Metabolic Syndrome in the Indian Context: A Review of its Biological and Social Determinants

Thesis submitted to Jawaharlal Nehru University
in fulfilment of the requirements
for the award of the degree of

Doctor of Philosophy

RANDEEP NEOG

Centre of Social Medicine and Community Health
School of Social Sciences
Jawaharlal Nehru University
New Delhi-110067
INDIA

2022

CENTRE OF SOCIAL MEDICINE AND COMMUNITY HEALTH
SCHOOL OF SOCIAL SCIENCES
JAWAHARLAL NEHRU UNIVERSITY
NEW DELHI-110067

Date: 17th August 2022

CERTIFICATE

This dissertation entitled **"METABOLIC SYNDROME IN THE INDIAN CONTEXT: A REVIEW OF ITS BIOLOGICAL AND SOCIAL DETERMINANTS"** is submitted in partial fulfilment of the requirements for the award of the degree of Doctor of Philosophy of Jawaharlal Nehru University. This thesis is my original work and has not been submitted in part or in full for any other degree of this University or any other University.

Randeep Neog

Randeep Neog

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

Rajib Dasgupta

Prof. Rajib Dasgupta
(Chairperson)

Rajib Dasgupta

Prof. Rajib Dasgupta
(Supervisor)

ACKNOWLEDGEMENT

The hope of earning a PhD from a prestigious institution like Jawaharlal Nehru University in Delhi makes me feel as though I might have accomplished something worthwhile in my life. It is equally challenging to relish this dream in the face of conflicting demands from life, and it is impossible to ignore all of the obligations that arise along the way. I had to question multiple times "whether I will be able to complete the PhD or not". I am able to break out of such pessimism because of able guidance of my respected supervisor, my parents' ongoing encouragement, my better half's steadfast support, and the presence of my daughter who serves as an inspiration whenever I am feeling down.

I would like to express my deepest sense of gratitude to my supervisor, *Professor Rajib Dasgupta*, without whom this thesis would not have been possible. His constant support and invaluable insights at every stage of my work endeavoured me to fulfil my dream.

I am thankful to all the faculty members of CSMCH, who over the time period at JNU since my MPH days nurtured me and groomed my thought process so that I can develop my own perspectives. My sincere thank to the other staff of CSMCH for their cooperation and support in my study. I extend thanks to *Dinesh Ji* of the Documentation Unit for his support as and when required.

I have to thank the Department of Epidemiology & International Public Health, Bielefeld University, Germany (WHO Collaborating Centre) for selecting me as an academic exchange fellow and giving me the opportunity to explore the vast literature available in its library.

I also take this opportunity to thank all my classmates, friends, and even juniors; whom I met in JNU; for their help in one way or another. I thank *Anil*, *Dr Anjali*, *Jisha*, *Kaushik*, *Paranjoy*, *Pranjal*, and *Rajesh* for their continued support and motivation over phone in spite of physical distances.

Words cannot adequately explain how grateful I am to my parents, *Mrs. Mary Neog* and *Dr. Pradeep Kumar Neog*, who have been instrumental in providing

encouragement for this piece of work. I know that they are going to cherish this accomplishment more than I will.

Finally, I acknowledge my wife, *Mrs. Rajlakhi Saikia*, for being a caring, understanding, and encouraging companion. My daughter, *Adritanaya*, deserves a special mention for cheerfully supporting her father's academic pursuits through her modest personal sacrifices.

Randeep Neog

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF GRAPHS

ACRONYMS

ACH:	Antidiuretic Hormone
ACTH:	Adrenocorticotropin Homrone
ACTH:	Adrenocorticotropin Hormone
AEE:	Activity-related Energy Expenditure
AHS:	Annual Health Survey
AMP:	Adenosine Monophosphate
ANS:	Autonomic Nervous System
AT:	Adipose Tissue
AVP:	Arginine Vasopressin
BMI:	Body Mass Index
BP:	Blood Pressure
BPA:	Bisphenol A
CAD:	Coronary Artery Disease
CAGR:	Compound Annual Growth Rate
CARDIA:	The Coronary Artery Risk Development in Young Adults
CDC:	Centre for Disease Control and Prevention
CES:	Central Economic Survey
CHARLS:	The China Health And Retirement Longitudinal Study
CRH:	Corticotropin-Releasing Hormone
CSDH:	Commission on Social Determinants of Health
CUPS:	The Chennai Urban Population Study
CURES:	Chennai Urban Rural Epidemiology Study
CVD:	Cardiovascular Disease
CVDRFS:	Cardiovascular Disease Risk Factor Study
DALYs:	Disability Adjusted Life Years

DDT: Dichlorodiphenyltrichloroethane

DDTC: Drug De-addiction and Treatment Center

DEXA: Dual Energy X-ray Absorptiometry

DLHS: District Level Health Survey

DM: Diabetes Mellitus

DNA: Deoxyribonucleic Acid

DOHaD: Developmental Origins of Health and Disease

EDCs: Endocrine Disrupting Chemicals

EGIR: European Group for the Study of Insulin Resistance

FAO: Food and Agriculture Organization

FFA: Free Fatty Acid

FFM: Fat Free Mass

FICCI: Federation of Indian Chambers of Commerce and Industry

FM: Fat Mass

GAS: General Adaptation Syndrome

GDM: Gestational Diabetes Mellitus

GDP: Gross Domestic Product

GH: Growth Hormone

GHANAISA: Ghanaian Health and Nutrition Analysis in Sydney, Australia

HDL: High Density Lipoprotein

HPA Axis: Hypothalamic-Pituitary-Adrenal Axis

IAP: Indian Academy of Paediatrics

ICD: International Classification of Disease

ICDS: Integrated Child Development Scheme

ICMR: Indian Council of Medical Research

ICO: Index of Central Obesity

IDF: International Diabetes Federation

IDRS: Indian Diabetes Risk Score

IGT: Impaired glucose tolerance

IL: Interleukin

IMS: The Indian Migration Study

IOTF: International Obesity Task Force

KIHD: Kuopio Ischaemic Heart Disease Risk Factor Study

LAP: Lipid Accumulation Product

LBW: Low Birth Weight

LC/NE: Locus Caeruleus/Norepinephrine

LPG: Liberalization, Privatization and Globalization

MDMS: Mid-Day Meal Scheme

MESA: The Multi-Ethnic Study of Atherosclerosis

MI: Myocardial Infraction

MPI: Multidimensional Poverty Index

NABARD: National Bank for Agriculture and Rural Development

NCD: Non-Communicable Disease

NCEP/ATP: National Cholesterol Education Programme/ Adult Treatment Panel

NFHS: National Family Health Survey

NFSA: National Food Security Act

NHANES: National Health and Nutrition Examination Survey

NIDDM: Non Insulin Dependent Diabetes Mellitus

NIN: National Institute of Nutrition

NNMB: National Nutrition Monitoring Bureau

NPCDCS: National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke

NRC: Nutritional Rehabilitation Center

NSS: National Sample Survey

OGTT: Oral Glucose Tolerance Test

OPHI: Oxford Poverty and Human Development Initiative

PCBs: Polychlorinated Biphenyls

PCDDs: Polychlorinated dibenzo-*p*-dioxins

PCDFs: Polychlorinated dibenzofurans

PDS: Public Distribution System

PGIMER: Post Graduate Institute of Medical Education and Research

PM: Particulate Matter

PNS: Parasympathetic Nervous System

POP: Persistent Organic Pollutant

PVC: Polyvinyl Chloride

RDA: Recommended Daily Allowance

REM: Rapid Eye Movement

RMR: Resting Metabolic Rate

RNA: Ribonucleic Acid

SAM: Severe Acute Malnutrition

SES: Socioeconomic Status

SFA: Saturated Fatty Acid

SHEEP: The Swedish Case Control Study in Stockholm

SNS: Sympathetic Nervous System

SSB: Sugar Sweetened Beverages

TAG: Triacylglycerol

TEE: Total Energy Expenditure

TEM: Thermic Effect of Meals

TFA: Trans Fatty Acid

TNF-α: Tumour Necrosis Factor-alpha

TV: Television

UNDP: United Nations Development Programme

US: United States

USA: United States of America

VLDL: Very Low Density Lipoprotein

WC: Waist Circumference

WHO: World Health Organization

WHR: Waist Hip Ratio

Chapter One

Introduction and Literature Review

1.1 Introduction:

One major challenge that the mankind is facing at present time due to the process of development and evolution is the burden of non-communicable diseases. In case of communicable diseases we can at least know the specific causative agent and intervene accordingly. On the other hand, the situation of non-communicable diseases is not the same because many macro level factors are acting on us starting from the utero and all throughout our life. These factors are acting at a slower rate but are adequate enough to show the implications by one's mid age or even earlier in case of developing nations. In developed nations the prevalence of communicable diseases has come down but that of non-communicable diseases has increased substantially. However the situation is worse in developing countries like India where the double burden of diseases is emerging as a matter of concern. While relentless efforts see success in taming some of the most dreaded infective causes of death, the lower economic classes that used to suffer the most from infectious diseases seem to benefit the most (as compared to the upper classes) from the controls applied to the same. However, the impact of NCDs brought by their complication potential and population ignorance is more indelible on the poor than the rich. In a country like India where unavailability, non-affordability, inaccessibility and inadequacy of health outreach services is a challenge which is encountered with time and across geographies; prevalence estimates of NCDs through surveys or even trend predictions based on repeated cross-sections or statistical modelling may not be precise. The rapid as well as varied and un-researched impact of economic development leaves the estimates even more unpredictable. Resultantly, the understanding of the incidence and how the natural histories of these NCDs unfold on the public health landscape is hazy. It is essential to look through the lenses of "life course epidemiology" to understand the determinants and subsequent policy generation. This study will focus on looking at the social determinants of metabolic syndrome; which act on the final common biological pathway; from the theoretical perspective based on the available relevant literature and data in Indian context.

1.2 Literature Review:

1.2.1 Definitions of Metabolic Syndrome:

Metabolic syndrome has drawn considerable attention in recent years but the concept can be dated back to 1600s when physician Nicolaes Tulp first documented the syndrome as 'hypertriglyceridemia syndrome' (Magliano, *et al*., 2008). The concept of constellation of various metabolic factors as health problem can be found quoted in the early part of twentieth century. However renewed interest in the topic grew when Reaven in 1988 proposed the concept of syndrome X (Wild and Byrne, 2005), which was described as the co-occurrence of glucose intolerance, insulin resistance, hyperinsulinemia, hypertension, increased of very low density lipoprotein (VLDL), and decreased of high density lipoprotein (HDL) (Reaven, 1988). "The metabolic syndrome consists of a constellation of metabolic abnormalities that confer increased risk of cardiovascular disease (CVD) and diabetes mellitus (DM)"- (Fauci *et al*., 2008). The constellation of metabolic disorders includes hyperglycemia, central obesity, decreased HDL-C, raised triglycerides, elevated blood pressure, and elevated sugar, which typically cluster together to a greater extent than predicted (Magliano, *et al*., 2008). Numerous synonyms and definitions of metabolic syndrome evolved over time until 1998 when the World Health Organization proposed a formal definition of metabolic syndrome (Alberti and Zimmet, 1998). Some of the common synonyms used for metabolic syndrome are:
(i) Syndrome X (ii) Metabolic syndrome X (iii) Dysmetabolic syndrome X (iv) Reaven syndrome (v) Android obesity syndrome (vi) Syndrome of affluence (vii) Insulin resistance syndrome (viii) Atherothrombogenic syndrome (ix) GHO (Glucose intolerance/ Hypertension/ Obesity) syndrome etc.

Though WHO had proposed a formal definition in 1998 and later modified it in 1999, several other organizations formulated their own definition of metabolic syndrome time to time. The definitions proposed by the European Group for the study of Insulin Resistance (EGIR) in year 1999, the National Cholesterol Education Programme Adult Treatment Panel III (NCEP/ATP III) in year 2001, and International Diabetes Federation (IDF) in year 2005 are worth mentioning (Alberti *et*

al., 2006). These organizations made effort to standardize the definition of metabolic syndrome by sharing similar criteria but in practical differed considerably.

Criteria	WHO 1999	EGIR 1999	NCEP ATP III 2001	IDF 2005
Fasting plasma glucose or diabetes status	Diabetes or impaired glucose tolerance or insulin resistance	≥ 6.1 mmol/l (110 mg/dl) but non-diabetic	≥ 6.1 mmol/l (110 mg/dl) or treatment	≥ 5.6 mmol/l (100 mg/dl) or previously diagnosed type 2 diabetes
Blood pressure	≥ 140/90 mm Hg raised	≥ 140/90 mmHg or treatment	≥ 130/ ≥ 85 mmHg or treatment	≥ 130/ ≥ 85 mmHg or treatment
Triglycerides/ HDL-cholesterol	≥ 1.7 mmol/l (150 mg/ dl) *and/or* Men: < 0.9 mmol/l (35 mg/ dl) Women: < 1.0 mmol/l (39 mg/ dl)	> 2.0 mmol/l (178 mg/ dl) *and/or* < 1.0 mmol/l (39 mg/ dl) or treatment	≥ 1.7 mmol/l (150 mg/ dl) *and/or* Men: < 1.03 mmol/l (40 mg/ dl) Women: < 1.29 mmol/l (50 mg/ dl) or treatment	≥ 1.7 mmol/l (150 mg/ dl) *and/or* Men: < 1.03 mmol/l (40 mg/ dl) Women: < 1.29 mmol/l (50 mg/ dl) or treatment
Obesity	Men: waist–hip ratio > 0.90 Women: waist–hip ratio > 0.85 and/or BMI > 30 kg/m^2	Men: waist circumference ≥ 94 cm Women: waist circumference ≥ 80 cm	Men: waist circumference > 102 cm Women: waist circumference > 88 cm	Men: waist circumference ≥ 94 cm Women: waist circumference ≥ 80 cm
Microalbuminuria	Urinary albumin excretion rate ≥ 20 μg/min or albumin:creatinine ratio ≥ 30 mg/g			

Table 1.1: Definitions of metabolic syndrome (Source: Wild and Byrne, 2005; Alberti *et al*., 2006; Magliano *et al*, 2008; Alberti *et al*., 2009)

The core of the WHO definition is glucose status and focused on detecting the cases of insulin resistance (Magliano *et al*., 2008). EGIR definition also relied on the insulin resistance by inclusion of fasting plasma glucose level. The NCEP ATP III definition which came several years later gave importance to all the components and stressed on relying on clinical judgements. The IDF tried a more practical definition of metabolic syndrome by placing central obesity as the core theme and gave emphasis on developing criteria for obesity (Magliano *et al*., 2008).

In year 2009 the new Joint Interim Societies definition of metabolic syndrome (Harm) tried to address all the obligations and put forward following criteria to define metabolic syndrome (Alberti *et al*., 2009):

(i) Men: waist circumference ≥ 85-102 cm; Women: waist circumference ≥ 80-90 cm (population and country specific)
(ii) Blood pressure ≥ 130/ ≥ 85 mmHg or treatment
(iii) Triglyceride ≥ 1.7 mmol/l (150 mg/ dl) or treatment
(iv) HDL Cholesterol Men: < 1.0 mmol/l (40 mg/ dl); Women: < 1.3 mmol/l (50 mg/ dl) or treatment
(v) Fasting plasma glucose ≥ 5.6 mmol/l (100 mg/dl) or previously diagnosed type 2 diabetes or treatment

As per consensus group statement by Misra *et al*. (2009), if a person has central obesity (it can be determined by measuring waist circumference and comparing with respect to ethnic specific values e.g. South Asians ≥ 90cm for male and ≥ 80cm for female) plus any two of the four factors mentioned in IDF definition then he can be defined as having metabolic syndrome. Hence the major features of the metabolic syndrome include central obesity, hyperglycemia, hypertriglyceridemia and hypertension. In order to understand metabolic syndrome several conceptual approaches have evolved to define the syndrome.

1.2.2 Existing Concepts and Studies:

The incidence of metabolic syndrome varies according to the character of different ethnic groups (Vijaya Krishna, 2011). Metabolic syndrome is common in Indians and genetic component can be linked for the pathogenesis. Thrifty genes could be held responsible for metabolic syndrome, because they maintain optimal levels of energy during the harsh periods of fasting (Groop, 2000). Thrifty traits that evolved during the period of intermittent famine would help in prolonging the survival when there was inadequate food supply (Landsberg, 2008). On the contrary the same traits would predispose to obesity and type 2 diabetes in presence of abundance of food supply (ibid). Hence the current epidemic state of metabolic syndrome may have its origin actually encrypted long ago to ensure survival in the wide swing of nutrition availability. The living example of Pima Indians of

southwestern United States who were once lean but now under the rage of obesity shows the potential of thrifty gene traits in the environment of excess food (ibid). The social history of famine in ancient India can be linked with this genetic component. Indians are more likely to experience various manifestations of metabolic syndrome because of known risk factors like abdominal obesity, a high prevalence of type 2 diabetes, hypertension, low levels of the beneficial high-density lipoprotein (HDL), a high level of triglycerides, hypercholesterolemia, and a sedentary lifestyle (Das, 2003). Insulin resistance is usually seen in these conditions and followed by hyperinsulinemia. However, insulin resistance may not occur in all the tissues of the body and muscle tissues show resistance early as compared to adipose tissues at the initial stages of metabolic syndrome (Hansen, *et al*., 1988). This is the reason why exercise is beneficial and halts the progression of metabolic syndrome by enhancing glucose utilization in muscles at the early stage (Das, 2003). Body fat distribution of Indians is different from west and persons in normal BMI (body mass index) range are found to have higher body fat or abdominal obesity. Obesity associated morbidity and mortality in humans is determined by the distribution of adipose tissue which is again predicted by genetic, environmental, and hormonal factors (Das, 2003).

One group identified insulin resistance as the important factor while the other group suggested visceral fat as the underlying cause (Magliano, *et al*., 2008). However the superimposition of these two approaches is desirable from both clinical and public health points (ibid). The pathophysiology of metabolic syndrome is typically explained in terms of insulin resistance, which is due to malfunction in insulin action. An excess of free fatty acids contributes to the development of insulin resistance (FFAs), which are predominantly produced from adipose tissue, and by the breakdown of lipoproteins inside tissues. A surplus of FFAs reduces the ability of insulin to control glucose absorption, and these FFAs build up as triglycerides in both skeletal and cardiac muscles. In a way to compensate the defect in insulin action and to retain the euglycemic state, mechanisms like modification of insulin secretion and/or insulin clearance are initiated. Ultimately, this fails due to defects in insulin secretion and progress from impaired glucose tolerance (IGT) to diabetes mellitus. Insulin on the other hand has a vasodilatation property which is lost with insulin resistance and making it one of the important factors of hypertension. Though this factor is thought to cause hypertension but still it is not very much clear on how

metabolic aberrations produce higher blood pressure. It is noteworthy to note that only 50% of people with essential hypertension also have insulin resistance (Zavaroni *et al*., 1992). The relative risk of DM and CVD increases many folds with metabolic syndrome. Framingham Offspring Study showed that the population with metabolic syndrome had attributable risk of developing type 2 DM was 62% (men) and 47% (women) and of CVD was 34% (men) and 16% (women) respectively.

Non communicable diseases are broadly caused by factors like physical inactivity, poor composition of diet (rich content of calories, fat, sugar, salt and poor in fruits and vegetables), and hamrful use of alcohol and tobacco etc (The Global Halth Policy Summit, 2012). These behavioural risk factors act on the biological pathways and give rise to the metabolic risk factors like hyperglycemia, hypertension, hyperlipidemia etc. in presence of larger underlying social determinants like poverty, urbanization, and globalization (Fig 1.1) (ibid).

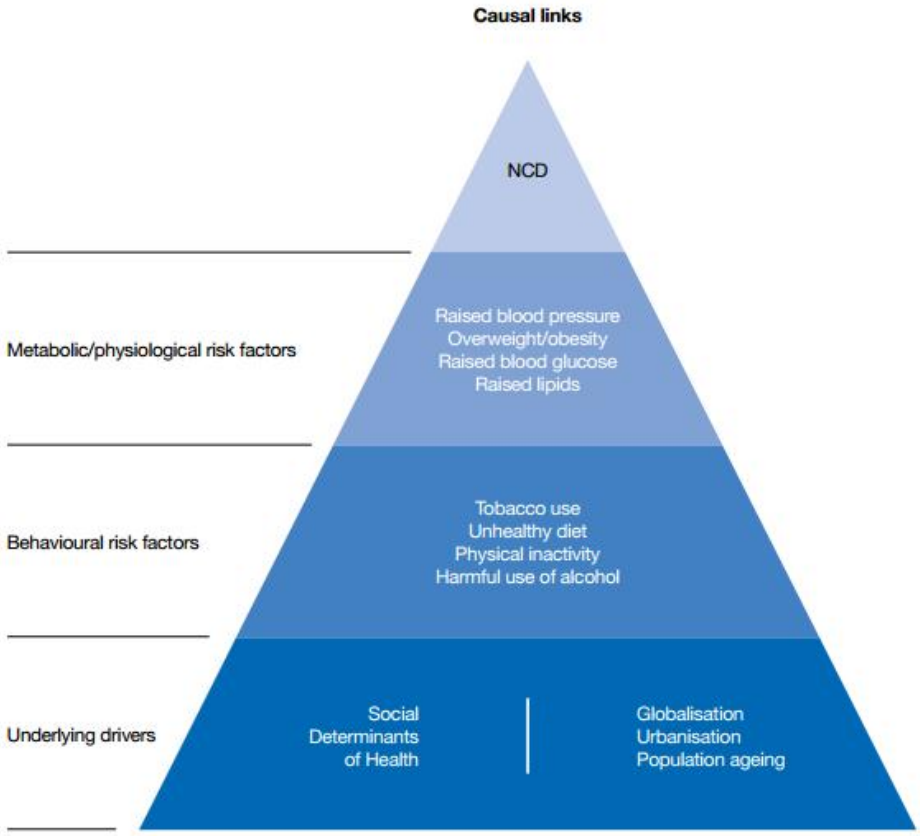


Fig 1.1: Causes of NCD (The Global Health Policy Summit, 2012)

In an effort to define and conceptualise metabolic syndrome, several approaches were proposed. Amongst them there are two most common approaches; in one

approach the metabolic syndrome is represented by a set of factors which are interlinked and clustered with each other and there is no known factor at the etiological core. Here an underlying feature is clear and there are clear association of potential underlying components with identified features (Magliano, *et al*., 2008). The alternative view assumes that there is a fundamental component at play that is connected to and the root cause of the other factors (ibid). These methods make no etiologic assumptions, and the components chosen are determined by statistical strength of connection. Subsequent investigation of associations are required to get an insight into the probable underlying causes (ibid).

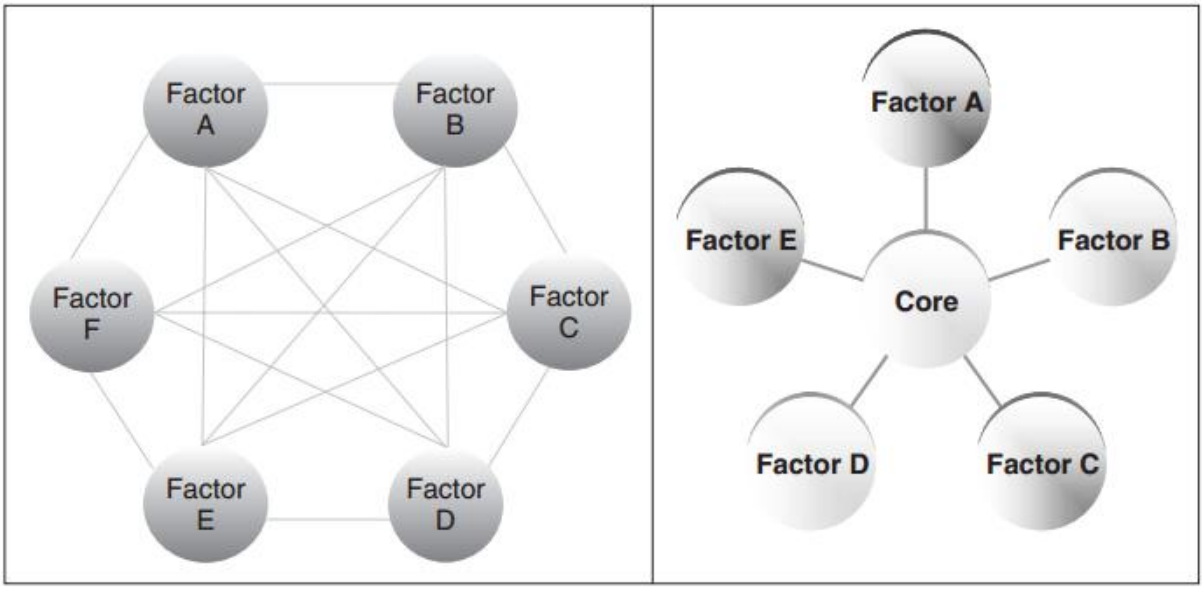


Fig 1.2: The two most common conceptual frameworks used to describe Metabolic syndrome (Adapted from Magliano, *et al*., 2008)

In general; genetic, environmental, and epigenetic variables interact to cause the majority of chronic diseases (Smith and Mill, 2011). Environmental factors proposed to act on the genes and bring about epigenetic changes (ibid). These can change the genomic expression and make subject vulnerable for chronic diseases. Establishing when such epigenetic changes (prior to diseases or as a secondary effect of other illness) may occur can be useful from public health point of view. Longitudinal epigenetic studies are required to overcome the current insufficient knowledge in this field.

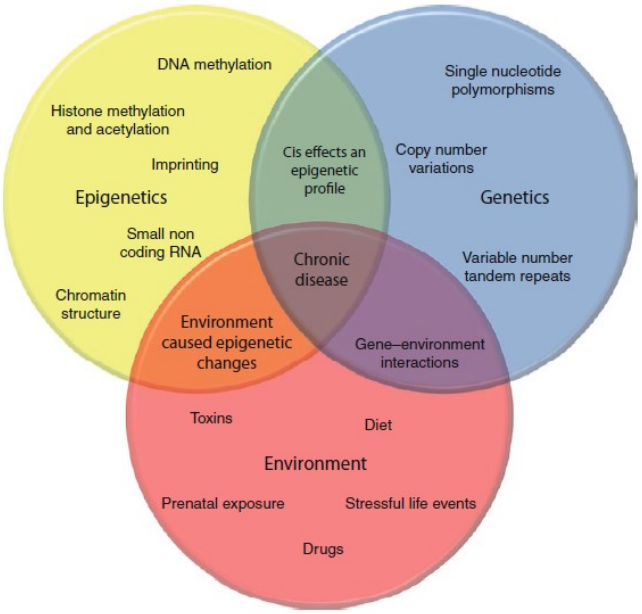


Fig 1.3: Interaction of genetic, environmenta, and epigenetic factors results in chronic diseases (Source: Adapted from Smith and Mill, 2011)

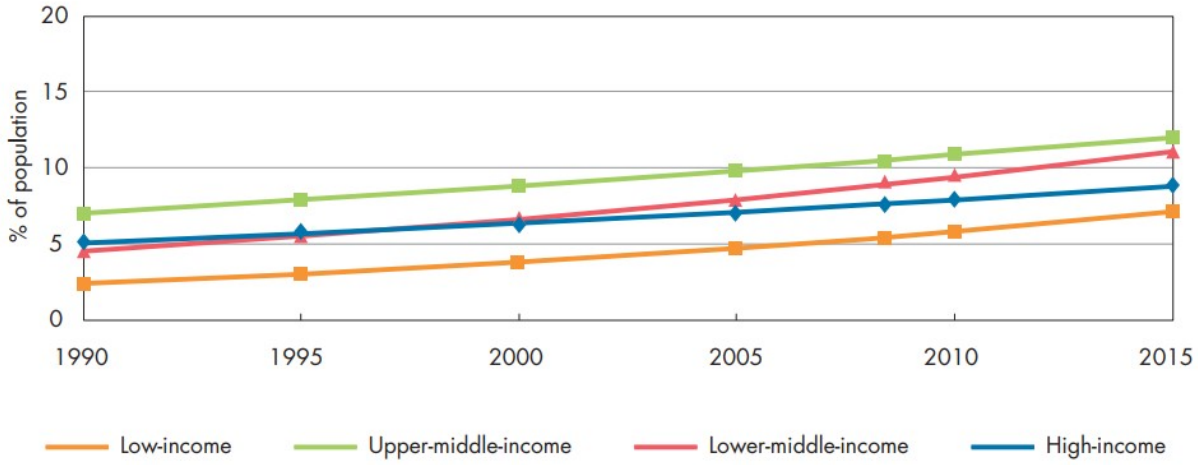
1.2.2.1 Obesity/Overweight/Weight Gain/BMI:

Strong relationship between obesity and metabolic syndrome do exist and it is observed that the relative risk of metabolic syndrome increases with increase in body mass index (BMI) in US population. Low birth weight, followed by rapid weight gain after 48 months of age, were found to be risk factors for adult glucose intolerance in five cohort studies of low- and middle-income countries (Norris *et al*., 2012). The 45-year British follow-up study revealed that poor glucose metabolism is linked to excessive BMI rise over the course of a person's lifetime and early onset of overweight or obesity (Power, *et al.*, 2011). The same study also showed that those who were obese in childhood and not there-after had a five fold risk of type 2 diabetes. In a cohort of Chinese adults, those with birth weights below 2500 g were 66 percent more likely to have more components of the metabolic syndrome than those with birth weights between 2500 and 3000 g, where chances of having these components were only 33 percent (Xiao, *et al*., 2010). The New Delhi Birth Cohort revealed that low BMI in infancy and rapid BMI rise during childhood and adolescence were risk factors for developing metabolic syndrome and impaired glucose tolerance (Fall, *et al.*, 2008). Indians have lower BMI than their Western counterpart; but despite lower BMI Indians are found to have a diabetes prevalence that is comparable to or higher than Western nations (Chan, *et al.*, 2009). The

Chennai Urban Population Study (CUPS) population had a mean BMI much lower than the Western population. Despite this, high risk of diabetes reported in South Indian population in the study (Mohan, *et al.*, 2003). Those who developed impaired glucose tolerance (IGT)/ diabetes were well below internationally recognised criteria for obesity (Sachdev, *et al.*, 2009). Asian Americans have a higher risk of cardiovascular disease and type 2 diabetes at low BMI than the European population, according to research on the connection between BMI and metabolic syndrome. This is because of the fact that the Asians living in their native land may have very different nutrition and physical activity profile than Asians who have immigrated to the US (Palaniappan, *et al*., 2011). Greater BMI gain in late childhood and adolescnce can be a predicting factor for increased adult adiposity and central obesity, and subsequent risk of metabolic disorder (Krishnaswamy, 2012). There are studies reporting that subcutaneous fat is associated with insulin resistance and visceral fat is associated with diabetes and metabolic syndrome (Sandeep, *et al.*, 2010). The same study found a significant relationship between metabolic syndrome and visceral fat but not subcutaneous fat among Asian Indians who do not have diabetes. Framingham Heart Study also support this hypothesis. In a cross sectional study carried out in the rural population of Wardha (Central India) showed a high prevalence of metabolic syndrome (nearly one in six persons) with central obesity directly associated with metabolic syndrome rather than general obesity (Deshmukh, *et al*., 2013). The same study also showed that dyslipidemia as a predominant factor of metabolic syndrome contributed by components like triglyceride and very low density lipoprotein (VLDL) levels. Visceral fat and the metabolic syndrome are linked by three different biological processes: Firstly, may be due to the anatomical location of the fat within the abdomen and its proximity to the portal venous system, direct drainage of free fatty acids to the liver induces hepatic insulin resistance and increases hepatic gluconeogenesis. Secondly, visceral adipocytes have more active lipolytic feature than subcutaneous adipocytes. Histological studies of Asian Indians have shown that adipocytes present in subcutaneous adipose tissue are compartively larger in size and are more resistant to the action of insulin (Misra, *et al.*, 2008). Thirdly, visceral adipose tissue specifically secrete biologically active peptides like visfatin and omentin that modulate glucose and lipid metabolism (Sandeep, *et al.*, 2010). For Asian Indians, study shows that waist circumference is a better index than BMI to identify the risk of metabolic syndrome (Mathias, *et al.*, 2009). In a Chinese cohort

study by Xiao *et al*. (2010) on low birth weight and metabolic syndrome showed increase prevalence of metabolic syndrome when modified cut-off values for waist circumference were used as recommended for Asians. Numerous studies have discovered a weak but statistically significant link between birth weight and an increased risk of developing diabetes as a child. In order to determine the relationship between birth weight and the risk of developing type 1 diabetes, a sizable population-based study comprising 1382602 live births was carried out in Norway from 1974 to 1998 (Stene *et al*., 2001). A linear increase in incidence of type 1 diabetes observed when there was increase in birth weight. This incidence was predicted in the study at 1.7% wih each 100gm increase in birth weight (ibid).

Childhood Obesity: Childhood obesity or overweight is becoming a global problem gradually. Gaining obesity at an early age increases the risk of future metabolic syndrome and hence we can expect a significant burden of cronic disorders. Global estimate of child overweight in 2008 showed that highest prevalence was amongst the upper middle income group countries (WHO, 2010). The problem is more alerming for lower middle income countries like India. Lower middle income countries were found to have the fastest rise of overweight in case of infants and young children. Following figure indicates this trend of overweight globally:



Graph 1.1: Infant and young child overweight trend as per Wold Bank income group countries from 1990 to 2015 (Source: Adapted from WHO Global Status report on NCDs 2010)

There is no national level representative data for children on prevalence of obesity and overweight in `India. Several school based surveys showed the prevalence of

overweight in the range of 15-25% (Naorem *et al*., 2013) matching the global trend of lower middle income countries. Exact estimation is important to know the magnitude of the problem in children as they are going to be the future cases of metabolic syndrome. With increasing chances of survival of LBW newborns, the possibility of becoming overweight/ obese or having metabolic syndrome in later part of life increases (ibid). Child directed marketing tactics are used to capture the future buyers by many food item producing companies. The level of affluence can be an important determining factor for overweight in children for obvious reasons. The easy availability of mechanical equipments and electronic entertainment systems for children or adolescents of higher socio-economic strata can be the highlighting factor here. A Chennai based urban study among 1193 school children of age group 8 to 15 years showed the overall prevalence of overweight at 12.1% and 15.5% among children and adolescents respectively (Tharkar and Viswanathan, 2009). The study also showed that prevalence of overweight (22%) and obesity (13.7%) was higher in girls as compared to boys. More interesting is that both overweight and obesity were maximum in girls belonging to affluent families (ibid). Media and advertisements influence children and teenagers easily in making family purchase or spending decisions. Short sleep duration of children has been found to be associated with obesity or overweight (Raj, *et al*., 2010).

Children's prevalence of the metabolic syndrome is observed to be influenced by obesity. The prevalence of the metabolic syndrome is closely correlated with the severity of obesity, according to a study conducted in the United States with 439 obese, 31 overweight, and 20 non-obese children and adolescents (Weiss *et al*., 2004). The same study also detected metabolic syndrome in half of the severely obese participants (ibid).

1.2.2.2 Nutrition Transition:

WHO Expert Committee (2002) opined that under-nutrition acts as protector of diabetes and India should have less diabetes cases because of high prevelance of under-nutrition in its population. On the contrary the problem is more in India. Equally important is the factor of nutrition transition and changes in diet as a result of the life-styles being colonised by Coca-Cola or McDonald's (Mitra, *et al.*, 2009). The

burden of under nutrition in India has increased as a result of the nutrition transition's negative effects, leading to a considerably greater prevalence of obesity and non-communicable diseases (Shetty, 2013). Five developments have disbalanced the equilibrium of calorie intake and calorie utilized: (i) decreased requirement of physical activity, (ii) growing calorie intake due to overall decrease in food price, (iii) rising cost of healthy food in comparison to unhealthy food, (iv) increase consumtion of outside food, and (v) women getting more participation in labour market (Yach *et al*., 2006). Modern men and women are equally focused on their careers, and women do not want to limit themselves to the conventional gender responsibilities of housework and childrearing. Days are getting shorter for work; therefore if individuals get time off from their busy work schedules, they attempt to use it for entertainment and leisure (Chitnis, 2019). Due to this modernization and engagement in the recreational activities there is paucity of time and hence many families opt for fast food products rather than utilizing the time in cooking (ibid). Rapid socioeconomic development resulting from globalisation made the traditional dietary patterns to disappear (Mitra, *et al.*, 2007) and there is substantial increase in saturated fat portion. In India, urban residents derive 32% of energy from fat compared with 17% in rural residents (Chan, *et al*., 2009). However rural areas are not left out of this transition (Kinra, *et al.*, 2010) and women devoting less time on cooking due to engagement in formal/informal or paid/unpaid works. This could be due to migration of male population for livelihood to the urban areas. This dietary change may also be influenced by the marketing of packaged food items. In a survey of Haryana's urban, rural, and urban slum dwellers, 90% of participants admitted to eating fewer than the WHO-recommended five servings of fruits and vegetables per day (Yadav, *et al*., 2008). Some people think that vegetarianism lowers the chance of getting diabetes. However, a multi-center Indian study found that vegetarians had a higher prevalence of diabetes (2.1–2.8%) than non-vegetarians (<2%) (Mitra, *et al.*, 2009). In a study by de-Oliveira *et al*., (2012) in Brazil showed that an adequate intake of fruits and an intake of more than 8 different items in the diet are protective of metabolic syndrome. Saturated fat consumption of >10% of total calorie intake represnted as a risk factor for diagnosis of metabolic syndrome (de Oliver *et al*., 2012).

The fast food culture has gripped our cities and majority of the immigrants are found to depend on unhealthy ‘junk’ foods (Mohan, *et al.*, 2007). In China, the fast

food chains increased from 3 in 1987 to 184 in 1997 and subsequently a whopping number of 546 in 2002 (Misra, *et al.*, 2008).

1.2.2.3 Physical Inactivity:

Occupation change, advent of newer technologies, and rapid urbanization have resulted in more sedentary nature of work and decrease in energy utilization. Instead of playing outside or engaging in other outdoor activities during leisure, people now prefer to relax within by watching television or playing video games on their phones or computers (Misra, *et al.*, 2008). Household activities have become more mechanized with use of equipments like microwave, washing machine, vaccum cleaner etc. Similarly in rural areas manual plowing of fields have been replaced by tractors and motor-cycles are used in large numbers instead of bicycles (ibid). In comparison to other ethnic groups South Asians are found to be less physically active (Kanjilal, *et al*., 2008). Again within South Asians the urban Indians lack the habit of doing exercise as compared to the Chinese or the Koreans, (Mitra *et al*., 2009). Indians prefer to sit in front of the television rather than going for a walk (ibid).

1.2.2.4 Stressors:

1.2.2.4.1 in utero: Human evolution have witnessed stressors like food shortage or famine and weight loss which lead to the development of metabolic adaptations. The 'thrifty gene' hypothesis proposed by Neel in 1962 is based on the fact that adults at present are experiencing marked changes in lifestyle or are being exposed to over nutrition which has been preceded by experience of great hardship during their early life because of wartime or civil unrest (Cockram, 2000; Mohan, *et al.*, 2007). In addition, low birth weight and exposure to undernutrition *in utero* can lead to altered genome expression, without any change in DNA codes, leading to permanent changes within the body through structural, metabolic, and physiological variations, a process called *epigenetics* (Chan, *et al.*, 2009). These early life events may influence the later susceptibility to IGT/diabetes with high dietary energy uptake and drop in physical activity level (Hoskote, *et al.*, 2008). Barker's hypothesis of developmental origins of adult disease also support this. The possible mechanisms involved includes altered fetal nutrition and increased glucocorticoid exposure. In such adverse situations, the

fetus is often found to make some reversible adaptations so that the immediate chances of survival improve. However, if these persist for long then fetus is compelled to adapt for irreversible changes which will manifest in later part of life (De Boo, *et al.*, 2006). Encountering adverse events during pregnancy can not only affect the offsprings of the ongoing pregnancy but *transgenetically* affect the next generation also (ibid).

1.2.2.4.2 in Employment Pattern: As hypothesized by Cassel (1974) the effect of social disorganization makes certain members of a population more susceptible; indeed, dominant members of the society are at an advantage than the others. In the Whitehall studies of British civil servants the health outcome is reflected in the employment hierarchy; those in the second grade (from top) are found to have worse health than those at the top of the hierarchy ladder (Brunner, *et al.*, 2006). The top civil servants are exposed to acute stress due to challenges which will be exciting, stimulating and, after the event, rewarding and emotionally satsfying. High efforts linked to high reward is generally health promoting (ibid).

Besides financial stability work has a number of other non-financial benefits and research has shown that job loss is a highly stressful life event. Recession and job cuts also act as stressors, particulary in an economy undergoing transformation. Employed persons with even low payrolls have been demonstrated to be more active and psychologically healthier than the unemployed (Bartley, *et al.*, 2006). Insufficient wage leads to low level of welfare benefits and ill-health of the working class making their numbers to increase who have become economically inactive (ibid).

1.2.2.4.3 in Migration: Migration for livelihoods, particulalry as a coping mechanism for chronic poverty or forced migration due to internal displacement, are always stressful. Migrants typically occupy subordinate positions than those who occupy position of power and prestige (Cassel, 1974). Chronic stress induced by structural inequality and lifestyle incongruity could result in impaired glycemic control due to migration. Stressors may interfere with personal ability of self-care and low income status limits the availability of appropriate nutrition (Spitzer, n.d.). Migrants usually put themselves at similar risk or even at worse health outcomes than the host population by trying to adopt the modes of life of the host location (Mohan, *et al.*,

2007). According to studies, compared to rural non-migrants, migrants who move from rural to urban areas had a higher frequency of obesity and metabolic syndrome (Ebrahim, *et al.*, 2010). Natural calamity can also act as a cause of stressor. Indian costal population affected by Tsunami in December 2004 was displaced and was under high stress. They showed a high prevalence of undetected diabetes/impaired glucose tolerance as compared to the unaffected control population (Ramachandran, *et al.*, 2006).

1.2.2.4.4 in Sleep deprivation: Insufficent sleep could lead to weight gain or obesity (Reavan, 2006). Pathological or behavioral adverse effects of sleep deprivation have been shown in several studies (AlDabal and BaHammam, 2011). Medical science has strong evidence of pathological sleep deprivation initiated glucose intolerance and hypertension. There are data from epidemiological and experimental studies which support this association and correlate behavioral sleep deprivation along with serious metabolic and endocrine consequences (AlDabal and BaHammam, 2011). However most of these studies are based out of India. In the Japan Collaborative Cohort Study, which involved a larger cohort of 104,010 Japanese respondents, self-reported data was evaluated and revealed that the mean sleep duration for men and women, respectively, was 7.5 hours and 7.1 hours (Tamakoshi and Ohno, 2004). School schedules are forcing children to lose sleep on everyday basis (Hansen *et al*, 2005). Insufficient sleep is found to be a common feature of shift work and hence pattern of employment can determine the sleep cycle of a worker (Wolk and Somers, 2006).

Stressor Pathways in Development of Metabolic Syndrome:

Stress due to various factors like psychological, biological and physical can be the major cause of metabolic syndrome. Chronic stressors are basically due to fight for survival and progress, and too much is desired in too little time. Certain stressors are unique for Indians and include: water scarcity, fear of losing employment, overtime working, lack of playgrounds and parks, irregular diet due to pressure of work, competitive environment, burden of education in students, and, replacement of joint families by nuclear families (Iyer, 2003). In response to stress two pathways (neuroendocrine pathway) involving nervous system and endocrine transmitters bring about metabolic and physiological changes (Brunner, *et al.*, 2006). Metabolic

syndrome can be due to inappropriate activation of HPA axis (Sridhar, *et al.*, 2002). Stress leads to HPA axis response and results in cortisol release into the blood stream and hormonal dysregulation. Intrauterine exposure to stress may activate the HPA axis and can be linked with health transition, metabolic syndrome and low birth weight.

1.2.2.4.5 Role of smoking or tobacco products and/or alcohol consumption:

Various tobacco products including smoking itself has been found to be associated with health problems. The pathogenesis of metabolic syndrome due to chronic exposure to tobacco products and smoking has enough documentations (Buckland *et al*., 2008). There are studies which demonstrate link between smoking and many components of metabolic syndrome. Alcohol consumption as definitive cause of metabolic syndrome is still controversial and need more exploration.

