPTER 10. DISCUSSION AND CONCLUSION

10.1. INTRODUCTION

India has the largest number of anemic individuals and one of the world's highest prevalence rates of anemia (IIPS, 2020). Anemia prevalence has marginally increased in India in the last two decades. Significant advancement has been achieved in iron biology; new areas continue to emerge from ongoing research, both basic and programmatic. Surprisingly, there is little documented success in addressing nutritional anemia at the public health level in developing countries, including India. The study's main objective was to review the nature and scope of nutritional anemia and explore biological and social determinants and programmatic approaches to nutritional anemia. The thesis explored and examined the breadth of literature to identify the reasons for high anemia prevalence and little documented success of programmes and policies at the public health level. The preceding chapters discussed the nature, causation, and intervention strategies for nutritional anemia. This chapter discusses the major findings with reference to the study's research questions and draws specific conclusions.

10.1.1. THE EPIDEMIOLOGY OF ANEMIA IS UNKNOWN AND CONTESTED

A clear and compelling definition of the problem could contribute greatly to controlling anemia. The thesis argued that a positivist biomedical definition of anemia, guided by haemoglobin thresholds, is one of the determinants of anemia. The positivist definition driving particular focus on haemoglobin thresholds amplifies the biological causal explanations and obscures the potential interventions in a way that contributes to the very problem. First, anemia is defined statistically in relation to changes in haemoglobin levels. The numerous social, economic, demographic, environmental and technical factors influencing haemoglobin levels are not factored into this definition. Second, haemoglobin is incorrectly used as a proxy for iron deficiency and vice versa. This methodological discrepancy has blurred the conceptual boundaries between nutritional anemia and iron deficiency, resulting in anemia and iron deficiency being understood as the same and iron deficiency as the sole cause of anemia. The multifactorial complexity of anemia is reduced to the dietary iron deficiency, discounting the role of various social factors in developing anemia. Therefore, a statistical and technical

definition of anemia leads to conceptual reductionism and inadvertently shifts the discourse to single etiology (iron deficiency) and single (iron-centric) interventions. It limits the scope to define anemia within the broad frameworks of health and nutrition and hampers the effective program prioritisation and targeting of anemia interventions.

10.1.1.1 ARE ANEMIA PREVALENCE ESTIMATES CREDIBLE ENOUGH?

The first step of an epidemiological inquiry involves accurately assessing the magnitude of prevalence, its patterns and distribution in population groups. The epidemiology of anemia is not well mapped. The exact prevalence of anemia is not known; the prevalence varies with the survey methodology. The two nationally representative surveys, CNNS and NFHS-4, report widely different prevalence estimates (40 % and 59 %, respectively) among children of the comparable age groups. Anemia prevalence reported by CNNS is 19 percentage points lower than NFHS. A lack of consensus on the exact magnitude of the problem raises questions over the reliability of the prevalence estimates of anemia in India. According to Sachdev et al. (2021), anemia prevalence in India is highly exaggerated (by 19 %). The global anemia prevalence is also questionable (Stoltzfus, 2001b).

10.1.1.2. ISSUES IN DEFINING CAUSES OF ANEMIA

Western biomedicine operates within a positivist construct in which the cause of the disease is isolated to a single origin. For a large part of public health discourse, iron deficiency has been universally assumed as the sole cause of anemia. It is important to recognise that neither all the causes of anemia are iron deficiency, nor all cases of iron deficiency may lead to anemia. The recent evidence shows that the contribution of iron to anemia is much lower (25-37 %) than previously expected (Petry et al., 2016). A non-linear and weak relationship exists between the two (Swaminathan et al., 2019).

Using 2019 GBD data, Gardner and Kassebaum identified as many as 35 nutritional and non-nutritional risk factors associated with anemia globally (Gardner & Kassebaum, 2020). Some of the risk factors included nutritional deficiencies of iron, vitamin A, folate, and vitamin B12, and non-nutritional factors such as infections, inflammations, thalassemia, and haemoglobinopathies (Kassebaum, 2013). The risk factors and their respective contribution varied according to age, sex, demography, and socio-economic status. Malarial infections are

the primary etiology in many regions of Africa, highlighting that infections and inflammations may play a more crucial role than nutritional deficiencies in infection endemic regions. (Engle-Stone et al., 2017). In many parts of central and south Asia, the Mediterranean, and sub-Saharan Africa, sickle cell traits and thalassemia might have a more critical role than malaria (Stevens, 2013).

10.1.1.3. UNKNOWN CAUSES OF ANEMIA

The causes of anemia are not well characterised; it largely remains unknown in developing countries, including India. Sarna and colleagues using CNNS data, showed that iron deficiency contributed to 24% of anemia, folate, or vitamin B12 deficiency, 23%, dimorphic anemia,12 %, and Inflammation 5% in children and adolescents aged 1-20 years in India. The study also highlighted that the cause of a large share of anemia (30-48%) is unknown (Sarna et al., 2020). There are regions with low iron deficiency and malaria but are still anemic. A large proportion of anemia remains following multimicronutrient supplementation and deworming programs in children and women, thus cannot all be attributed to nutritional and Chronic Inflammation. There are other unknown factors which explain anemia in such settings. Sachdev and colleagues concluded that the lack of physical exercise and fitness might partly explain the unknown causes (30-48 %) of anemia in India (Sachdev et al., 2021). Within Biomedicine, the cause of anemia is identified by biomarkers; only those causes are defined for which biomarkers are available. Those conditions which are outside the realm of biomedicine are not explained. Thus, unexplained anemia is a diagnosis of exclusion for which adequate markers and indicators are unavailable. The representative data on the prevalence, the patterns and distribution of causal factors and their respective contribution to anemia in a population, is lacking to map anemia's epidemiology.

10.2. THE CAUSE AND THE CONTEXT

Anemia is severe and endemic in one population and nearly absent in others. However, it is crucial to identify the risk factors without losing sight of underlying factors that cause anemia. The known risk factors are neither necessary nor sufficient to explain anemia in the population. The risk factors do not occur in isolation; their presence and contribution to the development of anemia are determined by socio-economic context.

10.2.1. INADEQUATE CONSUMPTION OF FOOD

Inadequate diet is one of the leading causes of anemia. NNMB surveys highlighted that average Indian household consumption of habitual diets such as cereals and millets, pulses, green leafy vegetables, milk products and nutrients such as energy, proteins, iron, and other micronutrients are lower than recommended. The consumption of meat products is grossly inadequate (NNMB, 2012). Nearly three-quarters of the total population consumed fewer calories than the recommended (Deaton & Drèze, 2009). For most Indians, cereal-based foods are the primary source of energy (~ 65 % in rural and ~50 % in urban India), the share of meat (5 %), dairy products (5%), and vegetables (1.5%) are minimum (K. M. Nair et al., 2016). NFHS shows that only 6 % of the population eats meat, fish, or chicken daily, 40 % weekly, and 30 % occasionally consume any form of non-vegetarian diet. Only ~10 % of children aged 6-23 months meet the criteria of WHO's minimum acceptable diet (MAD) (IIPS & ICF, 2017). The cereals contributed 60 %, Pulses 18%, vegetables 12 %, fruits 6 % and Meat 4 % of daily iron intake in a typical Indian diet (K. M. Nair et al., 2016).

This means that a large fraction of the Indian population is consuming inadequate energy, micronutrients, and macronutrients and less bioavailable nutrients from plant-based foods. Cereals-based Indian diets contain less bioavailable non-heme iron and high content of iron inhibitors such as phytates. The bioabsorption of nutrients is directly linked to access to diversified foods. Absorption of hematopoietic nutrients, including iron, is severely constrained in the absence of energy, macronutrients and micronutrients derived from food. In this regard, food availability and the food matrix composition are fundamental to addressing anemia.

10.2.2. LINKAGES BETWEEN SOCIO-ECONOMIC STATUS, UNDERNUTRITION, AND INFECTIONS

A cyclical relationship between undernutrition and infections exists. Nutritional deficiencies are known to exacerbate infection and vice versa. Most of the Indian population is characterised by food deprivation, severe nutrient deficiency, and a compromised biological potential of nutrient absorption and are also susceptible to infections and inflammations either due to nutritional deficiencies, poor environmental and unhygienic conditions, or most likely a combination of both. That is why anemia is highly prevalent in food-deprived, energy-scarce

people working as manual labourers and agricultural farmworkers living in poor sanitary and material conditions.

Open defecation (40 %), use of unimproved and shared toilet facilities (12%) and untreated water (62 %) is widely prevalent in India (IIPS & ICF, 2017). The lack of access to safe drinking water, unhygienic practices of open defecation, use of biofuels for cooking, and living in unfurnished houses aggravate anemia through infections and inflammations (Karlsson et al., 2020). Infections and inflammations may lead to inefficient utilisation of stored iron resulting in a functional iron deficiency (Kulkarni et al., 2021).

10.3. ANEMIA IS A SOCIAL PROBLEM

This study identified caste, class, gender, and religion as the structural determinants of anemia. Food education, occupation, food security, access to health services and WASH are the intermediate determinants. The structures of society bestow a socio-economic position, which creates differential access to income, education, and occupation, among others. Anemia is socially patterned, i.e., the prevalence of anemia typically follows the socio-economic gradient. Poor socio-economic conditions and household poverty identified by the use of biofuels, no latrine, no electricity, non-concrete houses, landlessness, absence of livestock ownership, lower wealth, food insecurity, working as wage labourers, lack of purchasing power are positively associated with increased risks of anemia (Nguyen et al., 2019). The disadvantaged groups are more likely to have poor socio-economic status. They are likely less educated, occupied in physically demanding jobs, have low purchasing power, limited access to diversified food and health care services, and are more vulnerable to work-related psychological stress. The poor access to resources for such groups indicates their social exclusion and explains the linkages between poverty and anemia. The differential distribution of material and other assets such as occupation, landholdings, housing, drinking water and sanitation may explain the differential rate of anemia across social groups (Chakrabarti et al., 2018).

According to Socio-economic Caste Census, nearly 90 % of the Indian population are casual manual labourers, foragers, pickers, and cultivators involved in gruesome, physically

challenging work conditions. SC, ST and OBCs constitute ~70 % of the Indian population[21]. Most of the poor are likely to be Dalits, other lower casts, tribal people, and Muslims. Women comprise a majority of the total agriculture and self-employed workforce. Therefore, a large section of the Indian population is poor, landless, manual casual labours and cultivators, barely surviving on the consumption of less than Rs 20 a day (Ansary & Das, 2018). Women and children among these groups are vulnerable to an enhanced risk of adverse consequences of poverty and deprivation, resulting in an increased risk of anemia (Sengupta et al., 2008).

Nutritional anemia is a reflection of inequities and outcomes of poverty, deprivation and social exclusion. This is because those living in poverty are characterised by monotonous diets with low bioavailable iron and other reoccurring nutrient deficiencies, combined with inhibiting factors such as phytates and high intakes of tea. In addition, there are high disease rates, infections, and inflammations due to compromised immunity, an unhygienic environment and poor access to health care services. The risk of anemia is likely to be higher among more disadvantaged social groups because of the intersectionality of caste, class, gender, and religion. The qualitative exploration of people's experiences and perceptions uncovers the hidden underlying mechanisms of clinical symptoms of anemia. The perpetual dizziness, headaches, weakness, and faintings reported by the anemic individuals are not a randomised list of items but are situated in narratives of daily life struggles against poverty, lack of food, women's lack of autonomy in food preferences, financial decisions, and health-seeking behaviours. The social adversities are biologically embodied and accommodated via reduced metabolic functions, reduced energy, and oxygen demand, resulting in fainting, dizziness, headaches, and other related symptoms. Thus, the clinical symptoms are biological manifestations of social adversities. Therefore, anemia is not merely a cluster of symptoms arising from discrete pathologies (nutrition deficiencies and infections). Rather, it is an illness deeply entrenched in poverty, deprivation, and social exclusion.

10.4. APPROACHES TO PROGRAMMES AND POLICIES

Iron supplementation is the central pillar in anemia treatment and prevention programmes, whether available in variable doses, frequency, or regimen. Food fortification, deworming, and behavioural change are complimentary anemia control strategies. The evidence shows that iron supplementation and wheat flour fortification trials can greatly reduce the risk of anemia (20%-

[21] https://secc.gov.in/getEmploymentAndIncomeRuralNationalReport.htm accessed on 04/04/2022.

70 %) and iron deficiency (52 %-72 %) (Das et al., 2019; De-Regil et al., 2011; Low et al., 2013; Peña-Rosas, De-Regil, Garcia-Casal, et al., 2015). In other cases, supplementation and fortification efficacy trials have not been found effective against anemia and iron deficiency (Peña-Rosas et al., 2019; Tam et al., 2020). The lack of consensus on optimal doses, frequency, and chemical and physical form of iron used in supplementation and fortification trials raises questions about the effectiveness of iron supplementation and fortification strategies.

Similarly, robust evidence on the effectiveness of deworming and behavioural interventions for anemia control is lacking. Taylor-Robinson et al. (2012), Salam et al. (2021), and Tanjong Ghogomu et al. (2018) demonstrated little or no effect. In contrast, Lo et al. (2018) showed the beneficial effects of deworming on anemia on anemia or haemoglobin indicators. The current approaches to behavioural interventions do not address underlying causes of behaviour changes and are likely to have a limited impact on anemia reduction (Barnes, 2015).