1.2.2.4 Environmental Pollutants:

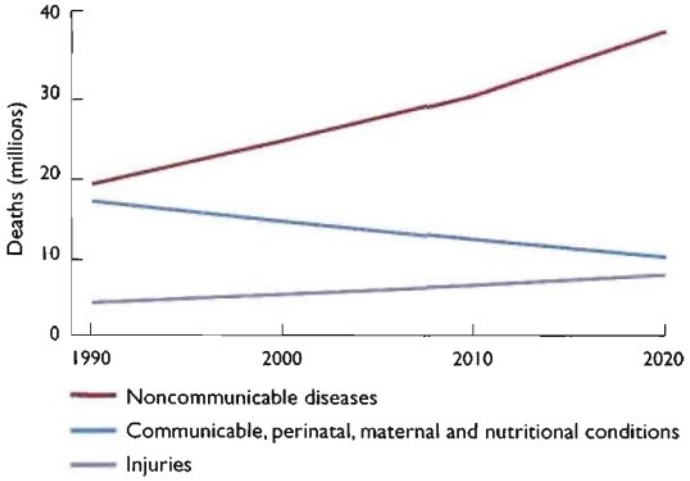
Exposure to Persistent Organic Pollutant (POP)s like DDT, PCBs (polychlorinated biphenyls) and dioxins increases the risk of both insulin resistance and metabolic disorder (Ruzzin, *et al.*, 2010). It is stated that even low concentration of pollutants are sufficient to initiate diabetes/metabolic syndrome in obese people (www.healthandenvironmentonline.com/2011/02/21/chemicals-and-diabetes-a-short-history as accessed on 08-08-2012). Dietary products like fish (lakes or rivers having high concentration of PCBs), meat and dairy products are the main sources of PCBs (Everett, *et al.*, 2011). PCBs and dioxins pile up in fatty tissues of animals and humans and are even reciculated in commercial food through animal feed used to accelerate growth (https://www.diabetesandenvironment.org/home/environmental-chemicals/persistent-organic-pollutants as accessed on 16-02-2022). A study in US has shown that higher level of POPs is directly proportionate to the prevalence of diabetes (Lee *et al*., 2006). The highest exposure group reported 37.7 times higher risk of diabetes than the group with lowest level of exposure (https://www.diabetesandenvironment.org/home/environmental-chemicals/persistent-organic-pollutants as accessed on 16-02-2022).

1.3 The Overall Scenario of Metabolic Syndrome:

There are numerous studies on prevalence of metabolic syndrome worldwide but are mostly focused on specific study populations and in certain geographies. These researches, which are predominately from developed or metropolitan areas of developing nations, indicate the prevalence of adult metabolic syndrome (Wild and Byrne, 2005). The criteria and cut off values followed in these studied for prevalence estimation are not similar and even modified as per requirement. In 2010, 285 million people worldwide, or 6.4% of the world's population, were estimated to have diabetes and the same is predicted at 371 million with prevalence of 8.3% for the year 2012 (IDF, 2011; 2012). It was also predicted that the number will rise to 438 million by the year 2030 (IDF, 2011). In 2025, it is anticipated that India, China, and the United States collectively would have the highest proportion of diabetics (Ramachandran, *et al*., 2002). Developing countries have reported the prevalence of diabetes at a younger age. In industrialized nations, most diabetics are typically over 65 years old, whereas in developing nations, the majority are between the ages of 45 and 64 (Wild, *et al*., 2004; Mitra, *et al*., 2007). This has significant socio-economic implications for developing nations. The World Economic Forum projected a global economic burden of $ 47 trillion as a severe threat to economic development due to the cases of NCDs by the year 2030 (Shetty, 2013).

Estimated 972 million people (333 million in developed countries and 639 million in developing countries) in the world are suffering from hypertension (Joshi, *et al*., 2007). Overall prevalence of hypertension globally (age ≥25years) was 40% in 2008 (WHO, 2010). Hypertension causes 7.5 million deaths, which accounts for 12.8% of total annual deaths, worldwide (ibid). Chennai Urban Rural Epidemiology Study (CURES) clearly shows that every fifth individual is hypertensive in Chennai.

The Global Burden of Disease by WHO in 1996 projected NCDs as the main cause of mortality by the year 2020 in developing regions. The projected trend in death by broad cause group is depicted in the graph below:



Graph 1.2: Projected trend of death in developing region by broad cause group (Source: Adapted from WHO, 1996)

Of the total global death of 57 million in year 2010; 36 million i.e. 63% is due to NCD and 1.3 million accounts for death due to diabetes (WHO, 2011). More than 16 million (40%) of these NCD deaths occurred prematurely under the age of 70 years (WHO, 2014). An estimated 3.96 million deaths worldwide is attributed by diabetes in the age group of 20-79 years which constitute 6.8% of global mortality in all ages (Roglic, *et al*., 2010). Between 2010 and 2020, the global number of fatalities from NCDs is anticipated to rise by 15% (WHO, 2011). The scenario was more heartening in low- and middle-income countries where almost three quarters (28 million) of all NCD deaths and majority of premature deaths (82%), under the age of 70 years, occurred in 2012 (WHO, 2014). NCDs are contributing around 60% (5.87 million) deaths out of all deaths in India (Nethan *et al*., 2017). Similar estimation of 6.0 million deaths from NCDs, constituting 62% of total mortality in the year 2016 was quoted by ICMR State Level Disease Burden Initiative (Ministry of Health and Family Welfare GoI, 2017).The highest number of death attributable to diabetes is expected to occur in countries with large population like India, China, United States of America, and Russian Federation (Roglic, *et al*., 2010). One of the disturbing facts is that while some countries documented some decline in the mortality and morbidity of some non-communicable diseases, but no such decline has been reported for diabetes (ibid).

The prevalence of metabolic syndrome is increasing in both urban and rural population of India with a range of 11% to 41% (Misra *et al*., 2008). In a cross-

sectional study, Prasad *et al*. found that the prevalence of metabolic syndrome was extremely high in the urban East Indian population at 33.5% (Prasad *et al*., 2012). Similarly a prevalence study for metabolic syndrome in Northern urban community showed a prevalence of 22.37% (Ravikiran *et al*., 2010). Chennai Urban Rural Epidemiology Study (CURES) is considered as one of the largest epidemiological study in India involving 26001 individuals selected randomly for diabetes screening. This study was one and only in its kind which tried to identify the prevalence of metabolic syndrome on representative population of Chennai metropolitan using WHO, ATPIII, and IDF criteria of metabolic syndrome (Deepa *et al*, 2007). Different prevalence rates of metabolic syndrome were recorded in the participated population (n=2350) i.e. 23.2% (WHO criteria), 18.3% (ATPIII criteria), 25.8% (IDF criteria), and 9.5% by using all the three criteria (ibid). Dyslipidemia, which is another component of metabolic syndrome, is very common in Asian Indians. Low HDL has been incorporated in several studies conducted in South Indian population (Prasad *et al*., 2012). Data and studies on diabetes are more available in comparison to other components of metabolic syndrome. IDF estimated around 40.9 million cases of diabetes in 2009 for India. Cases are expected to increase to 57.2 million in 2025 and 80.9 million in 2030 as estimated by WHO. More recently the ICMR-INDIAB study provides diabetic cases of India at 62.4 million and prediabetes at 77.2 million for the year 2011 (Anjana, *et al*., 2011). NFHS-5 data shows that 12% women and 14% men above the age of fifteen years have random blood glucose levels >140mg/dl. A fivefold increase in prevalence of diabetes from 2.1% to 12.1% recorded in urban adults at a national level survey conducted in six major cities in India from 1970 to 2000 (Mohan, *et al*., 2004). National NCD risk factor surveillance recorded a higher prevalence of diabetes in southern states (Mohan, *et al*., 2009). Chennai Urban Rural Epidemiology Study (CURES) showed an increase of prevalence from 8.3% to 14.3% from 1989 till 2004 indicating the increase of prevalence by 72.3% within the span of 14 years (ibid). Surveys conducted consecutively in the city of Madras (now Chennai) in 1988-89 and again in 1994-95 showed the increase of prevalence of diabetes from 8.2% to 11.6% and that of impaired glucose tolerance (IGT) from 8.7% to 9.1% (Ramachandran *et al*., 1997). The ratio between diabetes and IGT is significant in predicting future diabetes prevalence because it serves as an indicator of the population's "epidemic stage" (King and Rewers, 1993). Study in India showed that the onset of diabetes was before the age of 50 years in 54.1% of cases, indicating that

these subjects had developed it in their most productive years of life (Ramachandran, 2007). Females beyond 49 years of age constituted higher proportion of deaths than males in all regions (Roglic, *et al*., 2010). Chennai Urban Population Study (CUPS) showed nearly three times higher rates of overall mortality in subjects with diabetes than in non-diabetics [18.9 vs 5.3 per 1000 person-years] (Mohan, *et al*., 2009).

Diabetes has its economic implications at the individual, family and even at the country level. In an assessment by Indian Council of Medical Research (ICMR), diabetes results in 2263 thousand of DALYs lost annually (ICMR-MRC workshop, 2009; Gupta, n.d). Total amount needed to treat type 2 diabetes in India is estimated at around 2.2 billion USD (Ramachandran, 2007). Economist Intelligence Unit (EIU 2007) estimated the direct medical care costs for India at 2.1 percent of GDP (Mahal, *et al*., 2010). Diabetic individuals in India require 8 to 25% of their household income to meet the cost of treatment (Shobhana *et al*., 2000). Grover, *et al*. (2005) roughly assessed the cost of treatment for diabetes patient in North Indian hospital as INR 10,000 and another INR 4000 as losses on account of morbidity (ibid). Similarly hypertension accounts for 57 million DALYs or 3.7% of total DALYs (WHO, 2010).

Persons with diabetes are most frequently found to die because of cardiovascular diseases or renal failure rather than due to diabetes specific complications. According to reports, diabetic nephropathy is the main cause of chronic renal failure in India (Ramachandran, 2002). In a study conducted by Joshi, *et al* (2006) in East and West Godavari in Andhra Pradesh covering 45 villages, using verbal autopsy and ICD (International Classification of Disease) coding, the causes of death were recorded in between 1st October 2003 and 30th September 2004. The study recorded injuries (13%) followed by infectious diseases (12%), neoplasms (7%), diseases of the respiratory system (5%), and disorders of the circulatory system (32%) as the top causes of mortality (Joshi, *et al*., 2006). This study gives proof that people in rural India are most likely to have a far higher chance of dying from chronic illnesses and injuries than from infectious infections.

WHO has emphasised on preventing the major risks associated with chronic disease. “Preventing Chronic Diseases: A Vital Investment” a global status report by WHO gave stress on global response to address the major risks associated with

chronic disease worldwide (WHO, 2005). When compared to whites, blacks, Hispanics, and other Asians, Asian Indians have the greatest risk of coronary artery disease (CAD) as a result of dyslipidemia (Ardeshna *et al*., 2017).

Chapter Two

Conceptualisation of the Problem and Aim, Objective, Methodology of the Study

2.1 Conceptualisation of the problem:

The classical concept of causality in epidemiology is described by the epidemiological triad with agent, host, and environment as important components. External agent, susceptible host, and conducive environment interrelate in a variety of complex ways to produce disease. This model is more suitable for infectious diseases but does not work well for many non-communicable diseases. Model of multifactoral causation have been proposed to explain this. Rothaman's causal pies model (Rothman, 1976) tries to explain by comparing each contributing factor as piece of pie. When all the pieces of pie fall in place to complete the pie, it becomes sufficient cause for disease occurance. There may be several such suffient causes and each may have common component referred to as necessary cause. In case of metabolic syndrome certain sufficient causes (both biological and social) like obesity, nutrition, and stress have been identified and will be reviewed in this study. To complete the pie (suffient cause) the components of sufficient cause (pieces of pie) will be analysed in the Indian context. Studies and available data will also be reviewed to look for any necessary cause in the context of metabolic syndrome. As Rothman's model proposed that every piece of pie needs to be in place to complete the pie; similarly this review will look into the social causes as intergral part of the pie along with biological causes for diease occurance. Whether presumed to be necessary cause like obesity/overweight as common member of sufficient causes is really relevant for metabolic syndrome in Indian context needs to be explored.

There is no doubt that obesity, over weight, weight gain and/or BMI have strong association with metabolic syndrome. In case of Indian population BMI is not always true as a determining factor for metabolic syndrome; but central obesity and the pattern of weight gain are more relevant. Population specific BMI reference values are required for proper diagnosis and prevention of metabolic syndrome (Palaniappan, *et al*., 2011). Urbanization, mechanization, globalization leads to change in life style, physical activity, food habits and these in turn determine obesity and over weight. Population based surveys in developing countries involving 75 communities and covering 32 countries show that diabetes is rare in communities where traditional lifestyle has been followed (Hossain, *et al.*, 2007). Again low birth weight with obese childhood with even normal body weight thereafer can be a cause of adult type 2

diabetes. This questions the on going free meal or feeding programs because the rate at which the weight is gained also determines the prevalence of metabolic syndrome (Misra, *et al.*, 2008).

Low birth weight can be a reflection of the nutritional status of the mother. Poor nutrition of mother or exposure of foetus *in utero* to stressors can impend permanent changes in genome which can transmit to subsequent generations. This concept is true in case of Indian population which witnessed civil unrest, famine etc. in the past. With such inherent genomic changes some later generations may have improved in lifestyle/adequate food which the body is not programmed to deal with.

In UNDP Multidimensional Poverty Index (MPI) nutrition is kept as a key indicator for measuring health (UNDP, 2010). Countries with higher MPI headcounts have the tendency of more deprivation. Human Development Report 2010 shows that 55% of Indian population comes under MPI headcount and 42% lives with daily income of <1.25$ a day. As per the same report of year 2021 (survey conducted in 2015-2016) MPI headcount for India is 27.9% with 22.5% living below the international poverty line of 1.90$ per day (UNDP, 2021). Though people living below international poverty line has decreased considerably but in a high populous country like India these percentages will be huge in absolute numbers. Hence high prevalence of metabolic syndrome can be related as a result of poverty/deprivation for decades and not only due to epidemiological transitions. This also brings in the issue of inequity for determinants of health as raised through the four principles of Cassel (1974) and in the document of Commission on Social Determinants of Health (WHO). The Cassel's principles are summarised as-

(1) "….circumstances in which increased susceptibility to disease would occur would be those in which there is some evidence of social disorganization"

(2) The impact of these processes is not felt evenly by every member of a population. In comparison to dominating individuals, subordinates are more vulnerable.

(3) Processes (both biological and social) are protective.

(4) The presence of such differences in group dynamics would increase illness susceptibility rather than playing a specific etiology function.

The report of Commission on Social Determinants of Health (WHO, 2008) stressed on achieving health equity as 'social injustice is killing people on grand scale'. Poorest of the poor has the worst health outcome around the world, and even within better off countries. Health inequity is due to unequal distribution of income, goods, and services (CSDH, 2008).

Inadequate nutrition is a result of poverty and it also compels population to migrate to another place for livelihood. Poverty/chronic deprivation is a major cause of rural-urban migration in India.

Migrants try to adapt the lifestyle and food habits of new urban environment making them more vulnerable to impaired glucose tolerance. Barriers in maintaining the traditional eating habits by migrants are due to high price of fruits and vegetables and limited variety of food of choice (Misra, *et al.*, 2007). Change in dietary pattern is evident in both urban and rural population. Diet may be a determinant in development of diabetes/metabolic syndrome in two ways: by supply of calories and by the effects of particular foods (Mitra, *et al.*, 2009). Studies have indicated that persons with type 2 diabetes consume more saturated fat than participants without diabetes, as evidenced by their serum cholesterol ester, which has a larger proportion of saturated fatty acids than linoleic acid (a polyunsaturated fatty acid) (van Dam, 2003). Diets high in saturated fat decreases insulin sensitivity as compared to diets high in mono-saturated fat. Rigorous marketing tactics of packaged foods have invaded the rural markets and are becoming favourate pass-time food for children and in some occasions are about to replace the main meal. Rural women engaged in some sort of income generation activities to strengthen household economy made them to devote less time in cooking. Fast food or junk food has become the solution for many to save time. These issues are important and to be incorporated during the research with available secondary evidences while looking at the nutrition transition.

Different forms of stressors play important roles in the causation of metabolic syndrome. The mechanism of hypothalamic-pituitary-adrenal (HPA) axis is important to understand chronic stress. The hypothalamus and the pituitary gland of brain and the adrenal or suprarenal glands of each kidney constitute a complex set of interactions known as the HPA axis. Stressors act as triggers on hypothalamus to

secrete corticotropin-releasing hormone (CRH) and arginine vasopressin (AVP). Both then stimulates the posterior pituitary for release of adrenocorticotropin hormone (ACTH). ACTH drives the production of cortisol from the adrenal cortex (Guilliams, *et al.*, 2010). Chronic and repeated stressors can lead to HPA axis dysregulation and affecting end organ function. In subjects of metabolic syndrome the output of adrenaline and cortisol in 24 hour urine sample was found to be raised (Brunner, *et al*., 2006). Hence a normal functioning HPA axis progresses to HPA axis dysfunction under the stressors.

Socioeconomic status as derived from occupation are powerful indicators of heart disease or metabolic syndrome. Whitehall study stated that the gradation of employment proved to be a more powerful determinant for coronary diseases than other common risk factors like smoking, serum cholesterol, and blood pressure (Brunner, *et al*., 2006). Lack of variety of work, lack of social contact, hostility etc. are important factors (ibid). Lower employment grade was found to be directly related to the difficulty in clearing the glucose into body tissues for storage.

The stressors may start acting *in utero* and continue throughout life. In todays world we can find the competitive environment everywhere- starting from first enrollment in school to burden of education, from getting employment to fear of losing employment etc. Migration in the form of forced migration due to war, riot or natural calamity are very stressful. Even after migration the migrants occupy a subordinate position amongst the host population making them exposed to stressors. People undergo remarkable stress due to this new environment, socio-economic and language incongruity, job related obstacles, and absence of social support (Misra, *et al.*, 2007). Though social support is a very personal matter yet it has a wide spectrum of implications on health. Social support may be in the form of ‘emotional’ and ‘practical’ (Stansfeld, 2006). Subjects with belief such as “he is being cared for and

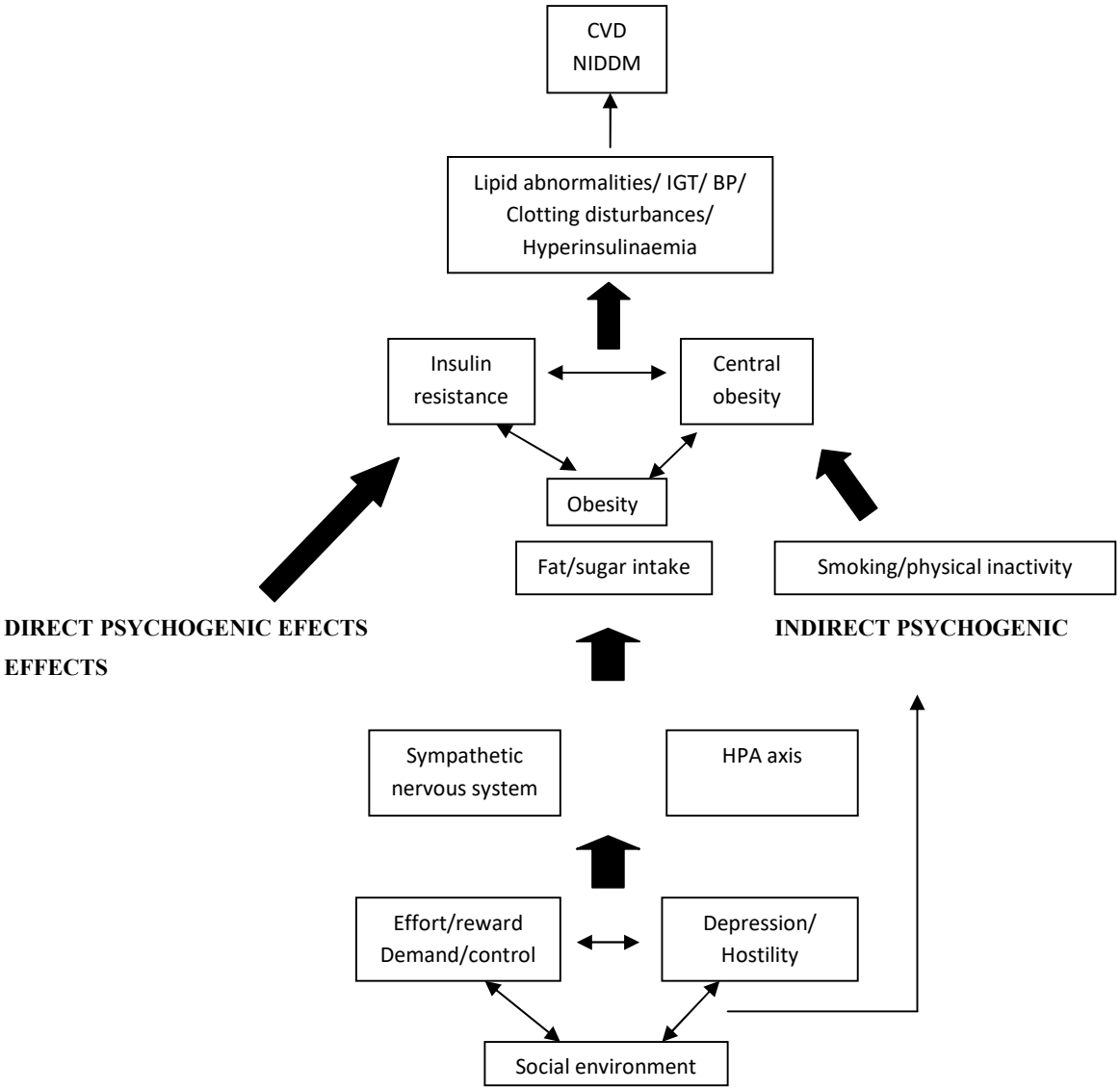


Fig 2.1: Psychosocial and biological pathways in CVD and NIDDM (Source: Adapted from Brunner, *et al*., 2006)

loved" are positive for health and put him into a network of social cohesion. Lower level of blood pressure, cortisol, adrenaline, and noradrenaline are found to be associated with high level of social support (ibid.). In case of migrants this social support and social cohesion is lacking due to the new environment; causing increased stress level and stimulation of HPA axis.

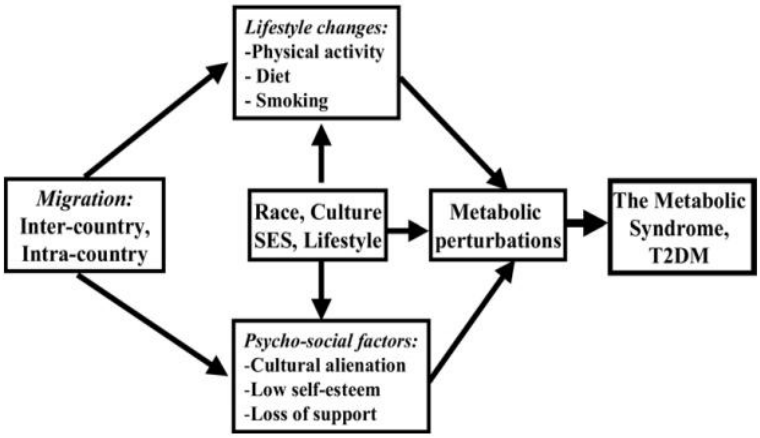


Fig 2.2: Interplay of multiple factors after migration (Source: Adapted from Misra, *et al.*, 2007)

Unemployment, axing of jobs due to recession are important stressors in present context for developing nation like India with a huge population. Employees at the top though pass through stressful periods but are inturrupted by the emotionally satisfying phases of rewards. On the other hand the subordinate employees are always under the stress for better performance due to pressure from boss or fear of losing the job. The Whitehall II study showed stepwise relationship between employment grade and prevalence of health related psychosocial factors (Brunner, *et al*., 2006). Two concepts of psychosocial work related stress are worth mentioning: the demand-control model and the effort-reward model (Marmot *et al*, 2006). The first model explores how low level of both decision making authority and skill utilization in job leads to higher risk of stressful experience. Such situation has a negative 'work-life balance' and decreases the likelihood of spending an active life beyond working hours. The second model is based on the imbalance between effort rendered at work and no equitable reward in return. Reward can be in terms of money, career, job security etc (ibid.). The Swedish case control study in Stockholm (SHEEP) reported that subjects with high demand and low control in their job were at higher risk of developing acute myocardial infarction (Hallqvist *et al*., 1998).

Risk factor epidemiology had the potential to give important understanding of the disease processes, but the concept was confined to the narrow definition of individual risks and without having any scope of emphasis on social and environmental factors (Dasgupta, 2003). On the other hand, the life course approach to chronic disease epidemiology includes studies that looks into the pathways (biological, behavioral,

and psychosocial) that operate in one's life course and even across generations (Ben-Shlomo, *et al.*, 2002). The life course model also helps us in understanding the diversities in the health and disease the populations experience over time, across geographies and within social groups (ibid). Recent reviews on trend of chronic diseases had strongly related factors from birth to adult life: the mother's body mass index, birth weight of child, growth trajectory of the child in early part, subsequent eating and physical activities, other behavious at adulthood (Yach *et al*., 2006).

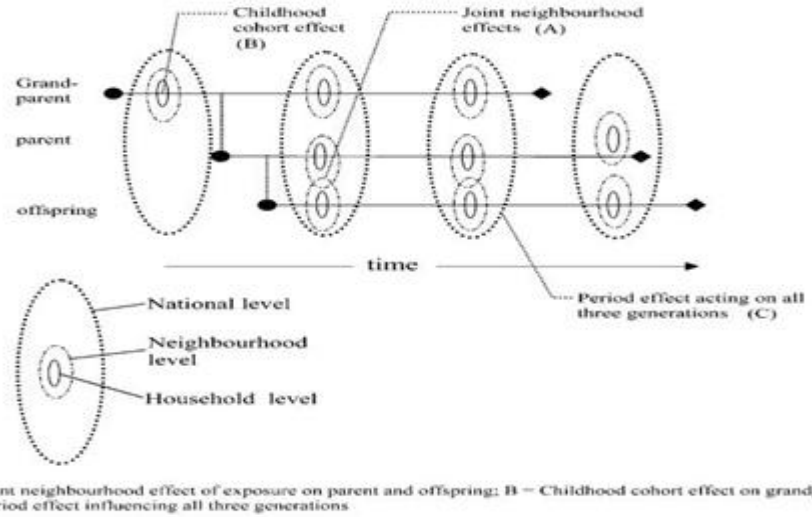


Fig 2.3: Multi-generational schema illustrating the possible influences of hierarchical and life course exposures on disease risk across three related individuals (Source: Adapted from Ben-Slomo, *et al*., 2002)

The whole concept of "proximal" and "distal" determinants of health has to be understand. The common idea is that the biological belongs to *proximal* and the social lies in the realm of *distal* (Krieger, 2008; CSDH-WHO, 2008). Proximal and distal divide actually creating splits rather than connecting them, and thereby "obscuring the intermingling of ecosystems, economics, politics, history, and specific exposures and processes at every level, macro to micro, from societal to inside the body" (Krieger, 2008). Hence knitting the proximal and distal determinants to get the multifactorial framework of "web of causation" is important.

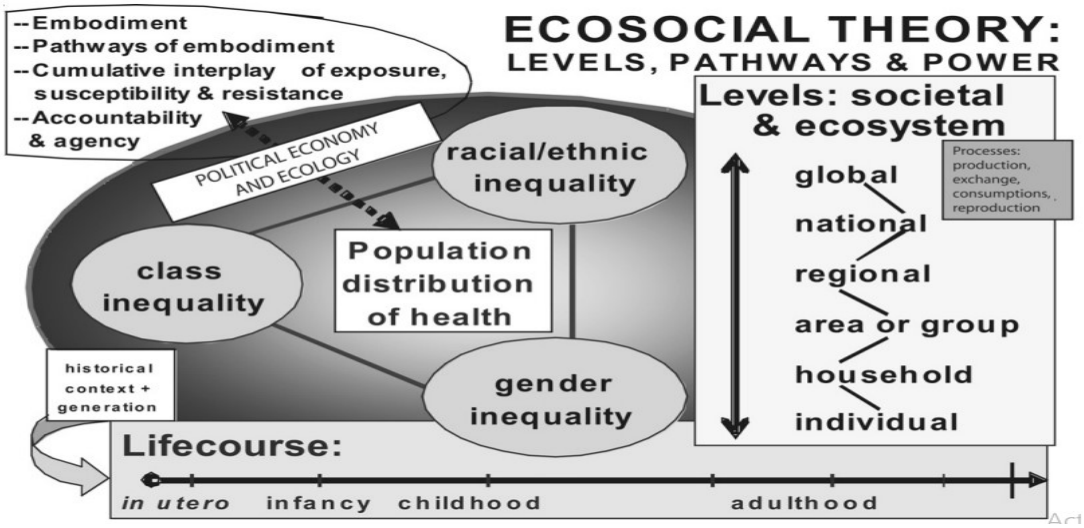


Fig 2.4: Ecosocial paradigm of disease (Source: Adapted from Krieger, 2008)

Several concepts are quoted above to give a framework on determinants across life-course starting from inside the body to the outside and from individual to global level. The impact on health outcome can be witnessed not only in individuals but also across generations. Health inequality is a phenomenon driven by the economic, racial, class and gender inequality at different phases of life. This is relevant in case of metabolic syndrome also. Advantageous group has a different set of life course than non-advantageous group to reach at metabolic syndrome. Advantageous group has the avenue to decrease or delay the progression. On the other hand such scopes are absent or minimal in case of non-advantageous group. These dynamics are reviewed in this study with support from relevant data.

The causality components can directly impact the health policy. Substantial evidence in favour of certain causality can mould the health policy. Till now it has been observed that health policies in respect to metabolic syndrome are focused mostly on biological causes. Risk assessment and risk reduction are inclined towards mitigation of biological causes. Policies tries to address obesity, less physical activity, high calorie diet, stress etc. by targeted measures rathen than looking at larger root causes. For example policy makers have to understand whether obesity or rate at which someone gains obesity is more important. Similarly less physical activity is a mean for weight gain but equally important to understand whether excessive physical activity by the marginalised can also be a hindrance for development and subsequent

metabolic syndrome. Life course approch has been looked as a challenge in health policy formulation due to difficulty in measuring the timescale for such long period (Exworthy, 2008). However it can not be neglected that certain information of life course are really important for risk profiling of metabolic syndrome. Moreover economic powerhouses and giant corporate lobbies also influence in drafting and implementation of health policies. As a result certain legislations are not that stringent on certain establised causalities.

2.2 Aim of the Study:

The final/proximate pathway of development of metabolic syndrome is biological. However, social factors interact with the biological processes to cause metabolic syndrome and this study is meant to analyze these social-biological linkages. The study will review the global and Indian studies available in the context and synthesise the Indian picture linking biological and social factors. Current Indian studies are rooted in the risk factor paradigm of epidemiology and is yet to take into consideration the life course epidemiology which is necessary for informing all policies that affect the social determinants of the disease and therefore require appropriate intervention at the policy level. Hence, at the end the review will recommend some policy clauses that can be considered to address the gaps.

2.3 Objective of the Study

The study will focus on delineating the pathways and interactions of the social and biological determinants leading to metabolic inflexibility and metabolic syndrome among poulations and also in rural to urban migrant populations with transfomation in nutrition (recognising that such changes are essentially ocurring in a millieu of undernutrition) and working and living patterns as the core of the inquiry. The review will also try to pave way for future research which need focus by bringing in the gaps in the available literature.

2.4 Methodology:

This study is purely based on review of existing literature from secondary sources. Before going to the methodology or method adapted for this review, we need to have an idea about some of the widely used review types which can be considered for this study. With the abundance of literature a variety of review types have evolved. However it is difficult to say how much these review types are able to retain their potential in true sense due to use of diverse terminologies (Grant and Booth, 2009).

(a) Critical review: Extensive literature search for critical analysis in narrative style without any quality assessment. Such reviews are starting point for further evaluation rather than final outcome.

(b) Literature review: Examination of wide range of published materials in narratives with analysis can be chronological, conceptual, thematic etc. It seeks to identify and build a base on previous work.

(c) Meta-analysis: More of a numerical analysis by graphs and tables with narratives. Statistically combines results of quantitative studies which need to be sufficiently similar for inclusion.

(d) Systematic review: A systematic search and synthesis of research materails and adhering to the review guidelines. Purposive or selective samling of materials aims to recommend on known facts and explores the future perspectives of unknown which impose some restriction on inclusion of studies.

(e) Mixed studies review: As name suggests it is a combination of methods with literature review being an essential component. The most important weakness of this review is that there is no consensus on what point the integration of qualitative and quantitative components should occur.

(f) Umbrella review: Focus is on broad condition or problem where evidences are compiled from multiple reviews. Without any search for primary studies the reviews tries to recommend for both known and unknown areas.

If we explore the above review types then limitations are observed in each while fulfilling the SALSA method (Search, Appraisal, Synthesis, and Analysis) to reach the endpoint. In this review study the importance has been given to follow the SALSA method to draw conclusions.

The secondary sources quoted in the references and bibliography of this study are used in a planned manner so that already mentioned objectives of the study can be addressed. Search of literature has been kept open as much as possible so that more findings can be incorporated in the study. The search of materials are structured in such a way that relevant literatures, as per requirement of each chapter, are included as much as possible. This will help in drawing a picture of social determinants of metabolic syndrome in Indian scenario and to ascertain the areas where more focus/studies are required. Relevant and most recent principles or hypotheses are tried to be included to build the theoritical base. Any contradictions or challenges raise against certain principles or hypotheses afterwards are also included in the review to know the relevance in Indian situation. Systematic literature selection has the possibility of narrowing down and hence has the disadvantages of either including the principles/hypotheses or their contradictions/challenges. Literature search on the basis of objective of the study is the core criteria. While looking for studies focus has been given to include those studies which represent larger population. However in case of non-availability of large scale studies, even smaller studies with important findings are also included in the review.

The first part of the study involves extensive review of literature to build a theoretical framework on how social and biological processes interact in metabolic syndrome. Some sources are not referred directly but have helped in understanding the study subject are quoted in bibliography section. Available quantitative data are used from secondary sources to project the problem in the context of prevalence, incidence, mortality, morbidity, economic burden etc. Some of the secondary data has been included in this section as follows to build the problem statement.

- Changes in physical activity in rural and urban population and the role of access to transport and mechanisation of work (including agriculture)
- Availability of packaged and processed foods in rural markets
- Determiants and processes of rural-urban migration
- Employment status, wage pattern etc. as stressors

2.5 Tools for Data Collection:

2.5.1 Review of Literature and Other Sources: Extensive literature review will include the materials like published books, articles from journals, internet sources, various reports of health organizations, newspaper reports etc. Such review will look at determinants such as obesity/BMI, nutrition transition, gene hypothesis, chronic deprivation, psychosocial factors and power relations as the causation of metabolic syndrome (DM/CVD/hypertension). Stress will be given to collect the secondary data from the original source with latest updation as much as possible. Sources to be used-

(i) data from reports of international organizations, agencies etc.

(ii) large scale national surveys- census of India/NSS/NFHS/NNMB etc.

(iii) published literatures- books/articles from journals/internet sources/various reports of health organizations/newspaper reports etc.

(iv) un-published data/thesis etc.

2.5.2 Resource Search: For this review study, online resource search has played an important role where priority is given to select the articles which meet the study objectives irrespective of period of publication or reporting. Books, thesis, newspapers etc. as available in hard bound form in libraries are also utilized as per requirement. Extensive PubMed, Google, and Google Scholar literature search was performed for theoretical concepts and supportive studies. Official websites of international organizations, research bodies, recognized institutes, departmental and ministerial web portals of Government of India, and other Govt. recognized bureaus or foundations are looked for annuals reports, guidelines, surveys, studies, reviews etc.

Extensive literature search has been performed using combination of keywords, chapter wise, depending on the contents of each chapter. Stepwise screening of literatures is done for inclusion or exclusion in the study. In the first step inclusions of articles are done depending on article title, description in the abstracts, and some weight age is also given on the year of publication. The titles and abstracts which are not at all relevant are excluded. In the second step full papers are reviewed in depths which are supposed to be included in the study. While doing so if it has been

observed that the publications are deficient in meeting the study objectives, then such publications are also excluded.

The resource search strategy performed is shown in the following figure:

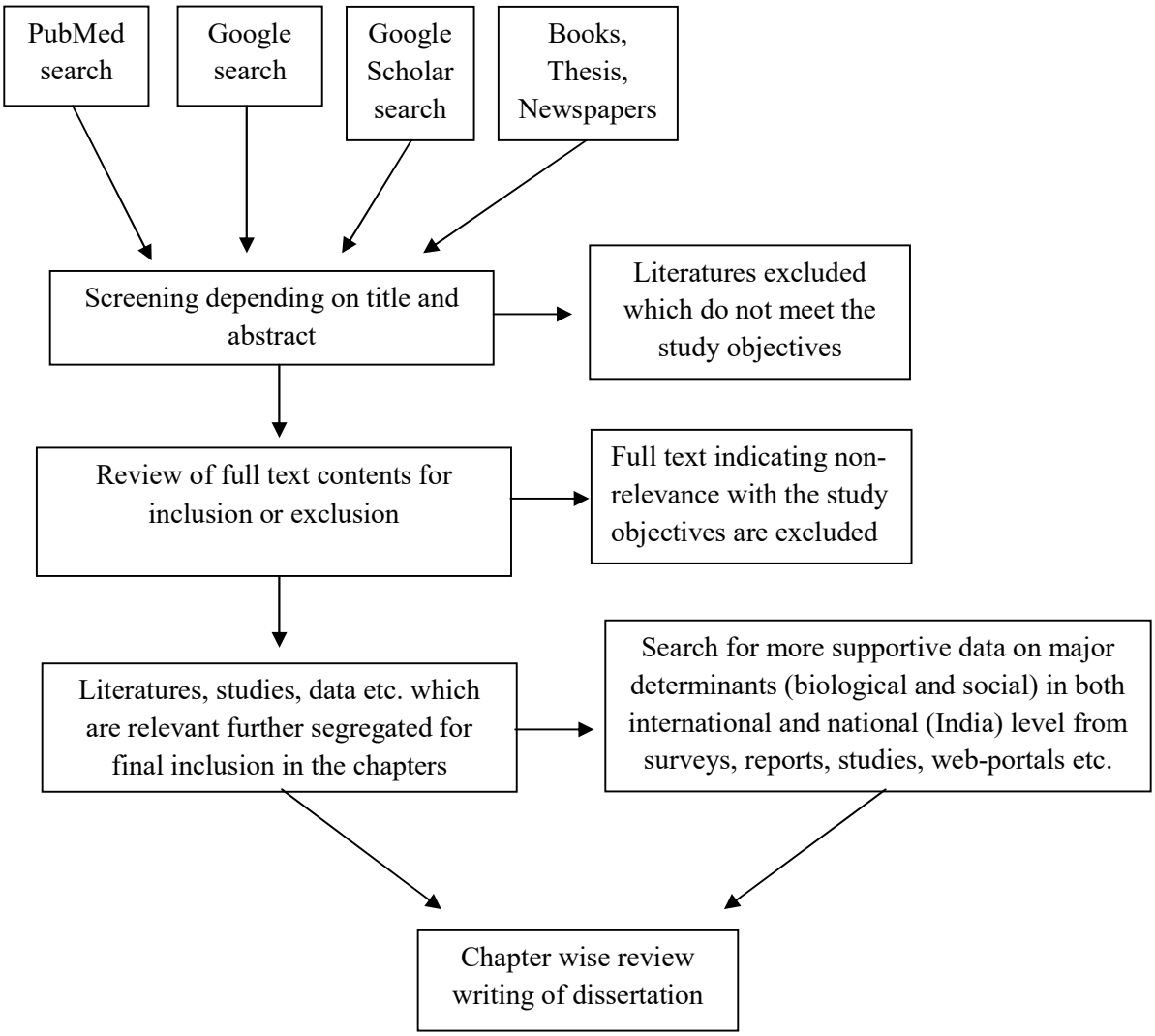


Fig 2.5: Flow diagram of resource search method

2.5.3 Keywords Used: Combination of key words used to search for resources are listed below:

(i) Chapter One (Introduction and literature review): Non-communicable diseases/NCD, metabolic syndrome, diabetes, hypertension, dyslipidemia, insulin resistance, glucose intolerance, definition, determinants, risk factors, incidence, prevalence, economic implications, world, India, obesity, overweight, weight gain, BMI, childhood obesity, birth weight, nutrition transition, physical inactivity,

stressors in utero, stressors in employment, stressors in migration, stressors in sleep deprivation, stressor pathway, HPA axis, smoking, tobacco, alcohol, and environmental pollutants.

(ii) Chapter Two (Conceptualisation of the problem): Metabolic syndrome, low birth weight, poverty/deprivation, social determinants of health, migrants, change in dietary patterns, stressors and metabolic syndrome, occupation and metabolic syndrome, unemployment and metabolic syndrome, life course approach, proximal determinants, and distal determinants.

(iii) Chapter Three (Biological concepts in relation to obesity, overweight, weight gain, BMI, body composition and environmental factors as determinants of metabolic syndrome): Metabolic syndrome, obesity, overweight, prevalence of obesity, central obesity, feeding behaviour, feeding behaviour mechanism, adipocyte/adipose tissue and obesity, inflammatory state, mediators of obesity, pro-inflammatory cytokines, low birth weight, catch up growth, thrifty phenotype, genes, programming, childhood obesity or overweight and prevalence, BMI, stages of obesity, waist circumference, waist-hip ratio, BMI and Indian population, advantages and limitations of BMI, physical activity, insufficient physical activity, urbanization in India, urbanization and physical activity, mechanization and its effect on physical activity, poor living condition, overcrowding, endocrine disrupting chemicals, persistent organic pollutants, heavy metals, and particulate matters.

(iv) Chapter Four (Nutrition transition and under nutrition as determinants of metabolic syndrome): Nutrition transition, stages of nutrition transition, demographic transition, epidemiological transition, India in nutrition transition, nutrition transition in relation to fat consumption, nutrition transition in relation to grain consumption, nutrition transition in relation to sugar consumption, sugar sweetened beverages, nutrition transition in relation to globalization/urbanization, eating out, fast food market, westernized diet, change in per capita calorie intake, National Food Security Act, PDS, ICDS, mid day meal scheme, migration as cause of nutrition transition, under-nutrition and metabolic syndrome, thrifty genotype, thrifty phenotype, foetal programming, developmental origin of health and disease, gene-environment

interaction, poor nutrition during critical phases of development, catch up growth, and anaemia.

(v) Chapter Five (Various stressors as determinants of metabolic syndrome): Stress definition, acute stress, chronic stress, stages of stress response, adaptation, biological pathway of stress, stress metabolic syndrome relation, stress and obesity, anxiety, stress eating, stress and HPA axis, stress in childhood, migration as stressor, migration scenario in India, employment as stressor, income as stressor, family life as stressor, sleep as stressor, REM and non-REM sleep, sleep deprivation and obesity, sleep and energy expenditure, sleep culture, sleep in adolescents, work pattern and sleep, education and stress, living condition as stressor, smoking/tobacco use and metabolic syndrome, mechanism to relate smoking/tobacco with metabolic syndrome, alcohol consumption and metabolic syndrome.

2.5.4 Review Material Analysis: Various review materials are collected by using the above keywords. Depending on title, abstract, and full content of these materials to meet the objectives and thematic areas; they are either selected or rejected for inclusion. In each chapter materials are segregated in such a way that the thematic areas such as (i) existing theoretical concepts, (ii) relevance of such concepts in western and Indian scenario, (iii) studies supporting such concepts, (iv) studies not supporting such concepts, (v) available data to support or contest such concepts etc. are addressed. Biological, social or any other relevant concepts/models are included to build the base of each chapter. Regarding inclusion of supporting data, stress has been given to analyse mostly the India relevant data. In discussion and conclusion chapter the gaps which need further exploration and are not clear in the reviewed chapters are analysed in details. The existing policies which need to re-look into certain aspects of metabolic syndrome are also included in this chapter.

Chapter Three

Biological Concepts in relation to Obesity, Overweight, Weight Gain, BMI, Body Composition and Environmental Factors as Determinants of Metabolic Syndrome

As it has been mentioned that the final common pathway for metabolic syndrome is biological, hence it is important to know the various biological concepts which predetermine the whole process. These concepts can be in relation to obesity, weight gain, BMI, body composition, and environmental factors directly or there can be web of connections influencing each others.

3.1 Obesity/Overweight:

In this section we will try to bring in the relevant concepts of obesity or overweight available and try to fit in the concepts relevant in Indian scenario.

Obesity/overweight has been identified as important risk factor for metabolic syndrome (Hu *et al*. 2007). Each component of metabolic syndrome deteriorates with increase in obesity and is found to be independent of age and sex (Raj *et al*., 2010). Impaired glucose tolerance is a condition that affects 197 million people worldwide as a result of obesity and the related metabolic syndrome (Hossain *et al*., 2007). More than half of adult in USA do not perform the recommended physical activity and two out of three are classified as overweight (ibid). National Health and Nutrition Examination Survey (NHANES) in USA showed that the prevalence of obesity has increased from 22.9% during 1988-1994 to 30.5% in 1999-2000 (Webber, 2009). According to data from the same study, each kilogram gained in weight increases the risk of diabetes by 4.5% (ibid). In 2004, a national multi-ethnic cross sectional population based survey in Malaysia (N=17211) revealed the prevalence of metabolic syndrome at 27.5% and that of central obesity at 36.9% respectively (Rampal *et al*., 2012). The increasing overweight trend has been witnessed in developed as well as developing countries across age and gender. The overweight epidemic is due to reduced energy output and increased energy input (Hu *et al*., 2007). A significant global population is unable to maintain the energy balance and leading to increased fat mass (Butler *et al*., 2006). A species' ability to adjust to changes in energy consumption and the amount of energy turned into triacylglycerol (TAG) and stored in adipocytes is crucial to its ability to survive (ibid). Patients with type 2 diabetes tend to have excessive amounts of body fat (Webber, 2009). An important contributing element to the emergence of insulin resistance is this adipose tissue abnormality (Rajala *et al.* 2003).

3.1.1 Obesity due to feeding behaviour:

Obesity/overweight is linked with the feeding behaviour, which itself is a complex behaviour, sensed by energy balance. Several gut and adipocyte secreted factors (integrated neuronal and endocrine signals) influence the hypothalamus of brain to influence food and fluid intake (Butler *et al.* 2006). Adipocytes/adipose tissues have highly active endocrine function and they secrete several endocrine factors termed as adipokines (Sanchez-Infantes *et al*. 2014). These adipokines or adipocytokines mediate multiple processes like insulin sensitivity and energy metabolism (Smith *et al*. 2005). We are not going into the details of these factors but some basics are important to understand the biology behind as they impound both stimulatory and inhibitory feeding effects. However role of such factors (hormone) like leptin and insulin are critical in the development of obesity/overweight. Positive energy balance induces adipocytes to secrete Leptin and later induces negative feedback through hypothalamus (Rajala *et al.* 2003). Normally leptin tries to suppress food intake, stimulates thermogenesis, enhances fatty acid oxidation and increases energy expenditure to maintain the energy homeostasis (Butler *et al.* 2006; Sanchez-Infantes *et al*., 2014). Low leptin levels indicate insufficient energy storage which enhances energy uptake and decreases energy expenditure; this in turn enhances the conversion of energy to fat and leads to positive energy balance and replenish the low leptin levels (Smith *et al*. 2005). For skeletal muscle, AMP-activated protein kinase serves as the connection between leptin and energy metabolism (AMPK).

Obesity and insulin resistance are both caused by abnormal leptin activity and release, which disturbs the pattern of energy consumption and utilization (Rajala *et al.* 2003). Insulin resistance is due to abnormal secretion of leptin by increased adipose mass as a result of abdominal obesity. On the other hand TAG and fatty acid accumulation in tissues can cause insulin resistance due to failure of adipocytes to store surplus calories (Butler *et al.* 2006). Diet induced reduction in central leptin and insulin signalling may stimulate the development of obesity (ibid).

3.1.2 Role adipocyte/adipose tissue in obesity:

The figure below explains the adipocyte/adipose tissue centred metabolic syndrome. Adipose tissue expansion is limited to a maximum capacity. Excess

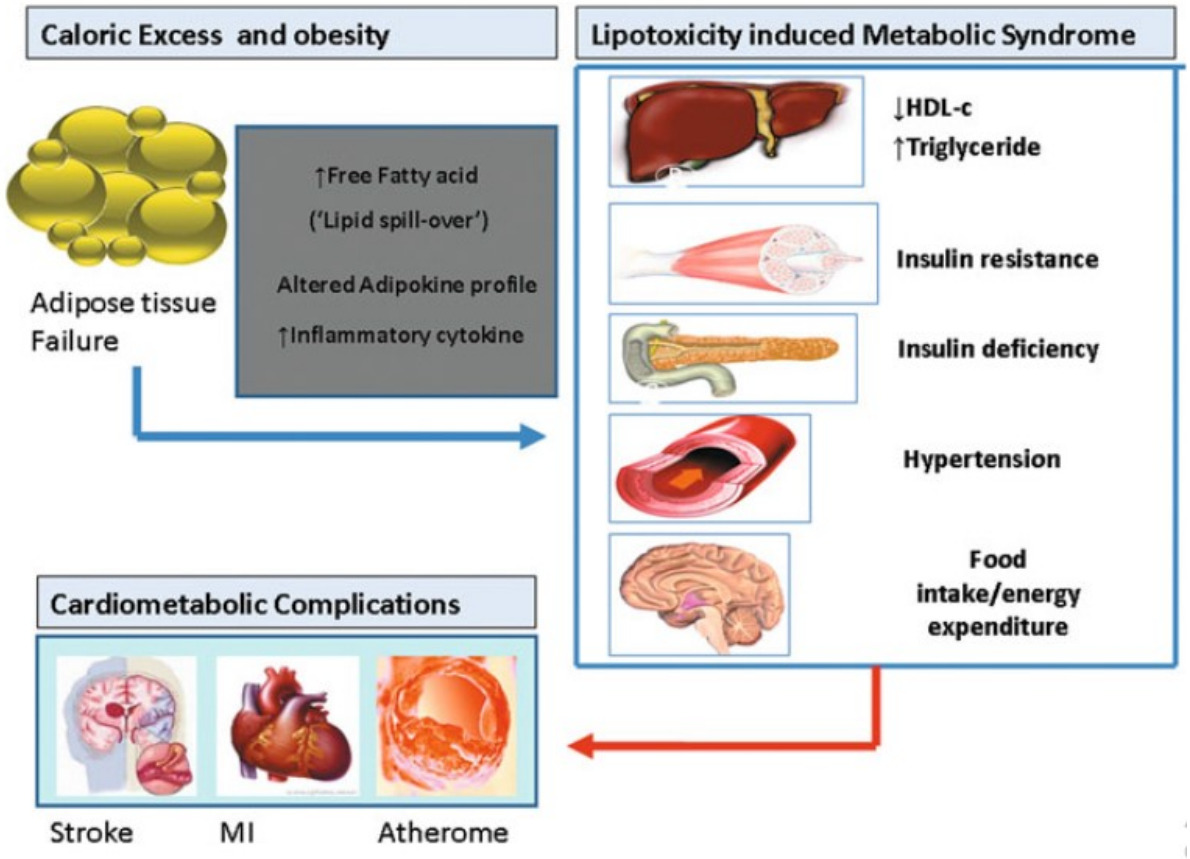


Fig 3.1: Metabolic syndrome from adipocyte perspective (Vidal-Puig, 2014)

accumulation of lipids in adipose tissue leads to lipid spill and hence lipid starts accumulating in non-adipocyte cells causing lipotoxic insult in the form of insulin resistance, tissue damage and inflammation (Dulloo *et al*., 2010). Any inflammatory event in our body is controlled by cytokine mediators, which are released by various cell types but especially by monocytes/macrophages (Wieser *et al*. 2014). In cases of obesity, macrophages can make up 40% of the total number of adipose tissue cells (Weisberg *et al*., 2003; Neels *et al*., 2006). It is also interesting to know that the magnitude of adiposity is directly proportionate to the accumulated macrophages in the adipose tissue (Weisberg *et al*., 2003). Adipose tissue (AT) expansion due to obesity causes local tissue microhypoxia and retention of macrophages around dead

adipocytes (ibid). As like in other inflammatory conditions, the macrophages clear the necrotic debris of these dead adipocyte cells by increasing its infiltration.

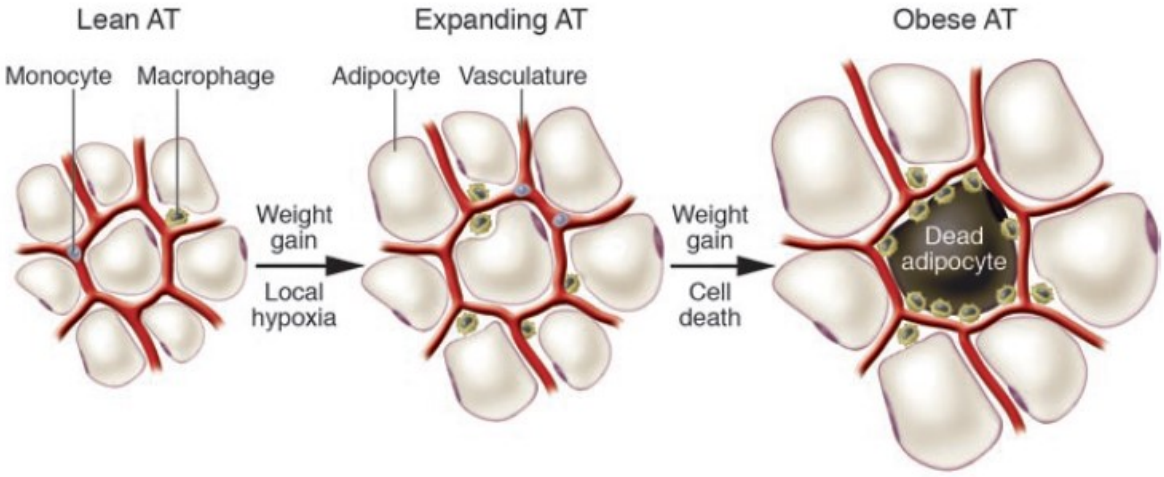


Fig 3.2: Stages of macrophage infiltration of adipose tissue leading to local hypoxia and cell death (Neels *et al*., 2006)

Pro-inflammatory cytokines including tumour necrosis factor-alpha (TNF-alpha), interleukin-1 (IL-1), and interleukin-6 (IL-6) are present in large amounts in adipose tissue. TNF-α is the first cytokine which provided a link between inflammation, obesity, and insulin resistance (Wieser *et al*. 2014). Therefore, obesity and chronic inflammatory state are associated and often referred to as 'metabolic inflammation' (Dulloo *et al*., 2010). The abnormal functioning of adipocytes/adipose tissue due to obesity and inflammatory state is the fundamental for development of metabolic syndrome or associated cardiometabolic complications. The detailed discussion on the adipocentric mechanism follows as explained by Vidal-Puig in the book "A System Biology Approach to Study Metabolic Syndrome". The adipose tissue will expand normally during the positive energy state until a stage of maximum expandability is reached. Eventually adipose tissues will fail to hold the surplus calories as fat which results in: (i) accumulation of fat in non-conducive sites like muscles, liver, beta cells of Pancreas etc. causing tissue dysfunction mediated by lipotoxicity phenomenon. (ii) adipocytes on becoming dysfunctional produce factors which promote insulin resistance. (iii) lipid induced inflammation of adipose tissue prevents its expansion and further aggravates insulin resistance. Lipolysis and fatty acid flow are increased due to insulin resistance and dysfunctional adipose tissue. This along with insulin resistance of liver increases the production of hepatic glucose

and TAG rich lipoproteins; and also increases the hepatic lipid accumulation. More availability of lipid to skeletal muscles boosts insulin resistance and lowers the insulin mediated glucose disposal known as impaired glucose tolerance. Finally systemic insulin resistance pushes to a pathological state where deterioration of metabolism progresses. This in turn worsens the insulin resistance further and the vicious cycle of metabolic dysfunction sets in. Adipocyte hypertrophy (Sanchez-Infantes *et al*., 2014) and adipocyte hyperplasia (De Ferranti *et al*, 2008) are evident in overweight and obesity respectively in an abnormal way. Adipocyte hyperplasia or adipogenesis is otherwise a normal developmental phenomenon that initiates in utero and continues so in lifetime (Sanchez-Infantes *et al*., 2014). Adipocyte hypertrophy causes local inflammation and mechanical stress which may disrupt adipose tissue function (Dulloo *et al*., 2010). In a cross sectional descriptive study in Brazil of 305 adults with metabolic syndrome during the period 2004 to 2008 showed higher adiposity (higher BMI, higher % Body fat, increased Muscle Mass Index) (de Oliveira *et al*., 2012). An epidemiological study on metabolic syndrome for a total 3785 subjects from Dehui in north eastern China showed central obesity in 36.1% (Wang *et al*., 2010). A similar cross sectional study in Guangdong southern China with 1206 participants had an overall 26.7% prevalence of metabolic syndrome. Amongst the obese 55.6% had metabolic syndrome, supporting the correlation (Li *et al*., 2010). According to a clinical investigation by Shelgikar *et al*., more than one-third of urban diabetics were diagnosed before the age of 35 and did not meet the prescribed BMI criterion for obesity (mean BMI=23.9). However they had central obesity (high waist-hip ratio) and skin fold ratio in subscapular-triceps region was also high (ibid).

3.1.3 Role of mediators in obesity:

Adipokines, inflammatory cytokines, and endothelial dysfunction are correlated with each other and with obesity (Meigs, 2008). Asian Indians have considerable endothelial dysfunction which can lead to alteration of activities in proinflammatory cytokines (interleukin-6 and TNF-α), nitrous oxide, endothelin-1, and procoagulant (elevation of fibrinogen, plasminogen activator inhibitor-1 etc.) (Eckel *et al*., 2005). The proinflammatory marker C - reactive protein concentrations vary amongst different ethnic groups and even within the same ethnic groups. For example the concentration of C-reactive protein is higher in healthy Asian Indians compared to

European white population and hence greater central obesity and insulin resistance (Eckel *et al*., 2005). BMI and C-reactive protein has direct positive correlation in case of affected children and adults (Das, 2005). Hyperglycemia has been a stimulus for increased level of C-reactive protein, interleukin-6 and tumour necrosis factor-α (ibid). Diets rich in saturated and trans-fats (high calorie) or protein stimulate the production of reactive oxygen by increasing the production of proinflammatory cytokines (Das, 2010). Free radical and proinflammatory cytokines leads to a state of oxidative stress which jeopardizes the antioxidant defense of various cells and tissues (Das, 2005). All these derailments could trigger and fasten insulin resistance and other related changes (Misra, 2003).

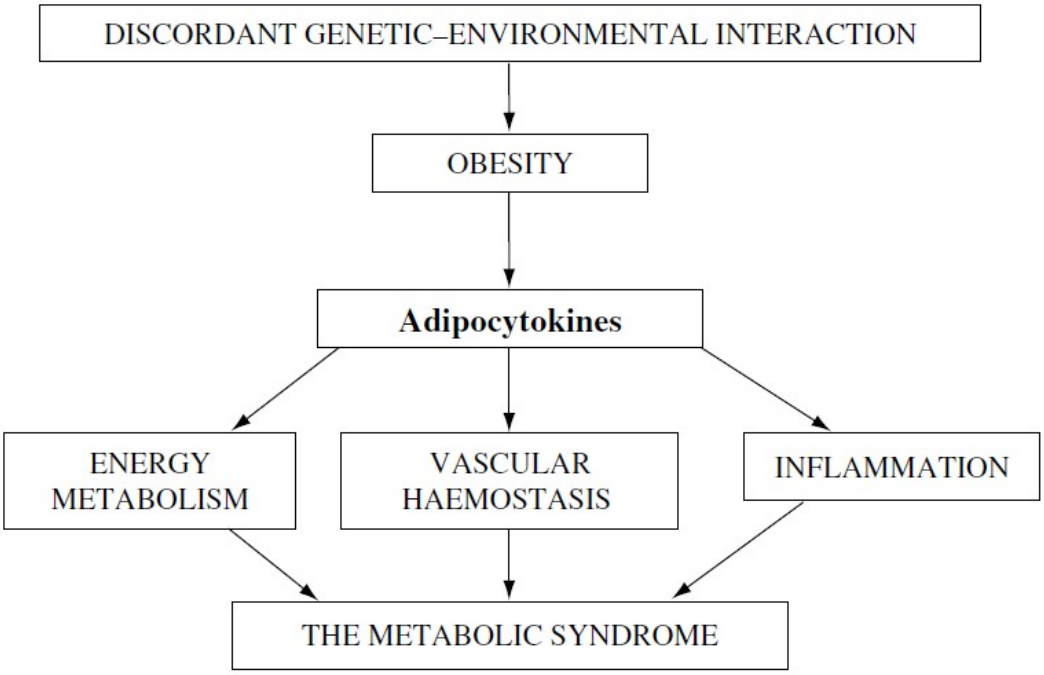


Fig 3.3: Adipocytokines in the pathogenesis of metabolic syndrome (Source: Adapted from Smith *et al*., 2005)

In the pathogenesis of metabolic syndrome it has been observed that major tissues like fat, liver, muscle, pancreas, and brain are interdependent and closely interlinked with the dysfunction of adipose tissue (Vidal-Puig, 2014). Free fatty acids are considered as the major messengers which communicates energy status with the above tissues (Smith *et al*., 2005). Obesity-related hepatic steatosis, which occurs when the liver accumulates fat without any evidence of alcohol consumption, is associated with insulin resistance (Misra, 2003).

With advancement of science and understanding of biology all body fats are now not considered as same. Adipocytes are now classified as white, brown, and beige adipocytes; and all are different in both morphological and functional characters (Saklayen, 2018).

3.1.4 Studies on obesity phenomenon:

Heavy mothers usually give birth to bigger babies who in adult stage may become obese also. A cohort of 14881 adolescents from around the United States participated in the Growing Up Today Study, which found that if full-term newborns had attained 1 kg more in their birth weight, the prevalence of overweight had increased by about 30% by the time they were 9 to 14 years old (Gillman *et al*., 2003). On the other hand babies who have a low birth weight due to adverse perinatal events (maternal nutritional deprivation) has the tendency to grow rapidly in childhood ("catch up growth") and become obese in adulthood (Misra *et al*., 2011; Xita *et al*., 2010; Mitra *et al*., 2009; Hossain *et al*., 2007; McMillen *et al*., 2005). This phenomenon is already observed in developing countries like India where better nutrition situation, more significantly in case of boys, leads to sudden surge of physical growth and subsequent obesity (Misra *et al*., 2011). Kuopio Ischaemic Heart Disease Risk Factor Study (KIHD), which tracked a cohort of men from the start of the late 1980s, was conducted on a middle-aged population in Finland (n=1005) showed two times more chances of metabolic syndrome in non-diabetic individuals having thinness at birth (Laaksonen *et al*., 2004). Though available studies may have ambiguities in between the relationship of birth weight and later BMI/insulin resistance (Mitchell *et al*., 2017), but people with light birth weight have shown higher insulin resistance (Newsome *et al*., 2003; Gluckman *et al*., 2004). A systematic literature review of prospective studies across world upto February 2013 had negative association in between birth length and adult abdominal adiposity (de Franca *et al*., 2014). The same review stated positive relation between birth weight and waist circumference on predominance but had inconsistent results between birth size and adult adiposity. The results of included studies varied from positive, significant, or no association between birth weight and adult anthropometric measures such as waist and hip circumference, waist-hip ratio etc. (ibid). The five cohort studies from Brazil, Guatemala, India, the Philippines, and South Africa had the inverse association of birth weight with risk of

adult glucose intolerance (Norris *et al*., 2011; Lakshmy *et al*., 2011). However the study also found that low birth weight and subsequent weight gain after 48 months at enhanced rate were risk factors for causing adult glucose intolerance (Norris *et al*., 2011).

An international cross sectional study on birth weight and subsequent BMI in children (6-7 years) showed a positive linear association i.e. for each Kg increase in birth weight the BMI increased by 0.47 (Mitchell *et al*., 2017). The combination of lower birth weight and higher attained BMI increases the later disease risk by many folds (Oken *et al*., 2003). Later outcomes are dependent on the growth during critical period of life like early childhood or even earlier than that viz. the intrauterine life. Intrauterine regulation of adipogenesis may be an important mechanism of the fetal origins of metabolic consequences (Yajnik, 2004). We have a diverse situation such as low birth weight with high central obesity and high birth weight with high BMI (Oken *et al*., 2003).

In obese individuals average energy output is lower than the input. Though less physical exercise by obese is held responsible for lower energy expenditure, but this cannot be the sole contributing factor as physical activities contribute only 15% of total energy expenditure by the body (Keen *et al*., 1979). Genetic factors predisposing obesity are important to explain this biological concept. A variation of 30-80% in BMI appears to be due to genetic factors as determined by studies (Kiranmala *et al*., 2013). Genetically determined insulin resistance has been proposed to result in poor insulin facilitated foetal growth, subsequent low birth weight, and insulin resistance in childhood and in adult life (McMillen *et al*., 2005). Besides Asian Indians, studies in other ethnic groups have shown that birth weight, body composition and body fat distribution are influenced by genetic factors (Misra, 2003). Stronger the family history, higher is the chance of getting metabolic disorder like diabetes. In a hospital based study of 140 subjects (20-59 years) who were first degree relatives of known diabetes cases showed higher diabetes prevalence than that in the non-diabetic control group (Mahanta *et al*., 2009). Depending on the programming probability, certain adult diseases may have foetal origins. The initiation of programming starts at a critical phase of development like pregnancy or early infancy when the provocation starts and has its lasting effect afterwards (Oken *et al*., 2003). Constant intrauterine

exposures may alter gene expression and cause a "thrifty phenotype" (ibid). This intrauterine programming has been explained by several probable mechanisms which also relate the later development of obesity and metabolic syndrome. According to the first mechanism, the foetal pancreas undergoes permanent structural alterations as a result of poor maternal nutrition and a lack of protein, impairing its ability to function normally (Oken *et al*., 2003). Another mechanism may be due to long term change in HPA axis mediated association of birth weight and metabolic syndrome (ibid). Studies on mice and bats reveal that single or polygenic natural gene mutation can produce obesity (Raj *et al*., 2010). Approximately 176 single gene mutations located at 11 different genes are linked to obesity (Kiranmala *et al*., 2013). Mutant genes are responsible for Leptin deficiency which in turn documented to be responsible for obesity (Raj *et al*., 2010). The identification of genes involved in obesity is a complex process and hence three fundamental study strategies followed. The first is a candidate gene association research, which examines the relationship between a certain genetic type and the obesity phenotype in order to comprehend the genetic mechanisms regulating food intake, insulin action and glucose metabolism, as well as energy expenditure and adipose tissue (Bastarrachea *et al*., 2006). The second approach, genome scan, using linkage analysis across generations identifies chromosomal regions with the help of polymorphic markers (ibid). The third approach utilizes messenger RNA (mRNA) based on the variations in gene expression as per tissue profiles (ibid). Besides, there are available evidences from animal models (Monogenic obesity, Oligogenic obesity) for genetic linkages of obesity (ibid). All these studies support the positive correlation with obesity and genetic factors.

Childhood obesity or overweight:

Childhood obesity/overweight needs nationwide study for prevalence trend. In India there are no well documented data on childhood obesity due to lack of large scale studies covering the entire country with its varied geographical, social and cultural norms. A systematic review by Ranjani *et al*. in India showed prevalence of childhood overweight and obesity at 19.3 percent (pooled data after 2010) as compared to earlier prevalence of 16.3 percent reported in year 2001-2005 (Ranjani *et al*., 2016). In a randomly selected survey of 2158 school children (7-14 years) from

different socio-economic classes of Indore district of Madhya Pradesh, found an overall prevalence of obesity at 14.97% with highest prevalence in the age group of 9-11 years (Siddiqui and Bose, 2012). Some of the key findings on children from Comprehensive National Nutrition Survey (2016-18) need to be looked seriously for further studies. The data on components of metabolic syndrome from the study gives us some ideas about the situation:

(a) There is growing risk of NCDs in the age groups of 5-9 years (children) and 10-19 years (adolescents) in India.
(b) One in ten is pre-diabetic and 1% is diabetic amongst school going children and adolescents.
(c) Five percent adolescents are hypertensive.
(d) Prevalence of dyslipidemia amongst school age children and adolescents varies from 3% to 34% depending upon serum total cholesterol, LDL, HDL, and triglyceride levels. (Comprehensive National Nutrition Survey, 2016-18)

Even though physical activity has been incorporated as a crucial part of the academic curriculum, an interesting discovery is that 48% of government schools in India lack playgrounds and sports facilities (Kiranmala *et al*., 2013). It is worth mentioning here that Indian Academy of Pediatrics (IAP) has already formulated a revised guideline for 5-18 years age group for defining overweight and obesity in children. The expert committee of IAP has recommended using 23 and 27 as cut offs on adult BMI chart for children to determine overweight and obesity respectively (Khadilkar *et al*., 2015).

3.2 BMI/Body Composition:

3.2.1 Obesity measurement:

Weight is considered as a definitive measure of obesity because heavy weight intended to indicate more body fat (Chumlea, 2006). However this is not always true as body weight is also depended with the variations in body water content and lean tissue (ibid). Moreover body weight is also dependent on the stature/height of the person. To overcome these variations weight is divided by stature/height square to formulate the body mass index (BMI). BMI was originally proposed by Quetelet in

1835 (Bray, 2007) and is a convincing tool for obesity screening (Bray *et al*., 2006). BMI has been used worldwide in the assessment and prevalence of obesity. There are many advantage of BMI being used as an obesity index. It helps in establishing relationship between body fatness, morbidity, mortality, and also in predicting the future risk (Chumlea, 2006). Calculation of BMI does not require any sophisticated equipment or set up and hence extensive national reference data are available worldwide (ibid). There are other methods like abdominal circumference, skin folds, bioelectric impedance analysis, body density, total body water, dual energy x-ray absorptiometry etc. are also available to assess obesity, but BMI is found to be the simplest and most informative of all at present (ibid). Operationally following levels of BMI are considered to segregate the stages of obesity:

- Normal weight = BMI 18.5–24.9 kg/m2
- Overweight = BMI 25–29.9 kg/m2
- Obesity = BMI >30 kg/m2
    - Class 1 = BMI 30–34.9 kg/m2
    - Class 2 = BMI 35–39.9 kg/m2
    - Class 3 = BMI >40 kg/m2 (Bray, 2007)

The second important measure to evaluate overweight and even most appropriate for determining central adiposity is waist circumference (Bray, 2007). At the level of the umbilicus or the suprailiac crest, measurements are frequently collected using a metal or non-elastic plastic tape (ibid). The recommended levels of waist circumference as per different expert groups are as follows:

Recommendation	Value for Males (in cm)	Value for Female (in cm)
National Heart, Lung and Blood Institute	<102	<88
International Diabetes Federation	<94	<80
Asian Obesity Task Force	<90	<80

Table 3.1: Recommended waist circumference (Bray, 2007)

3.2.2 Studies on obesity measurement:

BMI cutoff values for overweight and obesity show that the risk of chronic diseases increases as body fat percentage increases (Whitlock, 2009). A 45 year follow up study of birth cohort in England, Scotland, and Wales suggests that BMI gain in childhood influences diabetes risk, even in the absence of adult obesity (Power *et al*., 2011). There are several determining factors that are associated with increase or decrease score of BMI. Better BMI scores are connected with younger and middle-aged people, women, those with higher incomes and education, and people who live in cities (Chockalingam *et al*., 2011). BMI is frequently observed to be lower in elderly individuals, those with poor incomes, those with less formal education, those living in rural areas, and those who smoke (ibid). However, people of rural areas in past few years have witnessed the rise of BMI as well due to increase incidence of overweight and obesity as a result of rural development. Analysis of data from four continents in 57 prospective studies involving around 900,000 participants confirm that obesity (as determined by BMI) increases the rate of total mortality in both sexes in the age range from 35 to 89 years (Whitlock, 2009).

Our neighboring country China was once considered as having the leanest populations in the world, but overweight and obesity rate has escalated very rapidly now (Shen *et al*., 2011). Chinese people are more likely to experience central obesity, which increases their risk of metabolic side effects like cardiovascular disease. For this, the Working Group on Obesity in China proposed a BMI cutoff of 24 kg/m^2 for overweight and 28 kg/m^2 for obesity, respectively (Chen *et al*., 2006). To reduce overweight and obesity among Chinese people, the Chinese Ministry of Health has added these modifications to the recommendations, which differ from the original criteria (Shen *et al*., 2011). World Health Organization have recommended BMI as a method to define overweight and obesity but also proposed the customization of BMI ranges for specific subpopulations so that they are better suited (Palaniappan *et al*., 2011). The World Health Organization (WHO) and IOTF have recommended lower BMI cut-offs for Asian Indian adults of 23 kg/m^2 for overweight and 25 kg/m^2 for obesity, respectively (Ranjani *et al*., 2016). For Asians, the World Health Organization suggested a normal BMI of 18.5 to 23 (WHO, 2000; 2002). There are studies which question the credibility of BMI as a marker of obesity in case of Asian

populations. In addition to BMI, other accurate measures of adiposity, such as waist circumference, CT scans, and DEXA scans, may be used to determine obesity (Palaniappan *et al*., 2011). In case of waist circumference four body sites are preferred for measurement, but two sites are most commonly used as mentioned already (Bary, 2007; Palaniappan *et al*., 2011). There is lack of common consensus on optimal site for measurement, especially since it has variations by sex (Palaniappan *et al*., 2011). Rests of the methods are sophisticated ones and hence have their limitations for large community based studies. At the end, even after questions on the credibility, BMI has stood out as a reliable measure of adiposity or total body fat, regardless of height of a subject (Palaniappan *et al*., 2011; Chumlea, 2006).

In China, there is a fast spreading epidemic of metabolic syndrome, according to NCEP classification-based assessment. From 13.3 percent in 1992 to 15.1 percent in 2000, China has a higher prevalence of the metabolic syndrome (Shen *et al*., 2011). It is important to note that 64 million Chinese people had metabolic syndrome in 2000, but when the modified ATP III criteria for Asian populations were utilised, the number increased to 71 million (ibid). In a Hong Kong-based population study by Thomas, the increasing prevalence of metabolic syndrome among elderly Chinese was demonstrated (Thomas *et al*., 2005).

3.2.3 BMI as a tool of obesity assessment for Indian population:

Following the initial criterion of World Health Organization (WHO) for obesity [BMI >30 kg/m2], many studies in India have shown <10% prevalence of obesity in India, but in actual much higher values have been reported (Misra, 2003). While most people get diabetes if their BMI is in the range of 30-31, but in case of Indians it has been observed that a BMI of above 25 is enough to get diabetes (Mitra *et al*., 2009). Evidences suggest that the abnormality in body composition of Asian Indians is an important cause in the pathogenesis of metabolic abnormality. Misra (2003) has explained this variation of Asian Indians and the higher risk of metabolic derangements. First, Asian Indians by nature have more body fat than muscle mass as compared to Caucasians, African–Americans, and even other Asian ethnic groups. The original WHO cut-off criteria of BMI consider some Indians as ‘non-obese’ whereas they are actually obese when obesity is defined by using body fat as the

criteria. Hence the prevalence of obesity and overweight might be an underestimate in India (Khadilkar, *et al*., 2009). Second, the high prevalence of abdominal adiposity or central obesity even in people who are otherwise considered non-obese is perhaps equally important (Misra, 2003). Some investigators have given stress on the higher intra-abdominal fat mass, while some others have stressed on excess of truncal subcutaneous fat in Asian Indians as compared to Caucasians to be the risk factor behind. In Asian Indians, there is an excess of adipose tissue in both the abdomen subcutaneous tissue and the intra-abdominal region, while it is unclear which is more crucial for the etiology of insulin resistance. Adipose tissue is distributed more coaxially around the trunk than the extremities, and this is linked to the risk of developing chronic diseases like metabolic syndrome (Mitra *et al*., 2009; Baumgartner *et al*., 1995). The internationally accepted definition of BMI to screen normal and obese and also to identify abdominal obesity by use of waist circumference are mostly based on the data derived from Caucasian populations, and hence may not be suitable for Asian Indians and other Asian ethnic groups (Misra, 2003). A comparative analysis of African Americans and Asian Indians showed that later had higher percentage of body fat at each BMI (Yajnik, 2001). A study

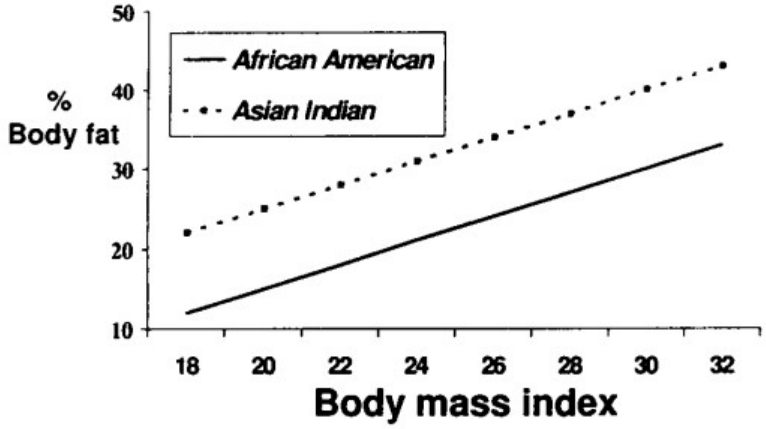


Fig 3.4: Regression lines between BMI and % body fat in Asian Indians and African Americans (Source: Adapted from Yajnik, 2001)

performed in the United States revealed that Indians have higher body fat percentages and posterior and central subcutaneous abdominal fat than Caucasians, which was attributed to higher levels of insulin resistance (Chandalia *et al*., 1999). Asians are at the same risk of developing cardiovascular disease even at smaller waist circumferences, according to studies used to determine prevalence rates using modified Asian criteria for waist circumference (90 cm for men and 80 cm for

women) (Shen *et al*., 2011).The normal body mass index considered as international standards is ≤25 kg/m^2, but the same should be considered at ≤23 kg/m^2 for Asian Indians as suggested by WHO (Mitra *et al*., 2009). However, these alterations do not apply to children and adolescents from India (Ranjani, *et al*. 2016). The value comparison for Indian children with that of US (NCHS 2000) and UK (1990) showed variations in corresponding BMI. The 75th percentile for Indian children was very close to the 85th percentile of US and UK data on BMI charts (Khadilkar *et al*., 2009).

The NFHS data clearly showed the increasing trend of BMI in Indian population irrespective of sex and rural-urban set up. However percentage of population who

	NFHS 5 (2019-21)			NFHS 4 (2015-16)			NFHS 3 (2005-06)		
	Urban	Rural	Total	Urban	Rural	Total	Urban	Rural	Total
% Women who are overweight or obese (BMI ≥ 25Kg/m^2)	33.2	19.7	24.0	31.3	15.0	20.6	28.9	8.6	14.8
% Men who are overweight or obese (BMI ≥ 25Kg/m^2)	29.8	19.3	22.9	26.6	14.3	18.9	22.2	7.3	12.1

Table 3.2: Percentage of men and women who are overweight or obese in India
(Source: NFHS-3; NFHS-4; NFHS-5)

were overweight or obese could be expected to increase if the revised cut off of BMI 23Kg/m^2 had been used. The exact magnitude of the problem was not reflected due to higher cut off value of BMI (BMI ≥ 25Kg/m^2) used in the survey. It is also interesting to observe that the BMI almost doubled in NFHS 4 compared to NFSH 3 and continued to rise in NFHS 5 in rural areas (both sexes) indicating a late but significant

change in lifestyle. Many of the poorest counties in the world have unexpectedly shown high levels of rural overweight (Popkin, 2010).

3.2.4 BMI and its limitations:

As mentioned already that BMI has a wider application worldwide but has its own limitations too. The measurement of body composition by BMI has significant limitations, and it also lacks sensitivity for identifying illness risks in the population with normal or modestly raised body weight (Dulloo *et al*., 2010). One important limitation of BMI is the inability to distinguish between FM (fat mass) and FFM (fat free mass or non-fat mass). For instance, bodybuilders and athletes who compete in other power sports (such as boxing, wrestling etc.) have low body fat percentages, but because of the existence of a higher amount of non-fat mass, their BMI is frequently listed as being in the overweight/obese range (Dulloo *et al*., 2010). The relationship between BMI and FM% varies according to ethnic groups and populations because body composition is affected by age, sex, race, genes and several environmental and behavioral factors (Baumgartner *et al*., 1995). Using only BMI criterion to access the nutritional status fail to distinguish between these divergent relationships (Dulloo *et al*., 2010). Asian Indians are found to deviate the most from Caucasians, with up to 5% more body fat at any BMI level (Bray, 2007; Dulloo *et al*., 2010). This leads to increased risks of metabolic derangement at lower BMI. Even use of FFM (related to height) and FM% (to assess the body fat store) can be misleading due to limited studies on exact measure of body fatness (Dulloo *et al*., 2010; Baumgartner *et al*., 1995). To overcome the grossness of BMI or gaps associated with expressing FM/ FFM only in absolute terms, it was proposed to do further partitioning of BMI by using FFM index (FFMI) and FM index (FMI) (ibid). BMI has been proposed to be divided into two subcomponents based on body composition:

$$\text{BMI (Kg/m}^2\text{)} = \text{FFMI (Kg/m}^2\text{)} + \text{FMI (Kg/m}^2\text{)}$$

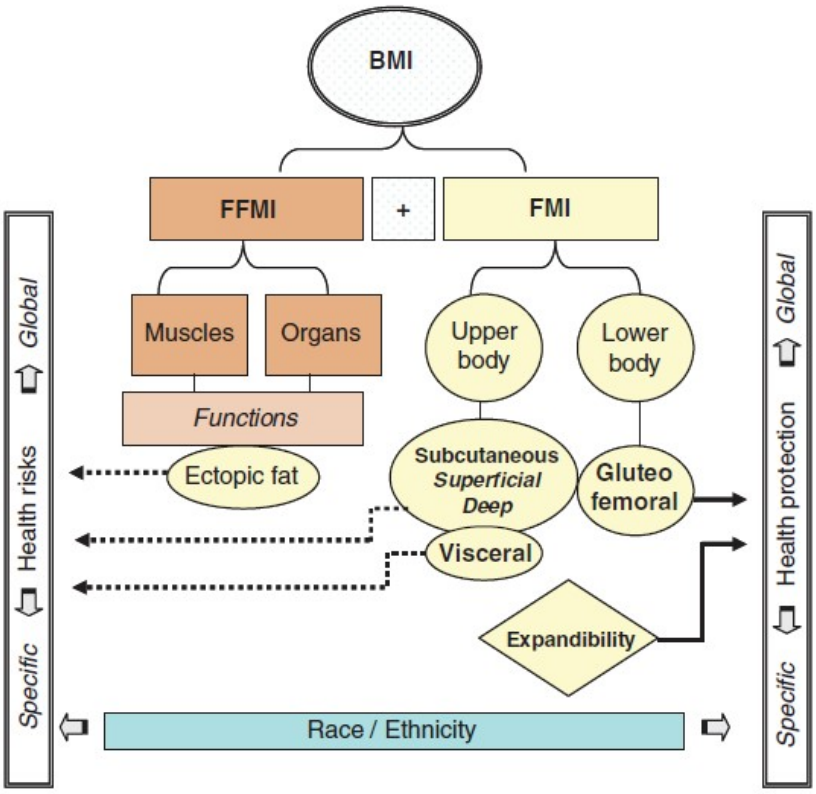


Fig 3.5: Partitioning of BMI into FMI and FFMI, followed by further partitioning into their sub-compartments (Adapted from Dulloo *et al*., 2010)

FFMI and FMI are helpful for comparing body composition in people of different heights, whereas BMI is a good and straightforward measure for tracking excess and deficit of body weights in people of different heights (Dulloo *et al*., 2010). FMI can be used to identify people with high BMI but no extra FM (ibid). Conversely, persons with 'normal' BMI but are at potential risk due to elevated FM can be identified by FMI too (ibid). By further dividing BMI into FMI and FFMI, it is beneficial going beyond BMI to fine-tune the assessment criteria for health risk and health protection (ibid).

3.3 Weight Gain:

3.3.1 Physical activity and weight gain:

Physical activity can be defined as "any body movement produced by muscle action that increases energy expenditure" (Swaminathan *et al*., 2013). Centre for Disease Covtrol and Prevention (CDC) America defined subjects who do not engage

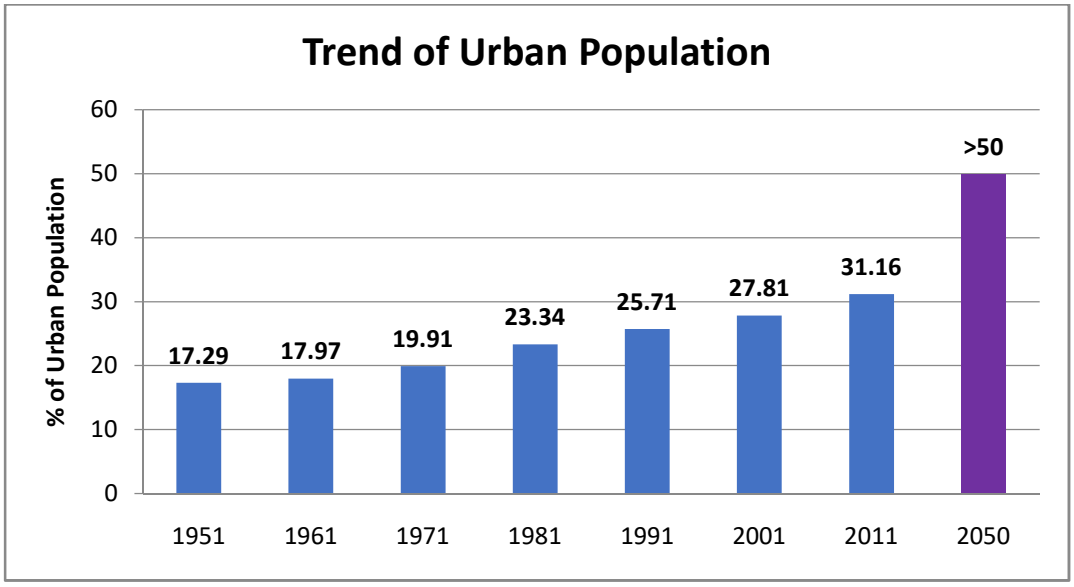
in at least 150 minutes of physical activity each week as physically inactive or sedentary (Kaur, 2014). Insufficient physical activity has also been defined as not doing moderate physical activity of at least one hour per day or moderate-to-vigorous activities of 20 minutes or more for at least three sessions per week (Swaminathan *et al*., 2013). Insufficient or no physical activity, sedentary behaviour due to various reasons can attribute to weight gain. From operational point 'sitting time' can be referred as sedentary behaviour rather than simply stating low level of physical activity (Edwardson *et al*., 2012). However, activities like lying down, sitting, watching television or using any screen based entertainment gadgets like computer, video game, play station, mobile etc. are referred to as sedentary behaviour (ibid). This behavioral problem initiates in the childhood with predominance in urban areas where children are not frequently exposed to diverse kind of physical exercise (Mitra *et al*., 2009). Due to limited avenues of physical activities in urban set up more hours are spent on computer screen or on cell phone or by watching television. The problem is more impounded by the later change in life style pattern. Approximately 75% of urban adolescents and young adults in India had been reported to be sedentary (Misra *et al*., 2004). These behavioral changes cannot be negated in rural set up as same changes may be happening lately compared to urban regions. Studies have revealed that one individual can spend more than half of their waking hours in sedentary activities (Edwardson *et al*., 2012). The odds of having metabolic syndrome increases by 73% when more time has been spent in sedentary life style (ibid). Physical inactivity and its relation with non-communicable diseases are poorly studied in the Indian scenario (Swaminathan *et al*., 2013). An US based randomized control trial showed that children watching TV for 4 plus hours per day or using a computer for one or more hours per day were 21.5% and 4.5% more likely to be overweight respectively (Epstein *et al*., 2008). In Hyderabad, 12 to 17-year old adolescents participated in a similar study that found that watching TV for more than three hours a day was associated with a higher prevalence of overweight and obesity than playing outside for more than six hours a week or doing household chores for more than three hours a day (Laxmaiah *et al*., 2007). A small school based randomized controlled trial in San Jose, Calif (USA) suggested that reduced use of television, videotape, and video game can be promising in preventing childhood obesity (Robinson, 1999). The main finding of this study is that watching television, eating junk food, and doing little physical activity are all linked to a higher prevalence of being overweight.