Experience from the BRINDA project in Bangladesh and Cambodia showed that National anemia policies focusing on iron delivering interventions, deworming, and behavioural programmes may be insufficient to reduce the anemia in contexts in which iron deficiency contributes only in low to a modest amount and where multiple confounding factors cause anemia. In such circumstances, other nutritional and covariates explained the anemia (Williams et al., 2019). Consistent with this finding, Swaminathan et al. (2019) showed that the northeastern states of Manipur, Nagaland, Mizoram, and Sikkim in India might benefit from iron interventions. In contrast, Rajasthan, Punjab, Himachal Pradesh, Madhya Pradesh, Uttar Pradesh, and Uttarakhand, despite the high prevalence of anemia, have less chance of anemia reduction with iron interventions, indicating that iron interventions might not work in these states. This finding highlights that iron interventions would have variable impacts across states. In many Indian states, an increase in iron intake through iron interventions would not significantly reduce anemia because of the other social confounding factors such as poverty and poor nutritional status. In a Poor socio-economic environment, the impact of iron interventions could be severely limited because of the poor absorption of iron and increasing iron intake is unlikely to address anemia.

10.4.1. ADDRESSING THE PROBLEM

> *"In current design, even if the coverage of the programme is 100 %, it will not yield desired results on anemia. Unless there is emphasis on access and affordability of balanced diet, protection of people living in unhealthy environment from disease burden, IFA supplementation would not work. Unless we do not have public health approach that encapisulating. Social determinants of health, we will not be able to improve anemia"* (Rajiv, T, personal communication, 07/02/2021)

One of the likely reasons for the failure of programmes and policies is the biomedicalised and clinical understanding of anemia as a public health problem. The evidence shows that more than biological, social factors play a crucial role in the population distribution of anemia. Therefore, socio-economic interventions can be beneficial in addressing the underlying causes of anemia. Improved socio-economic status, i.e., improvement in nutrition, increased consumption of diversified food, the decline in open defecation, improved sanitation, maternal schooling, coverage of health and nutrition programmes, and delayed pregnancy lead to a reduction in anemia drastically (Chakrabarti et al., 2018; Nguyen et al., 2019). Nguyen et al. (2018) showed that addressing the underlying causes of anemia reduced anemia more significantly than immediate determinants. These findings suggest that the optimal strategy may require a blend of nutrition-specific interventions (e.g., food aid) beyond single micronutrient interventions and nutrition-sensitive interventions among vulnerable groups.

In the Indian context, the causes of 30%-48 % of anemia are unknown. In such circumstances, the national anemia policies focusing mainly on iron interventions, deworming and behavioural change programs may be insufficient to reduce anemia prevalence. The unknown causes of anemia need to be identified and characterised to inform the program design. However, there is a possibility that unknown dimensions of anemia are embedded within the socio-economic and environmental context, and social interventions may also address the unknown causes.

10.5. CONCLUSION

Anemia is a contested and controversial public health problem. The controversy arises due to a lack of consensus on the constitution, prevalence, causes and appropriate intervention strategies for anemia. The contradictions result from the gap between biomedical and alternate discourses of anemia. The differential rates of anemia among social groups highlight that anemia is a reflection of social inequities characterised by poverty, deprivation, and social exclusion. Social inequities and experiences of a community are biologically embodied to manifest anemia. A community problem stemming from social reasons will require community-level socio-economic interventions. The iron interventions, deworming, and behavioural change strategies are medicalised interventions that have limited impact on addressing the underlying causes and are likely insufficient to reduce anemia alone. However, research shows that they may be helpful if used judiciously in conjunction with social interventions. We need epidemiologically sound, evidence-based, nutrition-specific, and nutrition-sensitive interventions to control and prevent anemia. Additional data on the prevalence and distribution of causal factors are required to inform the programmes and policies.

10.6. POLICY RECOMMENDATIONS

10.6.1. THE DEFINITION OF ANEMIA NEEDS TO BROADEN

The biomedical definition of anemia characterises anemia as a symptom or condition stemming from other diseases, conditions, or nutritional deficiencies. Therefore, the critical place for defining anemia as an illness of poverty and structural inequities is reduced to a singular etiology and as a statistical concept devoid of socio-economic realities of the time and place. Therefore, biological, social, economic, and environmental determinants should be factored into the definition to enhance the evaluation of determinants, estimation of prevalence and the management of anemia at the individual and population level.

10.6.2. EVIDENCE-BASED PROGRAMME

One of the reasons for the failures of programmes and policies are lack of adequate data to prioritise and target the interventions. For interventions to work, a clear epidemiological map of anemia, i.e., its prevalence in the population, patterns and distribution of the causal factors, is required. Additional data on population-specific etiology of iron and other nutritional deficiencies, inflammation status, and genetic and environmental (e.g., malaria) conditions are required at national, state, district and block levels to mount an effective response. In addition, there is an urgent need to focus on identifying the unknown causes.

10.6.3. APPROACH TO INTERVENTIONS

Piecemeal interventions are not sufficient to address anemia. The most effective approach for dealing with the multifactorial and deeply complex anemia problem is combining multiple and integrated strategies to reach all vulnerable groups. This can be done by combining nutrition-sensitive and nutrition-specific interventions and involving a wide range of sectors.

10.6.3.1. FOOD-BASED STRATEGIES

10.6.3.1.1. ENSURE AVAILABILITY, AFFORDABILITY, AND ACCESS TO DIVERSIFIED FOOD

Therefore, two approaches combined together should be used for anemia prevention and control programs. First, promoting the consumption of diversified foods, including vegetables, fruits, and non-vegetarian diets, through behavioural change and communications strategies. Second, integration of anemia control programmes with the programmes that ensure year-round availability, access, and affordability of culturally appropriate foods, particularly to vulnerable population groups. This can be achieved by strengthening the existing platforms, such as the public distribution system (PDS), ICDS and MDM programmes, and improving household food security through improving purchasing power, food for work programmes, direct/indirect subsidies, and combat rising food prices.

10.6.3.2. APPROACHES TO IMPROVE EXCLUSIVE BREASTFEEDING

The initiation and continuation of exclusive breastfeeding are abysmally low because of cultural and traditional practices, lack of education, health and nutrition awareness among mothers, lack of antenatal counselling on the feeding of infants, Inadequate, untrained and unsensitised health care support to mothers regarding IYCF, lack of family support for women, commercial promotion of baby foods as an alternative to breastfeeding, lack of proper support at community and workplace like maternity entitlements. Therefore, promoting exclusive breastfeeding will require a multidimensional approach that comprises raising awareness against unscientific dogmas, sensitisation, and training to health workers, improving the infrastructure, coverage, and accessibility of health services, empowering women and regulating the unethical advertising and promotion of baby foods rather than top-down, narrowly framed behavioural change interventions.

10.6.3.3. APPROACHES TO IMPROVE COMPLEMENTARY FEEDING

Poor education for mothers, low household income, lack of access to quality food and poor access to health services are some of the reasons for poor complementary feeding practices in India. An appropriate approach to increase the complementary feeding would be to target the

underlying causes and focus on strategies to improve the socio-economic status, illiteracy, purchasing power, and access to adequate health services.

10.6.3.2. MICRONUTRIENT SUPPLEMENTATION AND FORTIFICATION

The two strategies have the potential to significantly improve iron stores and haemoglobin levels either singly or in combination. However, a heterogeneous distribution of iron intake in different states means the differential requirement of iron. Therefore, one size fit all supplementation approach and pan India mandatory fortification also poses the risk of excess iron, particularly if both approaches are combined, especially in poor subjects where increasing iron intake is unlikely to address anemia. Iron supplementation and food fortification alone are insufficient to address anemia. They must be judiciously used in combination with other strategies guided by sound epidemiological evidence to gain maximum benefit.

Additionally, the recommended doses of iron are guided by operational convenience rather than backed by scientific evidence. Therefore, reducing iron doses to an optimum minimum can be one logical approach to minimise the adverse consequences. Micronutrient supplementation and fortification can be used as therapeutic short-term emergency measures.

10.6.3.3. DEWORMING PROGRAMMES AND WASH

The effect of deworming programmes on haemoglobin improvement or other nutritional outcomes is not apparent. Since preventive chemotherapy (deworming) does not break the cycle of infection and reinfection, populations living in poor environments are vulnerable to the risk of reoccurring infections. In these circumstances, periodic treatment and improvement in water, sanitation, and health education at the population level can reduce the transmission of soil-transmitted helminths and schistosome infections and increase the bioabsorption of nutrients, including iron. Therefore, deworming programmes should be strategically used in high-risk groups, simultaneously with concerted efforts on public provisioning of safe drinking water, hygienic toilets, and a clean environment to prevent and control anemia.

10.6.3.4. BEHAVIOURAL CHANGE COMMUNICATION STRATEGIES (BCCS)

Behaviours are embedded in a societal context. The decision to adopt or not to adopt a behaviour is determined by contextual factors. BCCS can be an important strategy to improve

the health and nutrition of the population if the underlying causes of not adhering to the healthy behaviours such as exclusive breastfeeding, complementary feedings, delayed cord clamping, and diversified foods are addressed in addition to behavioural change communication campaigns to promote the health and nutrition awareness.

10.6.3.5. MORE FOCUS ON VULNERABLE POPULATIONS AND CRITICAL LIFE STAGES

Women's physiology, such as pregnancy and menstruation, put them at considerably higher risk of anemia. The physiological vulnerability is embedded in the Indian social system, in which women are married earlier, do not have a choice over family planning and are not in a position to exercise autonomy in household decisions. The right approach would be to i) raise awareness at the community level about the consequences of early marriage and multiple births in the community, ii) increase educational opportunities and empowerment to girls, iii) improve health service delivery, access and use of contraceptive information and services.
Men are relatively at a lesser risk of anemia than their female counterparts. Adolescent males are not included in the anemia prevention and control strategies even though a large share of the adolescent male population is mild and moderately anemic. Therefore, adolescent males, particularly those belonging to disadvantaged populations, should also be given adequate focus on anemia control and prevention strategies.

10.6.3.6. INTERSECTORAL CONVERGENCE

Anemia is a multifactorial problem rooted in the social, economic, cultural, and environmental context. A concerted multisectoral approach is needed to alleviate socio-economic, cultural, and environmental problems in addition to the health sector. The broad-based interventions such as livelihood approaches, social safety nets, gender equality, education, and income generation programmes can improve overall nutritional status and anemia in several ways. The different sectors have an important role to play in preventing and controlling anemia. Agriculture and nutrition have linkages. Agriculture can improve food security, dietary diversity, access, and availability of nutrient-rich foods. Education can enhance awareness about health, hygiene, nutrition programs, deworming programmes, and iron-folic acid supplementation programmes. Infrastructure, planning and development can improve

sanitation and drinking water facilities, and the social services sector can be instrumental in poverty alleviation and livelihood improvement.

REFERENCES

Abraham, D., Kaliappan, S. P., Walson, J. L., & Ajjampur, S. S. R. (2018). Intervention strategies to reduce the burden of soil-transmitted helminths in India. *Indian Journal of Medical Research*, *147*, 533–544. https://doi.org/10.4103/ijmr.IJMR_881_18

Ackerson, L. K., & Subramanian, S. V. (2008). Domestic violence and chronic malnutrition among women and children in India. *American Journal of Epidemiology*, *167*(10), 1188–1196. https://doi.org/10.1093/aje/kwn049

Addo, O. Y., Emma, X. Y., Williams, A. M., Young, M. F., Sharma, A. J., Mei, Z., Kassebaum, N. J., Jefferds, M. E. D., & Suchdev, P. S. (2021). Evaluation of hemoglobin cutoff levels to define anemia among healthy individuals. *JAMA Network Open*, *4*(8), e2119123–e2119123.

Agrawal, S., Kim, R., Gausman, J., Sharma, S., Sankar, R., Joe, W., & Subramanian, S. V. (2019). Socio-economic patterning of food consumption and dietary diversity among Indian children: Evidence from NFHS-4. *European Journal of Clinical Nutrition*, *73*(10), 1361–1372. https://doi.org/10.1038/s41430-019-0406-0

Agrawal, S., Kumar, S., Ingole, V., Acharya, S., Wanjari, A., Bawankule, S., & Raisinghani, N. (2019). Does anemia affects cognitive functions in neurologically intact adult patients: Two year cross sectional study at rural tertiary care hospital. *Journal of Family Medicine and Primary Care*, *8*(9), 3005–3008. https://doi.org/10.4103/jfmpc.jfmpc_599_19

Albonjco, M., Stoltzfus, R. J., Savioli, L., Tielsch, J. M., Chwaya, H. M., Ercole, E., & Cancrini, G. (1998). Epidemiological evidence for a differential effect of hookworm species, Ancylostoma duodenale or Necator americanus, on iron status of children. *International Journal of Epidemiology*, *27*(3), 530–537.

Allen, L., & Ahluwalia, N. (1997). *Improving iron status through diet: The application of knowledge concerning dietary iron bioavailability in human populations*. Opportunities for Micronutrient Interverntions (OMNI) Project.

Allen, L., Casterline-Sabel, J., & Ramakrishnan, U. (2001). Prevalence and causes of nutritional anemias. *Nutritional Anemias*, 7–21.

Allen, L. H. (2000a). Anemia and iron deficiency: Effects on pregnancy outcome. *The American Journal of Clinical Nutrition*, *71*(5), 1280S-1284S.

Allen, L. H. (2000b). Ending Hidden Hunger: The History of Micronutrient Deficiency Control. *Background Analysis for the World Bank-UNICEF Nutrition Assessment Project World Bank (2000)*, 111–130.

Allen, L. H. (2002). Iron supplements: Scientific issues concerning efficacy and implications for research and programs. *Journal of Nutrition*, *132*(4 SUPPL.), 813–819. https://doi.org/10.1093/jn/132.4.813s

Allen, L. H. (2009). How common is vitamin B-12 deficiency? *The American Journal of Clinical Nutrition*, *89*(2), 693S-696S.

Anand, T., Rahi, M., Sharma, P., & Ingle, G. K. (2014). Issues in prevention of iron deficiency anemia in India. *Nutrition*, *30*(7–8), 764–770. https://doi.org/10.1016/j.nut.2013.11.022

Andrews, N. C. (2000). Iron metabolism: Iron deficiency and iron overload. *Annual Review of Genomics and Human Genetics*, *1*(1), 75–98.

Anne, M., Callahan, J., & Kang, H. (2013). Gender and caste intersectionality in the Indian context. *Human Resource Management*, *2013*(6), 31–48.

Ansary, R., & Das, B. (2018). Regional Patterns of Deprivation in India: An Assessment Based on Household Characteristics, Basic Amenities and Asset Possession. *Social Change*, *48*(3), 367–383. https://doi.org/10.1177/0049085718781663

Ansong, D., Akoto, A. O., Ocloo, D., & Ohene-Frempong, K. (2013). Sickle cell disease: Management options and challenges in developing countries. *Mediterranean Journal of Hematology and Infectious Diseases*, *5*(1).

Apte, S. V., & Iyengar, L. (1970). Absorption of dietary iron in pregnancy. *The American Journal of Clinical Nutrition*, *23*(1), 73–77.

Arabi, S. M., Ranjbar, G., Bahrami, L. S., Vafa, M., & Norouzy, A. (2020). The effect of vitamin D supplementation on hemoglobin concentration: A systematic review and meta-analysis. *Nutrition Journal*, *19*(1), 1–11.

Arlappa, N., Balakrishna, N., Laxmaiah, A., & Brahmam, G. N. V. (2010). Prevalence of anaemia among rural pre-school children of West Bengal, India. *Annals of Human Biology*, *37*(2), 231–242. https://doi.org/10.3109/03014460902991979

Awasthi, S., Peto, R., Read, S., Richards, S. M., Pande, V., Bundy, D., DEVTA (Deworming, & team, E. V. A. (2013). Population deworming every 6 months with albendazole in 1 million pre-school children in north India: DEVTA, a cluster-randomised trial. *The Lancet*, *381*(9876), 1478–1486.

Bailey, R. L., West, K. P., & Black, R. E. (2015). The epidemiology of global micronutrient deficiencies. *Annals of Nutrition and Metabolism*, *66*(suppl 2), 22–33. https://doi.org/10.1159/000371618

Baker, S. J. (1978). Nutritional anaemia—A major controllable public health problem. *Bulletin of the World Health Organization*, *56*(5), 659–675.

Baker, S. J., & DeMaeyer, E. M. (1979). Nutritional anemia: Its understanding and control with special reference to the work of the world health organization. *American Journal of Clinical Nutrition*, *32*(2), 368–417. https://doi.org/10.1093/ajcn/32.2.368

Balarajan, Y., Ramakrishnan, U., Özaltin, E., Shankar, A. H., & Subramanian, S. V. (2011). Anaemia in low-income and middle-income countries. *The Lancet*, *378*(9809), 2123–2135. https://doi.org/10.1016/S0140-6736(10)62304-5

Balarajan, Y. S., Fawzi, W. W., & Subramanian, S. V. (2013). Changing patterns of social inequalities in anaemia among women in India: Cross-sectional study using nationally representative data. *BMJ Open*, *3*, 2233–2233. https://doi.org/10.1136/bmjopen-2012

Baranwal, A., Baranwal, A., & Roy, N. (2014). Association of household environment and prevalence of anemia among children under-5 in India. *Frontiers in Public Health*, *2*, 196–196. https://doi.org/10.3389/fpubh.2014.00196

Barkley, J. S., Wheeler, K. S., & Pachón, H. (2015). Anaemia prevalence may be reduced among countries that fortify flour. *British Journal of Nutrition*, *114*(2), 265–273.

Barnes, B. R. (2015). Critiques of health behaviour change programmes: State of the science. *South African Journal of Psychology*, *45*(4), 430–438.

Bash, K. (2013). *The Perception of Maternal Anemia and the Effect of Nutritional Education: A Qualitative Analysis Among Village Mothers in Rural Kumaon, Uk*.

Bentley, M. E., & Griffiths, P. L. (2003). The burden of anemia among women in India. *European Journal of Clinical Nutrition*, *57*(1), 52–60. https://doi.org/10.1038/sj.ejcn.1601504

Bentley, P., & Parekh, A. (1998). *Perceptions Of Anemia And Health-Seeking Behavior Among Women In Four Indian States Technical Working Paper #9*.mothercare/johnsnow in

Berner, L. A., & Miller, D. D. (1985). Effects of dietary proteins on iron bioavailability—A review. *Food Chemistry*, *18*(1), 47–69.

Beutler, E. (2002). History of iron in medicine. *Blood Cells, Molecules & Diseases*, *29*(3), 297–308. https://doi.org/10.1006/bcmd.2002.0560

Beutler, E., & Waalen, J. (2006). The definition of anemia: What is the lower limit of normal of the blood hemoglobin concentration? *Blood*, *107*(5), 1747–1750. https://doi.org/10.1182/blood-2005-07-3046

Bharati, P., Shome, S., Chakrabarty, S., Bharati, S., & Pal, M. (2009). Burden of anemia and its socioeconomic determinants among adolescent girls in India. *Food and Nutrition Bulletin*, *30*(3), 217–226. https://doi.org/10.1177/156482650903000302

Bharati, S., Pal, M., & Bharati, P. (2019). Prevalence of anaemia among 6- to 59-month-old children in India: The latest picture through the NFHS-4. *Journal of Biosocial Science*, 1–11. https://doi.org/10.1017/S0021932019000294

Bharati, S., Pal, M., & Bharati, P. (2020). Prevalence of anaemia among 6- to 59-month-old children in India: The latest picture through the NFHS-4. *Journal of Biosocial Science*, *52*(1), 97–107. https://doi.org/10.1017/S0021932019000294

Bharati, S., Pal, M., Chakrabarty, S., & Bharati, P. (2015). Socioeconomic Determinants of Iron-Deficiency Anemia Among Children Aged 6 to 59 Months in India. *Asia-Pacific Journal of Public Health*, *27*(2), NP1432–NP1443. https://doi.org/10.1177/1010539513491417

Bharati, S., Pal, M., Sen, S., & Bharati, P. (2019a). Malnutrition and anaemia among adult women in India. *Journal of Biosocial Science*, *51*(5), 658–668. https://doi.org/10.1017/S002193201800041X

Bhatnagar, R. S., & Padilla-Zakour, O. I. (2021). Plant-Based Dietary Practices and Socioeconomic Factors That Influence Anemia in India. *Nutrients*, *13*(10), 3538.

Black, R. E., Victora, C. G., Walker, S. P., Bhutta, Z. A., Christian, P., de Onis, M., Ezzati, M., Grantham-McGregor, S., Katz, J., Martorell, R., & Uauy, R. (2013). Maternal and child undernutrition and overweight in low-income and middle-income countries. *The Lancet*, *382*(9890), 427–451. https://doi.org/10.1016/S0140-6736(13)60937-X

Braun, V., & Clarke, V. (2006). Qualitative Research in Psychology Using thematic analysis in psychology Using thematic analysis in psychology. *Qualitative Research in Psychology*, *3*(2), 77–101.

Bridle, C., Riemsma, R. P., Pattenden, J., Sowden, A. J., Mather, L., Watt, I. S., & Walker, A. (2005). Systematic review of the effectiveness of health behavior interventions based on the transtheoretical model. *Psychology & Health*, *20*(3), 283–301.

Bronfenbrenner, U., & Evans, G. W. (2000). Developmental science in the 21st century: Emerging questions, theoretical models, research designs and empirical findings. *Social Development*, *9*(1), 115–125. https://doi.org/10.1111/1467-9507.00114

Brumberg, J. J. (2016). *Chlorotic Girls , 1870-1920: A Historical Perspective on Female Adolescence Author (s): Joan Jacobs Brumberg Published by: Wiley on behalf of the Society for Research in Child Development Stable URL : http://www.jstor.org/stable/1130073 Accessed: 16-*. *53*(6), 1468–1477.

Camaschella, C., Nai, A., & Silvestri, L. (2020). Iron metabolism and iron disorders revisited in the hepcidin era. *Haematologica*, *105*(2), 260.

Cañete, A., Cano, E., Muñoz-Chápuli, R., & Carmona, R. (2017). Role of vitamin A/retinoic acid in regulation of embryonic and adult hematopoiesis. *Nutrients*, *9*(2), 159.

Chakrabarti, S., Georges, N., Majumder, M., Raykar, N., & Scott, S. (2018). Identifying sociodemographic, programmatic and dietary drivers of anaemia reduction in pregnant Indian women over 10 years. *Public Health Nutrition*, *21*(13), 2424–2433. https://doi.org/10.1017/S1368980018000903

Chandran, V., & Kirby, R. S. (2021). An analysis of maternal, social and household factors associated with childhood anemia. *International Journal of Environmental Research and Public Health*, *18*(6), 1–17. https://doi.org/10.3390/ijerph18063105

Chaparro, C. M., & Suchdev, P. S. (2019). Anemia epidemiology, pathophysiology, and etiology in low- and middle-income countries. *Annals of the New York Academy of Sciences*, 1–17. https://doi.org/10.1111/nyas.14092

Chatterjee, N., & Fernandes, G. (2014a). 'This is normal during pregnancy': A qualitative study of anaemia-related perceptions and practices among pregnant women in Mumbai, India. *Midwifery*, *30*(3), E56–E63. https://doi.org/10.1016/j.midw.2013.10.012

Chifman, J., Laubenbacher, R., & Torti, S. V. (2014). A systems biology approach to iron metabolism. *A Systems Biology Approach to Blood*, 201–225.

Chowdhury, T. K., & Roy, S. K. (2019). Prevalence of anaemia and associated factors among Oraon females of North 24 Parganas, West Bengal, India. *Anthropological Review*, *82*(1), 15–27. https://doi.org/10.2478/anre-2019-0002

Chyne, D. A. L., Meshram, I. I., Rajendran, A., Kodali, V., Getti, N., Roy, P., Kuhnlein, H. V., & Longvah, T. (2017). Nutritional status, food insecurity, and biodiversity among the Khasi in Meghalaya, North-East India. *Maternal and Child Nutrition*, *13*, e12557. https://doi.org/10.1111/mcn.12557

Coad, J., & Pedley, K. (2014). Iron deficiency and iron deficiency anemia in women. *Scandinavian Journal of Clinical and Laboratory Investigation*, *74*(sup244), 82–89. https://doi.org/10.3109/00365513.2014.936694

Cook, J. D., & Monsen, E. R. (1976). Food iron absorption in human subjects. III. Comparison of the effect of animal proteins on nonheme iron absorption. *The American Journal of Clinical Nutrition*, *29*(8), 859–867.

da Cunha, M. de S. B., Campos Hankins, N. A., & Arruda, S. F. (2019). Effect of vitamin A supplementation on iron status in humans: A systematic review and meta-analysis. *Critical Reviews in Food Science and Nutrition*, *59*(11), 1767–1781.

da Cunha, M. S., Siqueira, E. M., Trindade, L. S., & Arruda, S. F. (2014). Vitamin A deficiency modulates iron metabolism via ineffective erythropoiesis. *The Journal of Nutritional Biochemistry*, *25*(10), 1035–1044.

da Silva Lopes K, Takemoto Y, Garcia-Casal MN, Ota E, R. J. R. J. R. J., Kapil, R., Gupta, A., Who, Chan, M., Wong, C., Delforge, M., Selleslag, D., Triffet, A., Mineur, P., Bries, G., Graux, C., Trullemans, F., MacDonald, K., Abraham, I., Pluymers, W., Ravoet, C., Guidelines, O., Who, … Who. (2018). Nutrition-specific interventions for preventing and controlling anaemia throughout the life cycle: An overview of systematic reviews. *Journal of Nutrition*, *131*(1), 1–11. https://doi.org/10.4103/ijmr.IJMR

Dahlgren, G., & Whitehead, M. (2007). *Policies and strategies to promote social equity in health Background document to WHO – Strategy paper for Europe* (Vol. 14, Issue September1991, p. 67). https://core.ac.uk/download/pdf/6472456.pdf%0Ahttp://ideas.repec.org/p/hhs/ifswps/2007_014.html

Das, J. K., Salam, R. A., Mahmood, S. B., Moin, A., Kumar, R., Mukhtar, K., Lassi, Z. S., & Bhutta, Z. A. (2019). Food fortification with multiple micronutrients: Impact on health outcomes in general population. *Cochrane Database of Systematic Reviews*, *12*.