Sedentary behavior or reduced physical activity in today's world is not by choice but can be stated as a virtue of advancement in the field of science leading to mechanization in every step of life, growing urbanization etc. The rate at which these changes occur is directly proportionate to the weight gain vis-a-vis risk of metabolic syndrome.

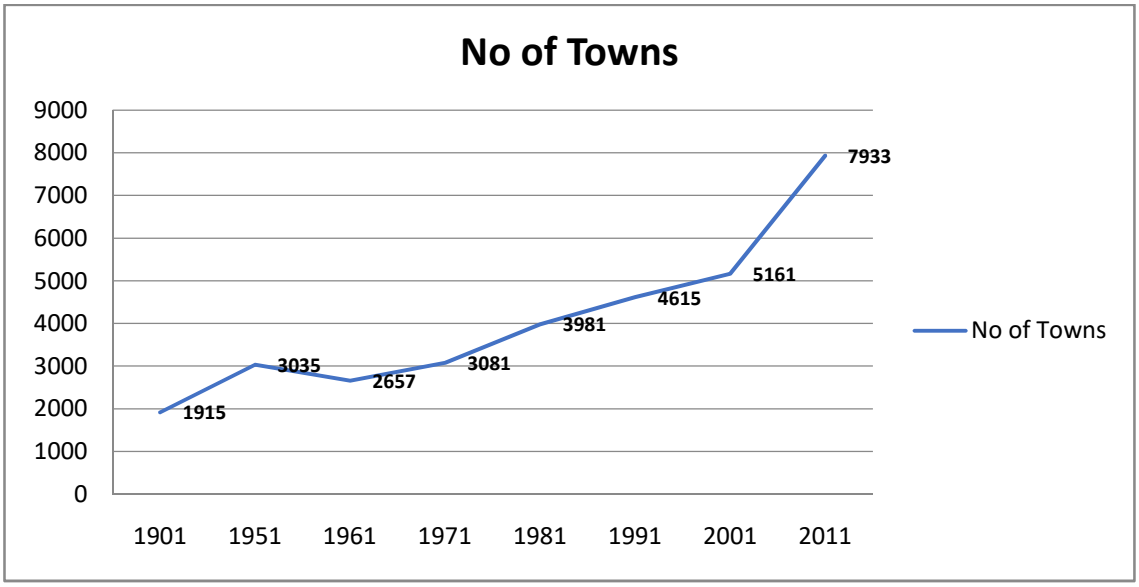
Studies across the world bring in the correlation between the pace of weight gain and earlier chances of metabolic syndrome. A 45 year follow up study of birth cohort in England, Scotland, and Wales suggest that excessive BMI gain at any life stage was associated with impaired glucose tolerance throughout the life span (Power *et al*., 2011). The same study suggested an association between overweight duration and impaired glucose tolerance i.e. longer the overweight duration greater would be the chances of abdominal obesity (ibid). New Delhi birth cohort shows that BMI/weight gain from 2 to 11 years of age has the higher risk of metabolic syndrome later (Fall *et al*., 2008). Greater risk of developing metabolic syndrome or its complications are associated with earlier onset and longer duration of obesity (Llyod *et al*., 2012).

3.3.3 Urbanization and physical activity:

There had been proportionate increase of Indian urban population from 20% to 28% during the period 1971 to 2001 and it is also projected to reach 36% by 2025 (Kiranmala *et al*., 2013). As per census 2011 report 31.2% of total population lives in towns. With an estimated annual average growth of 3% urban population (Misra *et al*., 2011) more than 50% of the country's population will be urban by year 2050 (MoHousing and Urban Affairs, 2018-19; Kiranmala *et al*., 2013). This implies that either all future population growth will take place in cities and/or that current rural areas will be completely urbanized (Kiranmala *et al*., 2013). The following figure clearly depicts that the percentage of urban population has increased almost two folds within a time span of 60 years (1951 to 2011).



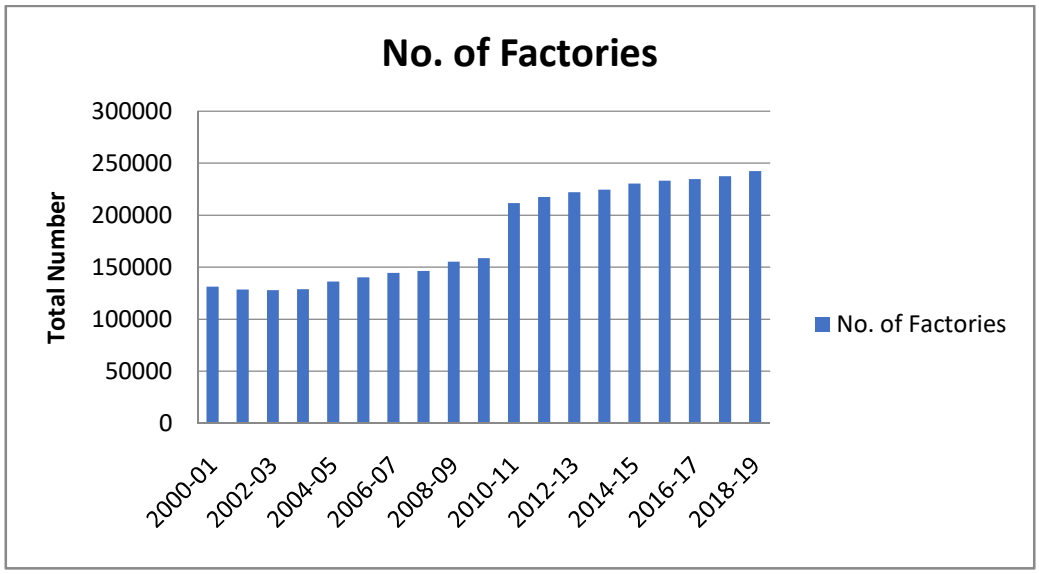
Graph 3.1: Trend of increase in % of urban population (Source: Census of India; MoHousing and Urban Affair)



Graph 3.2: Number of towns as per various census reports (Source: Census of India)

A considerable jump in the number of towns in India was observed from 5161 in year 2001 to 7933 in year 2011(Census of India, 2011). Urbanization has influenced the food consumption pattern by more energy dense and also by change in composition of food. Increased mechanization in the form of motorized transport, labour saving service sector etc. decreased the physical activity and contributed to an obesogenic environment (Kiranmala *et al*., 2013). Industrialization in India is also taking place at a steady pace leading to less labour intensive production processes.

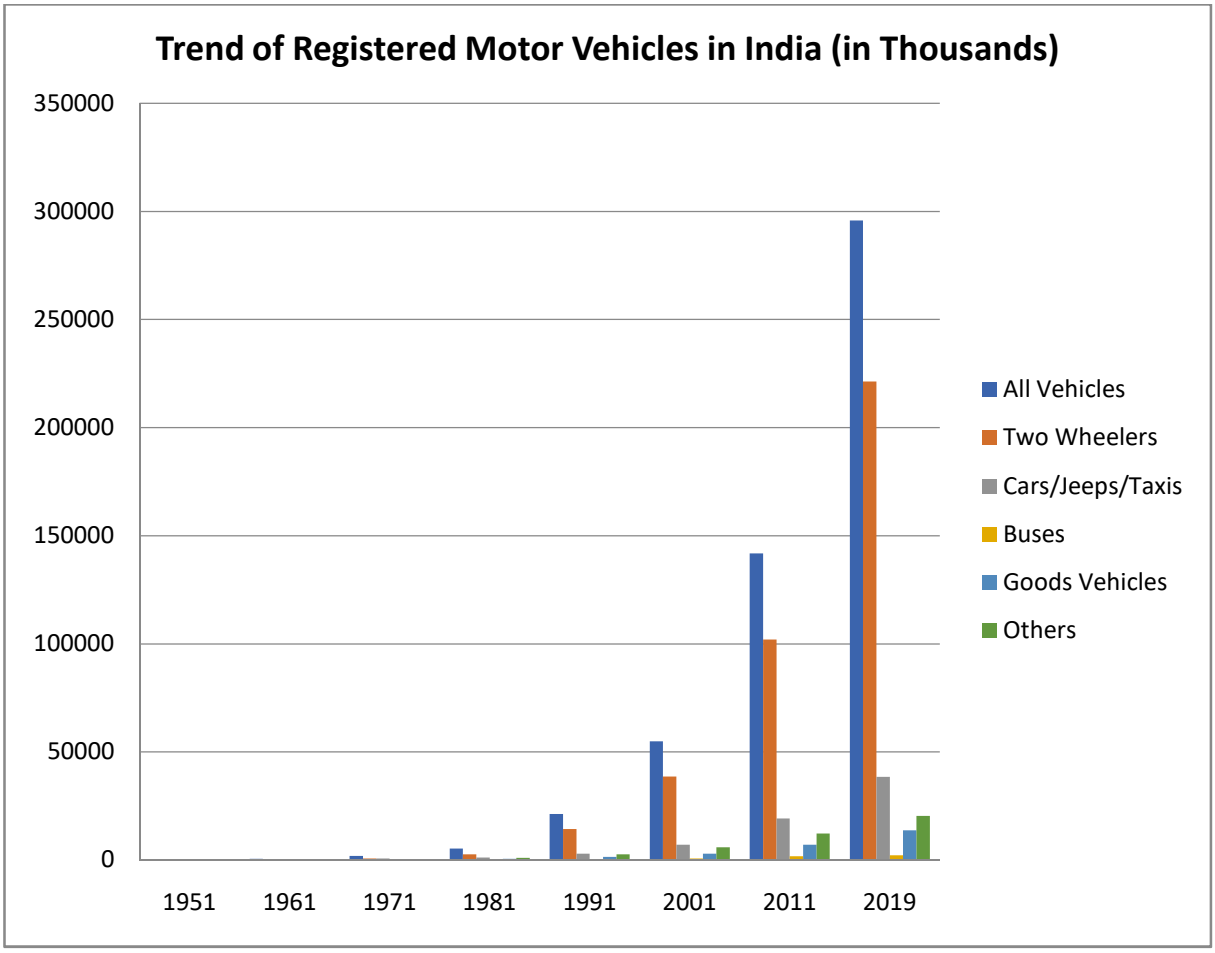
More industries mean production and availability of products which help customers in performing daily chorus with less physical labour.



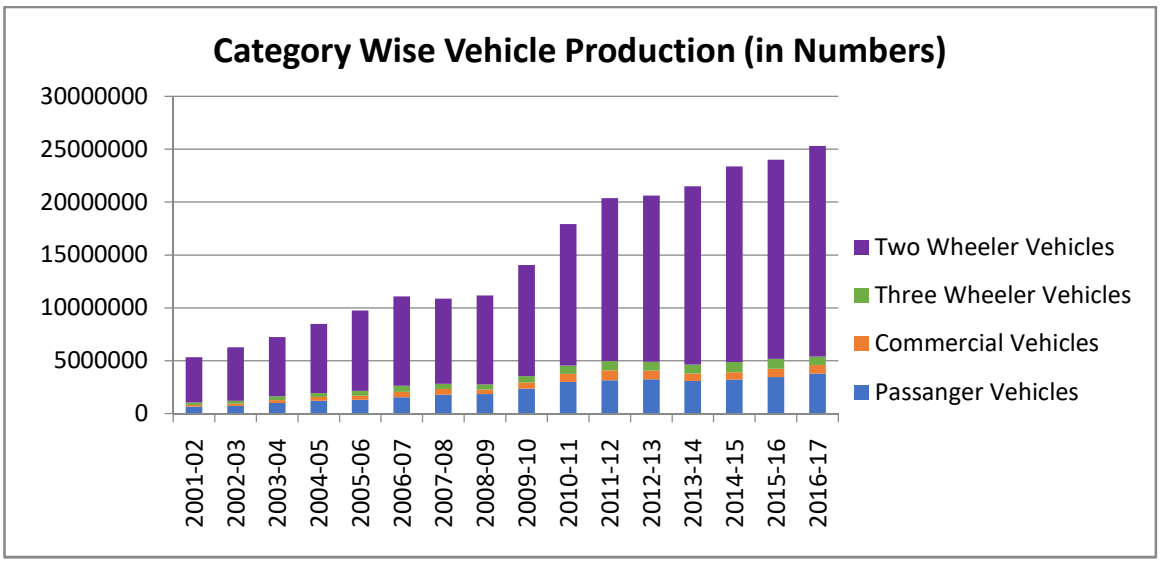
Graph 3.3: Growth of factories in India (Source: Adapted from Statistical Year Book India, 2011 and 2018; Annual Survey of Industries, 2015-16, 2016-17, 2017-18, 2018-19)

3.3.4 Mechanization and its effect on physical activity:

In India, a dramatic change in transportation sector is taking place. As because of increasing number of vehicle population, considerable physical energy has been saved by both urban and rural population. The graph below clearly shows the increase in all types of vehicle with more drastic increase in last two decades. One interesting trend is highest increase of two wheelers amongst all types. It may be presumed that the two wheelers are the most affordable and hence fits into the budget of many families. This also implies that a good proportion of Indian populations in the bracket of low or middle income category are having their own vehicle and becoming part of the mechanization process. According to a study conducted in eight Chinese provinces, men and women who live in households with motorised vehicles are 80% more likely to be obese than those who do not (Bell, *et al*., 2002).

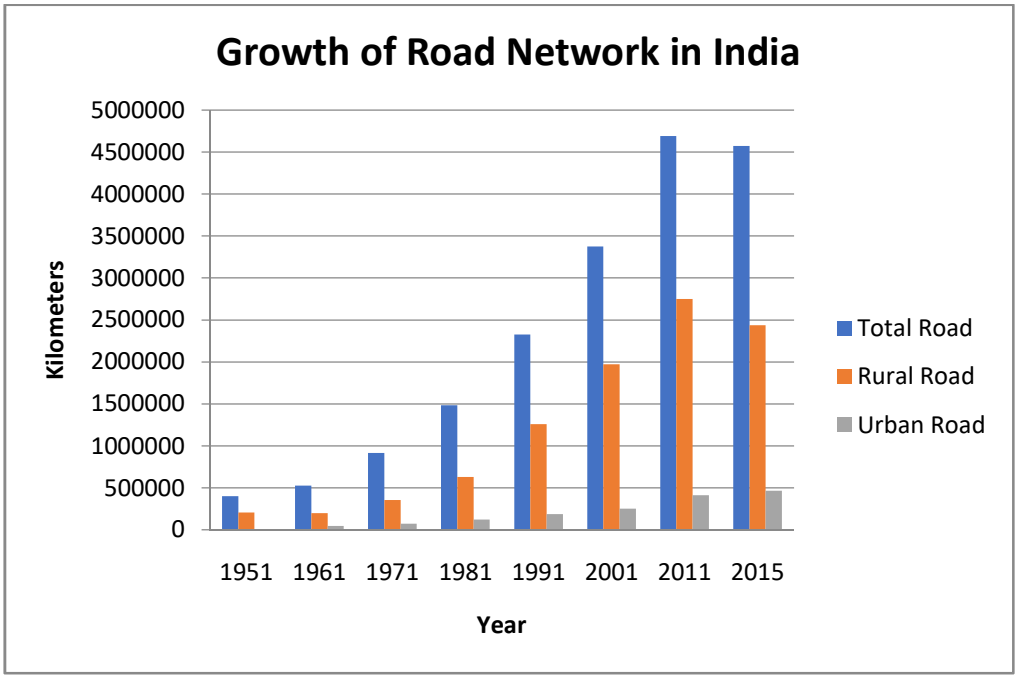


Graph 3.4: Category wise vehicle registration in India (in Thousands) (Source: Adapted from Road Transport Year Book, 2017-18 and 2018-19)



Graph 3.5: Category wise vehicle production trend (Source: Adapted from Statistical Year Book India, 2018)

Along with increase in vehicle population the strengthening of road network boosts the transportation sector. Motor able roads reaching out to even hard to reach areas changed the lifestyle of people. The graph below shows the growth of road network in India from 1951 to 2011. There has been steady increase in kilometer of road length and noticeably major proportions are happening in rural areas as compared to urban areas.



Graph 3.6: Growth of road network in India (Source: Adapted from India Transport Report- Moving India to 2032, 2014; Statistical Year Book India, 2018)

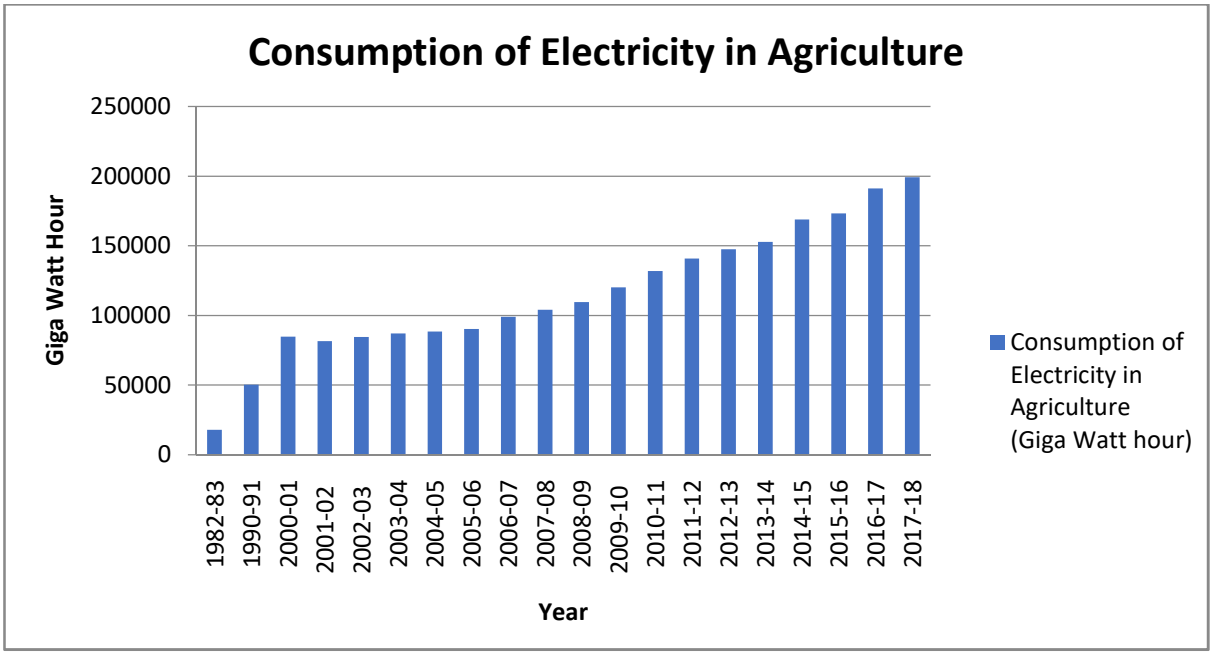
Another sector is going through tremendous mechanization is the agricultural sector. The sector is witnessing a considerable decrease in use of human and animal power. This shift is happening from traditional agricultural methods to modern mechanized methods in each and every step. The extent of mechanization at various levels were calculated as 40% in soil working and seed bed preparation, 29% in seeding and planting, 34% in plant protection, 37% in irrigation, and around 60-70% in harvesting and threshing (Grant Thornton India LLP, FICCI, 2015). Following table explains the power utilization shift by showing the percentage share of total power by human, animal, and tractor (other means are not included):

Year	Agricultural worker	Draught animal	Tractor (% share)
1971-72	15.11	45.26	7.49
1981-82	10.92	27.23	19.95
1991-92	8.62	16.55	30.21
2001-02	6.49	9.89	41.96
2005-06	5.77	8.02	46.7
2012-13	5.0	5.1	45.8

Table 3.3: Shift in percentage of power utilization in agriculture (Source: Adapted from NABARD, 2018)

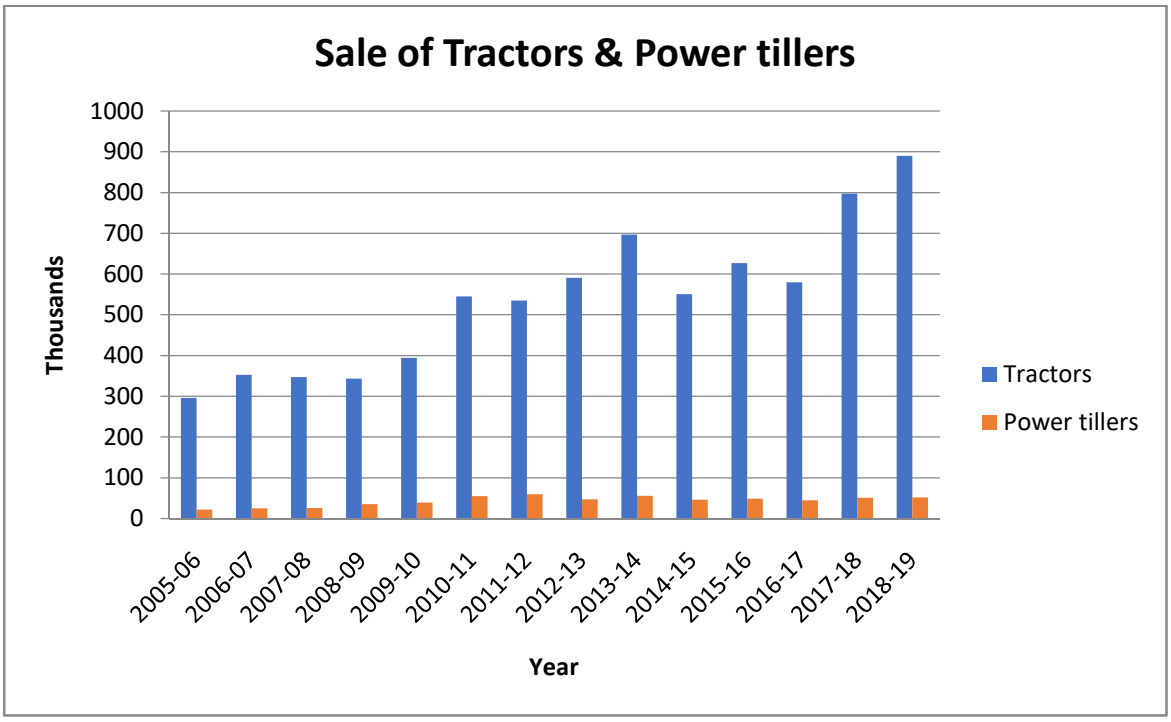
It is quite obvious from above data that the shares of farm power of agricultural workers have decreased by three times while the same has increased by six times for tractors within a span of 40 years.

An increase in demand and consumption of electrical power in agriculture is evident. The following figure shows that consumption pattern and with increase in utilization of electrical energy in agriculture there will be proportionate decrease of physical energy as well.



Graph 3.7: Consumption trend of electricity in agriculture (Source: Adapted from Ministry of Statistics and Programme Implementation, GoI; Ministry of Agriculture and Farmer Welfare, GoI)

Increasing trend of sale of tractors and power tillers as shown in the figure below also proves the process of mechanization in India. Moreover, government policies to subsidize the process of procurement of farm equipments for farmers fasten the mechanization process.



Graph 3.8: Trend of sale of tractors and power tillers (Source: Adapted from Ministry of Agriculture and Farmer Welfare, 2018; NABARD, 2018)

3.4 Environmental Factors:

Environment is a broad domain in relation to health. In this section discussion will be limited to environmental pollutants and various harmful chemicals which has clear evidence of association with metabolic syndrome. Environmetal factors act as important determinant in the pathogenesis of obesity or over weight and hence metabolic syndrome. Since mid 1850s the study of public health has always stressed on the interlinking of environmental health with infectious disease when John Snow determined the origins of a London cholera outbreak by using an environmental map (Feingold *et al*., 2010). This had clearly raised the issue of geography as a factor affecting the incidence of infectious diseases and the risk of transmission. There are several man-made chemicals and heavy metals that are released into the environment

as a result of the rapid industrialization and urbanization (Lee and Kim, 2016). Environmental factors with predisposition of genetic factors can lead to positive energy balance (Martins *et al*., 2014). One important analogy is that "genes load the gun and a permissive or toxic environment pulls the trigger" (Bray, 2007). Crowding, infections, and environmental pollution mediated fat cell stimulation may increase the risk of cardiovascular problems in Indian cities (Yajnik, 2001). Some of the NSS 76th round (2018) data tabulated below will give an idea of the living condition of Indian population. These data are of rural and urban combined and gives an idea that a good number of population/household in India still have poor living environment.

Average plinth level of house (meter)	0.4
Access to no latrine (% of population)	20.2
Households without drainage system (%)	28.3
Household garbage disposal in common place other than community dumping spot (%)	33.1
No arrangement of garbage collection system (%)	58.9
Households with stagnant water in or around the premises (%)	15.2
Households reporting problem of flies/mosquitoes (%)	45.3 (Severe) 51.1 (Moderate)

Table 3.4: Some indicators on living environment in India (Source: NSS 76th round 2018 report number 584)

Poor living conditions and overcrowding helps in repeated infection of inhabitants. Repeated infections cause inflammatory states which can yeild differential outcomes depending on the affected age group of the population. A special mention has to be given to the urban slum areas where poor living conditions are quite evident and hence population is more vulnerable. Along with poor living conditions the inhabitants are also exposed to the chemicals arising from waste which are frequently being handled for living. These chemicals are often those chemicals which are found to be pollutants or Endocrine Disrupting Chemicals (EDCs). Air pollutants play an important role in the subclinical inflammation and hence a positive corelation to metabolic syndrome can be hypothesized (Eze *et al*., 2015). Persistent organic pollutants (POPs) like organochlorine pesticides, polychlorinated biphenyls (PCBs), polychlorinated dibenzo-*p*-dioxins (PCDDs), and polychlorinated

dibenzofurans (PCDFs) are present in the environment and also in food chains even after consensus by the international community to limit their release (Ruzzin *et al*., 2010). Food items like fish, meat, and dairy products are the main source of POPs through contamination (Fisher, 1999). POPs have the capacity to cause insulin resistance and can disturb lipid and glucose metabolism (Ruzzin *et al*., 2010). POPs may activate nuclear receptors which in turn take different pathways to develop insulin resistance syndrome.

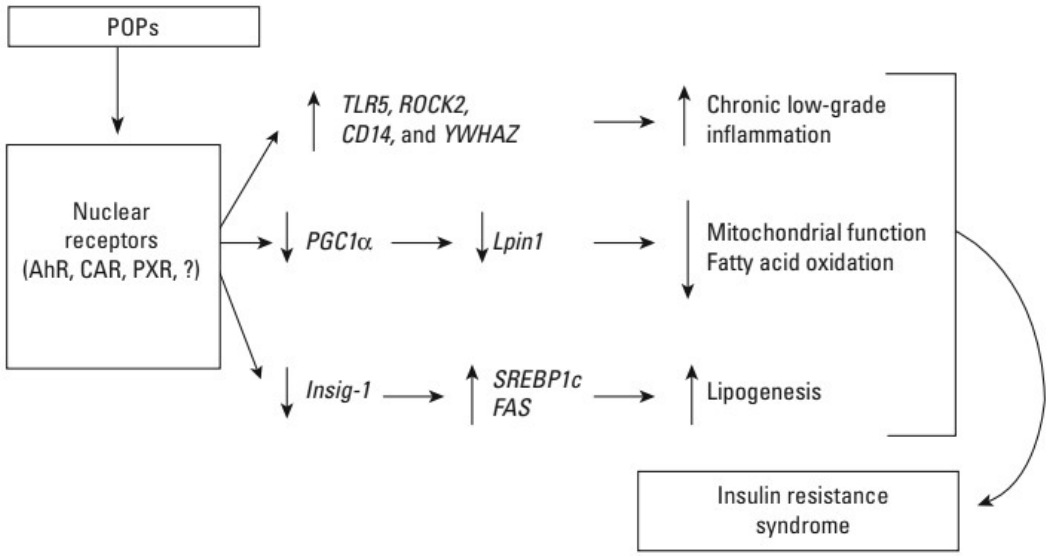


Fig 3.6: Possible mechanisms behind the POP exposed development of the insulin resistance (Source: Adapted from Ruzzin *et al*., 2010)

Some environmental pollutants act as Endocrine Disrupting Chemicals (EDCs) and interfere at different levels of metabolism and energy balance (Lubrano *et al*., 2013). As per World Health Organization/International Programme on Chemical Safety (WHO/IPCS, 2002) EDCs are defined as "an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub) populations". So EDCs can alter the function of endocrine system by mimicking the actions of natural hormones or by interfering the whole cycle of production to elimination (ibid). Chemicals that could affect any endogenous hormones that carry signals from one cell to another are now included in the category of "EDCs" in addition to those that fit the criteria outlined above (Barouki *et al*., 2012). There are so many chemicals identified as EDCs and more and more chemicals are added with time. Some of these substances show minimal health beneficial effect and most others not. EDCs modulate hormone

signalling and cause various levels of developmental and reproductive anomalies (Bagchi Bhattacharjee and Paul Khurana, 2014). Most of the concerned EDCs are synthetic chemicals of industrial origin. Most of these substances are solvents or lubricants, along with their byproducts such as polychlorinated biphenyls (PCBs) and dioxins, plastics, plasticizers [such as bisphenol A (BPA)], phthalates, pesticides (such as methoxychlor, chlorpyrifos, and DDT), fungicides (such as vinclozolin), herbicides (such as atrazine), and antibacterials (triclosan) (Barouki *et al*., 2012; Rajankar, 2018). These chemicals enter the food chain and start to build up in animal and human bodies (Barouki *et al*., 2012). Direct exposure can also happen through consuming polluted water, breathing contaminated air, and/or coming into contact with contaminated objects. Some potential EDCs with their source and key adverse effects mentioned below.

EDC	Key Source	Adverse Effects
Bisphenol A (BPA)	Used in plastic production	• Metabolic syndrome (Diabetes obesity) • Reproductive disorder
Triclosan	Cosmetics, soaps, detergents, toothpastes etc.	• Abnormal endocrine system • Weak immune system
Triclocarban	Personal care products, plastics	• Amplify effects of sex hormones
Phthalates	PVC plastic, solvents, toys	• Hepatotoxic • Teratogenic • Carcinogenic
Parabens	Cosmetics, foods, drugs	• Breast cancer
Nonylphenol	Clothing, paints, toys	• Endocrine disruption
Di-ethanolamine	Cosmetics, pharmaceuticals	• Liver cancer
Styrene	Plastics, disposable plates and cups, automobile	• Affect nervous system • Affect reproductive system

Table 3.5: Some key EDCs with their potential source and adverse effect (Source: Adapted from Rajankar, 2018)

BPA exposure causes disruption of several metabolic mechanisms and is crucial due to its extensive use in plastic industry. BPA has been found to contribute obesity in humans. EDCs have the potential to cause endocrine or metabolic abnormalities but also depends on at which critical period of development the exposure occurs (Barouki *et al*., 2012). All major endocrine organs like the pancreas, the thyroid gland and reproductive organs are vulnerable to endocrine disruption (ibid). This disruption involves HPA axis, which is key in the final common pathway of metabolic disorder. Barouki *et al* (2012) mentioned that if EDCs or other environmental chemicals are exposed during the crucial phases of development then functional changes in gene expression can occur. However such changes in the form of phenotypical deviations may not be observed at the time of birth even though exposure might have occured in utero. The changes in gene expresion may pass undiagnosed till there is increased risk of dysfunction or disease in later part of life. The phocomelia (congenital deformity where limbs are under developed or absent) caused by thalodomide exposure during pregnancy is a good example how chemicals could result in lasting adverse effects. Interestingly such exposures may not have any affect on the pregnant mother or may be insignificant from functional point of view. This also shows that such chemical exposures may not have visible effect on mature organs but may cause long term serious adverse effects on developing foetus. We all know that tissue development is controlled by genetic determinants and influenced by hormmones and growth factors. EDCs can influence this process by binding to hormone receptors and can alter the tissue specific functionality even in low doses. Effects of low dose EDCs may be more harmful than high dose as such dose-response relationship may be non-linear and hence skewed from the normal hormonal pathway. The majority EDCs and environmental factors do not cause genetic mutations or alter the DNA sequence but they may facilitate changes in gene expression, such as DNA methylation and histone acetylation, which might result in altered phenotypes or disease conditions (Barouki *et al*., 2012).

There are numerous studies to quote which have shown potential relationships between metabolic syndrome and exposure to heavy metals such as lead (Pb), mercury (Hg), and cadmium (Cd) (Lee and Kim, 2016). Blood cadmium levels and metabolic syndrome were shown to be significantly correlated in South Korean males participating in the Korean National Health and Nutrition Examination Survey (2008-

2012) (ibid). Blood cadmium levels were found to be higher in populations from north-eastern Asia i.e. Korean, Japanese, and Chinese as compared to western population because of consumption of rice as staple food by these Asian populations (Ikeda *et al*., 2000). Animal studies on rat and mice revealed that cadmium reduce glucose tolerance by damages pancreatic β cells and has diabetogenic effect (Lee and Kim, 2016). Lead (Pb) driven hypertension in human is a well established phenomenon (ibid).

As mentioned already all pollutants induce inflammatory responses as a determinant of metabolic syndrome. But this whole inflammatory process as driven by environmental toxicants can be modified by pathogens (Feingold *et al*., 2010). The severity of chronic disease progression or disease etiology depends on four possible scenarios as shown below. Pathogens and chemical toxicants interact in several ways leading to disease causation, which depends on the living conditions (Feingold *et al*., 2010). These scenarios are very much relevant for the vulnerable population living in urban slums with exposure to both pathogens and chemical toxicants.

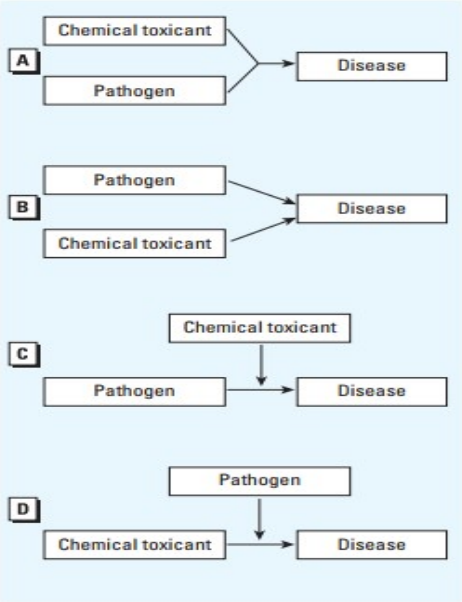


Fig 3.7: Scenarios in disease causation due to pathogen-chemical toxicants interaction (Source: Adapted from Feingold *et al*., 2010)

Particulate matter of <2.5 µm ($PM_{2.5}$) size has been found to exaggerate diet induced insulin resistance (Sun *et al*., 2009). $PM_{2.5}$ exposure enhances oxidative stress and inflammation in organ tissues leading to adipose inflammation and visceral adiposity (Sun *et al*., 2009; Wei *et al*., 2016). An experiment on mice for 24 weeks

where they were fed on high calorie diet along with exposure to concentrated ambient $PM_{2.5}$ or filtered air. The $PM_{2.5}$ exposed mice showed insulin resistance, visceral adiposity, and inflammatory changes (Sun *et al*., 2009). These findings provided evidence that chronic exposure to air pollution or $PM_{2.5}$ increases the risk of developing obesity and metabolic syndrome and helped in further understanding on how these particulates may modulate inflammatory responses in distant target organs (Sun *et al*., 2009; Wei *et al*., 2016). The whole mechanism of how particulate matter inhalation helps in the etio-pathogenesis of obesity and metabolic dysfunction has been shown below.

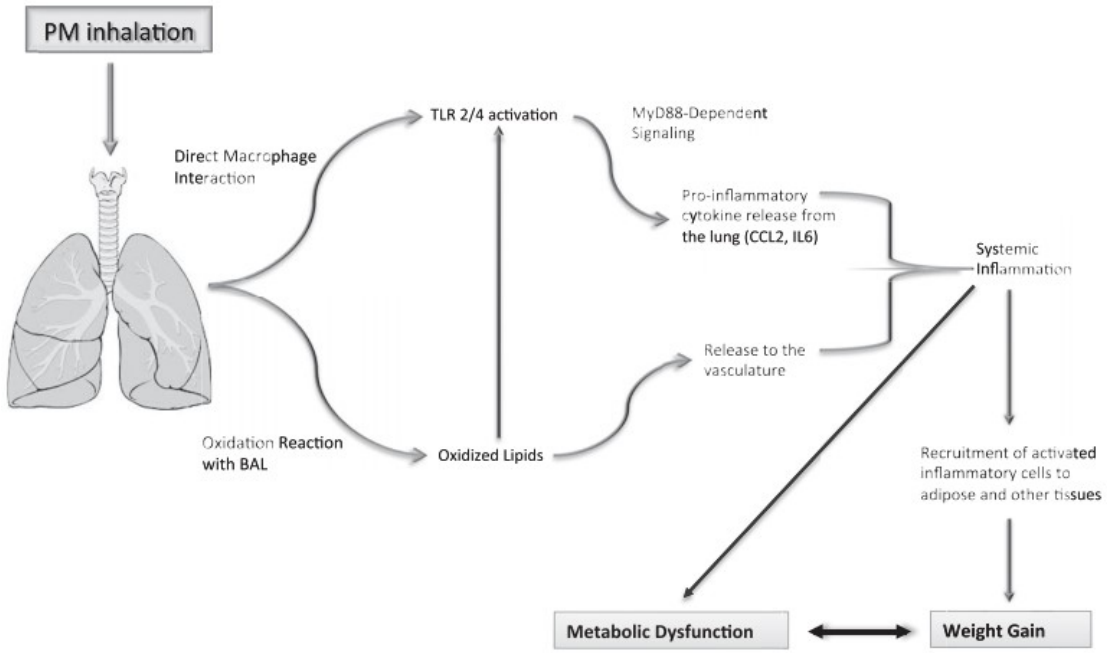


Fig 3.8: Particulate matter inhalation and mechanism of weight gain and metabolic dysfunction (Source: Adapted from Wei *et al*., 2016)

The vulnerable population living in urban slums are also prone to nutrition imbalance which may be due to work cycle or inability to procure nutritious food items. This nutritional imbalance along with exposure to environmental chemicals can pave a common mechanism in altering the gene expression. The final result can be variations in hormonal regulations and metabolism leading to increased disease risk. The figure below explains this mechanism.

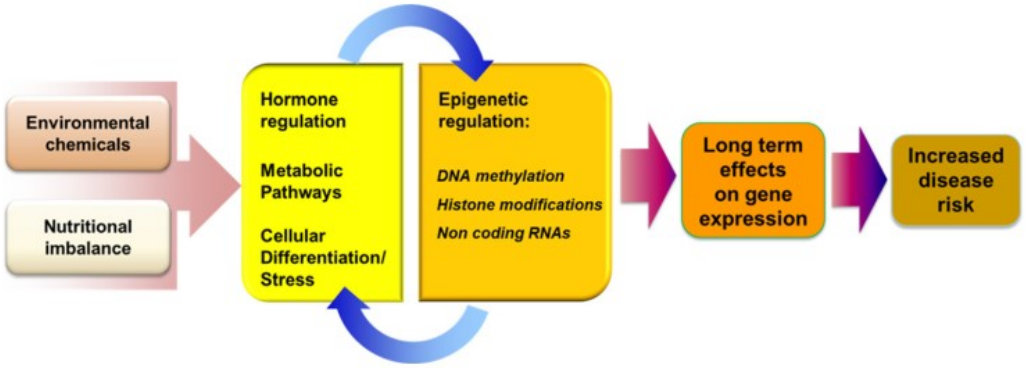


Fig 3.9: Common mechanism of environmental chemicals and nutritional imbalance leading to increased disease risk (Source: Adpated from Barouki *et al*., 2012)

Keeping in view of the adverse effects of EDCs on health, FAO and WHO joint food standard programme in 2019 has provided guidelines to promote internationally harmonized approach to address possible public health and trade issues arising from EDCs present in pesticides (FAO/WHO, 2019).

Chapter Four

Nutrition Transition and Under-nutrition as Determinants of Metabolic Syndrome

4.1 Nutrition Transition:

Diet unquestionably has a significant impact on the development of metabolic syndrome. The composition, frequency, and quantity of diet determine our health. Ayurveda prescribes: “When urine and stool have been properly eliminated, when mind is at peace, elements are balanced, stomach is free of wind, body is light, cognitive sense organs are efficient, and appetite is there, only then may you take food!” (Mitra *et al*., 2009). There is an ancient saying, “Those who eat only once are Yogis, and those who eat twice always remain happy and those who eat thrice remain acutely diseased” (ibid).

4.1.1 Demographic and epidemiological transition:

The world is going through the process of transition, both demographic and epidemiological, and is at various stages as per specific region or country. These stages determine the health status of its population depending on the already attained socio-economic status.

The demographic transition, which influences the population structure, is the change from high fertility and high mortality to low fertility and low mortality (Popkin, 2010; Shetty, 2013). This transition is observed during the evolution phase of a pre-industrial country into a more modern industrialized economy. Next is the epidemiological transition as formulated by Abdel Omran in 1971 (Shetty, 2013). India as a developing nation is going through rapid demographic transition with increase in life expectancy and side by side decline in birth rate. The share of population with age more than 60 years will be 179 million in 2026 (227% increase) from 54.7 million in 1991 in India (Shetty, 2002). It is estimated that aged population (>60 years) in India will be around 13.3% of total population in year 2026 (ibid). The gradual alteration in the population's age composition brought on by ageing along with adapted urban-industrial lifestyles has increased the prevalence of chronic and degenerative disease (Shetty, 2002; Popkin, 2010; Shetty, 2013).

Epidemiological transition indicates towards complex changes occurring in health, disease and death as a consequence of demographic, economic and social

changes (Shetty, 2002). Epidemiological transition has witnessed a spectacular fall in mortality due to fall in infectious disease, famine episodes, malnutrition, and poor environmental sanitation (Popkin, 2010). Developing nations like India are currently trailing behind industrialised nations in the epidemiologic transition process and are currently in the period of a decline in infectious disease mortality and an increase in chronic NCDs (Shetty, 2002; Shetty, 2013).

4.1.2 Stages of nutrition transition:

Agricultural and food system advancement have helped in increase in food availability. Changes in dietary consumption patterns due to better economic condition and urbanization lead to adverse health outcomes (Shetty, 2013). Within a few decades, the nineteenth-century agro-industrial revolution enhanced the amount of food produced. It was made possible by using scientific innovations in conventional agriculture, mechanisation, crop genetic modification, and the development of fertilisers and pesticides (Schmidhuber and Shetty, 2005). Food was being produced at such a rapid rate that the need was readily met. This made it possible to provide the expanding population with more food of higher quality at low costs. Increased fat consumption (mostly saturated fats of animal origin) and sugars have displaced the conventional dietary pattern (Shetty, 2013). Most of the traditional diets are not energy dense; having only low fat and are devoid of sugary beverages (Holmboe-Ottesen and Wandel, 2012). This consumption pattern of diet rich in fats, sugars, and refined and processed foods but low in fibre- often referred as Western diet (Popkin, 2003). Modernization of societies with economic development has fueled this consumption pattern and hence bears a casual linkage to the disease burden (Shetty, 2013). Such change in the composition and structure of the diet is referred to as the nutrition transition. The rise in non-communicable diseases and obesity prevalence are due to changes in body composition as contributed by the ageing population and countries moving through the stages of epidemiological, demographic and nutrition transitions (Shetty, 2013). Popkin divided the nutritional shift into three stages: (i) receding famine, (ii) degenerative disease, and (iii) behavioural transformation (Popkin, 2010).