Dasgupta, R., Roy, S., & Lakhanpaul, M. (2020). An uphill task for POSHAN Abhiyan: Examining the missing link of 'convergence'. *Indian Pediatrics*, *57*(2), 109–113.

de Pee, S. (2014). Proposing nutrients and nutrient levels for rice fortification. *Annals of the New York Academy of Sciences*, *1324*(1), 55–66.

De Silva, N., Ahmed, B.-N., Casapia, M., de Silva, H. J., Gyapong, J., Malecela, M., & Pathmeswaran, A. (2015). Cochrane reviews on deworming and the right to a healthy, worm-free life. *PLOS Neglected Tropical Diseases*, *9*(10), e0004203.

Deaton, A., & Drèze, J. (2009). Food and nutrition in India: Facts and interpretations. *Economic and Political Weekly*, 42–65.

DeFries, R., Chhatre, A., Davis, K. F., Dutta, A., Fanzo, J., Ghosh-Jerath, S., Myers, S., Rao, N. D., & Smith, M. R. (2018). Impact of Historical Changes in Coarse Cereals Consumption in India on Micronutrient Intake and Anemia Prevalence. *Food and Nutrition Bulletin*, *39*(3), 377–392. https://doi.org/10.1177/0379572118783492

DeMaeyer, E., & Adiels-Tegman, M. (1985). The prevalence of anaemia in the world. *World Health Statistics Quarterly. Rapport Trimestriel De Statistiques Sanitaires Mondiales*, *38*(3), 302–316.

DeMaeyer, E. M. (1989). *Preventing and controlling iron deficiency anaemia through primary health care*.

Denic, S., & Agarwal, M. M. (2007). Nutritional iron deficiency: An evolutionary perspective. *Nutrition*, *23*(7–8), 603–614. https://doi.org/10.1016/j.nut.2007.05.002

De-Regil, L. M., Jefferds, M. E. D., Sylvetsky, A. C., & Dowswell, T. (2011). Intermittent iron supplementation for improving nutrition and development in children under 12 years of age. *Cochrane Database of Systematic Reviews*, *12*.

Dev, S., & Babitt, J. L. (2017). Overview of iron metabolism in health and disease. *Hemodialysis International*, *21*, S6–S20.

Dhillon, P. K., Kumar, B., & Verma, H. K. (2021). Prevalence of Anemia in View of Socio-demographic and Health Status of Adolescent Girls Enrolled in Government School at Border-belt of Indian Punjab. *Ecology of Food and Nutrition*, *60*(2), 198–211. https://doi.org/10.1080/03670244.2020.1824160

Diamond-Smith, N. G., Gupta, M., Kaur, M., & Kumar, R. (2016). Determinants of Persistent Anemia in Poor, Urban Pregnant Women of Chandigarh City, North India: A Mixed Method Approach. *Food and Nutrition Bulletin*, *37*(2), 132–143. https://doi.org/10.1177/0379572116637721

Dutta, A., Mohapatra, M. K., Rath, M., Rout, S. K., Kadam, S., Nallalla, S., Balagopalan, K., Tiwari, D., Yunus, S., Behera, B. K., Patro, B. K., Mangaraj, M., Sahu, S., & Paithankar, P. (2020). Effect of caste on health, independent of economic disparity: Evidence from school children of two rural districts of India. *Sociology of Health & Illness*. https://doi.org/10.1111/1467-9566.13105

Dutta, P., & Sengupta, B. (2017). *SOCIOECONOMIC DETERMINANTS OF MATERNAL ANEMIA: A DISAGGREGATED LEVEL ANALYSIS FROM ASSAM, INDIA*. 71–87. https://doi.org/10.17501/icoph.2017.3109

Engle-Stone, R., Aaron, G. J., Huang, J., Wirth, J. P., Namaste, S. M., Williams, A. M., Peerson, J. M., Rohner, F., Varadhan, R., Addo, O. Y., Temple, V., Rayco-Solon, P., Macdonald, B., & Suchdev, P. S. (2017). Predictors of anemia in preschool children: Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) project. *The American Journal of Clinical Nutrition*, *106*(Suppl 1), 402S-415S. https://doi.org/10.3945/ajcn.116.142323

Evans-Agnew, R. A., Johnson, S., Liu, F., & Boutain, D. M. (2016). Applying critical discourse analysis in health policy research: Case studies in regional, organizational, and global health. *Policy, Politics, & Nursing Practice*, *17*(3), 136–146.

Ewert, B. (2020). Moving beyond the obsession with nudging individual behaviour: Towards a broader understanding of Behavioural Public Policy. *Public Policy and Administration*, *35*(3), 337–360.

Ezeamama, A. E., McGarvey, S. T., Acosta, L. P., Zierler, S., Manalo, D. L., Wu, H.-W., Kurtis, J. D., Mor, V., Olveda, R. M., & Friedman, J. F. (2008). The synergistic effect of concomitant schistosomiasis, hookworm, and trichuris infections on children's anemia burden. *PLoS Neglected Tropical Diseases*, *2*(6), e245.

FAO/WHO. (1988). Requirements of vitamin A, iron, folate and vitamin B12. In *Report of a Joint FAO/WHO Expert Consultation. Food and Nutrition series.* Rome FAO.

Farmer, P. E., Nizeye, B., Stulac, S., & Keshavjee, S. (2006). Structural violence and clinical medicine. *PLoS Medicine*, *3*(10), e449.

Fernandez-Gaxiola, A. C., & De-Regil, L. M. (2019). Intermittent iron supplementation for reducing anaemia and its associated impairments in adolescent and adult menstruating women. *Cochrane Database of Systematic Reviews*, *1*.

Ferrari, R. (2016). *Writing narrative style literature reviews*. *January*. https://doi.org/10.1179/2047480615Z.000000000329

Fiedler, J. L., Babu, S., Smitz, M.-F., Lividini, K., & Bermudez, O. (2012). Indian social safety net programs as platforms for introducing wheat flour fortification: A case study of Gujarat, India. *Food and Nutrition Bulletin*, *33*(1), 11–30. https://doi.org/10.1177/156482651203300102

Fishman, S. M., Christian, P., & West, K. P. (2000). The role of vitamins in the prevention and control of anaemia. *Public Health Nutrition*, *3*(2), 125–150.

Galloway, R., Dusch, E., Elder, L., Achadi, E., Grajeda, R., Hurtado, E., Favin, M., Kanani, S., Marsaban, J., Meda, N., Mona Moore, K., Morison, L., Raina, N., Rajaratnam, J., Rodriquez, J., & Stephen, C. (2002). Women's perceptions of iron deficiency and anemia prevention and control in eight developing countries. *Social Science and Medicine*, *55*(4), 529–544. https://doi.org/10.1016/S0277-9536(01)00185-X

Ganz, T. (2011). Hepcidin and iron regulation, 10 years later. *Blood, The Journal of the American Society of Hematology*, *117*(17), 4425–4433.

Garcia-Casal, M. N., Pasricha, S. R., Sharma, A. J., & Peña-Rosas, J. P. (2019). Use and interpretation of hemoglobin concentrations for assessing anemia status in individuals and populations: Results from a WHO technical meeting. *Annals of the New York Academy of Sciences*, *1450*, 5–14. https://doi.org/10.1111/nyas.14090

Gardner, W., & Kassebaum, N. (2020). Global, Regional, and National Prevalence of Anemia and Its Causes in 204 Countries and Territories, 1990–2019. *Current Developments in Nutrition*, *4*(Supplement_2), 830–830. https://doi.org/10.1093/cdn/nzaa053_035

Garrison, C. (2009). *Iron Disorders Institute Guide to Anemia*. Sourcebooks, Inc.

Gera, T., & Sachdev, H. P. S. (2002). Effect of iron supplementation on incidence of infectious illness in children: Systematic review. *Bmj-British Medical Journal*, *325*(7373), 1142-1144B. https://doi.org/10.1136/bmj.325.7373.1142

Gera, T., Sachdev, H. P. S., & Nestel, P. (2009). Effect of combining multiple micronutrients with iron supplementation on Hb response in children: Systematic review of randomized controlled trials. *Public Health Nutrition*, *12*(6), 756–773. https://doi.org/10.1017/S1368980008003145

Gera, T., Sachdev, H. P. S., Nestel, P., & Sachdev, S. S. (2007). Effect of iron supplementation on haemoglobin response in children: Systematic review of randomised controlled trials. *Journal of Pediatric Gastroenterology and Nutrition*, *44*(4), 468–486.

Gera, T., Sachdev, H. S., & Boy, E. (2012). Effect of iron-fortified foods on hematologic and biological outcomes: Systematic review of randomized controlled trials. *The American Journal of Clinical Nutrition*, *96*(2), 309–324.

Ghosh, R., & Bharati, P. (2003). Haemoglobin status of adult women of two ethnic groups living in a peri-urban area of Kolkata city, India: A micro-level study. In *Asia Pacific J Clin Nutr* (Vol. 12, Issue 4, pp. 451–459).

Ghosh, S. (2009). Exploring socioeconomic vulnerability of anaemia among women in Eastern Indian States. *Journal of Biosocial Science*, *41*(6), 763–787. https://doi.org/10.1017/S0021932009990149

Ghosh, S., Sinha, S., Shivakumar, N., Thomas, T., Sachdev, H. S., & Kurpad, A. V. (2019). Daily Iron Requirements in Healthy Indian Children and Adolescents. *Indian Pediatrics*, *56*(7), 551–555. https://doi.org/10.1007/s13312-019-1552-0

Ghosh, S., Sinha, S., Thomas, T., Sachdev, H. S., & Kurpad, A. V. (2019). Revisiting Dietary Iron Requirement and Deficiency in Indian Women: Implications for Food Iron Fortification and Supplementation. *Journal of Nutrition*, *149*(3), 366–371. https://doi.org/10.1093/jn/nxy283

Gillespie, S., Johnston, J. L., & Micronutrient Initiative (Association). (1998). *Expert consultation on anemia determinants and interventions: Proceedings of a conference held September 16-17, 1997, Ottawa, Canada*. Micronutrient Initiative.

Gillespie, S. & UNICEF. (1998). *Major issues in the control of iron deficiency*. IDRC, Ottawa, ON, CA.

Gonmei, Z., & Toteja, G. S. (2018). Micronutrient status of Indian population. *Indian Journal of Medical Research*, *148*(5), 511–521. https://doi.org/10.4103/ijmr.IJMR_1768_18

Gosdin, L., Martorell, R., Bartolini, R. M., Mehta, R., Srikantiah, S., & Young, M. F. (2018). The co-occurrence of anaemia and stunting in young children. *Maternal and Child Nutrition*, *14*(3). https://doi.org/10.1111/mcn.12597

Green, B. N., Johnson, C. D., & Adams, A. (2006). Writing narrative literature reviews for peer-reviewed journals: Secrets of the trade. *Journal of Chiropractic Medicine*, *5*(3), 101–117.

Gupta, S., Pingali, P., & Pinstrup-Andersen, P. (2019). Women's empowerment and nutrition status: The case of iron deficiency in India. *Food Policy*, *88*, 101763. https://doi.org/10.1016/j.foodpol.2019.101763

Haas, J. D., Rahn, M., Venkatramanan, S., Marquis, G. S., Wenger, M. J., Murray-Kolb, L. E., Wesley, A. S., & Reinhart, G. A. (2014). Double-Fortified Salt Is Efficacious in Improving Indicators of Iron Deficiency in Female Indian Tea Pickers. *Journal of Nutrition*, *144*(6), 957–964. https://doi.org/10.3945/jn.113.183228

Haden, R. L. (1938). HISTORICAL ASPECTS OF IRON THERAPY IN ANEMIA: CHAIRMAN'S ADDRESS. *Journal of the American Medical Association*, *111*(12), 1059–1061.

Hatfield, T. G., Withers, T. M., & Greaves, C. J. (2020). Systematic review of the effect of training interventions on the skills of health professionals in promoting health behaviour, with meta-analysis of subsequent effects on patient health behaviours. *BMC Health Services Research*, *20*(1), 1–9.

Hayes-conroy, J., & Colleges, W. S. (2015). *Available: NOW Available: NOW Available: NOW*.

Hennigar, S. R., McClung, J. P., Hatch-McChesney, A., Allen, J. T., Wilson, M. A., Carrigan, C. T., Murphy, N. E., Teien, H. K., Martini, S., & Gwin, J. A. (2021). Energy deficit increases hepcidin and exacerbates declines in dietary iron absorption following strenuous physical activity: A randomized-controlled cross-over trial. *The American Journal of Clinical Nutrition*, *113*(2), 359–369.

Herynk, J. W., & Janzen, J. M. (2014). From cell to symbol: A biocultural study of anemia and subjectivity among the Poqomchi' Maya in Guatemala. In *ProQuest Dissertations and Theses*.

Hunter, D. J., Popay, J., Tannahill, C., & Whitehead, M. (2010). Getting to grips with health inequalities at last? *BMJ (Online)*, *340*(7742), 323. https://doi.org/10.1136/bmj.c684

Hurrell, R., & Egli, I. (2010). Iron bioavailability and dietary reference values. *The American Journal of Clinical Nutrition*, *91*(5), 1461S-1467S.