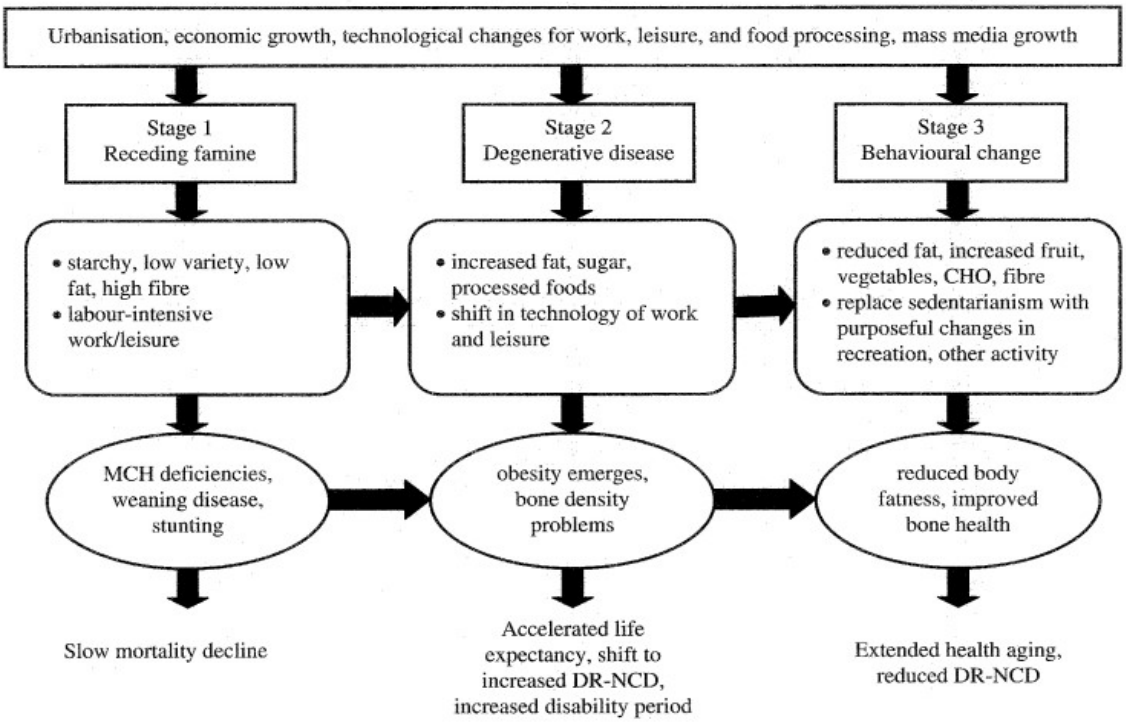


Fig 4.1: Stages of nutrition transition (Source: Adapted from Popkin, 2003)

Beginning in the 1960s, there was a global food crisis that resulted in population-wide famines, chronic undernourishment, and calorie deficits throughout the developing globe (Schmidhuber and Shetty, 2005). Large segment of Asian population was frequently hit by famines and in particular countries like China and India were badly affected at that time (ibid). Chronic under nutrition affected almost 40% of the population in developing nations (ibid). From 1970 to 2000 nutrition transition had gathered momentum due to green revolution and prevalence of undernourishment cam down in most of the major developing regions except a few (ibid). Nutrition transition has shifted the consumption patterns from carbohydrate based food products to calories derived from fat-based products (Siddiqui *et al*., 2019). While energy derived from fats has grown by 6% and energy derived from carbohydrates has fallen by 7% in between 1973 and 2004 due to changes in nutrition (Misra *et al*., 2011). Agro-industrial revolution started late in developing countries than the developed world and it took place more than a century afterwards. The factors which had helped in initiating the developed world's agro-industrial revolution at the beginning of the 1960s, took its turn afterwards for similar changes in the food and agricultural sectors of the developing world (Schmidhuber and Shetty, 2005). The same factors which brought revolution in developed world like high-yielding crops,

better irrigation, increased and improved supply chain, and vast mechanization had increased production and made food easily accessible to customers in emerging nations (ibid). These improvements were noticeable in developing countries where the average daily protein intake nearly doubled from about 40 to 70 g/person/day while the average daily calorie availability grew from around 1950 to 2680 kcals/person/day (ibid). However, in addition to these nutritional alterations, it has been discovered that South Asians are more likely to develop metabolic disorders when they consume an uneven quantity of fat, consume a lot of sodium, consume little dietary fibre, and engage in poor eating habits (Katulanda *et al*., 2012). Rapid urbanization has been the most important factor in affecting the consumption patterns (Schmidhuber and Shetty, 2005). Urbanization causes globalization of food consumption pattern due to modern and improved marketing and distribution system (ibid). Rigorous western distribution systems have displaced traditional diets with processed, sugary, fatty and as a whole more energy dense food (ibid). Enhanced foodstuff processing itself has its effect on food consumption patterns (ibid). Urbanization brings in more female participation in the work force and restricts the time consumed in cooking. As a result, people are moving away from labor-intensive traditional food preparations and toward precooked, simple food, snacks, or quick food from outside (ibid). The urban poor are particularly affected by the move to quick and convenient meals, and their diets tend to be deficient in fresh produce, pulses, potatoes, roots, and tubers while being high in sugar, salt, and fat (Schmidhuber and Shetty, 2005; Misra *et al*., 2011). In almost all countries of the world the per capita availability of cereals has decreased and is also contributing less energy share (Shetty, 2013). Both China and India are consuming more animal products and will be projected to continue the same in coming years ahead (Schmidhuber and Shetty, 2005). Higher consumption of animal products like meat and milk are related with a clear increase in the consumption of cholesterol and saturated fats (ibid). Increasing demand of animal source foods in low-income developing countries have projected a production of world's 63% of meat and 50% of milk by developing world alone by year 2020 (Popkin, 2003). The China example shows the following transitional changes: (i) the intake of cereals had decreased significantly in all income groups of both rural and urban population (ii) shift in consumption of coarse grains like millet, sorghum, and corn to finer grains (iii) increase consumption of animal products by affluent than poor, and by urban than

rural (iv) shift in energy source from carbohydrate to fat (ibid). Table below depicts the increasing global trend of calories from animal products. This growth was particularly rapid in East Asia as contributed by high (pig) meat consumption in China, and rapidly increasing milk consumption ("White Revolution") in South Asia.

	1962*	1970*	1980*	1990*	1998*	2015	2030
Calories/Person/Day							
World	281	301	321	351	380	397	438
Industrialized Countries	670	725	759	779	786	824	847
Developing Countries	117	133	165	214	284	345	393
Sub-Saharan Africa	106	112	125	115	108	120	138
Latin America	315	333	394	391	468	550	633
Near East/North Africa	215	220	278	264	261	312	362
East Asia	57	88	124	218	360	460	527
South Asia	113	106	118	158	185	247	314
Transition Countries	525	616	764	748	568	628	685

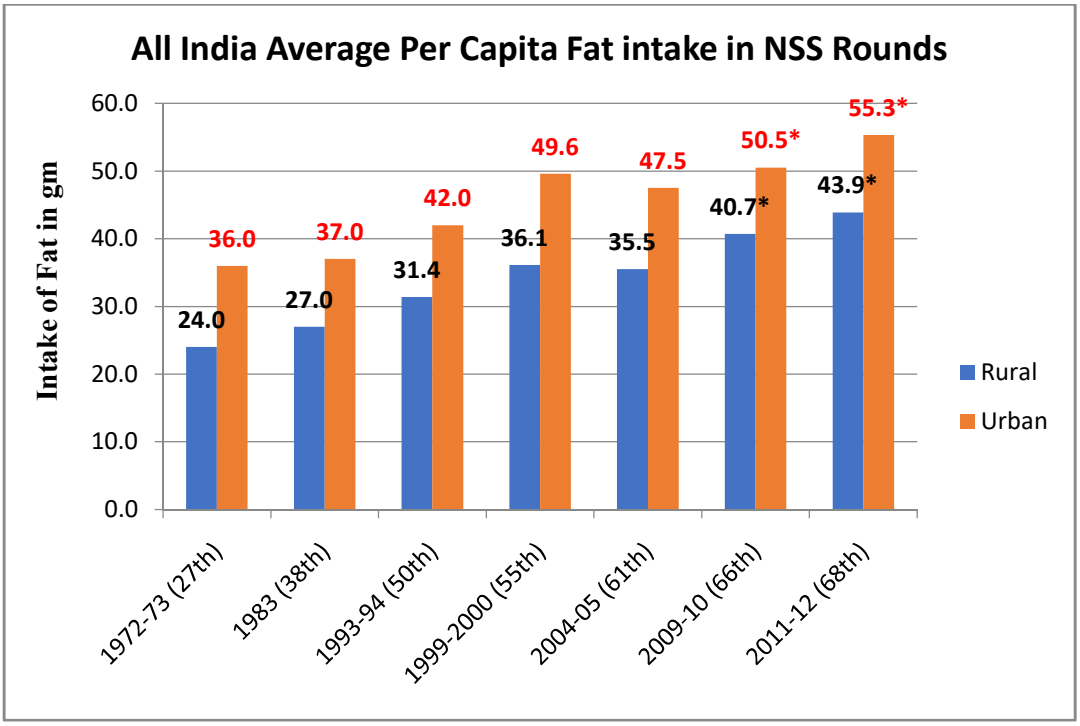
Table 4.1: Calorie availability from livestock products (Meats, Eggs, Milk, Dairy products) *3 year average centred on the year indicated (Source: Schmidhuber, J. and Shetty, P. 2005)

4.1.3 India in nutrition transition:

Surveys conducted by several national level organizations at different times indicated towards calorie adequacy in India by 1970s or by early part of 1980s (Shetty, 2002). Such findings do have its own controversy due to the disparities in intake of food as because of rural-urban and socio-economic divide. Gradual decrease in intake of cereals along with increase consumption of milk, milk products, animal products, fats, oils, and carbonated beverages have shifted the energy balance in India (Shetty, 2002; Misra *et al*., 2011; Shetty, 2013).

4.1.3.1 Change in fat intake:

As per food balance analysis of FAO (Food and Agriculture Organization), the intake of fat has been found to be increasing in developing nations (FAO/WHO, 1994). There is significant association between dietary fat intake and obesity when combined with limited physical activity (Bray *et al*., 2004). The body seems to adapt to high fat diet in slower rate in individuals with sedentary habits as compared to low fat diet (Lissner & Heitmann, 1995). Hindu Indians are traditionally strict vegetarians, in contrast to the Western diet's predominance on animal fats. The Indian cuisine has become more lacto-vegetarian as a result of industrialization (Mitra *et al*., 2007; Mitra *et al*., 2009). Consumption of vegetable oils at a high level has been seen in addition to the eating of meat, fish, eggs, and dairy products (ibid). Contrary to the west, developing countries like India actually witnessed the process of nutrition transition with increased production and/or import of oilseeds and vegetable oils (Popkin, 2003). Studies in China have shown a three times increase of individual intake of vegetable oil in all persons aged ≥2 years during the period of 1989–2006 (Popkin, 2010). The principal sources of these vegetable oils include soybean, sunflower, rapeseed, palm and groundnut (Popkin, 2003). High-fat diets are now affordable to low-income groups around the world, thanks to the widespread availability of relatively cheap vegetable oils (Shetty, 2013). ICMR Expert Consultation of National Institute of Nutrition, Hyderabad (2009) proposed that fat energy should contribute minimum 20% of total energy in case of Indians. It is necessary to further divide this total fat energy into 10% from visible sources (fats and oils) and 10% from invisible sources (food sources) (ICMR, 2009). The primary sources of "visible fats" are animal products, particularly butter and vegetable oils like *ghee* (clarified butter with high saturated fat) (Misra *et al*., 2011). However the ‘‘visible fat’’ (and oil) consumption pattern in India depends on the socioeconomic status and regional variations (ibid). There is positive relationship between total fat consumption and metabolic syndrome. According to the graph below, total fat consumption grew in India's rural and urban populations between 1973 and 2012 (NSS 68th round). Increase in supply of fats and oils since 1969 in India along with rising income have contributed to this increase in fat intake (Misra *et al*., 2011).



Graph 4.1: Average per capita per day fat intake for all India (rural and urban) as per NSS rounds. *Average of type 1 and type 2 data (Source: NSS 68th round).

The source of saturated fatty acids (SFAs) in Indian diets is mostly derived from butter, *ghee*, and coconut oil (in case of south India) (ibid). Polyunsaturated fat w-6 and w-3 are essential fats and these are only obtained from the diet (Mitra *et al*., 2007). Diets high in w-6 fat but poor in w-3 fat, which is the intake pattern of today's high fat containing food, have become a major risk factor (ibid). The mechanisms of insulin action and secretion are modulated by metabolites produced from w-6 and w-3 fat (ibid). It has been discovered that the metabolites of w-3 fats are heart protective and those of w-6 fats are thrombogenic and pro-inflammatory (ibid). We have a habit of discouraging the highly saturated traditional fats like *ghee* to tackle the health issues of high cholesterol level, and replace it with refined vegetable oil free of beneficial w-3 fat and high in unsaturated fat (ibid). The faulty ratio of w-6 and w-3 fat induces the risk factors for insulin resistance (ibid). Moreover, with invent of the process of hydrogenation helped in fluid oils to transform into spreadable margarine (Schmidhuber and Shetty, 2005). Although the technology aided in market penetration, it endangered people's health by turning beneficial unsaturated fatty acids into undesirable trans-fatty acids and non-essential fats (ibid). The harmful trans-fatty acids (TFAs) in Indian diets mostly derived from *Vanaspati*, which is widely used in low and middle class families due to low cost, easy to handle, and prolong shelf life

(Misra *et al*., 2011). Hence, with transition, the Indian diet at large started to have lesser saturated fat and cholesterol, and more polyunsaturated fat. Consuming trans-fatty acids concurrently raises LDL cholesterol levels, which are thought to promote obesity (*Vanaspati*) (Mitra *et al*., 2007). It is urged that Indians minimize their use of *Vanaspati* and instead switch to more traditional oils like mustard oil, coconut oil, and *ghee* when it was discovered that TFAs are to blame for the rising prevalence of type 2 diabetes mellitus (Mitra *et al*., 2009). In addition to being utilized in homes, TFA-rich *Vanaspati* is widely used in India by street sellers to prepare ready-to-eat, processed, baked, and fried dishes (Misra *et al*., 2011).

4.1.3.2 Change in grain consumption:

In India, consumers of all income levels have been switching from coarse grains like sorghum, barley, rye, maize, and millet to more refined cereals like rice and wheat (Shetty, 2013). Refined flour produce by modern milling procedures has better digestibility but destroys the beneficial characters like its texture, structure and valuable dietary fiber and also reduces their vitamins and minerals (Schmidhuber and Shetty, 2005). Higher levels of consumption of wheat in developing countries and especially refined white wheat flour, which lacks fiber, important minerals, and vitamins (ibid). The low intake of coarse cereals in urban areas and decreasing intake in rural areas over the last decade (1994–2004) has important implications for increasing insulin resistance (Misra *et al*., 2011). The Green Revolution in India raised food grain production from 72 million metric tons to nearly 200 million metric tons between the mid-1960s and late 1990s (Kiranmala *et al*., 2013). In a study on urban people from southern India, it was discovered that those who consumed the most refined grain (white rice grain) had a considerably higher frequency of metabolic syndrome (Misra *et al*., 2011).

4.1.3.3 Sugar consumption:

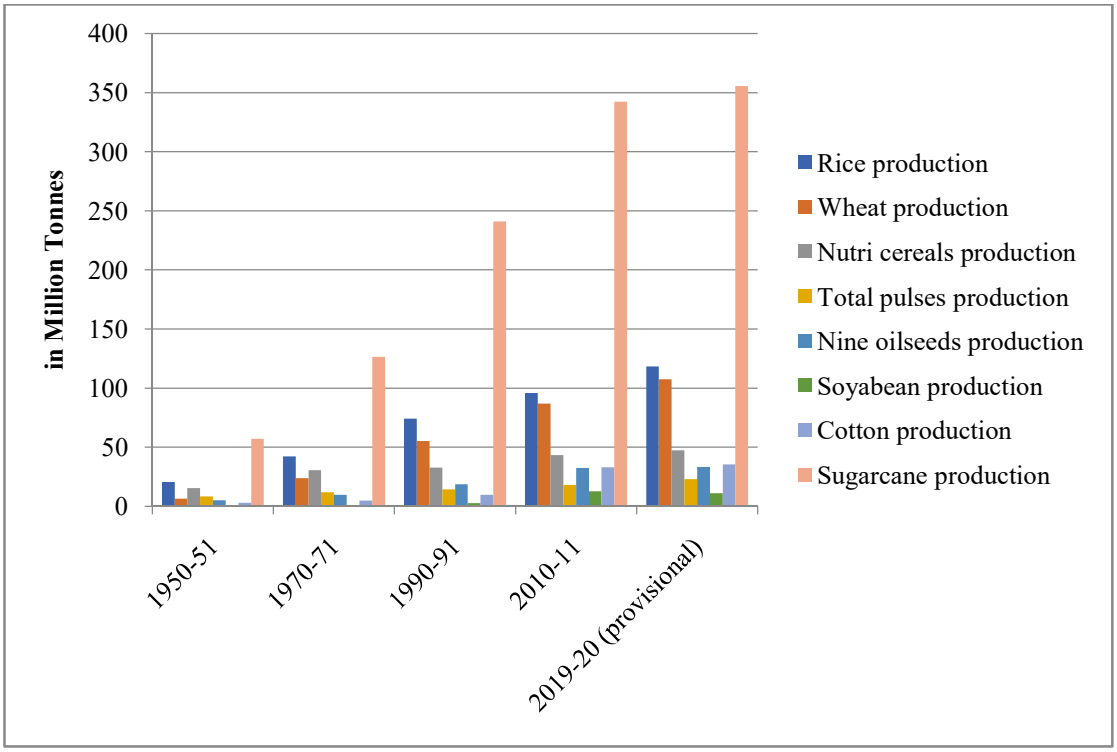
Increased consumption of added caloric sweeteners in developing countries hugely contributed as a determinant of obesity. Sugar is considered as the world's predominant caloric sweetener and overall trends show its increased consumption everywhere (Popkin, 2003; Schmidhuber and Shetty, 2005). In the 57th NSSO cycle,

sugar consumption was discovered to be greater above the suggested ICMR levels in 11 out of 20 Indian states (Vepa, 2010). Due to high sugar content, over intake of sweetened beverages may be related to India's rising rate of childhood obesity (Misra *et al*., 2011).

The soft drink business entered a new era with the help of the discovery of isomerase technology in the late 1960s (Havel, 2002). The process could turn half of a starch molecule into the sweet fructose, which differs from glucose, and the other half into the sugar molecule sucrose (ibid). The addition of this technology has a great role in obesity epidemic due to unique way of fructose absorption mechanism. It is important to understand the mechanism because restricting only fatty diets may not be effective in decreasing obesity without curbing on soft drinks. Fructose has a different mechanism of absorption from the gastrointestinal (GI) track than glucose. Fructose cannot stimulate the release of insulin from the pancreas like glucose does (Havel, 2002). Unlike fructose, which can enter muscle and other cells without the help of insulin, glucose requires insulin to do so (ibid). Once fructose is inside the cell, it can more efficiently provide the triglycerides than glucose by entering the glycerol pathways and increases the blood cholesterol and triglyceride levels (Havel, 2002; Mitra *et al*., 2007). Diet low in fat but high in carbohydrate inhibits the activity of enzymes which act as the gateway of fatty acid oxidation (Mitra *et al*., 2009). High carbohydrate intake actually inhibits the burning of excess fat (Mitra *et al*., 2007). High intake of fructose in the form of sucrose or corn syrup increases the risk of metabolic syndrome by elevated hepatic lipogenesis leading to dyslipidemia, hypertension and visceral adiposity (Holmboe-Ottesen and Wandel, 2012). Thus, rising consumption of soft drinks which contains fructose as carbohydrate due to the high-fructose corn syrup usage may be considered as a “fat equivalent” (Havel, 2002). This is why following extremely low-fat diets and continued consuming sweetened beverages do not result in the rapid weight loss that is anticipated (Mitra *et al*., 2007; Mitra *et al*., 2009). Moreover, sugar sweetened beverages fail to compensate as portion of total energy intake at subsequent meals; which means, obtaining energy from these beverages does not necessarily result in having less food in the subsequent meal (Schulze *et al*., 2004).

It is worth mentioning that such drinks are often termed as sugar sweetened beverages (SSB) and includes carbonated (fizzy) or non-carbonated (still) drinks (Mozaffarian, *et al*., 2011). They include not only soft drinks but other fruit drinks (except 100% fruit juice without added sweetener), ice tea, lemonade, powdered drinks with added sugar, and any other non-artificially sweetened drinks etc. In a meta-analysis conducted by Malik *et al*. (2010) showed a clear link between consumption of sugar sweetened beverages (SSB) and risk of metabolic syndrome. The same analysis showed that individuals who consume SSB often (1-2 servings/day) had higher relative risk (26%) of developing type 2 diabetes (Malik *et al*., 2010). A positive association was observed in between SSBs consumption and obesity when three prospective studies were reviewed with a total of 120,877 non-obese American adults who were followed for 20 years (Mozaffarian *et al*., 2011). In a cross-sectional study involving 5240 Mexican people aged 20 to 70 years, it was discovered that daily intake of more than two servings of sweetened beverages was linked to a two-fold increased risk of metabolic syndrome when compared with individuals not consuming sweetened beverages (Denova-Gutiérrez *et al*., 2010). Participants in the Framingham Heart Study who consumed one or more soft drink per day had a similar finding of a higher frequency of metabolic syndrome (Dhingra *et al*., 2007).

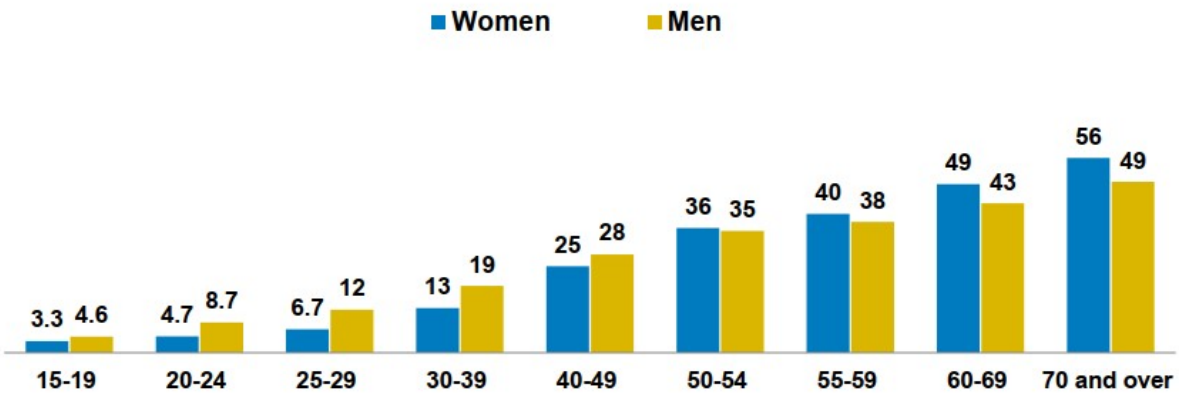
If we see the crop production pattern for last 70 years then it is quite evident that the production of sugarcane in India has risen steadily and exponentially. Gradual increases in rice and wheat production without much increase in nutri-cereals have supported the fact that there is shift in preference of cereal consumption. Interestingly the productions of nutri-cereals were more than the wheat production in between 1950 and 1970; and the whole paradigm of crop production changed from year 1990 onwards. India's opening of market in 1990s is an important factor for this shift and 'cash crops' like oilseeds, cotton, sugarcane etc. gradually started replacing the traditional crops. Globalization, India's opening of market compounded by change of food preference pushed cumulatively towards the nutrition transition.



Graph 4.2: Major crop production trend in India (Source: Directorate of Economics and Statistics, GoI; Department of Agriculture, Cooperation Farmers Welfare, GoI)

4.1.3.4 Salt consumption:

Salt consumption in excess of recommendation has been proved to be a major determinant in causing hypertension (an important component of metabolic syndrome). NFHS-5 (2019-20) has reported percentage of population with elevated blood pressure or taking medicines to control blood pressure at 30.2% (men) and 25.3% (women) in India. The same survey also reported that 39% (women) and 49% (men) aged fifteen years and above are pre-hypertensive. With age the prevalence of hypertension increases sharply but more worrisome is the increase in prevalence even in early age. NFHS-5 has reported an increase in prevalence of hypertension with increase in BMI.



Graph 4.3: Prevalence of hypertension by age (15 years and above) and sex (women and men) in India (Source: Adapted from NFHS-5)

Several population based studies conducted by ICMR, NSS, Chennai Urban Rural Epidemiology Study etc. at various times revealed the same finding that salt intake was far higher than the recommended amount of 5gm/person/day. A wide range of variation in salt consumption can be witnessed across states of India and between urban and rural population. The quantity of salt consumption is still high amongst these states and irrespective of rural-urban consumers (Arora *et al*., 2014). High contents of not only fat and sugar are reported from confectionery, packaged and processed food but also of salt. Market study shows that bulk purchase of 50-60% of total salt is carried out by processed food industries (Arora *et al*., 2014). Increase in consumption of packaged and processed food is taking place in every household and across all social strata in India (Dasgupta *et al*., 2015).

4.1.4 Impact of globalization and urbanization:

Globalization in simple terms means bringing the domestic economy closer to the international economy and is a consequence of liberalization (Vepa, 2010). We are all aware that dietary patterns, eating practises, and cooking techniques vary across India. Urbanization and migration cause a quick shift in the conventional dietary pattern, leading to a rise in the intake of "modern" foods (Mitra *et al*., 2009). In developing countries like India dietary shifting is occurring due to consumption of more fat, animal source food, and added caloric sweeteners (Popkin, 2003). Ageing populations and rapid income growth are two other significant factors that will continue to influence food consumption habits globally, according to Schmidhuber

and Shetty (2005). The gradual change in age pyramid changes the population composition where there is declining trend of young population and increase in ageing population. In such a scenario the major portion of total population will be economically active and engaged in income generation which is going to be spent on fewer numbers of children. What other developing countries can experience in future can be seen already in urban China. A booming economy and the strict one-child policy that has been in place for the last few decades have led to a situation where majority of family's income is spent on sole child. The condition is known as the "4:2:1 problem," in which the family's lone child receives a great deal of attention from 4 grandparents and 2 parents, especially when it comes to feeding, which has caused the incidence of overweight and obesity to rise sharply (Schmidhuber and Shetty, 2005). Hence a rapid nutrition transition can be expected after 2030 due to changes in the population dynamics (ageing), high income growth, and faster urbanization of developing countries (ibid). A scientific understanding is still limited in knowing the relationship between urbanization and food consumption (Pandey *et al*., 2020).

In recent few decades the energy intakes offered to people have increased due to an increase portion of food in per day plate because of frequent eat out culture. Fast food is one of the important dietary factors in causing obesity epidemic, which can be defined as convenience food (Pereira *et al*., 2005). Urbanization paved way for fast food industry because people started eating outside the home more frequently. Since eating out has turned to a normal habit, energy intake level from fast food has increased compared to energy expenditure in the body (Hensrud, 2004). A significant habit of eating outside the home has been witnessed since 80s (Finkelstein *et al*., 2005). Southern California in the 1940s may have been where the fast food industry's history began (Chitnis, 2019). The fast food industry has catered to the time constraints and sometimes to the budgetary constraints of consumers by giving quick access to affordable food, takeout, or even doorstep delivery services (Schmidhuber and Shetty, 2005). From 1 per 2000 Americans in 1980 to 1 per 1000 Americans in the year 2005, fast food establishments have risen significantly (Finkelstein *et al*., 2005). Fast food market in India had been projected at worth US$ 27.57 billion by 2020 (Anitharaj, 2018; Chitnis, 2019). Since only 10% of the Indian fast food sector is known to be organized, the actual market size may be far higher than what has been

estimated (Anitharaj, 2018). Survey says that Indian fast food industry is growing by 40% every year (Chitnis, 2019). FICCI PwC report states that Indian food service industry had total revenues of INR 337,500 crores in 2017 representing a CAGR (compound annual growth rate) of 8%. The same is projected to be INR 552,000 crores in 2022 representing a CAGR of 10%. This rate of growth is way ahead in comparison to some other neighbouring Asian fast food industries like South Korea and China which grew at CAGRs of 3.6% and 6.1% respectively over the same period in 2017 (FICCI PwC, 2018). Major global fast food players are changing the dynamics of the fast food industry in India. Following data of such major players will give an idea on how fast the industry is growing:

- Mc Donald's- targeted of opening 500 outlets in India by 2020.
- Dominos- in 2008 there were only 227 outlets but by 2017 it rose to 1126.
- Pizza Hut- around 700 outlets were planned by 2020.(Chitnis, 2019)

Though fast food culture has been presumed to be an urban phenomenon but gradually rural populations are also getting attracted to it. How much fast food culture has affected the rural life is an interesting topic of study because it is an ongoing process for India currently. A study conducted in rural Himachal Pradesh involving 425 children (12-18 years of age) studying in 30 government schools found high prevalence of (36%) of junk food consumption in last 24 hours (Gupta *et al*., 2018). The study also revealed that chips were the most commonly consumed item (71%) amongst all the junk foods by school aged children.

Studies suggest a positive correlation between the more frequent fast-food consumption and weight gain/overweight/obesity in adults and adolescents (Popkin, 2010). Due to a surge in fast food consumption by youngsters in USA, the energy contribution of fast food to the country's total energy consumption climbed from 2 percent in the late 1970s to 10 percent in the 1990s (Pereira *et al*., 2005). According to the Coronary Artery Risk Development in Young Adults (CARDIA) study, both young people of colour and those of white race acquire weight more frequently when they eat fast food. Increases in body weight and insulin resistance are strongly correlated with frequent trips to fast-food establishments as found in this multi-centric population-based prospective study of black and white men and women living in the

USA between 1985–1986 and 2000–2001 (Pereira *et al*., 2005). Prices for food items have a significant impact on our consumption patterns (Bray, 2007). It has been observed that the price of foods that are energy dense (rich in fat and sugar) has decreased since the beginning of the 1970s as compared to other food items. Since the early 1980s, the relative costs of foods heavy in sugar and fat have dropped when compared to fruits and vegetables (Bray, 2007). Fresh fruits and vegetables, seafood, and dairy all had price increases between 1985 and 2000 of 118%, 77%, and 56% respectively. In contrast, sugar and sweets saw a price increase of 46%, fats and oils saw a price increase of 35%, and carbonated drinks saw a price increase of only 20% (Finkelstein *et al*., 2005). Price determines the purchasing behavior of human beings and hence influences the selection of food item or even any other item. The likelihood of buying an item or food item depends on the lesser product cost and vice versa (Finkelstein *et al*., 2005). Therefore, the rise in the obesity pandemic is significantly influenced by food prices (ibid). Customers in developing countries are now more able to adopt food consumption habits that were previously only possible for consumers in wealthy countries due to the relative price drop of some energy-dense goods (Schmidhuber and Shetty, 2005). Instead of farmers or nutritionists, food manufacturers and retailers are the ones who shape the food environment around us (Finkelstein *et al*., 2005). Once this environment is set and the demand supply chain is established then the crop selection by the farmers are also influenced.

Metabolic syndrome in relation to nutrition has been poorly studied among south Asians including Indian (Katulanda *et al*., 2012). However it is quite obvious that the entire process of nutrition transition in India has started occurring through already discussed three stages. First stage saw customers switch from traditional staples to foods that were more common in "westernized" diets as famine conditions subsided (Misra *et al*., 2011). People are consuming more wheat such as bread, cakes, and cookies than other conventional foods, demonstrating how the world has changed (ibid). Cereals, pulses, fruits, and other low-fat foods are gradually being replaced by meat products and other high-fat foods (Law *et al*., 2020). As Indians are becoming more affluent, both rural and urban areas witnessed increased consumption of animal foods (Misra *et al*., 2011). Cross sectional analysis of 773 subjects from Adventis Health Study 2 showed that vegetarians (25.2%) have lowest association of metabolic

syndrome compared to non-vegetarians (39.7%) (Rizzo *et al*., 2011). In second stage, globalization showed its pronounced mark by influencing the consumers to had easy access to the varieties of fast or convenience foods which were processed, ready-to-eat, deep-fried, salted, sugared, spiced, and with added preservatives. In urban India, the consumption of biscuits, salted snacks, sweets, edible oils, and sugar grew throughout the 20-year period 1993–2005. (Misra *et al*., 2011). Currently, most Indians are in stage two of the nutrition transition (ibid). The nutrition transition coupled with sedentary lifestyles escalates the magnitude of metabolic syndrome (Schmidhuber and Shetty, 2005; Misra *et al*., 2011). In third stage, people belonging to the high socioeconomic class with good economic resources tend to realize the adversities associated with wrong eating habits. They try to adapt a healthy lifestyle by eating costly healthy foods and also by doing workouts in exercise facilities like gymnasium or by procuring expensive equipments at home (Misra *et al*., 2011). There is evidence that eating a lot of fruits and vegetables lowers the chance of developing metabolic syndrome. A nationwide study showed that dietary intake of fats and sugars was positively associated with overweight, and inversely associated with the intake of fruits and vegetables (ibid).

Decreased cereal intake was evident from NSSO data for past two decades (1993-2005) in both urban and rural population. However the quantity of total cereal intake was less in urban areas compared to the rural during this period (Misra *et al*., 2011). Though it has been presumed that the nutrition transition is a phenomenon affecting urban population, but changes are visible in rural set up also. A comprehensive public policy has been put in place by the government through the 2013 National Food Security Act (NFSA), to enable action to ensure that the most vulnerable and people living in poverty have access to enough food (Law *et al*., 2020). As a safety-net programme for food, the Public Distribution System (PDS) was created to offer low-income households necessities like rice and wheat at regulated, below-market prices (ibid). The marginalized has some assurance of not staying hungry due to economic constrains. In addition, government schemes like Integrated Child Development Scheme (ICDS) and the Mid-Day Meal Scheme (MDMS) have made the access to food easier. Despite a comprehensive set of government initiatives to offer food grains to the weaker section, an unusual variation in eating culture has been observed in the Indian context (Law *et al*., 2020). According to the calorie consumption pattern

in the table below, cereal consumption in India has experienced the greatest decline of any food group. Income growth and cheaper cereal prices would have increased the consumption of cereals in rural and urban households but in reality it is the opposite (ibid). The pattern reveals that Indian households are gradually replacing cheap cereals (such as coarse grains) with expensive ones (i.e. rice and wheat).

	Urban Sector				Rural Sector			
	1987-88	1993-94	2004-05	2011-12	1987-88	1993-94	2004-05	2011-12
Cereals	1323	1220	1225	1182	1684	1501	1426	1336
Egg/Fish/Meat	43	45	42	44	32	32	35	35
Edible Oil	190	191	202	237	114	127	160	199
Pulses	124	110	99	109	107	96	88	98
Vegetables & Fruits	133	134	126	121	101	112	114	108
Other Food	354	365	316	342	268	287	272	294

Table 4.2: Change in per capita calorie consumption per day from type of food consumed in India (Source: Adapted from Law *et al*., 2020)

Now let's look at the NSS data of various rounds to see whether similar observations can be reached. It is of no doubt that percentage of calorie derived from cereals has decreased over time in both rural and urban areas. Portion of vegetables and fruits have also been decreasing in food plate for both areas. On the contrary calorie contribution from pulses, nuts, oil seeds, meat, egg, fish, milk and milk products have slightly increased. There is significant increase in calorie contribution from oils, fats, and miscellaneous food products. Overall calorie consumption has decreased in both areas drastically. One interesting finding is that the amount of protein consumed has decreased though percentages of calorie contribution by various protein food groups have increased (Table 4.3). Significant increase in calorie contribution by miscellaneous food products may indicate towards consumption of "modern food items" or packaged food products or non-home cooked energy dense foods. This area needs more in depth studies in next rounds of NSS.

Indians may have acquired a dietary culture that differs from their long-standing traditional culture as a result of the effects of globalization and economic prosperity (Law *et al*., 2020). Since cereals are becoming less popular over time, income growth

		Percentage of calorie from different food groups									Average intake per diem per consumer unit		
Rural/ Urban	Year	Cereals	Roots & Tubers	Sugar & Honey	Pulses, Nuts & Oil seeds	Vegetables & Fruits	Meat, Egg & Fish	Milk & Milk products	Oils & Fats	Misc. food products	Calorie (Kcal)	Protein (gm)	Fat (gm)
Rural	1993-94	71.03	2.65	4.8	4.92	2.02	0.68	6.15	5.34	2.41	2683	75	39.1
	1999-2000	67.55	3.25	5.14	5.46	1.97	0.77	6.17	7.37	2.32	2668	73.4	44.9
	2011-12	61.1	3.01	4.9	5.2	1.85	0.82	7.07	9.01	7.04	2233	56.5	41.6
Urban	1993-94	58.53	2.54	6.21	6.05	3.26	1.02	8	8.79	5.6	2542	70.2	51.6
	1999-2000	55.05	2.9	6.15	6.86	2.94	1.12	8.23	11.24	5.52	2637	71.5	60.7
	2011-12	51.64	2.73	5.62	6.41	2.62	1.13	9.07	12.17	8.61	2206	55.7	52.5

Table 4.3: Trend of calorie contribution by food groups, protein, and fat on per diem basis (Source: NSS rounds 50th, 55th, and 68th)

and falling cereal prices haven't improved demand. The less favoured cereals in Indian households are a good example of changing food preferences in nutrition transition and its impact on health aspect (ibid). In rural set up calorie consumption is proportionate to the land holding size which means more the hectares of land in possession higher is the calorie intake (Siddiqui *et al*., 2019). The land reforms in India had made it possible for the rural sub section population to possess a piece of land for cultivation. Another important finding is that the households which get the subsidized food items through PDS system consume more calories than those households which are unable to access the PDS (ibid). How education influences the food diversity is an important aspect that needs to be studied upon extensively. Increasing education level decreases the total calorie consumption, but the contribution of calories from fat rises significantly (Siddiqui *et al*., 2019). In India, where the transition to a more nutritious diet is taking place, consumption of fat calories has gradually increased among both the rural population and the poorer urban households (ibid). The burden of overweight and prevalence of non-communicable diseases or metabolic disorders were initially concentrated in the high socio-economic group. However, with transition, the burden begins to shift to the lower socio-economic group as well and how much education plays the role of positive association for these groups need some detailed study (ibid).

In a recent study by Pandey *et al*. (2020) negated the concept of looking urbanization only as demographic process. By ignoring the economic, social, and cultural changes we may not be able to understand the process of urbanization. The

study emphasizes income growth along with urbanization as an important determinant in change in food consumption pattern. It is a known fact that disparities in income ultimately influence the health outcome (Shetty, 2002). Increase in purchasing power as prime factor coupled with other factors like food availability, food storage, change in food taste and preference etc. helped in nutrition transition (Vepa, 2010; Pandey *et al*., 2020).

Breakfast consumption has been linked to decreased body weight, according to Bray G.A. This is an important finding amidst the present lifestyle pattern in urban population. Late night work or different work shift pattern has made a section of the working class to rise late from bed and hence compels to skip the breakfast regularly. The hurriedness of employees to reach workplace on time or due to early morning school for children made them to skip the breakfast regularly or having it inadequately by taking some quick bites. Regular morning cereal consumption has been demonstrated to reduce BMI in adolescent females (Bray, 2007). Moreover, eating breakfast is associated with increase in eating frequently and decreases the gap between the meals. Breakfast has been considered as the most important meal of the day and has obvious health benefits.

There are differences between “fast food” and “junk food” though they are used interchangeably. All fast food may not be junk food (Keshari and Mishra, 2016). As per National Institute of Nutrition (NIN), Hyderabad “unhealthy or junk foods are those containing little or no proteins, vitamins, or minerals but are rich in salt, sugar and fats and are high in energy (calories).” Most of the processed or packed foods have unhealthy trans-fatty acids and additives (Keshari and Mishra, 2016). According to NIN, trans-fats should make up no more than 2% of total calories whereas WHO recommends it at 1%; but in reality Indian fast food contains high content of trans-fats (Johanson *et al*., 2012). Fast food eating culture in restaurants or any other eateries have changed the composition of food consumed. There are studies, as mentioned already, which drew attention on the consumption of calorically sweetened beverages and direct association with the epidemic of overweight. In USA it has been observed that more food consumption away from home leads to important dietary-behaviour shifts (Popkin, 2010).

A prospective birth cohort study of 568 Indian children revealed that a later introduction to regular solid meals and a longer breastfeeding duration are linked to a lower risk of increasing adiposity and a high BMI at age five (Caleyachetty *et al*., 2013). This is very relevant finding considering present scenario where women have to step out from home to the join the work force and not getting sufficient time to breastfeed her baby. The replacement of considerable portions of breastfeed with solid feed has increased adiposity in later life.

Low fiber content in diet due to various reasons and trivalent chromium deficiency has been considered as important nutritional etiological factors in causing diabetes (Keen *et al*., 1979).

4.1.5 Impact of migration:

Migrations in any form, whether within the nation or outside the nation, have its impact on change of food habits. Migrants are found to adopt the diet, lifestyle and socio-cultural practices (i.e. environmental factors) of the indigenous population and hence results in acquisition of disease pattern of the native population (Shetty, 2002). The health of immigrants are affected by nutrition transition (a global phenomenon) and dietary assimilation in new habitat (Holmboe-Ottesen and Wandel, 2012). When individuals of a minority group adopt the eating patterns of the dominant host community, this process is known as dietary assimilation (Satia-Abouta *et al*., 2002). This process of assimilation has been explained by various researchers by various models. Satia-Abouta *et al*. (2002) proposed that the host culture gets expose to the socio-economic and cultural factors of the immigrants. With time the host starts to influence the minor migrant group and changes occur in psychological factors, food preference, taste etc. leading to dietary deviations. Another model proposed by Kockturk-Runefors (1991) divided food into three categories: (a) ‘Staple foods’ like grains and tubers with high carbohydrate content (b) ‘Complementary foods’, which include items like meat, fish, eggs, milk, vegetables, etc. (c) ‘Accessory foods’, which include fats, oils, seasonings, desserts, nuts, etc. The model proposed that staple foods are more tightly attached to the cultural identity of a group than the other two categories of food and hence resist changes till end. The first category to go for change is the accessory foods because they are more driven by taste factor rather than

cultural identity. Since this category of food affects the health most, hence have important implications on migrant population. There are very few studies which compare the dietary changes of migrants with the similar non-migrant group from same place of origin.

How migration affected the health can be well witnessed in examples of South Asian migrants to United Kingdom. South Asian immigrants from the Indian subcontinent to the United Kingdom were found to have a higher relative risk of obesity, NIDDM, and coronary heart disease (CHD) than the local European population (McKeigue, 1997; Holmboe-Ottesen and Wandel, 2012). Evidence suggests that South Asian immigrants living in the US have metabolic syndrome twice as often as the country's native Caucasian population (Katulanda *et al*., 2012). Studies on South Asian immigrants who reside in other industrialized nations have discovered greater prevalence of metabolic syndrome and insulin resistance (ibid). The prevalence of diabetes among South Asians has been estimated to be five times higher than the native British population (Gholap *et al*., 2011). The prevalence of coronary artery disease in South Asian immigrants was three times higher than native population in developed counties (Katulanda *et al*., 2012). The mortality rate from diabetes has also been found to be on higher side in migrants who are natives of South Asia (Hadewijch *et al*., 2012).

Available studies on migrants have witnessed a gradual change in diet consumption in all the above three categories of food. According to a study conducted in Oslo, Norway, a significant number of immigrants from Pakistan and Sri Lanka consumed more meat and dairy products while eating fewer beans and lentils (Wandel *et al*., 2008). Majority in the above study group reported to consume more fat after migration (ibid). A Birmingham study revealed that South Asians prefer deep fried cuisine and consume more dairy items like butter, *ghee*, and full-fat milk than native Europeans do (Lip *et al*., 1995). To add more misery to the problem South Asian immigrants are found to consume more sugar-sweetened soft drinks (Malik *et al*., 2010). Extra energy ingested in the form of sugary drinks leads to rapid rise in blood glucose and insulin, which if taken frequently leads to glucose intolerance and insulin resistance (Holmboe-Ottesen and Wandel, 2012). A study on migrants from Ghana to Sydney known as Ghanaian Health and Nutrition analysis in Sydney,

Australia (GHANAISA) looked into the dietary changes and subsequent type 2 diabetes and obesity. The migrants were found to be suffering from high rate of metabolic disorder in western environment (Saleh *et al*., 2002) like the Indian migrants who shifted to United Kingdom. Migration changed the traditional food habit of these ethnic Ghanaians. Upon migration to Australia dietary changes like tropical root crops replaced by potato starch, fish being replaced by cheaper poultry and beef, decrease consumption of fruits etc. lead to increase consumption of saturated fat and decrease intake of helpful w-3 poly-unsaturated fat (Saleh *et al*., 2002). Migrants who migrate to high income countries witness increase in consumption of meat and reduction in intake of pulses (Holmboe-Ottesen and Wandel, 2012).

We can hypothesize that the trend of Western diet consumption is higher in urban natives and migrant groups (Bansal *et al*., 2010). The Indian Migration Study (IMS) was conducted on factory workers of Bangalore, Lucknow, Nagpur, and Hyderabad by making three distinctive groups for comparison- rural, rural to urban migrant, and urban. Again as per age group the young generations are fonder of Western food than aged group (ibid). Different pattern of occupational engagement in urban set up can be a reason behind in not getting enough time to cook the traditional food of choice. The Cardiovascular Disease Risk Factor Study (CVDRFS) in the same four Indian cities included non-migrant rural siblings of migrant urban factory employees and non-migrant urban siblings of migrant factory workers, revealed a higher prevalence of diabetes in urban migrants (12.5%) than in rural non-migrant siblings (4.5%) (Lyngdoh *et al*., 2006).

4.2 Under nutrition:

The link between chronic diseases in later life and under nutrition caused by a lack of macro- and micronutrients throughout prenatal and neonatal life appears to be a difficult and inconclusive issue (Misra *et al*., 2011). The timings and types of deficiency are crucial in determining the after effect at adult life. Several hypotheses have been proposed and even later criticized on developmental origin of adult diseases. The concepts of ‘thrifty gene’ and ‘thrifty phenotype’ were considered to be

the most promising explanations of insulin resistance at one era but were later discouraged with severe criticism.

4.2.1 Thrifty genotype and thrifty phenotype hypothesis:

Neel in 1962 hypothesized the 'thrifty genotype' concept to explain the prevalence of insulin resistance when population shifts from nutritional deprivation to abundance leading to obesity. Such genotype has been showcased in having survival advantage in chronic starvation period like the famines of South Asia or India (Forouhi, 2005). This survival was possible due to the capacity of the body to store extra energy and utilized it during the famines and food shortage. "Thrifty" gene hypothesized to aid in fat accumulation when calories are more readily available and later allowed reutilization during hunger (Baig, 2011). So these adverse conditions had been proposed in Neel orthodox hypothesis as the major force in shaping the genetic make-up for obesity and the metabolic syndrome (Speakman, 2006). It has been hypothesized that obese and overweight individuals have thrifty gene. This genetic predisposition has been thought to play a major role in accumulating fat as individuals differ substantially and there are evidences of strong familial tendencies (Baig *et al*., 2011). Even after 40 years or so since Neel proposed the thrifty gene hypothesis, no convincing gene candidate to support this hypothesis has been discovered. This hypothesis had been challenged later and more importance was given to gene-environment interaction (Speakman, 2006). The China Health And Retirement Longitudinal Study (CHARLS) in 2011 with 7262 participants observed the association between famine exposure during fetal period and childhood, and higher risk of hyperglycemia in adult females (SUN *et al*., 2018). The risk of metabolic syndrome was stronger with rural females who lived in rural areas of China, especially during gestation or early childhood (before 16 years of age), during the great famine (from the late 1950s to early 1960s) (Barouki *et al*., 2012; SUN *et al*., 2018). Long duration of famine and son preference while deciding on resource allocation might have deprived the daughters in receiving the same food and care. This had a lasting effect on health of female survivors which was observed in the study (SUN *et al*., 2018).

'Thrifty phenotype' hypothesis evolved due to the challenges faced by thrifty genotype hypothesis. It was proposed by Barker which stressed on the thriftiness aroused from the environmental conditions of the womb during development rather than genetic thriftiness. Poor nutrition during pregnancy has a negative impact on foetal growth, which leads to the development of metabolic syndrome as a result of long-lasting abnormalities in glucose and insulin metabolism (Webber, 2009). Such *in utero* environment has been presumed to 'programme' the susceptibility of later development of metabolic disease in the foetus (Armitage *et al*., 2004). The thrifty phenotype hypothesis attempts to explain the association between low birth weight and future development of metabolic disorders. It has been hypothesised that low birth weight leads to high prevalence of metabolic syndrome (hypertension, diabetes, CHD and insulin resistance etc.) in later life (Misra, 2003 and Das, 2005). Low birth weight babies have 10 times more chance of developing metabolic syndrome than babies with normal birth weights when they gain excess adiposity in early childhood (Das, 2005). Low birth weight babies indicate poor nutrition *in utero* and hence it has been speculated that as an adaptation mechanism the body starts storing body fats in an accelerated manner (Misra *et al*., 2011). This process is presumed to be programmed and hence carried forward to future generations. Barker has hypothesized that human body can be programmed by under nutrition (Barker, 1997). Fetal programming was developed as a result of the higher occurrence of metabolic syndrome or obesity in adults who were born with low birth weight or small for gestational age (Barker *et al*., 1990; Armitage *et al*., 2004; Baig *et al*., 2011). According to data, humans did not experience chronic starvation throughout the hunter-gatherer era, but with the advent of agriculture the issue of chronic starvation brought on by famines became more prevalent and significant (Baig *et al*., 2011). At that age it was quite obvious that crops were highly seasonal and weather dependent in nature and hence failure of even a single crop led to long-term food scarcity (ibid). Baig *et al*. (2011) argued that if we have to support the 'thrifty' hypothesis then people who had changed to agriculture should have developed obesity earlier. Similarly some ethnic groups from geographies with harsh winters should have increased frequency of obesity but actually it was opposite. Even groups like Australian aborigines who had given up hunter-gathering very recently developed high prevalence of diabetes and hypertension only after adapting to modern lifestyle. Since the ideas of a thrifty gene and a thrifty phenotype caused by foetal

programming are both flawed in various ways, alternative hypotheses have emerged in their place (Baig *et al*., 2011).

4.2.2 Developmental Origins of Health and Disease:

Instead of programming it is postulated that particular stages of fetal development are critical and if they are not properly followed through then the damage caused may be irremediable and there will be irreversible changes in the course of development (Susser and Stein, 1994). In the early stages of development when cells are differentiating and tissues are growing, development is malleable; therefore it enables the living creature to respond to the environment (Barouki *et al*., 2012). As a result, the initial theory that adult disease has a foetal base has been replaced by one that emphasizes the disease's developmental roots. The phrase has recently been changed to Developmental Origins of Health and Disease (DOHaD) (Barouki *et al*., 2012). In developing countries like India *in utero* or early-life adverse events caused by poor nutrition alters body composition and insulin resistance (Misra, 2003). The secretion and sensitivity to hormones like insulin and insulin like growth factors that promote foetal growth is reduced (Fall, 2013). The possible adverse contributory factors may damage tissues during development stage such as pancreatic β-cells, vascular endothelium and renal tubules (Misra, 2003). These damaged tissues may alter insulin secretion, endothelial dysfunction and can cause microalbuminuria respectively. The sensitivity of a tissue or system to adverse condition depends on whether it is fully developed or not (Barouki *et al*., 2012). Each tissue has different window period of sensitivity and hence the most sensitive period may vary from early childhood to puberty or even beyond for some tissues like brain and the reproductive system (ibid). This is crucial as extent of tissue plasticity affected can determine the future course of disease outcome. All cells of the body do not rely on insulin to take up nutrients, thus when insulin resistance arises, the uptake of nutrients by tissues that do depend on insulin is reduced. Consequently, tissues that are insulin independent, like the brain, have access to more nutrients than muscles that are insulin dependent (Baig *et al*., 2011). Putting it simply, insulin resistance leads to higher brain investment and decreased nutrient investment in the muscles (ibid). Lean tissues suffer from attrition due to such disinvestment or due to protein malnutrition (Misra *et al*., 2011). Similar to this, when the mother's nourishment is inadequate, the foetus sacrifices visceral

organs like the pancreas and liver in order to reroute the scarce resources to vital organs like the brain (Armitage *et al*., 2004). In order to control its growth and give priority to the development of vital tissues that need to mature more quickly, the foetus must adjust to the mother's poor nutrition (Fall, 2013). There is a reduction in blood/nutrient supply to the lower limbs of the body so that brain blood flow is preserved, and this ultimately sacrifices the muscle deposition and development of other vital organs like liver, pancreas and kidneys (ibid). There are evidences which support that maternal nutrition imbalance can induce the elements of metabolic syndrome in the offspring (Armitage *et al*., 2004). Lower birth weight is no longer thought to be a sole cause of later disease; rather, early-life restructuring of the body's tissues and realignment of the endocrine and metabolic axes brought on by a variety of adversities are given greater weight-age (Fall, 2013). Numerous animal studies demonstrate that prenatal malnutrition alters the way that insulin reacts to the metabolism of glucose and cholesterol as well as a number of other metabolic, endocrine, and immunological processes that are crucial from the perspective of human disease (Lucas, 1991). Studies on lamb have shown that when 50% nutritional restriction is implemented during the first half of pregnancy, followed by nutrient restoration there is no reduction in neonatal weight but causes development deviations of organs (liver and heart) at birth; which may be crucial as determinant for later development of the metabolic syndrome (Vonnahme *et al*., 2003). When mothers were under-feed from early to mid-gestation, the lambs exhibited increased birth weight gain and postnatal adiposity (Pillai *et al*., 2017). Similarly, maternal obesity has the possibility of increased fat accumulation in adult offspring (ibid). Other studies in animals appeared to produce features of metabolic syndrome when there was maternal dietary imbalance (Armitage *et al*., 2004). In rats, over-feeding during gestation found to alter development and functions of kidney in offspring (Pillai *et al*., 2017). Diet challenged pregnancies are observed to give impaired vascular endothelial cell dilatation in offspring and it appears to be one of the strongest phenotypes (Armitage *et al*., 2004).

4.2.3 Interplay of genes and environment:

As was already mentioned, there is no evidence of alleles that cause obesity or that can support the rate at which the obesity epidemic is spreading, suggesting that

genetics alone cannot explain this phenomenon (Baig *et al*., 2011). Gene-environment interplay is the most convincing perception. Environment in the form of poor nutrition or other adverse conditions *in utero* can cause epigenetic modifications which can pass on to next cell generation and even can be trans-generationally transmitted if germ cells are targeted (Barouki *et al*., 2012). DNA methylation, histone covalent modification, and non-coding RNA production are among the routes that have so far been identified (ibid). Hormones, cytokines, and dietary components can directly activate or inhibit receptors that cause gene expression by activating the relevant enzymes and pathways that regulate DNA methylation, non-coding RNAs, etc (ibid).

There are historical evidences of wartime Dutch famine during 1944-1945 on the offspring. The individuals had malnutrition whose mothers were exposed to that famine (Barouki *et al*., 2012). Interestingly the study was conducted more than 20 years after the famine had occurred to measure the severity of that exposure and also to study the several outcomes due to such exposure (Susser and Stein, 1994). In comparison to women exposed before or after the famine, it was found that those exposed during early pregnancy had a higher risk of producing children who would develop metabolic syndrome later in life (Barouki *et al*., 2012). The women exposed to Dutch Famine during the third trimester of gestation witnessed low birth weight babies and this pointed towards growth retardation as the underlying cause (Susser and Stein, 1994). Since the average daily calorie intake during the Dutch Famine was limited to 1680-3360 KJ, the timing of exposure during the gestation period was observed to be a significant factor in driving towards different outcomes (Armitage *et al*., 2004). To support this observation the study stated that increased adult obesity and glucose intolerance was associated with the famine exposure during late gestation while the same could result in hypertension if exposure occurred in the early phase of gestation (ibid). The underlying cause may be due to deranged hypothalamic function or can be due to rapid maternal weight gain in late pregnancy (Susser and Stein, 1994). However it is more likely that both these factors actually act together. Several types of genes associated in growth and metabolic regulation had varied levels of methylation, according to epigenetic research of people who were alive 60 years after the famine (Barouki *et al*., 2012). In more recent cohorts of people who had been exposed to the 1968–1970 Nigerian civil war famine in pregnancy and during

infancy, an increased risk of obesity, impaired glucose tolerance, and hypertension had been identified roughly 40 years later (Barouki *et al*., 2012).

4.2.4 Evidences supporting under nutrition as determinant of metabolic syndrome:

Poor nutrition exposure during gestation period is undoubtedly an important determinant. Along with timing of poor nutrition exposure, the type of diet consumed during gestational period is equally important. It has been correlated that the adequate consumption of maternal carbohydrate during the first trimester of pregnancy minimizes the gene methylation levels (Barouki *et al*., 2012). At the age of 6 to 9 years, methylation levels are linked to a child's adiposity (ibid). Maternal diet deficient in protein has its long term effect on the future progeny. Animal studies have shown impaired pancreatic β-cell function and increased blood pressure in later life for having exposure to intrauterine protein deficiency (Stanner *et al*., 1997). Women with high intake of carbohydrate but with protein deprivation during pregnancy leads to pronounced effect on the development of offspring, a situation likely to be more prevalent in malnourished populations of developing countries like India (ibid). Research has also been done on how iron affects the development of young rats. These investigations have shown that, despite being raised on a regular diet and having been exposed to maternal iron deficiency, the offspring of rats do show developmental programming of various elements of the metabolic syndrome (Armitage *et al*., 2004). Given that maternal anemia is common everywhere, regardless of social position or food supply, this model of iron deficiency is applicable to the majority of the world's population (ibid). Interestingly, rat models with iron restriction showed restricted growth at early age but no catch-up growth was witnessed in later phase despite providing them with better diet (ibid). These data might be sufficient to support the hypothesis that growth retardation affects the development and vascularisation of important organs at various stages of foetal development, resulting in reduced organ function and subsequent disease states in later life (Stanner *et al*., 1994). Studies on the effects of calorie, protein, and iron limitation as well as fat-feeding on the mother's diet have shown that some metabolic syndrome traits are programmed into the offspring (Armitage *et al*., 2004). This demonstrates the need of a balanced maternal diet for the health of the unborn child, but also how difficult it can be to achieve.

The siege of Leningrad (where caloric intake was reduced) failed to show any relation between birth weights and adult glucose homeostasis. Between September 8th, 1941, and January 27th, 1944, Leningrad was under siege by the Germans, who cut off supplies for the city, which is now known as St. Petersburg. In between 0.75 million to 1 million people out of total 2.4 million population died mostly from starvation (Stanner *et al*., 1994). Most of these deaths occurred during November 1941 to February 1942, known as the "hunger winter", when the siege was in full force. The city inhabitants were provided with only 250 g of bread for workers and 125 g for others (ibid). The average calorie intake was only around 300 calories for most of the citizens from the daily ration provided during this time and contained virtually no protein (Stanner *et al*., 1994). The situation improved with restoration of food supply when Lake Ladoga froze sufficiently in April/May 1942 to allow supplies to be transported across. Later, the subjects who had been subjected to the siege *in utero* showed a higher correlation between obesity and blood pressure (ibid).

The association between birth weight and disease risk in the future has been found to be U-shaped as per the analysis of the early epidemiological data (Barouki *et al*., 2012). Studies conducted in livestock species show reduced growth rates, reduced muscle fibre size, and increase in adiposity of offspring if there is either under-feeding or over-feeding during the gestation period (Pillai *et al*., 2017). Maternal markers such as obesity in the mother, rapid weight growth during pregnancy and gestational diabetes (GDM) can be used to detect foetal over nutrition. There is currently sufficient epidemiological data based on these markers to demonstrate that foetal over nutrition can result in offspring with phenotypes comparable to foetal under nutrition (Barouki *et al*., 2012). Both restricted and over feed maternal diet during early gestation can differentially modify the organogenesis of liver and kidneys leading to altered functioning (Pillai *et al*., 2017). Unaltered organ and tissue growth during foetal development is essential as well as crucial for optimal health and growth during postnatal life. In western countries, almost half of all expecting mothers are now estimated to be overweight, while in Asian nations, the prevalence of GDM has increased by up to 20%. (Barouki *et al*., 2012). Numerous studies have shown a connection between maternal obesity during pregnancy and the subsequent development of obesity and metabolic syndrome in children (Fall, 2013).

There are other important underlying causes of foetal under nutrition like rigorous physical labour before and during pregnancy and insufficient foetal supply most commonly caused by placental dysfunction (Barouki *et al*., 2012). Excessive workload before and during pregnancy is a very common situation in Indian context especially for the marginalized community. On the other hand, it was discovered that the placental weight was substantially correlated with both systolic and diastolic blood pressure viz-a-viz its function. Studies by Barker *et al*. (1990) found that by combining the placental weight and corresponding birth weight, predictions can be done on blood pressure and risk of hypertension among men and women aged around 50 years. In other words, highest blood pressure and risk of hypertension were found in case of small babies born with large placentas (Barker *et al*., 1990). We can emphasize that metabolic syndrome may be 'developmentally programmed' in adult offspring depending on placental insufficiency or because it was exposed to poor maternal nutrition *in utero* (Armitage *et al*., 2004).

Children who were born underweight and who did not obtain the recommended number of daily supplements during infancy and childhood had a higher chance of developing insulin resistance when they reached adolescence (Misra *et al*., 2011). Similar conclusions were drawn by Ashworth (1969) and Fjeld *et al*. (1989), where increased body fat accumulation had been witnessed in proportion to total weight gain as a result of nutritional rehabilitation of malnourished children (Schmidhuber and Shetty, 2005). This finding has important relevance in Indian scenario with respect to two nutrition rehabilitation program for children namely "Nutritional rehabilitation Centers (NRC)" for severely malnourished children and "Mid-day meal" for school children. India's current midday meal program, which provides pupils from disadvantaged socioeconomic backgrounds with free meals, needs to be closely monitored, and these kids should also be followed up, as there is evidence that these program are contributing to rising trends in obesity rates (Misra *et al*., 2011). The smallest newborns in the world are born in India, where almost one third have low birth weights (birth weights <2500 g). Some argue that the sole cause of diabetes and CHD epidemic in India is due to fetal under nutrition. If that is the case then heavier urban Indian babies (better nourished, mean weight 2900 g) would be expected to have lower rates of diabetes and CHD as compared to rural babies (mean weight 2650 g**)** (Yajnik, 2001). However, in actual diabetes and CHD are found to be 4-5 times

more common in urban than in rural India (Yajnik, 2001). Although fetal under nutrition is important, but postnatal nutrition and environment is equally important for the outcome. Hence disease manifestation depends on the considerable difference in the postnatal nutrient environment in comparison to what it had experienced *in utero* (Armitage *et al*., 2004). 'Catch-up growth' and its rate, where babies are born small but eventually pick up growth in the first month of life to reach the normal centiles, has been identified as a major risk factor for future development of metabolic syndrome and/or cardiovascular disease (ibid).

It is a proven fact that Indian mothers have been chronically malnourished. Study shows that rural Indian mothers were smaller with mean weight of 42 kg, mean height of 1.52 m, and mean BMI of 18.0 kg/m^2 as compared to Western mothers with weight of 63 kg, mean height of 1.63 m, and mean BMI of 23.5 kg/m^2 respectively (Yajnik, 2001). In terms of nutrition When compared to moms in the west, Indian mothers consume less protein and calories (~1800 kcal/day and 45 g protein/day compared with 2400 kcal/day and 90 g protein/day) (Yajnik, 2001). Maternal malnutrition is a recurring issue in countries with poor and middle incomes. Women falling in low income, low education attainment, food insecurity group remains vulnerable for inadequate and poor quality of diet (Barouki *et al*., 2012).

If we analyze some national level data for India there are obvious risks for high prevalence of metabolic syndrome with reference to above discussed factors. All rounds of NFHS data show a major percentage of women in their reproductive age group with BMI less than the normal figure. This indicates that a good proportion of women with child bearing age have poor nutrition status and same can be expected to continue during the gestation phase. It can also be expected that normal functioning of placenta is hampered due to nutritional insufficiency. Iron is crucial for the growth of the foetus, as has already been mentioned but NFHS data (all rounds) shows that more than half of reproductive age group women are always anemic. This is important because we can speculate that more than half the Indian expectant mothers' are passing the risk factor to their offspring. Of late the overweight/obesity of women is showing an increasing trend and more prominently in urban population. With increase in prevalence of maternal obesity and gestational diabetes the risk of child adiposity is high, so this needs more follow up.

Maternal poor nutrition status is reflected in the birth weight of the child. As mentioned already, one third of India's live birth are with low birth weight and hence with better nutrition the chances of adiposity increases later. The rate at which "catch up" growth occurs can decide the future path. NFHS data shows a good percentage of under-five children with stunting. Childhood stunting is considered as an adverse early life phenomenon which affects later susceptibility to obesity and subsequently causes diabetes or metabolic disorders (Webber, 2009). Other indicators like under weight and anaemia in children points towards poor nutrition during some vital post-gestational phases of life. If maturation or development of vital organs goes through bumpy rides then they deviate from the normal functionality. This holds the possibility of future disease risk with endocrine-metabolic dysfunction.

India	NFHS 5 (2019-21)			NFHS 4 (2015-16)			NFHS 3 (2005-06)
Indicators	Urban	Rural	Total	Urban	Rural	Total	Total
% of women (15-49 years) whose BMI below normal (BMI<18.5kg/m^2)	13.2	21.2	18.7	15.5	26.7	22.9	35.5
% of women (15-49 years) who are anaemic	53.8	58.7	57.0	50.8	54.3	53.1	55.3
% of women (15-49 years) who are overweight or obese (BMI≥25.0kg/m^2)	33.2	19.7	24.0	31.3	15.0	20.6	12.6
% of live births who reported low birth weight (<2.5kg)	-	-	-	17.6	18.5	18.2	22.0
% of children under 5 years who are stunted (height for age)	30.1	37.3	35.5	31.0	41.2	38.4	48.0
% of children under 5 years who are underweight (weight for age)	27.3	33.8	32.1	29.1	38.3	35.8	42.5
% of children 6-59 months who are anaemic (<11.0 g/dl)	64.2	68.3	67.1	56.0	59.5	58.6	69.4

Table 4.4: Indicators showing the scenario of malnutrition in India (Source: NFHS-4, 2015-16; NFHS-5, 2019-21)

The picture of maternal nutrition status is not rosy in India. Almost one third (NFHS 3) women in reproductive age group had BMI below the recommended value. Though the situation improved in NFHS 4 (one fourth women) and NFHS 5, but still a good proportion of women were below the recommended BMI in rural areas. Anemia being a chronic problem in India, more than half of women in reproductive age group is anemic and not much improvement was witnessed between NFHS 3 and NFHS 4 data but more deteriorating picture has been seen in NFHS 5. Poor nutrition status of Indian women is rightly reflected in the NFHS data which intend to affect the development of foetus. Overweight in women is gradually popping up but still it is more of an urban phenomenon than rural.

Iron deficiency is most vital in hampering the development of foetus and also in subsequent development of childhood. Programmatically in India importance has been given to tackle this problem. On the contrary we lack epidemiological data where deficiency of essential minerals and vitamins can impose during the critical phases of development of foetus and children. Poor diet quality is a major threat for non-accomplishment of the daily recommended allowances of minerals and vitamins.

Chapter Five

Various Stressors as Determinants of Metabolic Syndrome

In today's world stress in life is unavoidable and no one can escape it. When we talk about stress in life we usually indicate the various stressors which impact our health outcomes. From womb till tomb stressors are acting directly or indirectly on humans. When the threat to homeostasis exceeds a certain threshold, stress is described as a condition of threatened homeostasis or a state of disharmony, or as the perception of such, which activates adaptive responses (Chrousos and Gold, 1992; Rosmond, 2005; Chrousos, 2009). In simple terms, whenever we face any unfavorable situation our body tries to protect itself by the process of homeostasis by adapting some changes (Sharma, 2018). All creatures must maintain homeostasis, a complicated dynamic equilibrium, or re-establish by behavioral and physiological adaptive responses (Chrousos, 2009). In today's world, stress is progressively becoming more prevalent, and there is a large list of stressors that could have a negative mental or physical impact (Koski and Naukkarinen, 2017; Chrousos, 2009). Accidents, natural disasters, acts of terrorism or war, abuse of physical or sexual nature, grief, etc. are examples of external stressors, whereas internal stressors include anxiety, depression, and other emotional or behavioral illnesses (Pervanidou and Chrousos, 2011). Hence experience of both intense acute and chronic stress can exacerbate psychological as well as somatic conditions like obesity and metabolic syndrome (Pervanidou and Chrousos, 2012; Dwivedi *et al*., 2020). Complex life experiences including difficulties in relationships, health, employment, economics, and even social structure can be considered human stressors (Rosmond, 2005). To demonstrate the effects of stresses, both their intensity and duration must be considered (Chrousos, 2009). Stress can be acute (short duration), episodic (acute stress occurring too frequently), and chronic (long duration) and hence have varied health outcomes. All types of stress are not harmful or have negative impact on the body (Sharma, 2018). We will be focusing in this chapter on stressors which are important from social angle for metabolic syndrome.

5.1 Stress Response:

The response is subjective and can vary in different individuals even with similar intensity and duration. Moreover factors like age, gender, personality, health (both physical and mental) etc. do influence the stress response (Sharma, 2018). Hans Selye first developed a three staged profile of stress response also referred to as biologic

stress syndrome or the General Adaptation Syndrome (GAS) (Selye, 1976). The first stage is 'alarm reaction' where fight-or-flight response is evident and body shows the changes of first exposure to a stressor. In this stage either the body face the adversity or escape it. If exposure to stressors continues, the body tries to adapt to the situation utilizing all its resources and this stage is called 'stage of resistance'. The bodily changes that occurred in the first stage gradually disappear and adapt to the stressful situation. The body goes into recovery phase if mechanisms succeeded in overcoming the stressor effects (Sharma, 2018). Otherwise in the next stage adaptation energy is exhausted in the 'stage of exhaustion' due to the long continued exposure to the stressors. Prolong exhaustion stage can cause long term health effects like metabolic disorders.

The stress response is mediated by the involvement of three systems: the nervous system, the endocrine system and the immune system. The stress system, which is present in both the peripheral organs and the central nervous system, mediates the stress reaction (Pervanidou and Chrousos, 2011; Chrousos, 2009). The brainstem locus caeruleus/norepinephrine (LC/NE) system, which regulates arousal and autonomic (sympathetic) nervous system activity, and the hypothalamic corticotropin-releasing hormone (CRH) system, which regulates the hypothalamic-pituitary-adrenal (HPA) axis, make up the bulk of the stress system (Pervanidou and Chrousos, 2011; Pervanidou and Chrousos, 2012). Several etiological factors for obesity have been quite extensively studied but stress as a factor of obesity is poorly understood (Koski and Naukkarinen, 2017).

5.2 Biological Pathway of Stress:

The stress response starts with the first perception of the stressor. Hypothalamus in brain when encounters stress it activates the hypothalamic-pituitary-adrenal (HPA) axis, the sympathoadrenal system, and the autonomic nervous system (ANS) (Plotsky *et al*., 1989). The sympathetic nervous system (SNS) and parasympathetic nervous system make up the autonomic nervous system (PNS) (Sharma, 2018). Catecholamines like epinephrine (adrenaline) and nor-epinephrine (nor-adrenaline), which are released on stressor response, are responsible for the fight-or-flight response (Hall and Hall, 2021). In normal situations, adaptive changes in endocrine,

metabolic, and cardiovascular system can result from everyday stressors due to activation of the stress response that supports homeostasis (Pervanidou and Chrousos, 2012). Various changes occur in the body due to the release of catecholamines in order to proceed for fight or flight mechanism.

Adrenocorticotropin Homrone (ACTH), which is produced by the anterior pituitary gland in response to CRH, stimulates the adrenalglands in the kidney to release corticoids. Glucocorticoid released from adrenal cortex helps in energy generation which is required to withstand the adverse effects of stressors (Sharma, 2018). Besides, corticoids also suppress appetite and immune system, and induce feeling of depression and loss of control (ibid). The adrenal medulla releases catecholamines and has similar effects like the catecholamines of the sympathetic nervous system but in a more prolong way. ADH (Antidiuretic Hormone) secreted by hypothalamus regulates the fluid loss by re-absorption and regulates the blood pressure during stress (Hall and Hall, 2021).

Some other hormones of HPA axis like growth hormone (GH) and thyroid hormones (thyroxine and triiodothyronine) also play important role in stress system by influencing the vital functions of the body (Sharma, 2018). Stress mediators can have different effects on some important hormones of the body. Hypersecretion of insulin and growth hormone and hyposecretion of sex steroids can be witnessed due to chronic hypersecretion of these stress mediators. Such hormonal changes can lead to an increase in visceral adipose tissues' fat content and adverse metabolic consequences like metabolic syndrome (Pervanidou and Chrousos, 2011).

Hyperactivation of the Sympathetic Nervous System (SNS) in the body as a response to both acute and chronic stress also plays an important role in the pathway (Tsigos *et al*., 2020). Through intricate physiological mechanisms, SNS can mediate the stress response at different levels of the HPA axis and boost its activity (Herman *et al*., 2016). The final chronic stress results in the HPA axis's response being controlled by sex hormones like androgens and estrogens (Pasquali, 2012). The HPA axis and sex hormones may appear to be two independent systems, but they may actually work together to determine the aberrant response to prolonged stress, encouraging the development of abdominal fat (Tsigos *et al*., 2020). Lipoprotein

lipase, a lipid-storing enzyme, is found to be more abundant in adipose tissue with excess cortisol, especially visceral fat (Pasquali, 2012). Stress response has been revealed to have a significant relationship with metabolic syndrome and activation of the SNS as a key mediator along with the HPA axis (Herman *et al*., 2016).

5.3 The Paradigm of Stress and Metabolic Syndrome:

Several disorders can be contributed by the abnormally high concentrations of mostly cortisol, norepinephrine, and epinephrine as witnessed with deviations of activities in the already mentioned 'stress system' (Rosmond, 2005). HPA axis response is enhanced by high level of catecholamine, and CRH on the other hand seems to stimulate the sympathetic outflow (Tsigos *et al*., 2020). Different stressors can cause the HPA axis to react in different ways. When the HPA axis responds, it releases cortisol, which inhibits pancreatic β-cells' ability to secrete insulin and interferes with insulin activity at several levels (Rosmond, 2005). Cortisol normally regulates several physiological functions of adipose tissue like differentiation, distribution in body, and function. However, cortisol in excess can cause visceral obesity (Tsigos *et al*., 2020). Elevated cortisol and catecholamine levels indicate towards chronic hypersecretion of stress hormones. Buildup of fat over time, particularly in visceral adipose tissue can be seen due to elevated cortisol and catecholamine concentrations, leads to harmful metabolic effects such as arterial hypertension, dyslipidemia, and glucose intolerance (components of metabolic syndrome) (Tchernof and Despres, 2013). Insulin resistance is most likely due to significant increase in endogenous stress hormones and other inflammatory stress mediators in the body (Pervanidou and Chrousos, 2012). The complete range of the metabolic syndrome, which additionally includes visceral obesity, insulin resistance, and dyslipidemia, can be considered as having elevated cortisol levels as its primary cause (Rosmond, 2005).

The development and severity of metabolic disorder and other disorders of endocrine, autoimmune, cardio vascular etc. depend on the probability of individual's vulnerability or resilience to stress, and/or timing of stressors they were exposed to during the "critical stages" of development (Chrousos, 2009). Important periods for the consequences of significant acute or chronic stress include prenatal development,

infancy, childhood, and adolescence (Chrousos, 2009; Pervanidou and Chrousos, 2011; Pervanidou and Chrousos, 2012). Because these phases are crucial times of continual growth and significant brain plasticity, the presence of stressors throughout them can have long-lasting impacts (Pervanidou and Chrousos, 2011). Irreversible and permanent effects on metabolic system can be expected because of excessive activation of the stress system during these periods (ibid). Due to its persistent and long-lasting effects, chronic stress has received increased attention as a factor influencing the development of metabolic syndrome. Numerous physical, behavioural, and/or neuropsychiatric consequences of chronic stress are possible. Atherosclerotic cardiovascular disease, anxiety, depression, hypertension, obesity, type 2 diabetes, metabolic syndrome, excessive daytime sleepiness, and sleep problems are a few examples of its manifestations (Chrousos, 2009). In addition, children who have chronic changes in cortisol secretion may also experience changes in their stature, timing of puberty, and body composition (Pervanidou and Chrousos, 2012). Fasting cortisol concentration and cardiovascular risk variables showed considerable relationships in a cross-sectional cohort research in Mysore, South India (Ward *et al*., 2003). The study discovered links between cardiovascular risk variables and fasting cortisol concentration, particularly in men and women with higher BMI (ibid). Interestingly, while obesity alone amplifies the risk of CVDs in Caucasians, blood cortisol levels may serve as an independent risk factor for CVDs in South Asian individuals (ibid). To prove that those with greater circulating cortisol levels or increased stress response in young adulthood go on to acquire the metabolic syndrome later, longitudinal studies specifically looking at Asian Indian populations are needed. Incidence of CVDs was positively correlated with plasma cortisol/testosterone ratio, according to the Caerphilly Heart Study, which looked at a cohort of 2512 adult men in South Wales and is an important indicator of chronic stress exposure (Smith *et al*., 2005).

Both behavioural and biological factors are associated with chronic stress and obesity in both adults and children. It is clear that those who are constantly stressed out are more likely to become obese and experience various obesity-related issues (Pervanidou and Chrousos, 2011). Increase in waist circumference due to fat accumulation in visceral adipose tissue has been regarded as a sign of mal-adaptation to the exposure of chronic environmental stress (Pasquali, 2012). Chronic stress can

lead to a variety of metabolic co-morbidities due to simultaneous expression of both "anxious/depressive" as well as "obese" phenotype (Pervanidou and Chrousos, 2011). In other words chronic stress actually increases the risk of metabolic disorders by dual pathways. The dysregulation of the stress system is linked to anxiety disorders, depression, and other illnesses of failure to adaptation (Pervanidou and Chrousos, 2011). Anxiety and its association as a determinant of metabolic syndrome are still not well established. Studies have more directly linked metabolic problems such as altered lipid profiles and insulin resistance, elevated blood pressure, and abdominal obesity to depression (Skilton *et al*., 2007). Obesity and/or the metabolic syndrome are more likely to develop as a result of stress hormone changes seen in depression (ibid). Stress hormones cause insulin resistance and stop beta cells from secreting the insulin needed to maintain homeostasis (Baig *et al*., 2011).

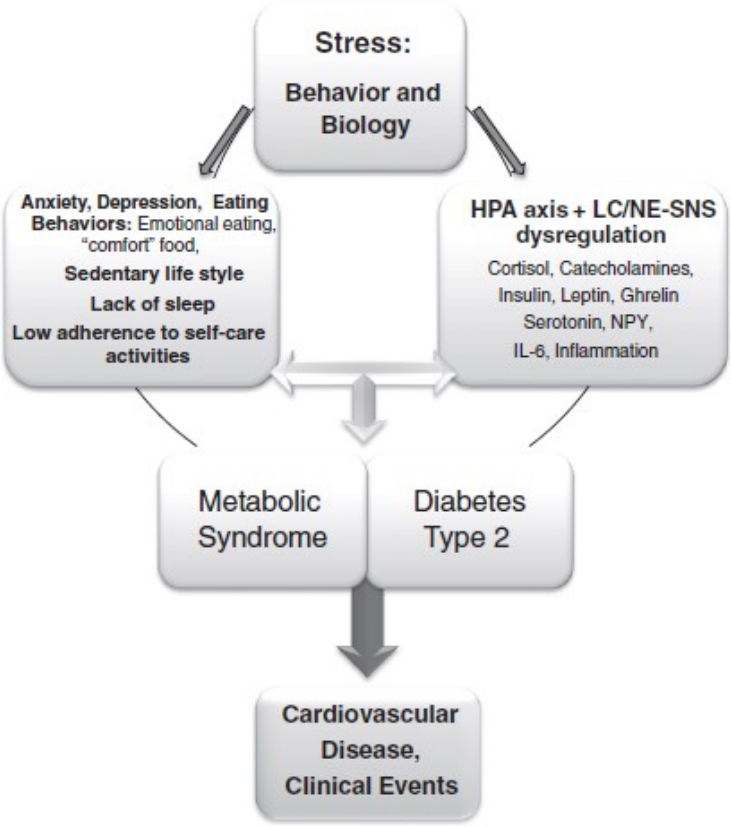


Fig 5.1: Biologic and behavior pathway linking obesity and metabolic syndrome (Source: Adapted from Pervanidou and Chrousos, 2012)

A dominant role played by Glucocorticoids is to regulate the stress-induced food intake (Pasquali, 2012). "Stress eating" as may be caused by stress hormone

imbalance is still a poorly defined area (Koski and Naukkarinen, 2017). Increased appetite and food intake play important role in the pathogenesis of obesity, but they on the other hand can represent or indicate towards behavior related clinical signs of depression also (Pervanidou and Chrousos, 2011). Relevant research indicate that people tend to select energy-dense diets and consume fewer vegetables while under stress (Ng and Jeffery, 2003; Mikolajczyk *et al*., 2009). In a study on monkeys, chronic physical and emotional stress that lasted for two years caused pathological behavioural changes (aggression), as well as nearly all the symptoms of the metabolic syndrome, including an increase in body weight and visceral fat deposition, insulin resistance, impaired glucose tolerance or diabetes, and dyslipidemia (Pasquali, 2012).

Health and life depend on the proper regulation of HPA stress axis (Herman *et al*., 2016). The neurobiology of stress is found to be associated with hunger and energy (Sinha and Jastreboff, 2013). There are other important determinants like our genetic background, epigenetic changes in life course, past history of stress, nature of the stressor, age, and critical phase of developmental of an individual that decides the direction of responses of HPA axis to stress (Pervanidou and Chrousos, 2012).

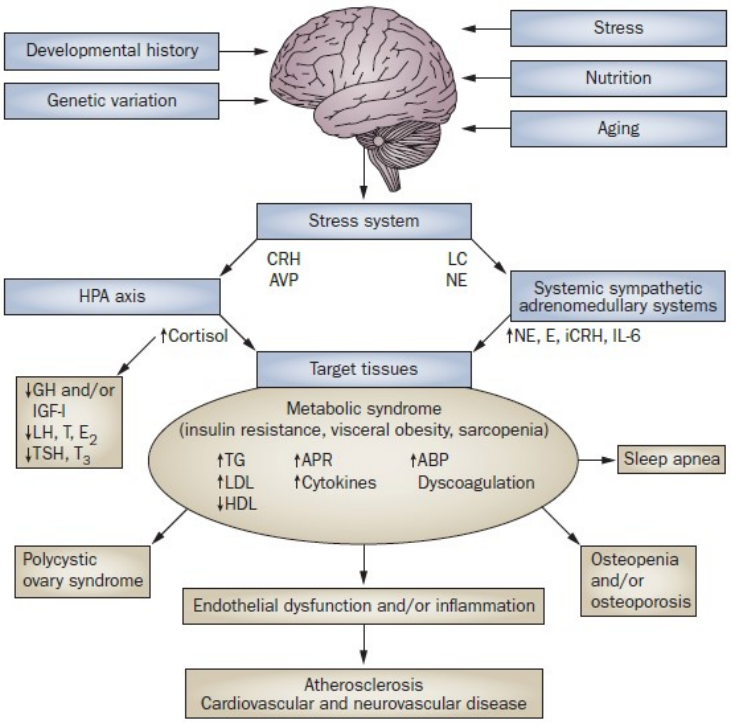


Fig 5.2: Chronic stress can lead to metabolic syndrome (Source: Adapted from Chrousos, 2009)

Competition, hostility, and social hierarchies are general behavioural traits that have been identified as key risk factors for stress (Rosmond, 2005). People are more prone to have recurrent HPA axis dysregulation if they are exposed to ongoing psychosocial and socioeconomic obstacles such a bad economy, low education, unemployment, and depression (ibid). Socioeconomic position (SEP) is a strong factor for prevalence of Type 2 diabetes as evident in several studies. When several SEP measuring indicators, such as education, occupation, income, etc., are employed, it has been discovered that there is an inverse relationship between SEP and diabetes prevalence (Maty *et al*., 2005). Low SEP individuals earn less money, have fewer job opportunities, and have less access to health care services and information (ibid). SEP exhibits patterns of many established risk factors, including increased body weight, a large waist circumference, and physical inactivity. In a large group of men and women employed in the British Civil Service, the groundbreaking Whitehall II study produced a longitudinal collection of data that explored the association between socioeconomic status (SES) and metabolic and cardiovascular outcomes. One of the advantages of the Whitehall II study is that the subjects were tracked prospectively rather than using a cross-sectional design, so the results can be interpreted as pointing to causal mechanisms rather than being merely co-relational. A sizable dataset produced by the Whitehall research has been utilised to examine the connection between social influences (i.e. SES) in people (Tamashiro, K.L. *et al*. 2011). When exposed to stress over an extended period of time, stress can cause short-term adaptive alterations in metabolism that turn into maladaptive modifications for the individual (ibid).

Stress in childhood has long term implications in future adult health. Childhood being critical phase of development, if exposed to stress even with short duration heavy exposure can have future adverse effects. Due to the Leningrad siege, which lasted from 1941 to 1944, Russia is a clear illustration of how early exposure to high levels of stress can lead to severe health outcomes in adulthood. The study on siege of Leningrad by Koupil *et al*. (2007) revealed that in comparison to those who were not exposed, women aged 6 to 8 years old and men aged 9 to 15 years old had greater systolic blood pressure in adulthood. The hypothesis that survivors of intense stress during childhood may face long-term bad health outcomes is further supported by the

observation that women and men who had survived a siege as children died more frequently from ischemic heart and cerebrovascular disease (Koupil *et al*., 2007).

Faulty life-style induces stress which may lead to more deposition of visceral fat and increase in waist circumference pushing towards insulin resistance (Mitra *et al*., 2009). Sleep problems and disorders are common health hazards in today's life. One of the most common signs of stress disorders is sleep problems, including problems with sleep onset, sleep duration, and sleep quality (Pervanidou and Chrousos, 2012). According to a prospective study, women who experienced abuse as children were far more likely to develop obesity in their early adult years than their non-abused peers because they were under very intense physical and emotional strain (Noll *et al*., 2007). Obese children associated with altered cortisol metabolism and stress related symptoms can amplify endocrine and metabolism related complications (Pervanidou and Chrousos, 2011). There are studies which suggested BMI and waist circumference as components of SEP and diabetes incidence pathway rather than as penultimate risk factor (Maty *et al*., 2005). Family problems like separation from parents have been found to have long term stressor effect and even can have behavioral issues (Koski and Naukkarinen, 2017).

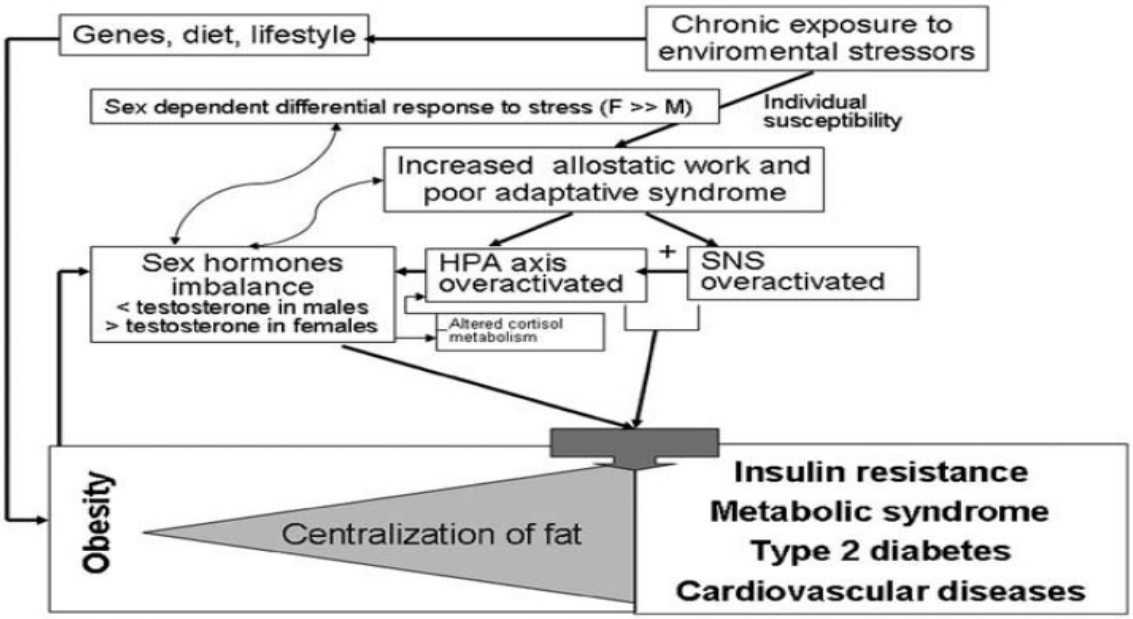


Fig 5.3: Combine effect of environmental stressors and other factors leading to metabolic syndrome (Source: Adapted from Pasquali, 2008)

How environmental stressors along with other important risk factors influence on stressor pathways leading to metabolic syndrome or metabolic diseases have been depicted in the above figure.