Hurrell, R. F. (2015). Flour fortification as a strategy to prevent anaemia. *British Journal of Nutrition*, *114*(4), 501–502.

Hurrell, R., Ranum, P., de Pee, S., Biebinger, R., Hulthen, L., Johnson, Q., & Lynch, S. (2010). Revised recommendations for iron fortification of wheat flour and an evaluation of the

expected impact of current national wheat flour fortification programs. *Food and Nutrition Bulletin*, *31*(1_suppl1), S7–S21.

ICMR. (2010). *Nutrient requirements and Recommended Dietary Allowances for Indians. A Report of the Expert Group of the Indian Council of Medical Research, National Institute of Nutrition Hyderabad; 2010*.

IIPS. (2020). *National Family Health Survey (NFHS-5) 2019–2020 fact sheets: Key Indicators 22 States/UTs from phase I. International Institute of Population Sciences, Ministry of Health and Family Welfare, Government of India*. http://rchiips.org/NFHS/NFHS-5_FCTS/NFHS-5%20State%20Factsheet%20Compendium_Phase-I.pdf

IIPS & ICF. (2017). *International Institute for Population Sciences (IIPS) and ICF. 2017. National Family Health Survey (NFHS-4), 2015-16: India. Mumbai: IIPS.*

Jackson, A. A. (2007). Anemia in severe undernutrition (malnutrition). *Nutritional Anemia*, 215.

Jilani, T., & Iqbal, M. P. (2011). Does vitamin E have a role in treatment and prevention of anemia? *Pakistan Journal of Pharmaceutical Sciences*, *24*(2), 237.

Kapil, U., Kapil, R., & Gupta, A. (2019). National Iron Plus Initiative: Current status & future strategy. *Indian Journal of Medical Research*, *150*(3), 239–247. https://doi.org/10.4103/ijmr.IJMR_1782_18

Kapur, D., Agarwal, K. N., & Agarwal, D. K. (2002). Nutritional anemia and its control. *Indian Journal of Pediatrics*, *69*(7), 607–616. https://doi.org/10.1007/BF02722690

Karakochuk, C. D., Hess, S. Y., Moorthy, D., Namaste, S., Parker, M. E., Rappaport, A. I., Wegmüller, R., & Dary, O. (2019). Measurement and interpretation of hemoglobin concentration in clinical and field settings: A narrative review. *Annals of the New York Academy of Sciences*. https://doi.org/10.1111/nyas.14003

Karlsson, O., Kim, R., Joe, W., & Subramanian, S. (2020). The relationship of household assets and amenities with child health outcomes: An exploratory cross-sectional study in India 2015-2016. *Ssm-Population Health*, *10*, 100513. https://doi.org/10.1016/j.ssmph.2019.100513

Kassebaum, N. J. (2013). *The Global Burden of Anemia*.

Kassebaum, N. J. & GBD 2013 Anemia Collaborators. (2016). The Global Burden of Anemia. *Hematology/Oncology Clinics of North America*, *30*(2), 247–308. https://doi.org/10.1016/j.hoc.2015.11.002

Kassebaum, N. J., Jasrasaria, R., Naghavi, M., Wulf, S. K., Johns, N., Lozano, R., Regan, M., Weatherall, D., Chou, D. P., Eisele, T. P., Flaxman, S. R., Pullan, R. L., Brooker, S. J., & Murray, C. J. L. (2013). A systematic analysis of global anemia burden from 1990 to 2010. *Blood*, *123*(5), 615–624. https://doi.org/10.1182/blood-2013-06-508325

Katsarou, A., & Pantopoulos, K. (2020). Basics and principles of cellular and systemic iron homeostasis. *Molecular Aspects of Medicine*, *75*, 100866.

Kavitha, N. (2011). Is young maternal age a risk factor for sexually transmitted diseases and anaemia in India? An examination in urban and rural areas. *Journal of Health Management*, *13*(3), 279–300. https://doi.org/10.1177/097206341101300303

Kelkitli, E., Ozturk, N., Aslan, N. A., Kilic-Baygutalp, N., Bayraktutan, Z., Kurt, N., Bakan, N., & Bakan, E. (2016). Serum zinc levels in patients with iron deficiency anemia and its association with symptoms of iron deficiency anemia. *Annals of Hematology*, *95*(5), 751–756.

Khan, J. H., Hassan, T., & Shamshad. (2014). Incidence of Poverty and Level of Socio-Economic Deprivation in India. *The Journal of Developing Areas*, *48*(2), 21–38. https://doi.org/10.1353/jda.2014.0031

Kinyoki, D., Osgood-Zimmerman, A. E., Bhattacharjee, N. V., Kassebaum, N. J., & Hay, S. I. (2021). Anemia prevalence in women of reproductive age in low-and middle-income countries between 2000 and 2018. *Nature Medicine*, *27*(10), 1761–1782.

Knovich, M. A., Il'yasova, D., Ivanova, A., & Molnár, I. (2008). The association between serum copper and anaemia in the adult Second National Health and Nutrition Examination Survey (NHANES II) population. *British Journal of Nutrition*, *99*(6), 1226–1229.

Kothari, M. T., Coile, A., Huestis, A., Pullum, T., Garrett, D., & Engmann, C. (2019). Exploring associations between water, sanitation, and anemia through 47 nationally representative demographic and health surveys. *Annals of the New York Academy of Sciences*, *1450*(1), 249–267. https://doi.org/10.1111/nyas.14109

Kreiger, N. (1994). *EPIDEMIOLOGY AND THE WEB OF CAUSATION: HAS ANYONE SEEN THE SPIDER?*

Krieger, N. (2005). Embodiment: A conceptual glossary for epidemiology. *Journal of Epidemiology and Community Health*, *59*(5), 350–355. https://doi.org/10.1136/jech.2004.024562

Krieger, N. (2011). *Epidemiology and the people's health: Theory and context*. Oxford University Press.

Krishnaswamy, S., Bhattarai, D., Bharti, B., Bhatia, P., Das, R., & Bansal, D. (2017). Iron Deficiency and Iron Deficiency Anemia in 3-5 months-old, Breastfed Healthy Infants. *Indian Journal of Pediatrics*, *84*(7), 505–508. https://doi.org/10.1007/s12098-017-2330-4

Krupp, K., Placek, C. D., Wilcox, M., Ravi, K., Srinivas, V., Arun, A., & Madhivanan, P. (2018). Financial decision making power is associated with moderate to severe anemia: A prospective cohort study among pregnant women in rural South India. *Midwifery*, *61*, 15–21. https://doi.org/10.1016/j.midw.2018.02.014

Kubzansky, L., Seeman, T. E., & Glymour, M. M. (2014). Biological pathways linking social conditions and health: Plausible mechanisms and emerging puzzles. *Social Epidemiology: New Perspectives on Social Determinants of Global Population Health*, 512–561.

Kulkarni, B., Peter, R., Ghosh, S., Pullakhandam, R., Thomas, T., Reddy, G. B., Rajkumar, H., Kapil, U., Deb, S., & Johnston, R. (2021). Prevalence of iron deficiency and its sociodemographic patterning in Indian children and adolescents: Findings from the Comprehensive National Nutrition Survey 2016–18. *The Journal of Nutrition*, *151*(8), 2422–2434.

Kundu, S., Kumari, S., Maji, B., Ray, D., & Kumar, A. (2013). *Nutritional status and productivity of female tea pluckers of a tea garden in Dooars , West Bengal*. *3*(1), 3101–3106.

Lamstein, S., Stillman, T., Koniz-Booher, P., Aakesson, A., Collaiezzi, B., Williams, T., Beall, K., & Anson, M. (2014). Evidence of effective approaches to social and behavior change communication for preventing and reducing stunting and anemia: Report from a systematic literature review. *USAID/Strengthening Partnerships, Results, and Innovations in Nutrition Globally (SPRING) Project, Arlington*.

Larsen, D. A., Grisham, T., Slawsky, E., & Narine, L. (2017). An individual-level meta-analysis assessing the impact of community-level sanitation access on child stunting, anemia, and diarrhea: Evidence from DHS and MICS surveys. *PLoS Neglected Tropical Diseases*, *11*(6), e0005591. https://doi.org/10.1371/journal.pntd.0005591

Laxmaiah, A., Arlappa, N., Balakrishna, N., Mallikarjuna Rao, K., Galreddy, C., Kumar, S., Ravindranath, M., & Brahmam, G. N. V. (2013). Prevalence and determinants of

micronutrient deficiencies among rural children of eight states in India. *Annals of Nutrition and Metabolism*, *62*(3), 231–241. https://doi.org/10.1159/000348674

Little, M., Zivot, C., Humphries, S., Dodd, W., Patel, K., & Dewey, C. (2018). Burden and determinants of anemia in a rural population in South India: A cross-sectional study. *Anemia*, *2018*. https://doi.org/10.1155/2018/7123976

Lo, N. C., Snyder, J., Addiss, D. G., Heft-Neal, S., Andrews, J. R., & Bendavid, E. (2018). Deworming in pre-school age children: A global empirical analysis of health outcomes. *Plos Neglected Tropical Diseases*, *12*(5), e0006500. https://doi.org/10.1371/journal.pntd.0006500

Longvah, T., Khutsoh, B., Meshram, I. I., Krishna, S., Kodali, V., Roy, P., & Kuhnlein, H. V. (2017). Mother and child nutrition among the Chakhesang tribe in the state of Nagaland, North-East India. *Maternal and Child Nutrition*, *13*, e12558. https://doi.org/10.1111/mcn.12558

Loudon, I. (1984). The diseases called chlorosis1. *Psychological Medicine*, *14*(1), 27–36.

Low, M., Farrell, A., Biggs, B.-A., & Pasricha, S.-R. (2013). Effects of daily iron supplementation in primary-school–aged children: Systematic review and meta-analysis of randomized controlled trials. *Cmaj*, *185*(17), E791–E802.

Lozoff, B., Klein, N. K., & Prabucki, K. M. (1986). Iron-deficient anemic infants at play. *Journal of Developmental and Behavioral Pediatrics: JDBP*, *7*(3), 152–158.

Mahapatra, S., Parker, M. E., Dave, N., Zobrist, S. C., Shajie Arul, D., King, A., Betigeri, A., & Sachdeva, R. (2021). Micronutrient-fortified rice improves haemoglobin, anaemia prevalence and cognitive performance among schoolchildren in Gujarat, India: A case-control study. *International Journal of Food Sciences and Nutrition*, *72*(5), 690–703.

Majia, L. A., Hodges, R. E., Arroyave, G., Viteri, F., & Torun, B. (1977). Vitamin A deficiency and anemia in Central American children. *The American Journal of Clinical Nutrition*, *30*(7), 1175–1184.

McCullagh, P. (2016). Mind, the gap. *Communications in Computer and Information Science*, *621*, 102–112. https://doi.org/10.1007/978-3-319-41769-1_8

McKay, A. K., Pyne, D. B., Burke, L. M., & Peeling, P. (2020). Iron metabolism: Interactions with energy and carbohydrate availability. *Nutrients*, *12*(12), 3692.

McLean, E., de Benoist, B., & Allen, L. H. (2008). Review of the magnitude of folate and vitamin B12 deficiencies worldwide. *Food and Nutrition Bulletin*, *29*(2_suppl1), S38–S51.

Mejia, L. A. (1993). Role of vitamin A in iron deficiency anemia. *Nestle Nutrition Workshop Series*, *30*, 93–93.

Mejía, L. A., & Chew, F. (1988). Hematological effect of supplementing anemic children with vitamin A alone and in combination with iron. *The American Journal of Clinical Nutrition*, *48*(3), 595–600.

Merrill, R. D., Burke, R. M., Northrop-Clewes, C. A., Rayco-Solon, P., Flores-Ayala, R., Namaste, S. M., Serdula, M. K., & Suchdev, P. S. (2017). Factors associated with inflammation in preschool children and women of reproductive age: Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) project. *The American Journal of Clinical Nutrition*, *106*, 348S-358S. https://doi.org/10.3945/ajcn.116.142315

Michelazzo, F. B., Oliveira, J. M., Stefanello, J., Luzia, L. A., & Rondó, P. H. (2013). The influence of vitamin A supplementation on iron status. *Nutrients*, *5*(11), 4399–4413.

Miski, A. M.-A., & Kratzer, F. H. (1977). Effects of dietary protein, glycine, and tryptophan on iron metabolism in the growing chick. *The Journal of Nutrition*, *107*(1), 24–34.

Mohanram, M., Kulkarni, K. A., & Reddy, V. (1977). Hematological studies in vitamin A deficient children. *International Journal for Vitamin and Nutrition Research.*

Internationale Zeitschrift Fur Vitamin-Und Ernahrungsforschung. Journal International de Vitaminologie et de Nutrition, *47*(4), 389–393.

MOHFW. (1991). *Policy on control of Nutritional anaemia, National Nutritional Anaemia control programme*. https://hetv.org/pdf/anaemia-policy.pdf

MoHFW. (2013). *Guidelines for control of Iron deficiency Anaemia,National iron Plus Initiave, towards infnite potential in an anaemia free India, Ministry of Health and Family Welfare, Government of India*. https://www.nhm.gov.in/images/pdf/programmes/child-health/guidelines/Control-of-Iron-Deficiency-Anaemia.pdf

MoHFW. (2018). *Intensified national iron plus initiative (I-NIPI): Operational guidelines for programme managers*. https://anemiamuktbharat.info/wp-content/uploads/2019/09/Anemia-Mukt-Bharat-Brochure_English.pdf

MOHFW & UNICEF. (2019). *Comprehensive National Nutrition Survey- 2016-18, National Report*.

Montresor, A., Addiss, D., Albonico, M., Ali, S. M., Ault, S. K., Gabrielli, A.-F., Garba, A., Gasimov, E., Gyorkos, T., & Jamsheed, M. A. (2015). Methodological bias can lead the Cochrane Collaboration to irrelevance in public health decision-making. *PLoS Neglected Tropical Diseases*, *9*(10), e0004165.

Moretti, D., Goede, J. S., Zeder, C., Jiskra, M., Chatzinakou, V., Tjalsma, H., Melse-Boonstra, A., Brittenham, G., Swinkels, D. W., & Zimmermann, M. B. (2015). Oral iron supplements increase hepcidin and decrease iron absorption from daily or twice-daily doses in iron-depleted young women. *Blood, The Journal of the American Society of Hematology*, *126*(17), 1981–1989.

Moretti, D., Zimmermann, M. B., Muthayya, S., Thankachan, P., Lee, T.-C., Kurpad, A. V., & Hurrell, R. F. (2006). Extruded rice fortified with micronized ground ferric pyrophosphate reduces iron deficiency in Indian schoolchildren: A double-blind randomized controlled trial. *American Journal of Clinical Nutrition*, *84*(4), 822–829.

Mudur, G. (2015). *Deworming programme in India sparks controversy*. British Medical Journal Publishing Group.

Muncie Jr, H. L., & Campbell, J. S. (2009). Alpha and beta thalassemia. *American Family Physician*, *80*(4), 339–344.

Muthayya, S., Thankachan, P., Hirve, S., Amalrajan, V., Thomas, T., Lubree, H., Agarwal, D., Srinivasan, K., Hurrell, R. F., & Yajnik, C. S. (2012). Iron fortification of whole wheat flour reduces iron deficiency and iron deficiency anemia and increases body iron stores in Indian school-aged children. *The Journal of Nutrition*, *142*(11), 1997–2003.

MW&CD. (2007). *Review of the Policy regarding micronutrient – Iron, folic acid (IFA), Ministry of Women & Child Development, New Delhi*. https://nhm.gov.in/images/pdf/programmes/child-health/guidelines/goi_ifa.pdf

Myint, Z. W., Oo, T. H., Thein, K. Z., Tun, A. M., & Saeed, H. (2018). Copper deficiency anemia. *Annals of Hematology*, *97*(9), 1527–1534.

Nair, K. M., Fernandez-Rao, S., Nagalla, B., Kankipati, R. V., Punjal, R., Augustine, L. F., Hurley, K. M., Tilton, N., Harding, K. B., Reinhart, G., & Black, M. M. (2016). Characterisation of anaemia and associated factors among infants and pre-schoolers from rural India. *Public Health Nutrition*, *19*(5), 861–871. https://doi.org/10.1017/S1368980015002050

Nair, K. M., & Iyengar, V. (2009). Iron content, bioavailability & factors affecting iron status of Indians. *Indian Journal of Medical Research*, *130*(5), 634–645.

Nair, M. K., Augustine, L. F., & Konapur, A. (2016). Food-based interventions to modify diet quality and diversity to address multiple micronutrient deficiency. *Frontiers in Public Health*, *3*, 277.

Nairz, M., Theurl, I., Wolf, D., & Weiss, G. (2016). Iron deficiency or anemia of inflammation? *Wiener Medizinische Wochenschrift*, *166*(13), 411–423.

Namaste, S. M., Aaron, G. J., Varadhan, R., Peerson, J. M., & Suchdev, P. S. (2017). Methodologic approach for the Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) project. *The American Journal of Clinical Nutrition*, *106*, 333S-347S. https://doi.org/10.3945/ajcn.116.142273

Nancy Carter, R. N., Bryant-Lukosius, D., & Alba DiCenso, R. N. (2014). The use of triangulation in qualitative research. *Oncology Nursing Forum*, *41*(5), 545.

Nayar, K. R. (2007). Social exclusion, caste & health: A review based on the social determinants framework. *Indian Journal of Medical Research*.

NDD. (2015). *National deworming day: Operational guidelines. Child health division. New Delhi: Ministry of Health and Family Welfare, government of India Posted: 2016*. https://nhm.gov.in/images/pdf/NDD/Guidelines/NDD_Operational_Guidelines.pdf

Neufeld, L. M., Larson, L. M., Kurpad, A., Mburu, S., Martorell, R., & Brown, K. H. (2019). Hemoglobin concentration and anemia diagnosis in venous and capillary blood: Biological basis and policy implications. *Annals of the New York Academy of Sciences*, *1450*(1), 172–189. https://doi.org/10.1111/nyas.14139

Nguyen, P. H., Scott, S., Avula, R., Tran, L. M., & Menon, P. (2018). Trends and drivers of change in the prevalence of anaemia among 1 million women and children in India, 2006 to 2016. *BMJ Global Health*, *3*(5), 1–12. https://doi.org/10.1136/bmjgh-2018-001010

Nguyen, P. H., Scott, S., Neupane, S., Tran, L. M., & Menon, P. (2019). Social, biological, and programmatic factors linking adolescent pregnancy and early childhood undernutrition: A path analysis of India's 2016 National Family and Health Survey. *The Lancet Child and Adolescent Health*, *3*(7), 463–473. https://doi.org/10.1016/S2352-4642(19)30110-5

NIN Annual Report. (2005). *Annual Report 2005-06. National Institute of Nutrition, Indian Council of Medical Research; p. 18-26*. https://www.nin.res.in/annualreports.html

NNMB. (2012). *Diet and nutritional status of Rural population, prevalence of hypertension and diabetes among adults and infant and young child feeding practices—Report of third repeat survey* (pp. 1–322). http://nnmbindia.org/1_NNMB_Third_Repeat_Rural_Survey___Technicl_Report_26.pdf

NNMB. (2017). *Diet and Nutritional Status of Urban Population in India and Prevalence of Obesity, Hypertension, Diabetes and Hyperlipidedemia in Urban Men and Women. A brief NNMB Urban Nutrition report, National Institute of Nutrition, ICMR*.

Onyeneho, N. G., Ozumba, B. C., Chalupowski, M., & Subramanian, S. V. (2020). Risk Factors of Childhood and Maternal Anemia in India. *International Quarterly of Community Health Education*, *40*(3), 209–217. https://doi.org/10.1177/0272684X19874278

Page, C. M., Patel, A., & Hibberd, P. L. (2015). Does Smoke from Biomass Fuel Contribute to Anemia in Pregnant Women in Nagpur, India? A Cross-Sectional Study. *Plos One*, *10*(5), e0127890. https://doi.org/10.1371/journal.pone.0127890

Pal, P. P., Sharma, S., Sarkar, T. K., & Mitra, P. (2013). Iron and Folic Acid Consumption by the Ante-natal Mothers in a Rural Area of India in 2010. *International Journal of Preventive Medicine*, *4*(10), 1213–1216.

Panth, M., Shatrugna, V., Yasodhara, P., & Sivakumar, B. (1990). Effect of vitamin A supplementation on haemoglobin and vitamin A levels during pregnancy. *British Journal of Nutrition*, *64*(2), 351–358.

Papathakis, P., & Piwoz, E. (2008). Nutrition and Tuberculosis: A review of the literature and considerations for TB control programs. *United States Agency for International Development, Africa's Health 2010 Project*, 1.

Paré, G., & Kitsiou, S. (2017). Methods for literature reviews. In *Handbook of eHealth Evaluation: An Evidence-based Approach [Internet]*. University of Victoria.

Pasiakos, S. M., Margolis, L. M., Murphy, N. E., McClung, H. L., Martini, S., Gundersen, Y., Castellani, J. W., Karl, J. P., Teien, H. K., & Madslien, E. H. (2016). Effects of exercise mode, energy, and macronutrient interventions on inflammation during military training. *Physiological Reports*, *4*(11), e12820.

Pasricha, S., Drakesmith, H., Black, J., Hipgrave, D., & Biggs, B. (2013). *Review Article Control of iron de fi ciency anemia in low- and middle-income countries*. *121*(14), 1–3. https://doi.org/10.1182/blood-2012-09-453522.The

Pasricha, S. R., Black, J., Muthayya, S., Shet, A., Bhat, V., Nagaraj, S., Prashanth, N. S., Sudarshan, H., Biggs, B. A., & Shet, A. S. (2010). Determinants of anemia among young children in rural India. *Pediatrics*, *126*(1). https://doi.org/10.1542/peds.2009-3108

Paul, P., Chouhan, P., & Zaveri, A. (2019). Impact of child marriage on nutritional status and anaemia of children under 5 years of age: Empirical evidence from India. *Public Health*, *177*, 95–101. https://doi.org/10.1016/j.puhe.2019.08.008

Pearce, N. (1997). Traditional epidemiology, modern epidemiology and public health. *Epidemiologia e Prevenzione*, *21*(2), 92–99.

Peeling, P., Dawson, B., Goodman, C., Landers, G., & Trinder, D. (2008). Athletic induced iron deficiency: New insights into the role of inflammation, cytokines and hormones. *European Journal of Applied Physiology*, *103*(4), 381–391.

Peeling, P., Dawson, B., Goodman, C., Landers, G., Wiegerinck, E. T., Swinkels, D. W., & Trinder, D. (2009). Effects of exercise on hepcidin response and iron metabolism during recovery. *International Journal of Sport Nutrition and Exercise Metabolism*, *19*(6), 583–597.

Peña-Rosas, J. P., De-Regil, L. M., Garcia-Casal, M. N., & Dowswell, T. (2015). Daily oral iron supplementation during pregnancy. *Cochrane Database of Systematic Reviews*, *7*.

Peña-Rosas, J. P., De-Regil, L. M., Malave, H. G., Flores-Urrutia, M. C., & Dowswell, T. (2015). Intermittent oral iron supplementation during pregnancy. *Cochrane Database of Systematic Reviews*, *10*.

Peña-Rosas, J. P., Mithra, P., Unnikrishnan, B., Kumar, N., De-Regil, L. M., Nair, N. S., Garcia-Casal, M. N., & Solon, J. A. (2019). Fortification of rice with vitamins and minerals for addressing micronutrient malnutrition. *Cochrane Database of Systematic Reviews*, *10*.

Perumal, V. (2014). Reproductive risk factors assessment for anaemia among pregnant women in India using a multinomial logistic regression model. *Tropical Medicine & International Health : TM & IH*, *19*(7). https://doi.org/10.1111/tmi.12312

Peters, D. H. (2009). *Improving health service delivery in developing countries: From evidence to action*. World Bank Publications.

Petry, N., Olofin, I., Hurrell, R. F., Boy, E., Wirth, J. P., Moursi, M., Angel, M. D., & Rohner, F. (2016). The proportion of anemia associated with iron deficiency in low, medium, and high human development index countries: A systematic analysis of national surveys. *Nutrients*, *8*(11), 1–17. https://doi.org/10.3390/nu8110693

Pollitt, E. (2001). The developmental and probabilistic nature of the functional consequences of iron-deficiency anemia in children. *The Journal of Nutrition*, *131*(2), 669S-675S.

Poskitt, E. M. E. (2003). Early history of iron deficiency. In *British Journal of Haematology*. https://doi.org/10.1046/j.1365-2141.2003.04529.x

Powers, H. J. (2003). Riboflavin (vitamin B-2) and health. *The American Journal of Clinical Nutrition*, *77*(6), 1352–1360.

Powers, H. J., Hill, M. H., Mushtaq, S., Dainty, J. R., Majsak-Newman, G., & Williams, E. A. (2011). Correcting a marginal riboflavin deficiency improves hematologic status in young women in the United Kingdom (RIBOFEM). *The American Journal of Clinical Nutrition*, *93*(6), 1274–1284.

Radhika, A. G., Sharma, A. K., Perumal, V., Sinha, A., Sriganesh, V., Kulshreshtha, V., & Kriplani, A. (2019). Parenteral versus oral iron for treatment of iron deficiency anaemia during pregnancy and post-partum: A systematic review. *The Journal of Obstetrics and Gynecology of India*, *69*(1), 13–24.

Ramakrishnan, U. (2001). *Nutritional Anemias*.

Rana, M. J., & Goli, S. (2017). The returns of family planning: Macro-level assessment of the effect of contraceptive use on women's anaemia and childhood undernutrition. *Journal of Biosocial Science*, *49*(6). https://doi.org/10.1017/S0021932016000717

Rao, N., Vijayasarathy, C., & Prabhavathi, T. (1983). Iron absorption from habitual diets of Indians studied by the extrinsic tag technique. *Indian Journal of Medical Research*.