5.4 Migration as stressor:

Migration or moving from one location to another in quest of a better way of life is a constant activity and a significant aspect of the development of humanity (Bhati, 2015). “Migration refers to the movement of an individual or family or group of persons from one place to another place with change in residence for a number of reasons like social, cultural, economic and noneconomic factors” (Singh, 2016). The most unpredictable factor in population increase is thought to be migration, which is also seen to be the factor that has the most influence on cultural, political, and economic issues (Singh, 1998). Migration is always stressful, whether it is brought on by the forced migration of refugees and internally displaced persons or by the movement of those seeking employment and a better quality of life (Carballo and Siem, 2006). People who are forced to leave their home country have increased stress, which may increase the risk of developing future health issues or aggravate current ones (Dwivedi *et al*., 2020). It is important to recognise that migration is a complicated process that affects development, security, and other societal issues rather than simply seeing it as a simple movement of people across borders (Singh, 2016). In the majority of nations, if not the entire world, there have been documented large-scale migrations of people from villages to towns, towns to other towns, and even one country to another, concurrent with industrialization and economic progress (Singh, 1998). Uprooting oneself from one's original land, leaving behind loved ones, moving in challenging physical and psychosocial circumstances, and dealing with the hard reality of resettling in an unfamiliar environment that may not be accommodating are all aspects of migration (Carballo and Siem, 2006). With more than 230 million individuals affected globally, migration has been labelled as one of the biggest social and political crises of the twenty-first century (Singh, 2016). From a demographic perspective, there are three factors that influence population increase in any given location, with migration coming in third after fertility and mortality (Singh, 1998). Interesting enough, migration does not occur inside the biological framework,

although both fertility and mortality do (ibid). Due to globalisation, continuing economic and demographic differences, and other factors, rural to urban migration is the most prevalent and growing type of migration (Singh, 2016).

Natural population increase, the eventual categorization of rural regions as urban, and rural to urban migration are the three main reasons that drive the expansion of this phenomenon (Bhati, 2015). The key factor accelerating urbanisation in developing nations is rural-to-urban migration (Singh, 2016). Though once rural to rural migration was dominant but the proportion of this migration has declined steadily with time (Singh, 1998). In addition to rural to urban migration, there has also been a rise in urban to urban movement, particularly from small urban towns to large urban cities (Singh, 1998; Singh, 2016). Similarly the short distance migration has decreased with time in comparison to medium and long distance migration (Singh, 1998). It has been observed that most of the long distance movements are rural to urban or urban to urban. This is the prime factor of significant increase in migrant population in urban areas. If this trend persists then long distance streams can be presumed to be the dominant migration streams in future (Singh, 1998).

According to research, migrants and refugees in host countries frequently experience chronic loneliness and despair (Carballo and Siem, 2006). Though there are other determinants but stress aroused has been coined as the key determinant of metabolic syndrome in migrants (ibid). Studies undertaken in European countries show that immigrants had greater rates of non-communicable diseases such as hypertension, diabetes, obesity, and metabolic syndrome than the native population overall (Dwivedi *et al*., 2020). How over eating can be a compensatory mechanism to deal with stress has been discussed already. Additionally, migrants frequently struggle with adjusting to new eating customs and foodstuffs, which might increase their risk of developing metabolic diseases (Carballo and Siem, 2006). Detailed discussion has been done in chapter of nutrition transition regarding consumption of food containing more fat and less fibre in host place than their original home with subsequent health problems.

Indian citizens enjoy the freedom to move freely around the country for any cause, including in search of a better way of life, as mandated by the country's

constitution. In addition, India introduced its new economic policy in 1991 under the name LPG (Liberalization, Privatization, and Globalization), which enhanced the nation's economy and increased work opportunities, luring migrants to urban areas (Singh, 2016). In India, the rate of net rural to urban migration grew from 21.2% to 24.1% between 1991 and 2001 (ibid). Misra *et al*. reported this migration rate to increase exponentially in India from 11.9% (in 1931) to 27.8% (in 2001) (Misra *et al*., 2011). Work related factors are the main cause of migration in about 40% of cases from rural to urban area (Bhati, 2015). Collectively, Bihar and Uttar Pradesh account for up to 70% of all migration to India (Bhati, 2015). Despite Maharashtra not being a border state, interesting information from Eldis Community claims that around 41% of all migrants came from Uttar Pradesh. Similar to in-migration, out-migration from Orissa preferred Gujarat and Maharashtra as the destination, which contributes about 34%. In the case of Bihar, approximately 50% of them have migrated to West Bengal, Maharashtra, Uttar Pradesh, and Jharkhand. Moreover one-third of the Tamil Nadu population moved to Karnataka, and the remainder mostly chose Kerala, Maharashtra, and Uttar Pradesh. This general trend reveals that among all Indian regions, Maharashtra receives the greatest number of migrants looking for labour or professional opportunities (Bhati, 2015). Mumbai, which is known as India's financial capital, has been the driving force behind it.

In addition to human pain and suffering, it is recognized that several health problems are linked to mass migration during war, riots, hunger, natural calamities, or owing to strong economic reasons (Dwivedi *et al*., 2020). Owing to riots that took place in West Pakistan (now Bangladesh) and East Pakistan (August 15, 1947), India has a history of experiencing large-scale migration both before and during independence. The personal and societal tragedies related to partition, riots, etc. have been the subject of numerous studies and publications, but little is known about the long-term metabolic abnormalities these events have on the migrating population (Dwivedi *et al*., 2020). Dwivedi *et al*. at the National Heart Institute in New Delhi (India) from January 2016 to June 2019 conducted a brief observational research on ethnic Indian migrants (n = 30) from West Pakistan and ethnic Indian inhabitants of Delhi (n = 30). The majority of the migrants were in their early infancy (5–10 years old) when they migrated to India, and both migrants and non-migrants were in their seventh decade of life at the time of this study. The majority of immigrants had

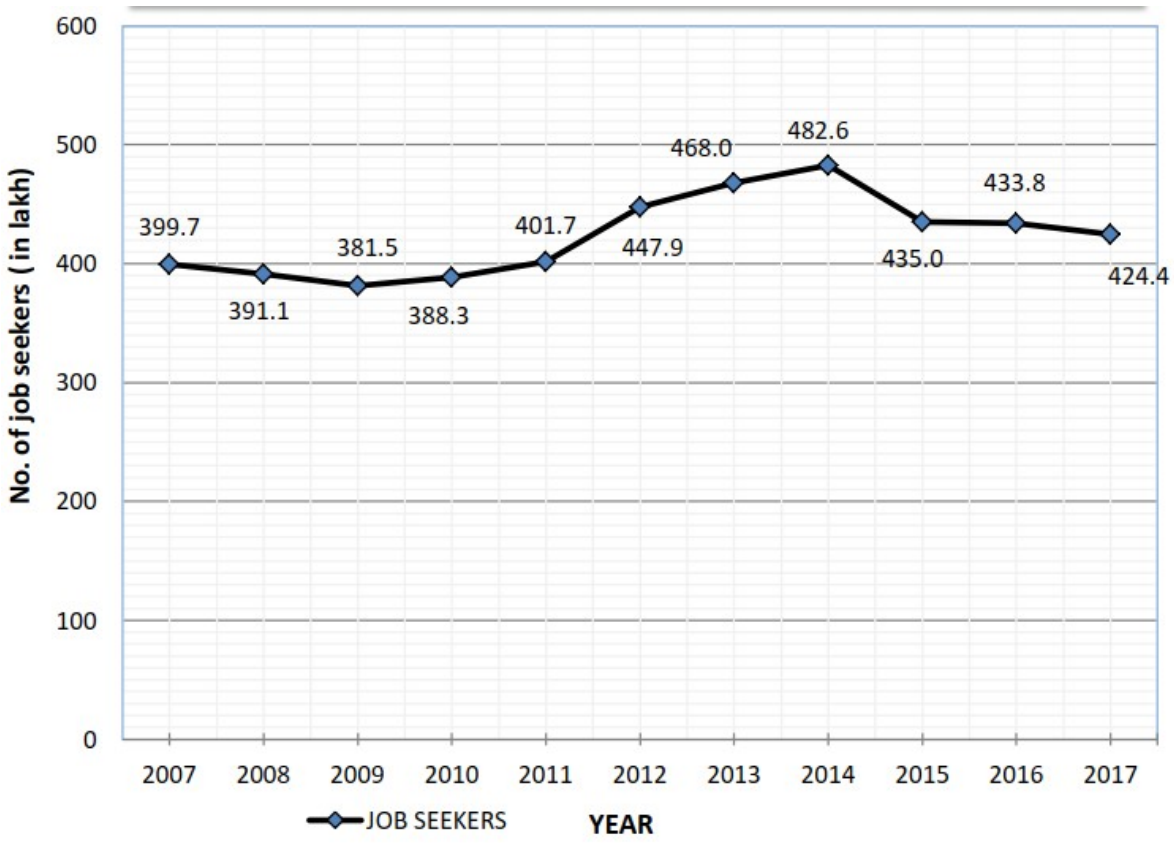
hypertension, either on their own (20%) or in combination with another condition (63.3%) *viz*. hypertension and diabetes, coronary artery disease and hypertension, coronary artery disease and diabetes, and coronary artery disease and stroke at the time of study. Non-migrants on the other hand had 16.6% (statistically not significant) alone with hypertension or had such a combination in only 36.8% of the cases (Dwivedi *et al*., 2020).

In 6510 industrial employees from Lucknow, Nagpur, Hyderabad, and Banglore, the impact of rural to urban migration on the prevalence of obesity and diabetes was investigated. According to the study, there has been a rise in obesity among rural migrants who have moved to metropolitan regions, putting them at the same risk as urban residents (Ebrahim *et al*., 2010). Even today studies which look into dramatic upsurge in the incidence of metabolic disorder following exposure to stress due to mass migration are very rare to find worldwide. Fang *et al*. (2015) investigated the relationships between stress and insulin resistance in Chinese American women who were foreign born. The study was conducted in southeastern Pennsylvania from October 2005 to April 2008, where 423 women recruited to complete questionnaires who reported stressful life events. Initial assumption was that due to change in dietary habits there had been high disease risk. However, later data negated this assumption as risk factors like diet or obesity alone failed to explain the disease risk transition as principle factor (Fang *et al*., 2015). Then, it was stated that immigrants experience significant stress due to a number of difficulties, including language barriers (Zhang *et al*., 2012), being away from family and having limited access to social networks (Pickett and Wilkinson, 2008), as well as being exposed to racism and discrimination that they had not previously encountered in their own country of origin (Gee *et al*., 2009). Chinese immigrant women were found to experience more severe effects due to stressors related to lack of social support network in the host country (Taylor *et al*., 2007). Most importantly, even after such correlations this field is still ignored and there are hardly any studies which look into Chinese migration stress and consequent increase in the prevalence of metabolic diseases (Lee *et al*., 2011).

India too has no studies which look into the internal migration stress and incidence of metabolic syndrome. Epidemiological, experimental, or interventional studies are required in India to establish the causality of migration stress.

5.5 Employment and income as stressors:

There is evidence that social and economic inequalities are linked to health issues such as non-communicable diseases (Pradeepa *et al*., 2003). We all know that income is directly related to employment/livelihood and both are interdependent factors. Type of employment decides the income and hence the quality of life. A positive influence on health and lifestyle may be expected with better income and prestige received from an occupation (Nair, 2010). Good income and job appraisals can help better living conditions and adoption to healthier lifestyle along with access to quality healthcare (ibid). Number of job seekers in India has not come down as per below graph; indicating not everyone is lucky to have a job and hence quality life.



Graph 5.1: Trend in live register of all job seekers in all India bases (Source: Adapted from Employment Exchange Statistics GoI, 2018).

Data of registered job seekers and placement also gives a gloomy picture. Placement rate has not gone up indicating that new job generation is low. Certain proportion of population will always be unemployed; means they will be under constant stress.

Year	All job seekers (in Lakh)		Educated job seekers (10th std. & above)(in Lakh)	
	Registration	Placement	Registration	Placement
2005	54.4	1.7	41.3	0.9
2010	61.9	5.1	49.4	3.9
2011	62.1	4.7	52.9	3.3
2012	97.2	4.3	87.4	2.8
2013	59.7	3.5	50.1	2.3
2014	59.6	3.4	50.0	2.3
2015	69.4	3.9	41.7	2.5
2016	59.6	4.1	29.7	2.9
2017	39.5	4.2		

Table 5.1: Trend of job seekers and placement for all India (All and educated)
(Source: Adapted from Employment Exchange Statistics GoI, 2017 & 2018)

Getting a job may decrease the stress level to certain extent but can be the cause of other stressors. Contract or temporary type of employment can be the cause of constant stress due to job insecurity. More than half of the urban labour force is employed in the unorganised, informal, and future uncertain sectors (Bhati, 2015). Similarly if there is irregularity in salary payment or job loss, they can act as tremendous stressors. The NSS data shows that not much has changed over the years in type of employment especially for casual workers. Approximately around 30% employees of total are working as casual workers for last few decades, indicating that uncertainty prevails consistently. Self employed category also bears a certain level of uncertainty as compared to regular employment. Hence only 10-18% regular employees can be considered as having secured future. We can indirectly imply that majority of workers/employees in India are in constant stress due to lack of job security.

In India, with huge population, unemployment rate is high and queue of candidates for vacant job is long. In such scenario everybody tries to give his best,

NSS round	Self employed	Regular employees	Casual workers
38th (1983)	605	103	292
55th (1999-2000)	550	88	362
68th (2011-12)	522	179	299

Table 5.2: Type of employment (per 1000) for both rural and urban as per NSS rounds in India (Source: NSS rounds 38th, 55th, and 68th)

even in most stressed situation, so that no one replaces him. The Harris and Todaro model says that more migrant workers are attracted by creation of job opportunities in urban areas and when a saturation level is reached then no new jobs can actually increase the unemployment (Bhati, 2015). Hence getting employed is a stressful life event and sustaining the same with job satisfaction is another one. Situations such as work stress and unemployment have shown to increase the cortisol levels in some studies (Cota *et al*., 2001). The stress level can be different depending on the type of worker in similar set of work place. The managerial level workers may have different stress than the labour intense workers. The Chennai Urban Population Study (CUPS), an epidemiological investigation including 1262 participants, has as one of its goals the evaluation of the dyslipidemia patterns in two distinct socioeconomic groups residing in the same urban South Indian city. Socioeconomic determinants had an impact on the pattern of dyslipidemia, with dyslipidemia being more prevalent and severe in the medium income group of this urban South Indian population (Pradeepa *et al*., 2003). The middle income group was found to have a significantly greater prevalence of elevated cholesterol levels. The CUPS study also showed that some metabolic syndrome components are more common in middle-class people than low-income people (Pradeepa *et al*., 2003). Such findings of middle income group actually indicate towards lifestyle transition and encountering more stress to achieve the aspirations of next income group.

Quoted as the ‘adaptation syndrome’, referred to the faster transition in socioeconomic status occurring in developing countries, has been cited as one of the causes for the increased prevalence of the various metabolic syndrome symptoms in more affluent individuals (Mohan *et al*., 2001). Chinese researchers from the National

Diabetes Prevention Control Co-operative Group found that when economies improve and people adopt more modern lifestyles, the prevalence of diabetes rises (ibid). Similar results have been recorded from our neighbouring developing countries, such as Malaysia and Bangladesh (Ali *et al*., 1993; Sayeed *et al*., 1997).

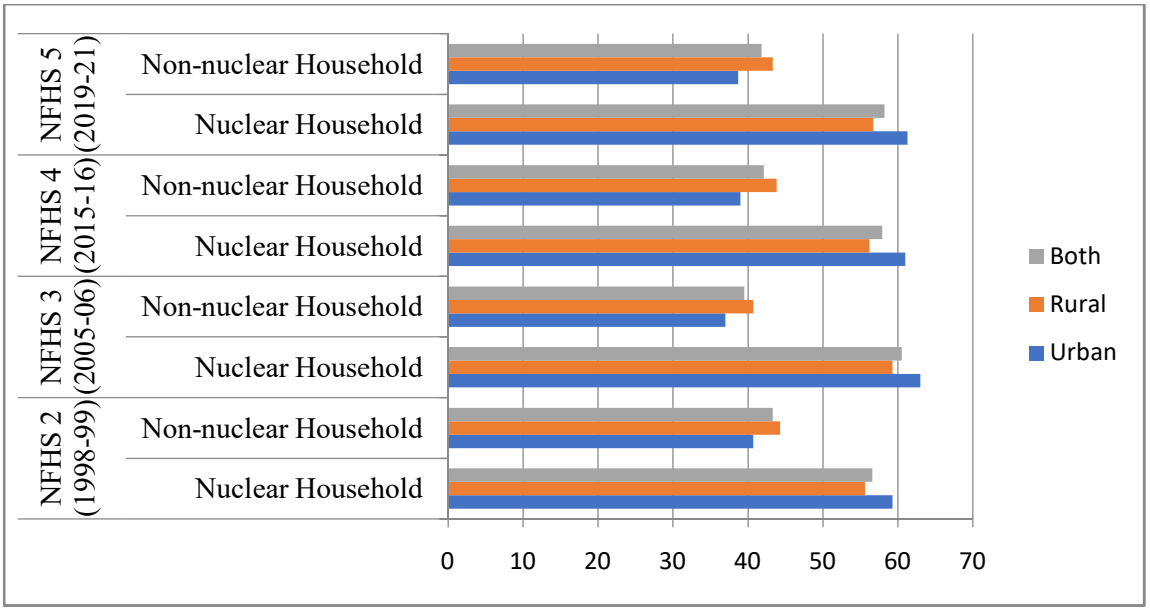
Studies have revealed that metabolic syndrome is often associated with sedentary occupations due to physical inactivity with added job related stressors. In similar line with landmark Whitehall study, a cross sectional study between June 2008 to December 2008 of 651 employees in an Indian plant site showed an overall crude prevalence of metabolic syndrome of 18.5% with largest category being the managers and senior officials (Nair, 2010).

Shift work has a strong possibility to contribute towards metabolic syndrome. There are studies which directly linked metabolic changes with shift work (Wolk and Somers, 2006). Shift work may exert diurnal variation and changes the circadian blood pressure with more probability towards hypertension (Yamasaki *et al*., 1998; Kitamura *et al*., 2002). Shift work also causes additional metabolic syndrome symptoms such as abdominal obesity, glucose intolerance, and dyslipidemia (Karlsson *et al*., 2001; Nagaya *et al*., 2002; Di Lorenzo *et al*., 2003; Karlsson *et al*., 2003). Besides, shift work acts as potential oxidative stressor to enhance release of harmful oxidants in the body (Sharifian *et al*., 2005). Shift work or working hours as determinant of metabolic syndrome need more studies in Indian scenario. All above studies are based in foreign soil and we need to reciprocate similar studies in India to see whether same results can be derived or not.

5.6 Family composition as stressor:

India is going through demographic, epidemiological, nutritional transitions as discussed already. India is simultaneously going through social-economic and cultural transitions too. There are studies to support such transitions but there are scarcities of studies which look into socio-economic and cultural transitions as stressors. Due to economic reason such as livelihood or as impact of westernization generations are becoming more inclined towards individualistic lifestyle and somehow leaving behind traditional values. Traditional joint families are breaking into smaller nuclear families

and have now become the characteristic feature of the Indian society. Nuclear households are defined as "households that are comprised of a married couple or a man or a woman living alone or with unmarried children (biological, adopted, or fostered), with or without unrelated individuals" (NFHS 3). Three out of five families in India are found to be nuclear and are found to be an overall picture of entire country (NFHS 2; NFHS 3; NFHS 4). The following graph, based on various rounds of NFHS data, indicates towards this fact and shows the shift in last few decades. Though the percentage of nuclear family is more in urban area compared to rural area but rural society is not very far behind in this phenomenon. This indicates that Indian society is going collectively through the path of westernization and hence preferring to be independent like west (Bhati, 2005). The number of working mothers and single parents is raising as more men and women desire independence in their careers and personal lives (ibid).



Graph 5.2: Trend of percentage of nuclear and non-nuclear households in India (Source: NFHS 2; NFHS 3; NFHS 4)

There is even increase in cases of divorce or broken families in India. Though India has documented the lowest rate of divorce in the world, but this is changing with time. Census data of 2011 revealed that 0.24% of total married population and 0.11% of total population are divorced in India (Census, 2011). We may presume that the rate of divorce is low because of under reporting due to various reasons; common being social stigma attached with it. Moreover, most of the marriages are still not

being registered in the court of law and hence their status is not known in due course. On the other hand separation rate amongst couple was found to be three times higher than the divorce rate (Jacob and Chattopadhyay, 2016). High rate of separation gives an indication that the rate of divorce may also be high. We need studies and data to support this statement.

Above two social issues are given emphasis as stressors, because they not only put the concerned members on psychological turmoil but also the immediate family members (like offspring, parents, in-laws etc.). Joint family gives a sense of social security both economically and mentally. A family with several generations together are found to be bonded strongly and hence are better equipped to face any consequences in life. On the contrary, individualistic nature of nuclear family makes members more vulnerable to the exposure of life's struggles. It actually reciprocates an old proverb "Unite we stand, divide we fall". Though it is not possible to measure whether such psychological conditions are more in nuclear family or in joint family, but long term comparative studies may give valuable inputs as importance of such stressors for metabolic syndrome.

Child has been found to be the cementing factor in motivating couples to stay together even under stressed and strained relationship (Vincent and D'Mello, 2018). It is obvious that such families will continue to be in stressful environment. In case of divorce or broken families, psychological and developmental effect on offspring can be long term and pronounced. Anxiety, depression, agitating behaviour etc. can be witnessed in child of such families. Long term health outcomes in such child due to the stressor effect as a consequence of behaviour change should be studied upon.

5.7 Sleep as stressor:

We all know that humans spend one third of their life asleep. Sleep can be described as "a physiological state characterized by lack of response to environmental stimuli" (Krueger *et al*., 2016). Although many hypotheses have been proposed to explain why people sleep, including those involving energy repair, thermoregulation, waste elimination, neural connection, and plasticity enhancement, sleep still remains a difficult mystery for researchers (Knutson *et al*., 2007; Krueger *et al*., 2016). Rapid

eye movement (REM) sleep and non-REM (NREM) sleep are the two primary phases of sleep in both humans and other mammals (Colten and Altevogt, 2006). REM sleep constitutes 20-25% and NREM sleep constitutes 75-80% of the whole sleep cycle (ibid). Both phases of sleep are important for normal physiological wellbeing of humans. Even today, we do not fully grasp the range of sleep functions, despite a variety of medical knowledge and recent advances in the study of sleep medicine (Dinges, 2006). Even though sleep is an essential activity for life, many questions about why humans sleep, what encourages sleep, what awakens people, or how many hours of "restorative sleep" are necessary etc. is still unanswered (AlDabal and BaHammam, 2011). There is little doubt that sleep is crucial for sustaining the body and brain's regular functions, and that sleep loss or sleep deprivation has been linked to a variety of physiological and psychological illnesses (Knutson *et al*., 2007). For instance, sleep deprivation has been connected to metabolic diseases like diabetes, hypertension, and obesity in healthy persons (Colten and Altevogt, 2006; Pervanidou and Chrousos, 2012) and increases the risk of heart attack and stroke (Colten and Altevogt, 2006; Cappuccio *et al*., 2011; Dettoni *et al*., 2012).

Only obesity and a lack of exercise fall short in explaining the growing epidemic of glucose intolerance and the metabolic syndrome. Obese people exhibit a roughly inverse linear relationship between weight and sleep, which suggests that getting less sleep is linked to being overweight and obese (Gangwisch *et al*., 2005; Vorona *et al*., 2005). It has been found that the chance of being obese is reduced by 80% for every additional hour of sleep (Knutson *et al*., 2007). According to recent research, sleep disruptions can cause a variety of physiological problems, one of which is the development of insulin resistance, which also contributes to weight gain. Thus, the increased incidence of the metabolic syndrome and insulin resistance across the population may be explained by the greater frequency of both qualitative and quantitative sleep disorders (AlDabal and BaHammam, 2011). A range of pathways, including insulin resistance and anomalies in the neuroendocrine system that controls hunger, may relate sleep loss to an increased risk of obesity and diabetes (Knutson *et al*., 2007). Sleep deprivation may impact energy balance and promote weight gain due to an increase in appetite, more time awake to eat, or excessive food intake, as well as a decrease in energy expenditure (Knutson *et al*., 2007; AlDabal and BaHammam, 2011). The activity of hypothalamic-pituitary-adrenal axis is affected by the

significant hormonal changes brought about by sleep deprivation. In addition, such hormonal changes are accompanied by a state of altered inflammatory and pro-inflammatory pathways leading to collective metabolic derangements (AlDabal and BaHammam, 2011). Experimental investigations have demonstrated that lack of sleep increases inflammatory and pro-inflammatory markers, which are signs of physical stress (Mullington *et al*., 2010). Stressful situations are frequently known to disturb the sleep/wake patterns and are also important regulators of circulating leptin in the body, which control food intake and energy balance and may be a factor in the emergence of obesity (Pervanidou and Chrousos, 2012). As mentioned already body can have multiple physiological changes because of sleep deprivation, but increase in cortisol level has an important role (AlDabal and BaHammam, 2011). Cortisol being an important derivative of stress pathway has already been discussed.

Another important area where we need more knowledge is to know the effect of sleep deprivation on total energy expenditure (TEE). The total amount of daily energy expenditure (TEE) is typically determined by three factors: (a) resting metabolic rate (RMR), which is defined as the energy expenditure of a person laying in bed in the morning following sleep as well as in the fasting state; RMR accounts for about 60% of TEE in people with sedentary occupations. (b) Thermic effect of meals (TEM), which accounts for approximately 10% of TEE and is the energy expenditure associated with the digestion, absorption, metabolism, and storage of food (c) energy used for all other activities is known as activity-related energy expenditure, or AEE (Knutson *et al*., 2007). It has not been directly investigated if sleep loss in humans affects TEE or any of its spending components (ibid). A schematic pathway of sleep deprivation leading to insulin resistance and diabetes is shown in Fig 5.4.

Chronic sleep restriction is a recent tendency that has been seen to emerge over the previous two to three decades (Reaven, 2006). Worldwide trends toward adopting a 24/7 lifestyle, longer work hours and shifts, 24/7 availability of goods, and 24 hour global connectivity have all led to significant changes in sleep culture (AlDabal and BaHammam, 2011; Cappuccio and Miller, 2017). Several studies amongst Americans

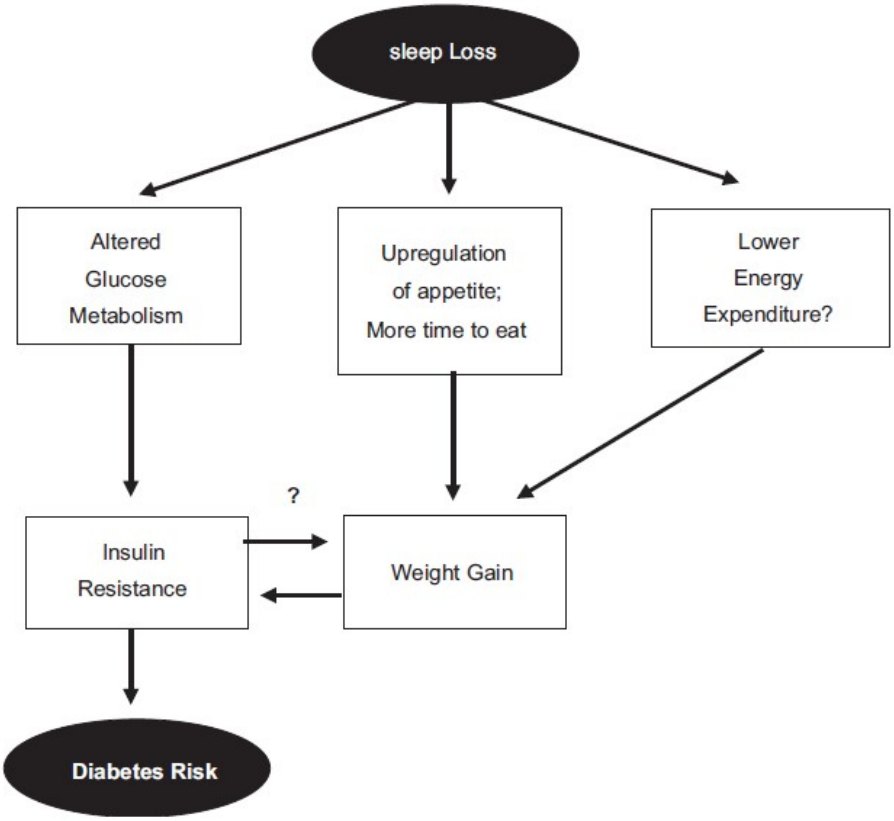


Fig 5.4: Schematic pathways showing sleep loss to diabetes risk (Source: Adapted from Knutson, *et al*., 2007; Knutson and Cauter, 2008)

since 1960s have shown curtailment of sleep duration per night from 8.0-8.9 hours to 7.0 hours in 1995 and 6.0 hours or less in 2004 (Knutson and Cauter, 2008). In a cross-sectional self-reported population-based study conducted in the United States with 110,441 adult participants (over the age of 18), 28.3 percent of participants reported sleeping for less than 6 hours, 63.3 percent reported sleeping for 7 or 8 hours, and 8.5 percent reported sleeping for more than 9 hours (Krueger and Friedman, 2009). According to a national poll carried out in 2014 by the National Sleep Foundation in America, almost 55% of kids and teenagers do not get enough sleep each night (Buxton *et al*., 2015). Additionally, insufficient sleep is increasingly prevalent as people get older e.g. 8 percent of children aged 6 to 11 sleep for less than seven hours and 23% sleep for eight hours each night, but 56 percent of teenagers aged 15 to 17 slept for less than seven hours each night (ibid). Insufficient sleep duration was found in a substantial population-based cohort research of Chinese adults in Singapore, where 58,044 participants were selected from the Singapore Chinese Health Study (Shankar *et al*., 2008). The majority of participants who were eligible for the study reported sleeping for 7 hours per night on average (33%),

followed by 8 hours per night on average (27.49%), 6 hours per night (23.43%), less than 5 hours per night (9.38%), and more than 9 hours per night (6.63%) (ibid).

One significant epidemiological finding was the inverse connection between the amount of sleep and the prevalence of obesity worldwide during the past few decades (Cappuccio and Miller, 2017). In the United States, obesity prevalence has increased at the same time that average sleep duration has decreased, validating the aforementioned observation (Reaven, 2006). There are several reports which support sleep duration as a determinant of adiposity (Shigeta *et al*., 2001). In an American longitudinal research, 915 children were tracked from birth to age three, higher BMI and obesity was showed to be associated with sleep of less than 12 hours per day in infancy (Taveras *et al*., 2008). Additionally, a sample of 8274 Japanese kids revealed a dose-response association between insufficient sleep and juvenile obesity (Sekine *et al*., 2002). A thorough review and meta-analysis of the connection between sleep duration and childhood obesity was conducted by Chen *et al*. showed that the risk of obesity increased by 58 percent for children with shorter sleep durations and by 92 percent for those with the lowest sleep durations. For every additional hour of sleep, this risk was shown to be lowered by 9% (Chen *et al*., 2008). A total of 1037 participants born between April 1972 and March 1973 in Dunedin, New Zealand were recruited as part of the longest prospective birth cohort study and when their BMIs were calculated at the age of 32, it was interestingly discovered that shorter childhood sleep durations were substantially linked to greater adult body weights (Landhuis *et al*., 2008). Significant increase in the risk of obesity among boys and girls of 10 to 19 years age groups of Arab children were reported in a sample of 5,877 children when sleep time was ≤7 hours (Bawazeer *et al*., 2009). Reduced insulin sensitivity is observed with varied durations of sleep loss (Gonzalez-Ortiz *et al*., 2000) as well as due to extended sleep debt brought on by consistently getting less than 6 hours of sleep each night (Shigeta *et al*., 2001). Reduced glucose tolerance and a blunted insulin response to glucose were observed in an interventional trial where healthy volunteers were only allowed to sleep for four hours each night for six nights in a row (Spiegel *et al*., 1999). Sleep loss can affect the metabolic syndrome's other symptoms, such as blood pressure increases, in addition to visceral obesity (Reaven, 2006). Moreover psychological problems like anxiety and depression have been found to be

associated with early life sleep problems (Gregory *et al*., 2005). The cascade of sleep deprivation and metabolic changes can be represented in the following flow diagram:

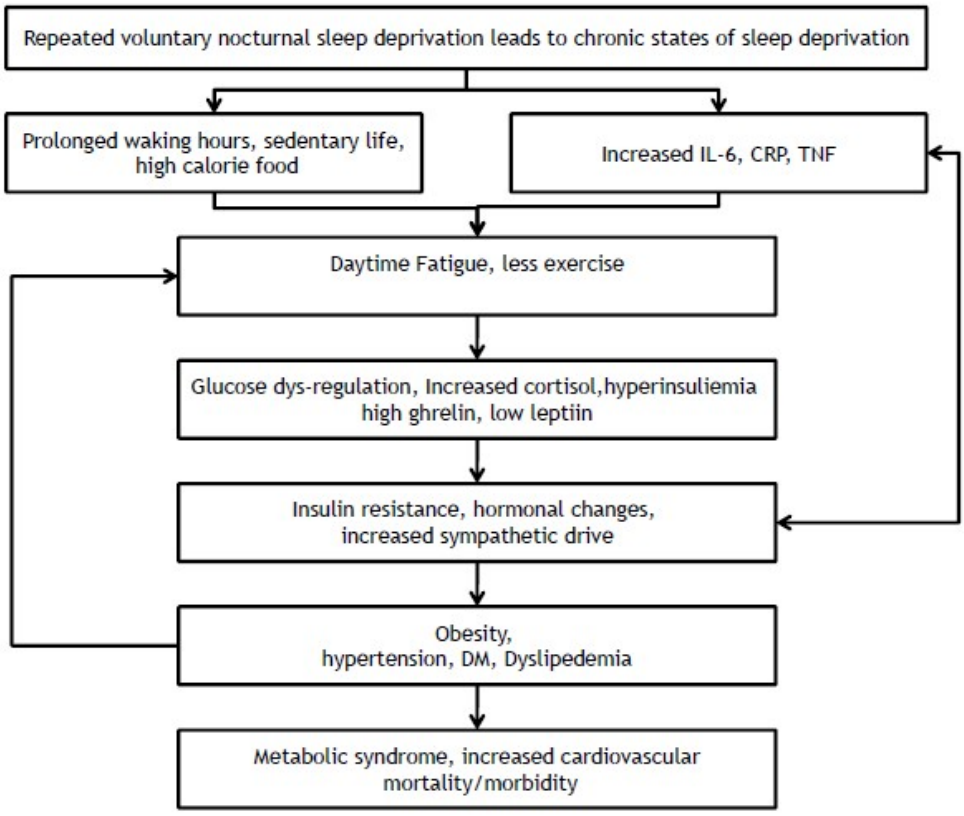


Fig 5.5: Algorithm for interaction between sleep deprivation and metabolic changes (Source: Adapted from AlDabal and BaHammam, 2011)

Recent research has shown that adolescents typically prefer to stay up later and get up later each day, which is less prevalent in older adults and pre-adolescents (Hansen *et al*., 2005). However, inadequate sleep in school-aged children and adolescents is commonly attributed to early school start times and academic workload (Wheaton *et al*., 2016). In school-age children and teenagers, excessive exposure to electronic media, such as television, computers, electronic gaming consoles, mobile phones, and music players, results in delayed bedtime and short sleep duration due to early academic activity (Cain and Gradisar, 2010). Due to their early start times in the morning and delayed sleep at night, high school students in the United States used to experience sleep deprivation during the entire school week. In a study conducted by Hansen *et al*., a total of 60 children kept sleep/wake diaries from the beginning of August until two weeks following the beginning of the school year in September (in year 1997). In the week after the start of school, the study found that teenagers lost up

to 120 minutes of sleep every night, and that weekend sleep time was much longer (by around 30 minutes) than it was throughout the school year. The overall amount of sleep was found to be higher on weekends, suggesting that teenagers were trying to make up for the sleep they had missed during the week. Sleep loss of students has adverse effects on neuro-cognitive performance, mood, and health leading to poor morning performance, compared with afternoon performance (Hansen *et al*., 2005).

Another common feature of sleep deprivation is due to engagement in shift work. In comparison to weekday workers, shift workers who work at night typically get less sleep. This idea, which contends that shift work causes sleep deprivation with negative metabolic effects, may have important consequences for population-based interventions to stop the rise of metabolic diseases in the modern workplace culture (Wolk and Somers, 2006).

It was discovered throughout the literature search that the majority of studies on sleep patterns in teens and other age groups were from the West (Gupta *et al*., 2008). To obtain accurate published data from India on this crucial yet understudied topic, research on teenage sleep patterns is essential. In a study by Gupta *et al*., 1920 students in Grades 9 through 12 from three Delhi-area schools were included, and their sleep patterns were evaluated on a variety of factors, including total daily sleep time, time to bed, sleep latency, nocturnal awakenings, wake-up time, time to get out of bed, daytime napping, nap duration, the impact of skipping naps, etc. The study gave some important findings: (a) wake up time varied significantly amongst adolescents and it got delayed with the advancing Grades (b) presence of television, internet, or any other media in the child's bedroom made them to sleep late and wake-up late, such children used to spend less time in bed and were more tired during the day (c) this study sample had increased prevalence of daytime napping and daytime sleepiness whose incidence increased with higher Grades (Gupta *et al*., 2008). According to a study conducted on urban and semi-urban South Indian youngsters, those who sleep for shorter periods of time (less than 8.5 hours per day) are more likely to be overweight than those who sleep for longer periods of time (more than 9.5 hours per day) (Kuriyan *et al*., 2013). Sleep anomalies and its long term effect on health in respect to metabolic disorder is a topic that needs attention and long term

follow up. How much changing lifestyle in India is impacting sleep pattern and is that impact well enough to drive up to the metabolic outcomes?

5.8 Education as stressor:

Education in the form of "pressure learning" can be a stressor which has not been studied well from metabolic syndrome angle. The competition to do better than peers or learn things quickly than others can be a tremendous stressor. Children are more vulnerable to such stressor though young people are equally prone due to career related stress. Moreover, there are factors which can be considered as barriers of physical activity in children or which can induce sedentary behaviour are time constrains due to the volume of home work, negative experiences in school, own peer pressure to perform better, and sense of lack of energy (Swaminathan and Vaz, 2013). Increase incidence of suicide amongst teenagers and young aged is reported on daily basis in India. Under performance in studies than what has been expected is a major cause of such catastrophe. Even if we ignore such catastrophe, health related problems will obviously be there due to educational stressors. Highest level of education (tertiary education) and good monthly household income (≥ LKR 50,000) was observed to have the highest prevalence of metabolic syndrome in a study on Sri Lankan adults (Katulanda *et al*., 2012). The Alameda County Study attempted to link socioeconomic level and diabetes incidence during a 34-year period (1965-1999) using a sample size of 6147 people. A total 318 (5.2%) of the 6147 patients at baseline who participated in the 34-year trial reported getting diabetes (Maty *et al*., 2005). In stark contrast to the Sri Lankan study, this research revealed that having less than 12 years of education was linked to a 90% higher risk of diabetes than having more than 12 years of education (ibid). The study found that disadvantage in educational attainment due to socioeconomic reasons is a significant factor in determining the incidence of Type 2 diabetes in adults (Maty *et al*., 2005). Similarly, stress-related with low educational status can be strongly associated with abdominal obesity (Pasquali, 2012). These contrasting findings need to be further investigated keeping following three perspectives in mind. Firstly, is it due to low education level the health awareness level is so low that subjects are unable decide on the healthy lifestyle practices. Secondly, educational stresses are so high and prolong that in the race of attaining educational qualification the health ultimately suffers. Lastly,

subjects who are unable to handle the educational stress, drops down before completion of educational goals.

5.9 Housing, water, sanitation as stressors:

Housing, water, and sanitation are basic components of living condition. These factors are hardly studied as stressors in relation to metabolic syndrome. In developed countries where living conditions of people are better, they are never considered as factors of concern. However in developing countries like India these components are of major concern both in rural and urban set up. We have sufficient data for India which shows that poor housing condition, struggle to collect potable water, and poor sanitation are still rampant. Such poor living condition can encounter the inhabitants with repeated infections, as well as mental and physical stress. Repeated infection, inflammation, triggering of pro-inflammatory factors and endothelial dysfunction are established biological pathway of obesity/adiposity. We may propose that repeated infections during critical phases of development (childhood) can also initiate stress mechanism. Now inflammatory and stress mechanisms can act together or they may be independent of each other. To establish infections as stressor we need to conduct long term epidemiological studies.

Similarly fetching water from far flung areas or to queue up for collection can be a cause of both physical and mental stress. Moreover poor quality of drinking water can cause repeated infections of an individual. Poor housing and sanitation are other reasons of repeated infections. As vulnerability and stress related to these factors cannot be measured directly hence some other indirect parameters have to be utilized to estimate the magnitude of stress. Following data can be of help in assessing the living condition and throw some light on the problem in India.

	Urban	Rural	All
Households having principal source of drinking water within dwelling (NSS 76th round, 2018)	56.1%	27.5%	37.3%
Households with exclusive access to a better primary drinking water source within the home's boundaries and with enough water accessible year-round (NSS 76th round, 2018)	50.5%	42.0%	45.0%
Drinking water not treated or not required to be treated (NSS 76th round, 2018)	50.9%	72.8%	65.3%
Households having no access to latrine (NSS 76th round, 2018)	3.8%	28.7%	20.2%
Bad condition of structure of house (NSS 76th round, 2018)	6.9%	14.9%	12.2%
Percent of households with houses that have stagnant water issues inside or outside the house (NSS 76th round, 2018)	12.6%	16.6%	15.2%
Households without drainage facility (NSS 76th round, 2018)	8.0%	38.9%	28.3%

Table 5.3: Data on some salient indicators of living condition in India for both rural and urban set up (Source: NSS 76th round, 2018)

Some of the above parameters are already mentioned in previous chapter of environmental factors as cause of infection and obesity. Principle source of drinking water within easy reach (within dwelling) is still a big problem in India (37.3%) and more serious in rural area. All together only 45.0% households have exclusive drinking water source located within their premises and water sufficiently available throughout the year. Accessibility of drinking water is not easy in good number of households and it requires enough of physical and mental stress to fulfill the need. In the survey there is no scope to analyze the water quality but we can presume that majority of population i.e. 65.3% (rural and urban combined) are drinking untreated water or water which is presumed to be safe without treatment. Bad structure of house

(12.2%), water stagnation around house (15.2%), no access to latrine (20.2%), and lack of proper drainage facility (28.3%) etc. are other indicators of poor living condition. All these factors indicate towards increased vulnerability to frequent infections. Moreover these data are from recent NSS round which shows a grave picture even after significant improvement in the situation. It can easily be presumed that the situation might be more deteriorating few decades back which likely to have adverse consequences till now.

5.10 Smoking or tobacco use and/or alcohol consumption as determinant:

Smoking or use of other tobacco products and/or consumption of alcohol has its implications on society as well as on health. The habit of using such products cannot be considered as stressors but these habits at many times are justified by users to overcome stress. It is important to ascertain how use of such products can enhance the process of metabolic syndrome in presence of other risk factors.