Rao, S., Joshi, S., Bhide, P., Puranik, B., & Asawari, K. (2014). Dietary diversification for prevention of anaemia among women of childbearing age from rural India. *Public Health Nutrition*, *17*(4), 939–947. https://doi.org/10.1017/S1368980013001006

Rao, S., Joshi, S., Bhide, P., Puranik, B., & Kanade, A. (2011). Social dimensions related to anaemia among women of childbearing age from rural India. *Public Health Nutrition*, *14*(2), 365–372. https://doi.org/10.1017/S1368980010002776

Raphael, D. (2006). Social determinants of health: Present status, unanswered questions, and future directions. *International Journal of Health Services: Planning, Administration, Evaluation*, *36*(4), 651–677. https://doi.org/10.2190/3MW4-1EK3-DGRQ-2CRF

Redig, A. J., & Berliner, N. (2013). Pathogenesis and clinical implications of HIV-related anemia in 2013. *Hematology 2013, the American Society of Hematology Education Program Book*, *2013*(1), 377–381.

Reveiz, L., Gyte, G. M., Cuervo, L. G., & Casasbuenas, A. (2011). Treatments for iron-deficiency anaemia in pregnancy. *Cochrane Database of Systematic Reviews*, *10*.

Ridgway, E., Baker, P., Woods, J., & Lawrence, M. (2019). Historical developments and paradigm shifts in public health nutrition science, guidance and policy actions: A narrative review. *Nutrients*, *11*(3). https://doi.org/10.3390/nu11030531

Rogozińska, E., Daru, J., Nicolaides, M., Amezcua-Prieto, C., Robinson, S., Wang, R., Godolphin, P. J., Saborido, C. M., Zamora, J., & Khan, K. S. (2021). Iron preparations for women of reproductive age with iron deficiency anaemia in pregnancy (FRIDA): A systematic review and network meta-analysis. *The Lancet Haematology*, *8*(7), e503–e512.

Rohner, F., Zimmermann, M. B., Wegmueller, R., Tschannen, A. B., & Hurrell, R. F. (2007). Mild riboflavin deficiency is highly prevalent in school-age children but does not increase risk for anaemia in Cote d'Ivoire. *British Journal of Nutrition*, *97*(5), 970–976.

Rokade, S., Mog, M., & Mondal, N. A. (2020). Nutritional status among tribal women in Maharashtra, India: Spatial variations and determinants. *Clinical Epidemiology and Global Health*, *8*(4), 1360–1365. https://doi.org/10.1016/j.cegh.2020.05.012

Rowe, S., & Carr, A. C. (2020). Global vitamin C status and prevalence of deficiency: A cause for concern? *Nutrients*, *12*(7), 2008.

Sabharwal, N. S., & Sonalkar, W. (2015). Dalit Women in India: At the Crossroads of Gender, Class, and Caste NIDHI SADANA SABHARWAL AND WANDANA SONALKAR. *Global Justice : Theory Practice Rhetoric*, *8*(1). https://doi.org/10.21248/GJN.8.1.54

Sachdev, H. S., Porwal, A., Acharya, R., Ashraf, S., Ramesh, S., Khan, N., Kapil, U., Kurpad, A. V., & Sarna, A. (2021). Haemoglobin thresholds to define anaemia in a national sample of healthy children and adolescents aged 1–19 years in India: A population-based study. *The Lancet Global Health*, *9*(6), e822–e831.

Safiri, S., Kolahi, A.-A., Noori, M., Nejadghaderi, S. A., Karamzad, N., Bragazzi, N. L., Sullman, M. J., Abdollahi, M., Collins, G. S., & Kaufman, J. S. (2021). Burden of anemia and its underlying causes in 204 countries and territories, 1990–2019: Results from the Global Burden of Disease Study 2019. *Journal of Hematology & Oncology*, *14*(1), 1–16.

Salam, N., & Azam, S. (2017). Prevalence and distribution of soil-transmitted helminth infections in India. *BMC Public Health*, *17*(1), 1–12.

Salam, R. A., Das, J. K., & Bhutta, Z. A. (2021). Effect of mass deworming with antihelminthics for soil-transmitted helminths during pregnancy. *Cochrane Database of Systematic Reviews*, *5*.

Sarkar, R., Rose, A., Mohan, V. R., Ajjampur, S. S. R., Veluswamy, V., Srinivasan, R., Muliyil, J., Rajshekhar, V., George, K., Balraj, V., Grassly, N. C., Anderson, R. M., Brooker, S. J., & Kang, G. (2017). Study design and baseline results of an open-label cluster randomized community-intervention trial to assess the effectiveness of a modified mass deworming program in reducing hookworm infection in a tribal population in southern India. *Contemporary Clinical Trials Communications*, *5*, 49–55. https://doi.org/10.1016/j.conctc.2016.12.002

Sarna, A., Porwal, A., Ramesh, S., Agrawal, P. K., Acharya, R., Johnston, R., Khan, N., Sachdev, H. P. S., Nair, K. M., & Ramakrishnan, L. (2020). Characterisation of the types of anaemia prevalent among children and adolescents aged 1–19 years in India: A population-based study. *The Lancet Child & Adolescent Health*, *4*(7), 515–525.

Sattarzadeh, M., & Zlotkin, S. H. (1999). Iron is well absorbed by healthy adults after ingestion of double-fortified (iron and dextran-coated iodine) table salt and urinary iodine excretion is unaffected. *The Journal of Nutrition*, *129*(1), 117–121.

Saxena, C. N., & Srivastava, N. (2009). ICDS in India: Policy,design and delivery issues. *IDS Bulletin*, *40*(4), 45–52.

Schümann, K., & Solomons, N. W. (2017). Perspective: What makes it so difficult to mitigate worldwide anemia prevalence? *Advances in Nutrition*. https://doi.org/10.3945/an.116.013847

Scott, J. M. (2007). Nutritional anemia: B-vitamins. *Nutritional Anemia*, 111.

Scott, S. P., Chen-Edinboro, L. P., Caulfield, L. E., & Murray-Kolb, L. E. (2014). The impact of anemia on child mortality: An updated review. *Nutrients*, *6*(12), 5915–5932.

Sedlander, E., Long, M. W., Mohanty, S., Munjral, A., Bingenheimer, J. B., Yilma, H., & Rimal, R. N. (2020). Moving beyond individual barriers and identifying multi-level strategies to reduce anemia in Odisha India. *Bmc Public Health*, *20*(1), 457. https://doi.org/10.1186/s12889-020-08574-z

Semba, R. D., & Bloem, M. W. (2002). The anemia of vitamin A deficiency: Epidemiology and pathogenesis. *European Journal of Clinical Nutrition*, *56*(4), 271–281.

Sengupta, A., Kannan, K. P., & Raveendran, G. (2008). India's common people: Who are they, how many are they and how do they live? *Economic & Political Weekly*, *43*(11), 49–63.

Sheftel, A. D., Mason, A. B., & Ponka, P. (2012). The long history of iron in the Universe and in health and disease. *Biochimica et Biophysica Acta - General Subjects*, *1820*(3), 161–187. https://doi.org/10.1016/j.bbagen.2011.08.002

Shet, A. S., Zwarenstein, M., Rao, A., Jebaraj, P., Arumugam, K., Atkins, S., Mascarenhas, M., Klar, N., & Galanti, M. R. (2019). Effect of a Community Health Worker-Delivered

Parental Education and Counseling Intervention on Anemia Cure Rates in Rural Indian Children: A Pragmatic Cluster Randomized Clinical Trial. *Jama Pediatrics*, *173*(9), 826–834. https://doi.org/10.1001/jamapediatrics.2019.2087

Shi, Q., Leng, W., Wazir, R., Li, J., Yao, Q., Mi, C., Yang, J., & Xing, A. (2015). Intravenous iron sucrose versus oral iron in the treatment of pregnancy with iron deficiency anaemia: A systematic review. *Gynecologic and Obstetric Investigation*, *80*(3), 170–178.

Shi, Z., Zhen, S., Wittert, G. A., Yuan, B., Zuo, H., & Taylor, A. W. (2014). Inadequate riboflavin intake and anemia risk in a Chinese population: Five-year follow up of the Jiangsu Nutrition Study. *PLoS One*, *9*(2), e88862.

Silva Neto, L. G. R., Santos Neto, J. E. dos, Bueno, N. B., de Oliveira, S. L., & Ataide, T. da R. (2019). Effects of iron supplementation versus dietary iron on the nutritional iron status: Systematic review with meta-analysis of randomized controlled trials. *Critical Reviews in Food Science and Nutrition*, *59*(16), 2553–2561.

Singh, M. B., Fotedar, R., & Lakshminarayana, J. (2005). Occupational morbidities and their association with nutrition and environmental factors among textile workers of desert areas of Rajasthan, India. *Journal of Occupational Health*, *47*(5), 371–377. https://doi.org/10.1539/joh.47.371

Smith, E. M., & Tangpricha, V. (2015). Vitamin D and anemia: Insights into an emerging association. *Current Opinion in Endocrinology, Diabetes, and Obesity*, *22*(6), 432.

Smith, J. L., & Brooker, S. (2010). Impact of hookworm infection and deworming on anaemia in non-pregnant populations: A systematic review. *Tropical Medicine & International Health*, *15*(7), 776–795.

Smith, K. E., Hunter, D. J., & Blackman, T. I. M. (2009). Divergence or convergence? Health inequalities and. *Critical Policy Studies*, *29*(2), 216–242.

Snilstveit, B., Oliver, S., & Vojtkova, M. (2012). Narrative approaches to systematic review and synthesis of evidence for international development policy and practice. *Journal of Development Effectiveness*, *4*(3), 409–429. https://doi.org/10.1080/19439342.2012.710641

Solar, O., & Irwin, A. (2010). *A conceptual framework for action on the social determinants of health.* 79–79.

Sood, S. K., Ramachandran, K., Rani, K., Ramalingaswami, V., Mathan, V. I., Ponniah, J., & Baker, S. J. (1979). WHO sponsored collaborative studies on nutritional anaemia in India. *British Journal of Nutrition*, *42*(3), 399–406. https://doi.org/10.1079/BJN19790130

Spottiswoode, N., Duffy, P. E., & Drakesmith, H. (2014). Iron, anemia and hepcidin in malaria. *Frontiers in Pharmacology*, *5*, 125.

Steiger, G., Müller-Fischer, N., Cori, H., & Conde-Petit, B. (2014). Fortification of rice: Technologies and nutrients. *Annals of the New York Academy of Sciences*, *1324*(1), 29–39.

Stevens. (2013). *"Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995–2011: A systematic analysis of population-representative data". Apple Books.*

Stiller, C. K., Golembiewski, S. K. E., Golembiewski, M., Mondal, S., Biesalski, H.-K., & Scherbaum, V. (2020). Prevalence of Undernutrition and Anemia among. *International Journal of Environmental Research and Public Health*, *17*(342), 1–32.

Stoffel, N. U., von Siebenthal, H. K., Moretti, D., & Zimmermann, M. B. (2020). Oral iron supplementation in iron-deficient women: How much and how often? *Molecular Aspects of Medicine*, 100865.

Stoffel, N. U., Zeder, C., Brittenham, G. M., Moretti, D., & Zimmermann, M. B. (2020). Iron absorption from supplements is greater with alternate day than with consecutive day dosing in iron-deficient anemic women. *Haematologica*, *105*(5), 1232.

Stoltzfus, R. J. (2001a). Iron-deficiency anemia: Reexamining the nature and magnitude of the public health problem. Summary: Implications for research and programs. *The Journal of Nutrition*, *131*(2S-2), 697S-700S; discussion 700S-701S. https://doi.org/10.1093/jn/131.2.697S

Stoltzfus, R. J. (2001b). Defining Iron-Deficiency Anemia in Public Health Terms: A Time for Reflection. *The Journal of Nutrition*, *131*(2), 565S-567S. https://doi.org/10.1093/jn/131.2.565S

Stoltzfus, R. J., & Dreyfuss, M. L. (1998). *Guidelines for the use of iron supplements to prevent and treat iron deficiency anemia*. ILSI Pr.

Stuart-Macadam & Kent. (1992). *Diet, Demography and Disease: Changing Perspectives on Anemia.TransactionPublishers*. https://books.google.co.in/books?hl=en&lr=&id=cgeKq1IjPpwC&oi=fnd&pg=PP9&dq=Diet,+Demography+and+Disease:+Changing+Perspectives+on+Anemia&ots=3gYzCakF5w&sig=UoEWsq4D47p5WJqVy0zZ91z6_SE&redir_esc=y#v=onepage&q=Diet%2C%20Demography%20and%20Disease%3A%20Changing%20Perspectives%20on%20Anemia&f=false

Stuart-Macadam, P. (2006). Integrative Anthropology: A Focus on Iron-Deficiency Anemia. *Archaeological Papers of the American Anthropological Association*, *16*(1), 129–137. https://doi.org/10.1525/ap3a.2006.16.1.129

Subasinghe, A. K., Walker, K. Z., Evans, R. G., Srikanth, V., Arabshahi, S., Kartik, K., Kalyanram, K., & Thrift, A. G. (2014). Association between Farming and Chronic Energy Deficiency in Rural South India. *Plos One*, *9*(1), e87423. https://doi.org/10.1371/journal.pone.0087423

Subramanian, S., Ackerson, L., Subramanyam, M., & Sivaramakrishnan, K. (2008). Health inequalities in India: The axes of stratification. *The Brown Journal of World Affairs*, *14*(2), 127–138.

Susser, M. (1985). Epidemiology in the United States after world war II: The evolution of technique. *Epidemiologic Reviews*, *7*(1), 147–177. https://doi.org/10.1093/oxfordjournals.epirev.a036280

Swaminathan, S., Ghosh, S., Varghese, J. S., Sachdev, H. S., Kurpad, A., & Thomas, T. (2019). Dietary Iron Intake and Anemia Are Weakly Associated, Limiting Effective Iron Fortification Strategies in India. *Journal of Nutrition*, *149*(5), 831–839. https://doi.org/10.1093/jn/nxz009

Tam, E., Keats, E. C., Rind, F., Das, J. K., & Bhutta, Z. A. (2020). Micronutrient supplementation and fortification interventions on health and development outcomes among children under-five in low-and middle-income countries: A systematic review and meta-analysis. *Nutrients*, *12*(2), 289.

Tandara, L., & Salamunic, I. (2012). Iron metabolism: Current facts and future directions. *Biochemia Medica*, *22*(3), 311–328.

Tandon, R., Jain, A., & Malhotra, P. (2018). Management of Iron Deficiency Anemia in Pregnancy in India. *Indian Journal of Hematology and Blood Transfusion*, *34*(2), 204–215. https://doi.org/10.1007/s12288-018-0949-6

Tanjong Ghogomu, E., Suresh, S., Rayco-Solon, P., Hossain, A., McGowan, J., Peña-Rosas, J. P., & Welch, V. (2018). Deworming in non-pregnant adolescent girls and adult women: A systematic review and meta-analysis. *Systematic Reviews*, *7*(1), 1–16.

Taylor-Robinson, D. C., Maayan, N., Soares-Weiser, K., Donegan, S., & Garner, P. (2012). Deworming drugs for soil-transmitted intestinal worms in children: Effects on

nutritional indicators, haemoglobin and school performance. *Cochrane Database of Systematic Reviews*, *11*.

Thankachan, P., Muthayya, S., Walczyk, T., Kurpad, A. V., & Hurrell, R. F. (2007). An analysis of the etiology of anemia and iron deficiency in young women of low socioeconomic status in Bangalore, India. In *Food and Nutrition Bulletin* (Vol. 28, Issue 3).

Thankachan, P., Rah, J. H., Thomas, T., Selvam, S., Amalrajan, V., Srinivasan, K., Steiger, G., & Kurpad, A. V. (2012). Multiple Micronutrient-Fortified Rice Affects Physical Performance and Plasma Vitamin B-12 and Homocysteine Concentrations of Indian School Children. *Journal of Nutrition*, *142*(5), 846–852. https://doi.org/10.3945/jn.111.149021

Thankachan, P., Walczyk, T., Muthayya, S., Kurpad, A. V., & Hurrell, R. F. (2008). Iron absorption in young Indian women: The interaction of iron status with the influence of tea and ascorbic acid. *American Journal of Clinical Nutrition*, *87*(4), 881–886.

Thomas, C. E., Gaffney-Stomberg, E., Sun, B.-H., O'Brien, K. O., Kerstetter, J. E., & Insogna, K. L. (2013). Increasing dietary protein acutely augments intestinal iron transporter expression and significantly increases iron absorption in rats. *The FASEB Journal*, *27*(6), 2476–2483.

Thompson, B. (2007). Food-based approaches for combating iron deficiency. *Nutritional Anemia*, *337*, 1–21.

Thurnham, D. I., & Northrop-Clewes, C. A. (2007). Infection and the etiology of anemia. *Nutritional Anemia*, 231–256.

Trigo, B. (1999). Anemia and vampires: Figures to govern the colony, Puerto Rico, 1880 to 1904. *Comparative Studies in Society and History*, *41*(1), 104–123. https://doi.org/10.1017/s0010417599001887

UNICEF. (1990). *Strategy for improved nutrition of children and women in developing countries* (pp. 13–24). https://doi.org/10.1007/BF02810402

USAID. (2013). Conceptual Frameworks for Anemia. *Usaid Task Force for Anaemia*, *October*.

Varghese, R., & Roy, M. (2019). Coresidence with mother-in-law and maternal anemia in rural India. *Social Science and Medicine*, *226*, 37–46. https://doi.org/10.1016/j.socscimed.2019.02.027

Vart, P., Jaglan, A., & Shafique, K. (2015). Caste-based social inequalities and childhood anemia in India: Results from the National Family Health Survey (NFHS) 2005-2006 Chronic Disease epidemiology. *BMC Public Health*, *15*(1), 1–8. https://doi.org/10.1186/s12889-015-1881-4

Viana, M. B. (2011). Anemia and infection: A complex relationship. *Revista Brasileira de Hematologia e Hemoterapia*, *33*(2), 90–92. https://doi.org/10.5581/1516-8484.20110024

Vijaya Bhaskar, A. V., Nithya, D. J., Raju, S., & Bhavani, R. V. (2017). Establishing integrated agriculture-nutrition programmes to diversify household food and diets in rural India. *Food Security*, *9*(5), 981–999. https://doi.org/10.1007/s12571-017-0721-z

Vos, T., Abajobir, A. A., Abate, K. H., Abbafati, C., Abbas, K. M., Abd-Allah, F., Abdulkader, R. S., Abdulle, A. M., Abebo, T. A., & Abera, S. F. (2017). Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: A systematic analysis for the Global Burden of Disease Study 2016. *The Lancet*, *390*(10100), 1211–1259.

Wailoo, K. (1999). *Drawing Blood Technology and disease identity in Twentieth century America*. Jhu press.

Wander, K., Shell-Duncan, B., & McDade, T. W. (2009). Evaluation of iron deficiency as a nutritional adaptation to infectious disease: An evolutionary medicine perspective.

American Journal of Human Biology, *21*(2), 172–179. https://doi.org/10.1002/ajhb.20839

Weiss, G., & Goodnough, L. T. (2005). Anemia of chronic disease. *New England Journal of Medicine*, *352*(10), 1011–1023.

Welch, V. A., Ghogomu, E., Hossain, A., Awasthi, S., Bhutta, Z., Cumberbatch, C., Fletcher, R., McGowan, J., Krishnaratne, S., & Kristjansson, E. (2016). Deworming and adjuvant interventions for improving the developmental health and well-being of children in low-and middle-income countries: A systematic review and network meta-analysis. *Campbell Systematic Reviews*, *12*(1), 1–383.

Wendt, A., Waid, J., Müller-Hauser, A., Kyei, N., Sobhan, S., & Gabrysch, S. (2020). Do hemoglobin concentration and anemia prevalence differ between capillary and venous blood and between analysis methods? *Current Developments in Nutrition*, *4*(Supplement_2), 922–922.

West Jr, K. P., Gernand, A., & Sommer, A. (2007). Vitamin A in nutritional anemia. *Nutritional Anemia*, 133–153.

WHO. (1994). *Report of the WHO Informal Consultation on Hookworm Infection and Anaemia in Girls and Women.5-7 December 1994 Schistosomiasis and Intestinal Parasites Unit Division of Control of Tropical Diseases (Formerly: Programme of Intestinal Para*.

WHO. (2001). *Iron Deficiency Anaemia :Assessment, Prevention, and Control: A guide for programme managers*. https://doi.org/10.1016/j.paed.2017.08.004

WHO. (2004). Vitamin and mineral requirements in human nutrition. In *Report of a joint FAO/WHO expert consultation, Bangkok, Thailand, 21–30 September 1998* (pp. 194–216). World Health Organization Geneva.

WHO. (2006). *Guidelines on food fortification with micronutrients/edited by Lindsay Allen...[et al.]*.

WHO. (2007). *Assessing the iron status of populations: Report of a joint World Health Organization/ Centers for Disease Control and Prevention technical consultation on the assessment of iron status at the population level, 2nd ed., Geneva, World Health Organization*. https://www.who.int/publications-detail-redirect/9789241596107

WHO. (2008a). Closing the gap in a generation. *Health Equity Through Action on the Social Determinants of Health*, 246–246. https://doi.org/10.1080/17441692.2010.514617

WHO. (2008c). *Worldwide prevalence of anaemia 1993-2005*. http://whqlibdoc.who.int/publications/2008/9789241596657_eng.pdf

WHO. (2009). *Global prevalence of vitamin A deficiency in populations at risk 1995-2005: WHO global database on vitamin A deficiency*. World Health Organization.

WHO. (2010). *Anaemia Prevention Along The Life-Cycle*.

WHO. (2011a). *Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity* (pp. 1–6). http://scholar.google.com/scholar?hl=en&btnG=Search&q=intitle:Haemoglobin+concentrations+for+the+diagnosis+of+anaemia+and+assessment+of+severity#1

WHO. (2011b). The global prevalence of anaemia in 2011. *Who*, 1–48.

WHO. (2016). Strategies to prevent anaemia: Recommendations from an Expert Group Consultation. *World Health Organization*, *December*, 5–6.

WHO. (2017). Nutritional Anaemias: Tools for Effective Prevention. In *World Health Organization* (p. 83).

WHO, FAO, UNICEF, GAIN, MI, & FFI. (2009). *Recommendations on wheat and maize flour fortification. Meeting Report: Interim Consensus Statement. Geneva, World Health Organization*. http://www.who.int/nutrition/publications/micronutrients/wheat_maize_fort.pdf

WHO, W. (1959). *Iron Deficiency anaemia-Report of a study group.* (pp. 143–162) [WHO].

WHO, W. (1968). *Nutritional anaemias. Report of a WHO group of experts.* (pp. 1–29).
WHO, W. (1972). *Nutritional anaemias. Report of a WHO group of experts.*
WHO, W. (1993). *Prevention And Management Of Severe Anaemia In Pregnancy: A report of a Technical Working group*.
Williams, A. M., Addo, O. Y., Grosse, S. D., Kassebaum, N. J., Rankin, Z., Ballesteros, K. E., Olsen, H. E., Sharma, A. J., Jefferds, M. E., & Mei, Z. (2019). Data needed to respond appropriately to anemia when it is a public health problem. *Annals of the New York Academy of Sciences*, *1450*(1), 268–280. https://doi.org/10.1111/nyas.14175
Wirth, J. P., Woodruff, B. A., Engle-Stone, R., Namaste, S. M., Temple, V. J., Petry, N., Macdonald, B., Suchdev, P. S., Rohner, F., & Aaron, G. J. (2017). Predictors of anemia in women of reproductive age: Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) project. *The American Journal of Clinical Nutrition*, *106*(Suppl 1), 416S-427S. https://doi.org/10.3945/ajcn.116.143073
Wiseman, E. M., Bar-El Dadon, S., & Reifen, R. (2017). The vicious cycle of vitamin a deficiency: A review. *Critical Reviews in Food Science and Nutrition*, *57*(17), 3703–3714.
World Health Organization & UNICEF. (2004). *Focusing on anaemia: Towards an integrated approach for effective anaemia control: Joint statement by the World Health Organization and the United Nations Children's Fund*. (pp. 1-sheet).
Yadu, C. R., & Satheesha, B, Y., C. R. ,. &. Satheesha, B. (2016). Agrarian Question in India. *Economic and Political Weekly*, *51*(16), 7–8.
Yang, F., Liu, X., & Zha, P. (2018). Trends in Socioeconomic Inequalities and Prevalence of Anemia Among Children and Nonpregnant Women in Low- and Middle-Income Countries. *JAMA Network Open*, *1*(5), e182899–e182899. https://doi.org/10.1001/jamanetworkopen.2018.2899
Zarychanski, R., Rimmer, E., & Houston, D. S. (2012). Anaemia: Adaptive Mechanisms and Consequences. *ELS*.
Zhang, Y., & Wildemuth, B. M. (2009). Qualitative analysis of content Applications of Social Research Methods to Questions. *Information and Library Science*.
Zimmermann, M. B. (2007). Interactions between iron and vitamin A, riboflavin, copper, and zinc in the etiology of anemia. *Nutritional Anemia*, 199.
Zimmermann, M. B., & Hurrell, R. F. (2007). Nutritional iron defi ciency. *Www.Thelancet.Com*, *370*(11).

ANNEXURES

Institutional Ethics Review Board, JNU (IERB Ref No 2021/Student/ 269)

Interview schedule for Key informants

1. What do you think is the reason why nutritional anemia prevalence reduction over the period is minimal at national scale, and why prevalence in many states has increased in the recent past despite many efforts?

2. What are the nutritional and non-nutritional causes of anemia?
    a. What are the nutritional deficiencies other than iron?
    b. What are non-nutritional factors?
    c. Do we know enough on nutritional and non-nutritional causes, their prevalence and distribution to take epidemiologically sound and informed decision on anemia mitigation?
    d. Or what do we do not know about anemia?

3. Do you think, current approaches and intervention strategies (AMB) have potential to reduce anemia significantly if effectively implemented?
    a. If not, why so?

4. What advantages do Anemia Mukt Bharat (AMB) have over earlier programmes?

5. Does AMB programme address all the known causal factors of anemia?

        i. Does AMB intend to address unknown causes or recognizes unknown factors that need to be identified?

6. What shortcomings do you see in the design of AMB and what changes would you suggest/recommend overcoming those shortcomings/lacunae?

7. Is there anything else that you would like to tell us so that we have a better understanding of the nutritional anemia as a public health problem, or are there any issues you feel are important that we have not touched upon during the interview?