5.10.1 Smoking or tobacco use:

According to certain research, smoking is a significant but modifiable risk factor for developing metabolic syndrome. Korea National Health and Nutrition Examination Survey in 1998 obtained data for 3452 adult men (≥20 years) which showed significant dose-dependent association of cigarette smoking with metabolic syndrome (Woo Oh *et al*., 2005). In another cross sectional study in Korea (from April 2009 to December 2010) out of 1,852 subjects 31.8% were non-smokers, 56.2% were intermediate smokers, and 12.0% were heavy smokers. The prevalence of metabolic syndrome were 29.4%, 33.7%, and 42.2% respectively; clearly indicating that prevalence of metabolic syndrome had increased as smoking level increased (Hwang *et al*., 2014). Similar findings were attained in a cross sectional study in Seoul from July 2017 to March 2019 with 808 participants (<40 years age) where cigarette smokers had a 2.4 fold greater risk of metabolic syndrome (Kim *et al*., 2021). In comparison to participants who did not smoke, middle-aged Japanese male office workers who frequently smoked tobacco had a 1.07–1.66 times higher chance of developing metabolic syndrome (Nakanishi *et al*., 2005). Among 1146 men with

varying smoking statuses, including non-smokers, former smokers, and current smokers, a community-based study carried out between October 2004 and September 2005 in a major city in Central Taiwan revealed that current smokers had a significantly higher risk of developing the metabolic syndrome than the other two groups (Chen *et al*., 2008). An identical correlation was found in a study conducted by 398 Thai volunteers (aged 21 to 62) in Bangkok, Thailand's suburban and urban residential zones (Suriyaprom *et al*., 2010). Teenagers who use tobacco products, either actively or passively, who are overweight or at danger of becoming overweight have a four times increased chance of having the metabolic syndrome (Weitzman *et al*., 2005). A study with a one-year follow-up period found that current smokers had a greater risk of metabolic syndrome than non-smokers, independent of age, BMI, insulin resistance, and other lifestyle factors (Kawada *et al*., 2010). Men who smoke more than 20 cigarettes a day have a higher chance of developing diabetes than non-smokers, according to the Physicians' Health Study of America, which monitored 21,068 male physicians from the ages of 40 to 84 years for a period of 12 years (Manson *et al*., 2000). The risk of getting metabolic disease was found to be 31 percent higher in smokers who smoked more than 20 cigarettes per day than in smokers who smoked fewer than 20 cigarettes per day in a similar cross-sectional investigation in Brazil with 65 smokers (age 18-60 years) (Gouveia *et al*., 2020). Cross sectional study conducted in Puerto Rico in 856 adults from 2005 to 2007 also supports an increased risk of metabolic syndrome among current smokers, particularly those with a heavier consumption (Calo *et al*., 2013). Smoking seems to accelerate visceral fat accumulation leading to increased waist circumference and promote obesity-related disorders (Cena *et al*., 2011). In a meta-analysis of prospective studies that included an analysis of 13 trials with 56,691 participants and 8,688 cases, Sun *et al*. (2012) demonstrated a strong positive connection between active smoking and risk of metabolic syndrome. Heavy smokers were more likely to acquire metabolic syndrome than light smokers, and active male smokers were more likely to do so than non-smokers (Sun *et al*., 2012). The Multi-Ethnic Study of Atherosclerosis (MESA) included males and females between the ages of 45 and 84 who self-identified as non-Hispanic White, African-American, Hispanic, or Chinese American, a multicenter cohort study, between 2000 and 2002. This study found that current smoking is associated with metabolic syndrome, prevalence of high waist circumference, low HDL-C and elevated triglyceride despite having lower BMI

(Berlin *et al*., 2012). However many studies did not find any correlation between smoking history with lipid profile-related variables, making it a controversial topic (Gouveia *et al*., 2020). Study by Berlin *et al*. also found higher inflammatory markers among current smokers compared to never or former smokers. According to statistics from the Framingham research, smokers who are obese have a 14-year decline in life expectancy by the time they are 40 years old (Peeters *et al*., 2003).

The recent Global Adult Tobacco Survey report of India (2016-17) stated that 28.6% adults (>15 years age) have been using tobacco in some form. The rate has been 42.4% for men and 14.2% for women. If we analyse the trend with NFHS data then there is a gradual decrease in tobacco users in India like many other developing countries. However the bad news is that the prevalence of smokeless tobacco use continues to rise with decline in smoking rate (Gupta *et al*., 2004). The use of smokeless tobacco has received relatively lesser attention in studies even after derangements associated with metabolic syndrome (Balhara, 2012). Overall prevalence of smokeless tobacco in India was 21.4% with 29.6% in men and 12.8% in women (Global Adult Tobacco Survey report of India, 2016-17)

	NFHS 3 (2005-06)	NFHS 4 (2015-16)	NFHS 5 (2019-21)
Men who use any kind of tobacco (%)	57.0	44.5	38.0
Women who use any kind of tobacco (%)	10.8	6.8	8.9

Table 5.4: Tobacco use among adults in India (15-49 years) (Source: NFHS 4 and NFHS 5)

In a position statement on tobacco use and metabolic syndrome by Uttar Pradesh Association of Physicians of India has held smoking as an important risk factor for metabolic syndrome (Balhara *et al*., 2017).

Mechanism by which smoking or tobacco promotes metabolic syndrome:

Smokers are more hyperinsulinemic in response to an oral glucose load and have greater insulin resistance than non-smokers (Manson *et al*., 2000). Additionally,

smoking cigarettes can reduce insulin sensitivity by raising blood levels of insulin-antagonistic compounds like catecholamines, cortisol, and growth hormone (Nakanishi *et al*., 2005). Smokers' fasting plasma cortisol concentrations are higher than non-smokers', and there may be an imbalance of the sex hormones for men and women (Friedman *et al*., 1987). By having a direct harmful effect on the pancreas, beta cell function, and the insulin receptor; nicotine, carbon monoxide, and other metabolites generated from tobacco also play significant roles in insulin resistance (Borisova and Georgieva, 1991; Cena *et al*., 2011). Furthermore, several mechanisms have been proposed by several researchers on how cigarette smoking promotes dyslipidemia (Slagter *et al*., 2013). Leptin has drawn interest because of its potential links to tobacco use and body weight. The link between Leptin and adiposity is more complicated when multiple factors are at play. There are still conflicting results on Leptin levels in smokers and further investigations are required (Cena *et al*., 2011). Whatever contradictions are there but smoking in no doubt causes hormonal imbalance which consequent upon insulin resistance as a result of central fat accumulation (ibid). Increased levels of inflammatory markers including C reactive protein and fibrinogen have been linked to smoking and other obesity variables (Balhara, 2012).

5.10.2 Alcohol consumption:

Alcohol consumption and its relation with health is complex (Lee and Jang, 2021); and equally complex is the association of alcohol with each component of metabolic syndrome. This complexity is due to the dose relation and also with the quality of alcohol consumed in developing countries like India. Low to moderate alcohol intake (15-30 gram ethanol/day) has been stated to be beneficial for health while high alcohol intake (>45-60 gram ethanol/day) increases the risk (Elmadhun and Sellke, 2013; Lee and Jang, 2021). In most of the cases people start as low to moderate drinkers but with time they turn to be heavy drinkers because of addiction to alcohol. Epidemiological evidences support the incidence of metabolic syndrome with alcohol consumption but still data on this issue are not consistent rather controversial (Ala'a *et al*., 2009; Sun *et al*., 2013). A meta analysis of six prospective studies with 28,862 participants and 3305 cases of metabolic syndrome revealed that heavy alcohol consumption was linked to an increased risk of developing the

condition, whereas very light alcohol consumption appeared to be linked to a decreased risk of the same (Sun *et al*., 2013). The association of alcohol consumption with metabolic syndrome has been referred as J-shaped (Ala'a *et al*., 2009; Trisrivirat *et al*., 2021) while with insulin resistance as U-shaped (Sun *et al*., 2013). In another meta-analysis of seven observational studies by Ala'a *et al*. suggested "responsible alcohol intake" to be associated with a reduced prevalence of metabolic syndrome. Results of a cross-sectional study with 400 participants chosen from the family medicine department's outpatient unit at Chiang Mai University's school of medicine (Thailand), between December 2016 and January 2017 suggested that alcohol consumption is frequently linked to an increased risk of metabolic syndrome (Trisrivirat *et al*., 2021). In a Korean cross-sectional study 12,830 current drinkers were recruited where prevalence of metabolic syndrome was 26.2% in men and 17.5% in women, and drinking quantity and binge drinking frequency were found to be positively associated with metabolic syndrome in both sexes (Lee and Jang, 2021). A systematic review and meta-analysis of articles from countries like USA, Brazil, Switzerland, Germany, and India demonstrated that more than 1 in 5 persons with alcohol use disorder had metabolic syndrome (Vancampfort *et al*., 2016).

Analysis of 1529 participants of the National Health and Nutrition Examination Survey (1999-2002) in U.S. adults showed that drinking in excess of dietary recommendation and binge drinking increased the risk of metabolic syndrome (Fan *et al*., 2008). The Brazilian Longitudinal Study of Adult Health (ELSA-Brasil) included 14,375 current or retired government servants (aged 35 to 74), and a cross-sectional analysis revealed a strong correlation between alcohol consumption and metabolic syndrome (44%) (Vieira *et al*., 2016). The study also found that timing of alcohol consumption and beverage type determines the outcome of metabolic syndrome or its components.

There are scarcity of studies in India reporting prevalence of metabolic syndrome and substance abuse including alcohol consumption. In a study conducted in between July-December 2009 at the Drug De-addiction and Treatment Center (DDTC) of the Psychiatry department at the multispecialty general hospital of Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh (India) prevalence of metabolic syndrome was 24.6% (n=110) in alcohol dependent group (Mattoo *et al*.,

2011). In the same set up a cross sectional study was conducted from July 2009 to June 2010 involving 100 alcohol dependent patients and also using both genetic (n=50) and healthy (n=50) controls. In contrast to prior research, the prevalence of metabolic syndrome was fairly low in alcohol-dependent people (27% and 18%, respectively, using IDF and NCEP ATP III criteria), compared to healthy controls (30% and 20% using IDF and NCEP ATP III criteria respectively) (Aneja *et al*., 2013). A small cross-sectional study involving 50 alcohol-dependent patients (18-55 years old) at the Department of Psychiatry, Victoria Hospital, affiliated with Bangalore Medical College and Research Institute, Bengaluru, from October 2014 to May 2016 revealed a 14 percent prevalence of metabolic syndrome (Saiyadali *et al*., 2020).

The LifeLines Cohort Research is a multidisciplinary prospective population-based cohort study that was conducted in the north-eastern part of the Netherlands between December 2006 and December 2012 (Slagter *et al*., 2014). The study having 64,046 participants tried to evaluate the combined effect of smoking and alcohol on metabolic syndrome. Like other studies, this study also found favourable association between light alcohol consumption and components of metabolic syndrome. Interestingly, light alcohol consumption had been stated in the study to moderate the negative association of smoking with metabolic syndrome (Slagter *et al*., 2014). Studies mentioned above are showing discrepant results on whether alcohol consumption is protective or threat to metabolic syndrome. This could be partially explained by varying consumption habits in various study populations or by under reporting of consumption pattern (as most studies are dependent on self declaration of alcohol consumption) (Fan *et al*., 2008). Studies on the association between diverse alcohol consumption patterns or types of beverages and the metabolic syndrome are uncommon in India, where the majority of studies to date have focused on prevalence estimation or dosage response relationships. Higher regular drinking rates, exceeding dietary recommendations, and binge drinking were all linked to an increased risk of developing the metabolic syndrome (Fan *et al*., 2008). Lower prevalence of metabolic syndrome with moderate alcohol consumption has been reported from various studies on American and European population (Rosell *et al*., 2003).

Like smoking NFHS data show a decreasing trend in alcohol consumption. However, this trend is going to be beneficial or harmful in the prevalence of metabolic syndrome needs further follow up.

	NFHS 3 (2005-06)	NFHS 4 (2015-16)	NFHS 5 (2019-21)
Men who consume alcohol (%)	31.9	29.2	18.8
Women who consume alcohol (%)	2.2	1.2	1.3

Table 5.5: Alcohol consumption among adults in India (15-49 years) (Source: NFHS 4 and NFHS 5 factsheet)

5.11 Inadequate studies in India:

Studies and data on stress and its metabolic effect in India scenario are inadequate to draw a definitive conclusion. We need long term follow up studies with inclusion of important stress factors even though there are obvious hindrances in conducting such studies. For instance, it is challenging to translate the effects of experimental sleep restriction from the laboratory to the real world, making it difficult to link various aspects of sleep deprivation as a causal factor with metabolic syndrome (Reaven, 2006). Researchers have to look beyond the lens of obesity/adiposity as the final determinant to address these deficiencies. We need to come out from the tendency to relate metabolic syndrome via obesity/adiposity pathway for most of the determinants, as it may not be suitable for Asian Indian phenotype. Some studies on Chinese migrants already supported this and we also need to conduct such studies in Indian population to substantiate that claim. Once it is done then we have to look into various aspects of smoking/tobacco/alcohol use as next derivative of metabolic syndrome.

Chapter Six

Discussions and Conclusions

6.1 Discussions:

The review has looked into various biological and social determinants of metabolic syndrome in Indian context. While going through literatures it has been found that biological or micro level determinants have been studied well but with some unaddressed issues which need further clarity. On the other hand important social determinants (macro level) have been considered indispensable as cause of metabolic syndrome but in depth long follow up studies on social determinants are deficient. Certain areas are still in dark which need more analysis. A detailed discussion on the basis of reviewed literature as follows:

6.1.1 Definition of Metabolic Syndrome and risk assessment:

There are several definitions in medical textbooks or as proposed by various organizations for metabolic syndrome. These definitions are modified or amended time to time to meet the variations as per geography and/or ethnicity. Most of these definitions are based on biological risk factors and on their clinical parameters. But these definitions are deficient in looking at other important risk factors like positive or negative energy balance. The available definitions do not give any scope to make out the energy balance status of an individual as they do not look into the physical activity in terms of calories, or energy consumed in the form of food. Energy consumed, energy utilized, and energy deposited in the body is important as risk factors for metabolic syndrome. Energy deficiencies at crucial times of development are also important for future outcome of metabolic syndrome in self or in future progeny. Calculating out the energy surplus or deficiency as risk factors to predict the probability of metabolic syndrome is crucial from both preventive and planning point of view. The existing definitions are not capable of capturing this important aspect.

The most accepted WHO definition of metabolic syndrome has also been criticised for not able to address certain aspects. WHO includes Type 2 diabetes as a criterion in the definition but keep no scope for the diagnosis of metabolic syndrome in those individuals who are at risk of developing diabetes later. Additionally, the WHO definition includes oral glucose

tolerance test (OGTT) or 2-hour post glucose challenge to determine the status of impaired glucose tolerance. However these tests are considered by many as less practical with an added cost but with a small added value in predicting risk (Grundy *et al*., 2004).

Indian Diabetes Risk Score (IDRS) has been proposed in predicting metabolic syndrome and cardiovascular disease with score value ≥60 as per the proposed score table below (Parikh and Mohan, 2012). The physical activity component has been included in this risk score. However a more specific quantification of physical activity would have given a better prediction in risk score.

Indian Diabetes Risk Score (IDRS)	
Parameter	Score
Age (years): <35 35-49 ≥50	 0 20 30
Abdominal obesity: Waist<80cm(female), <90cm(male) Waist≥80-89cm(female), ≥90-99cm(male) Waist≥90cm(female), ≥100cm(male)	 0 10 20
Physical activity: Exercise regular+ strenuous work Exercise regular or strenuous work No exercise and sedentary work	 0 20 30
Family history: No family history Either parent Both parents Minimum score	 0 10 20 0

Table 6.1: Indian Diabetes Risk Score (Source: Parikh and Mohan, 2012)

A similar index named Lipid Accumulation Product (LAP) has been proposed to identify metabolic syndrome using WC and fasting triglyceride levels (mmol/L) as parameters (Parikh and Mohan, 2012). But their accuracy has to be studied upon and more in depth studies are required to reach into a definitive conclusion.

The above scoring system though tried to include the physical activity component but still lack one important aspect i.e. calorie intake in respect to food consumed. There are reference levels for recommended daily allowance (RDA) of calorie intake and we even have estimates for calorie contribution by various macro components of food. The calorie consumed can be easily calculated with reference to the food history for each and every individual. The positive or negative energy balance can be calculated out if we can quantify the physical activity in terms of calories burnt and relate it with the food consumed.

In Indian context when we have a skewed population with diverse food consumption pattern and varied physical activity, knowing positive or negative energy balance is important to determine the risk factors. As because of such variations the same factor can play different roles in different situation and ultimately act as determinants of metabolic syndrome. In urban set up positive energy balance can be due to less physical activities and more energy dense food and hence act as the primary determinant of metabolic syndrome. On the other hand in rural poverty driven and labour intense situation negative energy balance leading to developmental compromises can be the primary determinant of metabolic syndrome. Again if we look at the urban migrant population who has intense hardship for livelihood and living in pavers and slums of cities; they do have similar negative energy balance even after staying in urban environment. This linking of social status and energy balance is crucial to predict the probable pathway involved in future causation of metabolic syndrome. Our knowledge about physical activity is not sufficient across multiple domains and hence lack in age stratified data, comparisons across geography (regions) and location (rural to urban) etc. in India. Ramachandran *et al*. (2004) has developed a scoring system to calculate the

physical activity. Such kind of tool should be incorporated in risk assessment at field level to know the energy balance.

Categories of occupation	Does your work involve mostly sitting/standing/walking?	Does your work involve moderate activity, e.g. brisk walking, fetching water from wells, moderate agricultural work, e.g. sowing seeds, weeding, painting buildings, household work etc?	Does your work involve vigorous manual activity?	Additional activities: Do you use a cycle or engage in sports activities?	Total
(i)Manual labourers (including masons, carpenters and those who carry loads, and agricultural work, e.g. ploughing and tilling) (ii)Office jobs or desk work (iii)House wives and retired	Answer: Yes Minimum score=1	Answer: Yes Score =2 (45 min/day) Score=3 (45–240 min/day) Score=4 (240–480 min/day) Maximum score=28 (4x7 days/week)	Answer: Yes Score=5 (15–60 min/day) Score=6 (60–240 min/day) Score=7 (240–600 min/day) Maximum score=49 (7×7 days/week)	Answer: Yes Score=1 (45 min/day) Score=2 (45–240 min/day) Score=3 (240–360 min/day) Maximum score=21 (3×7 days/week)	70

persons (iv)Persons unable to work					

Quartiles of physical activity	Score
1 Sedentary 2 Light 3 Moderate 4 Strenuous	1-17 18-34 35-51 >51

Table 6.2: Physical activity scoring system (Source: Adapted from Ramachandran *et al*., 2004)

If we further narrow down to the children regarding physical activity patterns in India then there are large gaps in our knowledge. Future studies should try to capture these gaps so that we can have a clear picture on energy status which can further help in risk assessment.

6.1.2 National data on metabolic syndrome:

No nationally representative data on the prevalence of metabolic syndrome are available from any of the South Asian countries (Katulanda *et al*., 2012). Hence it is evident that India is also lacking in regular and systematic data recording of the components of metabolic syndrome. The data which gives us a clear picture on the blood glucose level, blood pressure, lipid level etc. in case of Indian population, is lacking. WHO estimated data on diabetes, hypertension, raised cholesterol etc. are available (Global status report on NCD 2010 of WHO) but need re-estimation and continuous update. National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS) was launched in India in 2010 to control NCDs. The programme has all the necessary objectives like early diagnosis and management. Up till December 2013, around 5.33 crore people of India have been screened for diabetes and hypertension (NPCDCS Information System, MoHFW). This kind of screening process must be continuous and more focus has to be given on the vulnerable sections. Health services system

should be strengthened in such a way that it can detect not only clinically confirmed cases of diabetes, hypertension, hyperlipidemia etc. but should also be able to capture the at risk population of future metabolic syndrome. A well organized and structured health services system is required which can capture these data on daily basis upon first contact with the at risk population. NFHS data do reflect the obesity/overweight data of India but must be an underestimation due to the international cut offs are used as the standard. To fulfill the early diagnosis and management objectives, a strong and correct data base is required from grass root to national level. Even screening process should cover all the population of the country and should not be in bits and pieces.

6.1.3 BMI or other alternatives:

There are sequences of stages in the life course to reach to the final outcome of metabolic syndrome and weight being an important determinant for this outcome. Obesity or overweight is undoubtedly a risk factor for future metabolic syndrome. Correct assessment of obesity/overweight is very important for future prevention or management of metabolic syndrome. But early identification, treatment and prevention of metabolic syndrome is a major challenge for healthcare professionals. Whatever tools for assessment are available at present, BMI in no doubt is the most preferred and widely used tool of assessment of body weight. In field situations we just need weight measuring instrument and measuring tap to calculate the BMI. It is quite easy and convenient to use, without any sophistication, in resource constraints countries like India. A very minimal or no training/orientation required for field staff to do the above measurements. Even the existing field staffs are familiar in measuring weight and height on regular basis. We have witnessed them doing such measurements with ease since the birth of a baby to record the progress/rate of growth etc. Even after all the advantages of BMI it excludes a major chunk of population, more specific in Asian Indian context, which are actually at risk of metabolic syndrome. BMI can measure the excess weight but fails to detect the degree of adiposity, which is very much relevant

for Asian Indians. BMI as a parameter is best suited in field situation but lack in sensitivity.

There are other parameters as proposed to replace BMI or to complement in such a way, that they fill up the gaps of each other. Waist Circumference (WC) has been used on regular basis and has been even observed to replace BMI in most recent definitions of metabolic syndrome. Like BMI we need only measuring tap to measure WC. However it has its own disadvantages owing to the different recommended body levels of measurements and were already discussed in previous chapter. We have emphasized on the importance of measuring waist circumference but it has its own limitations in predicting visceral fat accumulation and further risk assessment of the metabolic syndrome. As an alternative the index of central obesity (ICO) has been proposed and defined as the ratio of the WC to the height. So in simple terms ICO translates 'if your waist size is more than half of your height, you should consult your doctor' (Parikh and Mohan, 2012). Hence persons with ICO>0.5 should be evaluated for high blood pressures, pre-diabetes, and hyperlipidemia or metabolic syndrome (ibid). This index like others needs to be examined thoroughly before reaching on any final conclusion.

If we need to continue using the existing parameters then firm guidelines in defining cutoffs must be established for numerous obesity indicators in Asian Indians, such as BMI, waist circumference, waist to hip ratio, and percentage of body fat (Joshi, 2003). Universal BMI cutoff points are discouraged by experts (Durenberg *et al*., 2002). WHO expert consultation (2004) has already recommended the modified BMI ranges and also supported inclusion of waist circumference to refine BMI values. The suggested categories are: underweight <18.5 kg/m^2; at acceptable risk 18.5-23 kg/m^2; increased risk 23-27.5 kg/m^2; and high risk ≥27.5 kg/m^2 (WHO expert consultation, 2004). If possible country specific combinations of some parameters can be considered so that they complement the deficiencies of each other and strengthen the risk assessment capacity. We need to consider the combination of BMI and WC or waist hip ratio (WHR) in Indian context as simple tools for risk assessment. This kind of combinations is important for

specific population like Asian Indian urban or migrant population. They tend to have a larger percentage of body fat even when their BMI is lower, a higher waist hip ratio (WHR) even when their waist circumference is relatively low, and less non-fat body mass compared to ethnic groups (Joshi, 2003). We need to conduct more studies which look into the sensitivity of such combinations in risk assessment. Some investigators of west have argued that due to linear relation between BMI and WC, no significant additional information can be provided by inclusion of WC measurement (Farin *et al*., 2005). Measuring WC has been considered as just the refining of already predicted risk using BMI (Despres *et al*., 2008). As the body composition of west is very much different from Asian Indian population, hence we need nationwide studies to determine whether such correlations are linear or not in our context. In a positive sign the most recent NFHS-5 has incorporated for the first time the population with a waist-hip-ratio which has high risk. Irrespective of gender and rural-urban divide the data on waist to hip ratio is of major concern for India.

	Urban	Rural	Total
% of women with high risk waist to hip ratio (≥0.85)	59.9	55.2	56.7
% of men with high risk waist to hip ratio (≥0.90)	50.1	46.4	47.7

Table 6.3: Percentage of population with high risk waist hip ratio (Source: NFHS-5, 2019-21)

More than half of India's population are carrying the risk of central adiposity and hence have high probability of future metabolic syndrome. Studies show that overall Asian populations had lower BMIs than Caucasians while having higher Body Fat Percentages. Generally speaking, their BF percent was 3-5 percent higher for the same BMI, but for the same BF percent, their BMI was 3–4 units lower than Caucasians (Deurenberg *et al*., 2002). The below figure explains the discrepancy of BMI and BF%. Subject A and B have same BF% but due to shorter legs of A he will have high BMI value. Because of same body fat both should have equal risk but higher BMI

score makes subject A more vulnerable. Similarly subject C and D has same BMI and hence are at equal risk. But due to big frame of C he will have more lean mass and hence less BF%, making him less vulnerable than D.

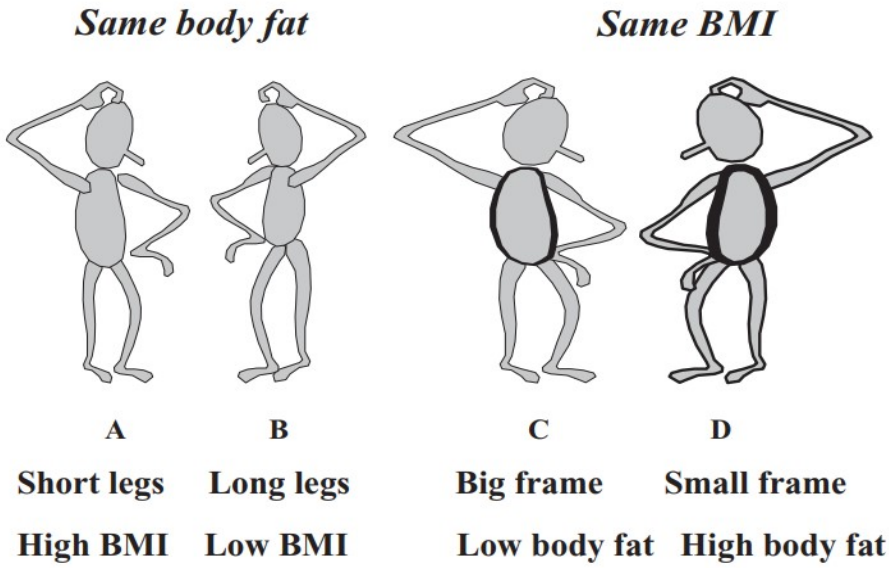


Fig 6.1: Risk assessment discrepancy of BMI and BF% (Source: Adapted from Durenberg *et al*., 2002)

BMI in children is another aspect that needs more research and more specific cut offs. Proper risk assessment at early age is important to know the future prospect of metabolic syndrome. It has been observed that BMI varies substantially as per age and gender in case of children. In case of adults simple cut offs are enough without any further division on the basis of sex and age. However in case of children the BMI cut-off points used to classify obesity should be sex-age-specific. Guidelines with such cut offs are required to be developed and implemented.

6.1.4 Over nutrition or under nutrition:

Over nutrition as an important determinant of obesity and metabolic syndrome has been extensively studied till now. We have sufficient supporting evidences for this phenomenon. Over nutrition in combination with other determinants can hasten the process. Physical inactivity has been considered as the most important determinants amongst all. However, can we have

enough studies to support that subjects with over nutrition and active lifestyle manage to delay the progression of metabolic syndrome? In other words, can we have enough evidences to hypothesise that even with obesity a person can delay the progression of metabolic syndrome by keeping himself physically active?

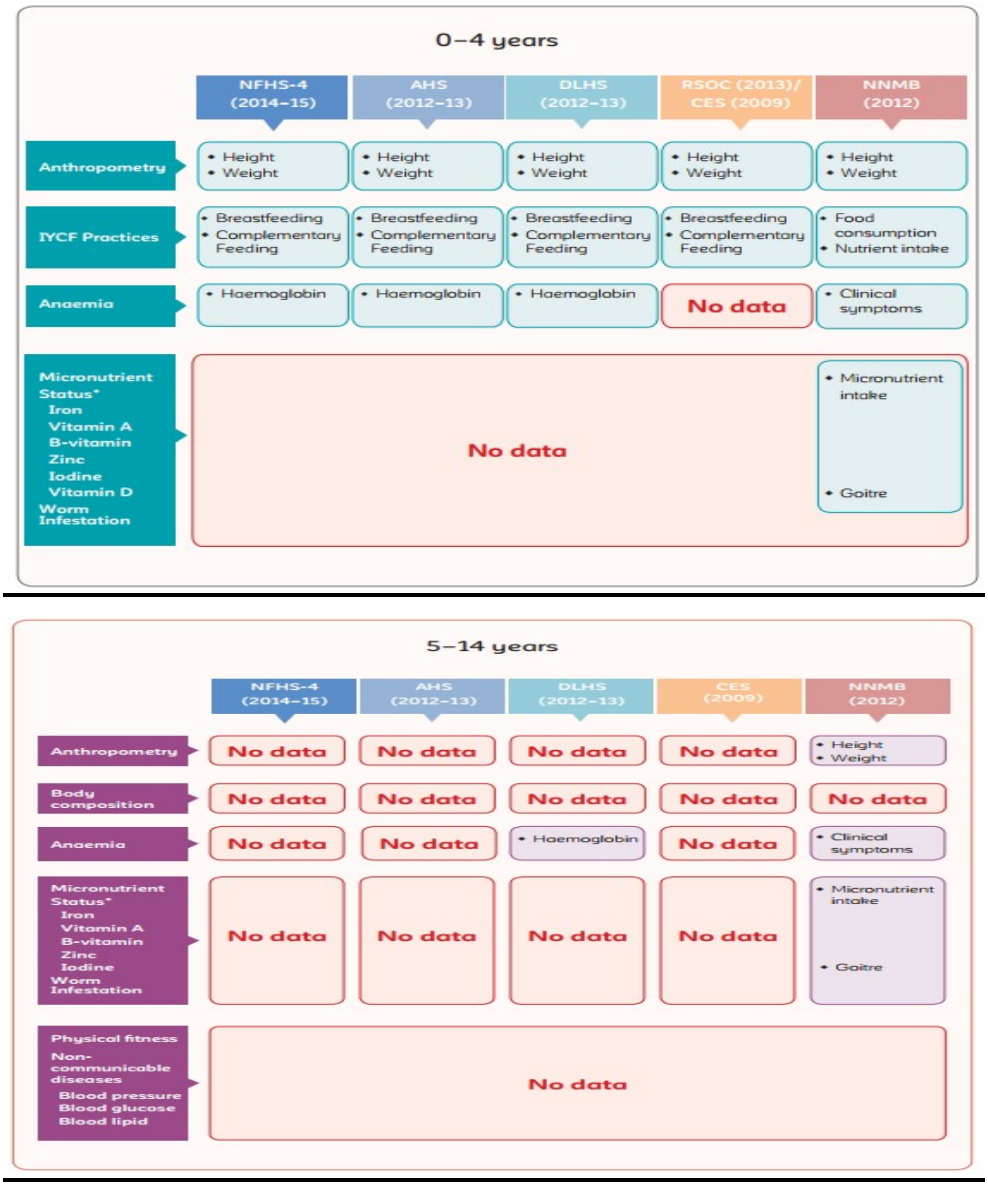
Now in contrast to over nutrition can under nutrition is an important determinant of metabolic syndrome? If so; it can be of importance in social conditions where poverty is prevalent. We have to look from the life course epidemiology angle starting from *utero* onwards with continuing situation of poverty and hardship. Poverty and hardship can cause under nutrition to the developing foetus at critical developmental stages leading to permanent changes. Even if there is improvement in poverty situation and adequate nutrition later on, the already compromised organs cannot withstand it. These irreversible changes in organs can continue to hamper the normal development in the next generation establishing a vicious cycle. We do not know if early-life protein deprivation affects the physiological makeup of skeletal muscle, a common Indian scenario, so that normal functions are compromised (Misra and Vikram, 2004). This aspect of poverty as determinant of metabolic syndrome has been poorly studied.

It is of no doubt that both over nutrition and under nutrition have similar and important implications on future metabolic syndrome depending on at which critical phases of development such changes had occurred. Determining the balanced maternal and neonatal nutrition during the critical phases of development to minimise the future prevalence of metabolic syndrome will be crucial but important.

6.1.5 Lack of national nutrition data:

Whatever surveys are being conducted till now they lack or provide limited information (a) on micronutrient deficiencies across age groups (b) on nutrition indicators beyond 5 years age group (c) on NCDs for children (d) on measures of adiposity which correlates with NCDs in the age group 5-19 years

(Comprehensive National Nutrition Survey, 2016-18). National level surveys like NFHS, DLHS, AHS, CES, NNMB etc. are unable to address several areas. Nutrition being an important determinant in crucial phases of development to decide the future course of metabolic syndrome; we should plan for studies to address these gaps. Following figure gives us a clear picture on data gaps as per such important age groups:



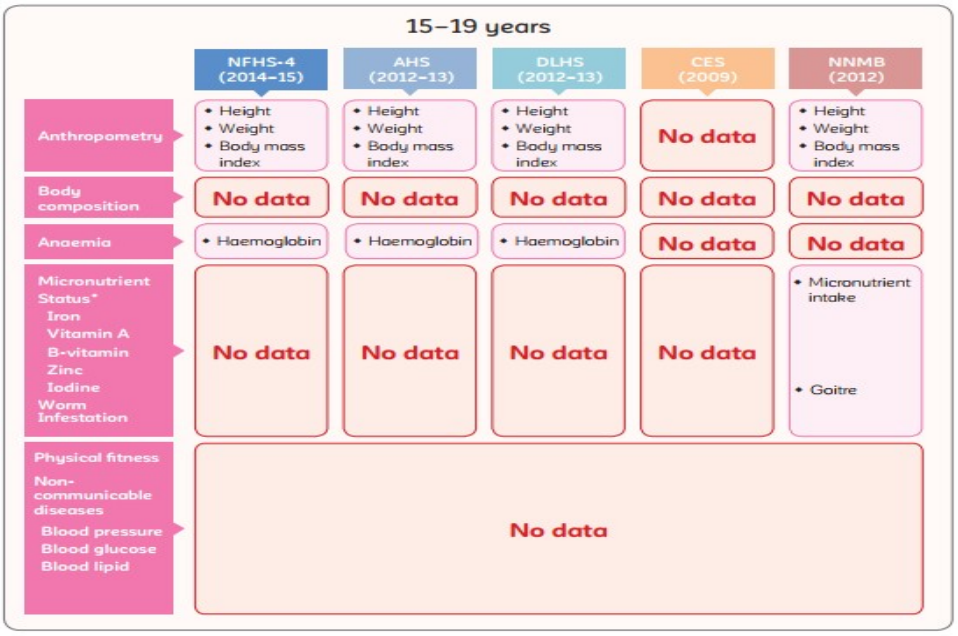


Fig 6.2: Data gaps of various surveys on nutrition (Source: Comprehensive National Nutrition Survey, 2016-18)

6.1.6 Balance between macro and micro nutrients in maternal and child diet:

What is the optimal amount of macro or micro nutrient required in maternal and child diet to be in good health? Can we be able to standardized the requirement of macro or micro nutrients for various races, genders etc.? Will these diet standardizations at critical phases of life are optimal to avoid future metabolic syndrome if we ignore the life course where subject(s) or their ancestor(s) might had gone through severe socio-economic hardships?

Above queries are relevant but might be difficult to achieve the prescribed balance owing to the complexity of the diet menu as determined by personal and environmental factors. Keeping this in view, a recent document "What India Eats" by ICMR-NIN has been published to understand (i) food group and macronutrient consumed as per region (ii) how different food groups contribute in the form of energy, protein, fat and carbohydrate (iii) how much population actually consuming food as per recommendation of ICMR-NIN (iv) region wise variation of obesity, hypertension and diabetes (Hemalatha *et al*., 2020). ICMR-NIN has developed "My Plate for the Day" on the basis of recommended dietary allowances (RDA) to design the proportions of energy

contribution from different food groups to attain 2000 Kcal of Indian diet. My plate for the day as developed by ICMR-NIN recommends 45% energy/calorie from cereals and millets, 17% of calories from pulses and meat, and 10% from milk and milk products to achieve 2000 Kcal. Following table illustrates the prescribed proportion of foods from different food groups:

Food Groups	Foods to be consumed per day (weight of raw food in gram)	% of total energy/day from each food group	Total energy/day (Kcal) from each food group	Total protein/day (gram) from each food group
Cereals	270	45	900	20
Pulses*	90	17	340	21
Milk/Curd (ml)	300	10	200	10
Vegetables+ (green leafy vegetables)	350	5	100	4
Fruits#	150	3	67	1
Nuts & Seeds	20	8	150	4
Fats & Oils$	27	12	243	-

Table 6.4: Recommended daily consumption of various food groups (Source: Adapted from ICMR-NIN my plate, 2020)

*Egg/fish/meat can substitute pulses
+Prescribed amount of vegetables (excluding potato) may be consumed in either cooked form or salad
#Prefer fresh fruits (avoid juices)
$Use different varieties of cooking oils, vegetables, fruits, nuts etc. to obtain a variety of phytonutrients, vitamins, minerals, and bioactive compounds

From theoretical point the above recommendations look good but are far away to achieve in Indian scenario where we have so much of regional, cultural, and economic variations. The document clearly mentions that above recommendations do not have therapeutic implications but can optimise the prevalence of non-communicable diseases if coupled with other healthy behaviours or lifestyle. It is a matter of doubt how many can achieve the above recommendations on daily basis even after belonging to the well off

category of the society. People who belong to the marginalized section of the society, achieving these diet goals are nothing more than fairy tales. For them a plate which fills their tummy and do not let them stay hungry would be the biggest achievement of the day. The document itself gives a contrasting picture on percentage of population in India who actually consume food groups as recommended. Major population is unable to meet the dietary recommendations in both rural and urban areas. Interestingly people in rural areas are seemed to meet the fat requirement as recommended indicating towards nutrition transition and inclination towards energy dense food. The picture is more or less similar if we further segregate to regional level.

Food groups	Rural		Urban	
	% people with recommended intakes	% people not taking recommended intakes	% people with recommended intakes	% people not taking recommended intakes
Cereals	1.5	98.5	21.6	78.4
Pulses	7.2	92.8	16.4	83.6
Total fat	97.4	2.6	74.9	25.1
Milk and milk products	8.7	91.3	14.3	85.7
Vegetables	8.8	91.2	17.0	83.0
Fruits	15.9	84.1	28.6	71.4
Nuts	14.3	85.7	17.9	82.1
Others	91.9	8.1	62.5	37.5

Table 6.5: Percent of adult population consuming recommended food intakes in rural and urban areas of India (Source: What India Eats ICMR-NIN, 2020)

It may be a rare occasion when a perfect balance of macro and micro nutrients can be found in population, especially in maternal and child diet. Most of the studies are found to be oriented with calorie (macro) intake and their relation with obesity. Studies which look into the role of macro nutrients in the development of vital organs during critical phases of life are rare. Similarly studies which look into the correlation of micro nutrients in diet and how they influence the development of vital organs during critical phases of life are not adequate. Laboratory based animal studies are there but we need to have long term follow up dietary studies as per social and economic condition. To understand the function performed by macro- and micronutrients during intrauterine development (from maternal diet) and neonatal periods and the risk of obesity and the metabolic syndrome in adulthood, extensive research on the basis of social stratification is needed in India. In other words, comparative studies need to be conducted to know how same macro- and micronutrients bring out different metabolic outcomes in different social groups.

6.1.7 Does public distribution system (PDS) need to focus on providing a healthy food basket?

The core objective of PDS is that no one stays hungry. Even the poorest of the poor in the society should be protected by the food safety net. However, when we look into the food basket, the program mainly focuses on providing subsidised sugar, rice and wheat to the poor. The nutrition transition in India has changed the taste bud of consumers and hence PDS has to come out of the historically inclined policy towards staple grains only. It is high time for government to make the PDS basket more diversified by not focusing only on cereals but other healthy products. A diversified basket will enhance the accessibility and availability of various food items even to the poorest, which is required to deal with the food insecurity as well as nutritional deficiencies. The policy should be such that PDS either promotes coarse grains instead of fine grains or push for inclusion of fibre rich healthy food items like fruits and vegetables.

6.1.8 Is ongoing nutrition rehabilitation programs stand out in optimizing the diet as per need?

The important ongoing nutrition rehabilitation programs in India are (i) Nutrition Rehabilitation Center (NRC) for low birth weight babies (ii) Mid day meal program for school going children. These two programs are important from metabolic disorder point because they cover the crucial phases of development in neonates and children.

(i) NRC: The main objective of establishing NRCs under the guidance of Ministry of Health and Family Welfare is to manage the children with severe acute malnutrition (SAM) in the age range of 6-59months. The first and foremost job of NRC is to correct the nutrition deficiencies through nutrition supplementation. Although such centers take the opportunity to provide other services like nutrition counseling, immunization, family planning etc. but here we will be focusing on the nutrition rehabilitation aspect only. For SAM children with medical complications, initial stabilization may have to be provided at higher facility like district hospital or sub-division hospital for a period up to 1 week. Once stabilization is done, the rehabilitation phase continues for next 2-6 weeks and usually the initial 2 weeks of this phase are spent at NRC. Initially a "starter diet" with low in protein but high in carbohydrate is started and then switched to "catch up diet" with high calorie and protein. The "Operational guideline on facility based management of children with SAM (2011)" has detail nutrition reference chart and even has diet recipe for both facility and community management. The monitoring is done on the basis of weight measurement and weight gain is considered as a successful indicator of NRC. The guideline clearly mentions that "encourage the child to eat as much as possible, so the child can gain weight rapidly" is somehow contrary to the initial hypothesis as mentioned in previous chapter that 'catch-up growth', where babies are born small but grow rapidly to achieve the normal, has been identified as a risk factor for the later development of metabolic syndrome. SAM children are

expected to have somewhat compromised development of vital organs and hence cannot be expected to handle the dietary surge. Moreover, over dependence on parameters like weight and height to monitor the growth of SAM children can be good indicators from NRC outcome point but may fail to differentiate whether the weight gain is due to muscle mass or fat mass. For Asian Indians this aspect is very important as discussed earlier. It is high time to do some long term follow up/retrospective studied to know the future effect on low birth weight babies of NRCs who got rehabilitations in the form of nutrition supplements to gain the prescribed weight. In a way to reduce the under five mortality are we creating a pool of children which will be living with chronic morbidities in adult life?

(ii) Mid Day Meal Program: India has a long history of mid day meal program in school. Initially it was presumed that school meal program would exert a positive effect on school enrolment and attendance, but could not be ascertained later. The program also tried to break the age old caste, class, and gender divide by sitting together and sharing a common meal (Ministry of Education GoI, 2006). It has to be kept in mind that the program is a 'nutrition support' and does not intend to replace the major meals of the day. But in practical, schools are being enrolled by children of various socio-economic back ground, such nutrition support serves differently to different children. For children of well to do families such free meals may serve as additional meals; whereas the same can be a major meal for the under privileged. Free meal programs in school of developing countries like India to control the under nutrition can actually increase the childhood obesity by enhancing the adiposity among those with minimal under nutrition. The program does not have the scope to regularly monitor the growth of children and accordingly the calorie adjustment. Hence it is difficult to know for whom the free meals are replenishing the deficient calorie and for whom adding the excess calorie. The umbrella coverage of all school going children with prescribed calorie intake without accessing the actual calorie requirement and socio-economic background may be problematic from future metabolic disorder point. Regular follow up of

school going children is required by using proper parameters to monitor weight gain (for both muscle and fat mass).

6.1.9 Other areas of nutrition that need focus:

(i) We do not have enough studies to know the driving forces beneath in changing the pattern of consumer preference for food items. When Indians started to achieve the economic sustainability, why dietary habits have diverted towards more energy dense Western style of diet?

(ii) Globalization and urbanization is no doubt creating nutrition transition in India similar to rest of the world. Eating out or meals consumed away from home has become a more frequent activity. No national level survey tries to capture this aspect in order to see the portion of meal which is not home cooked. Most of the non-home cooked foods are found to be energy dense with minimal nutritional value. What proportion of population in India consumes outside food on regular basis is a topic of analysis to do the risk estimation.

(iii) "Frequent small meals" are always encouraged by physicians for good health. Nationwide studies pertaining to large interval between meals and their correlation with increase incidence of metabolic syndrome have not been conducted. Once this correlation is established, we can go further to ascertain the determinants behind the long gaps between major meals. People having sufficient purchasing power but irregular eating time table because of tight job schedule can be a reason. Busy work schedule compels to eat out regularly as there is no time to cook at home. "Brunch" is a very common word used by many to indicate a meal taken in late morning as a combination of two major meals i.e. breakfast and lunch. The above diet irregularities are very common in urban set up.

On the other hand people in the lowest strata can have long gaps or at times may have to skip some meals due to insufficient purchasing

power. This kind of scenario can easily be witnessed in extreme poverty situation irrespective of urban or rural area. In most recent report published by Global Hunger Index (GHI) India has been placed at 101st rank amongst the 116 countries. With India's GHI score of 27.5 hunger level has been marked as serious (https://www.globalhungerindex.org). Poor GHI score indicates inadequate food supply (under nourishment), child under nutrition, and under five mortality rate. Such contrasting social dynamics need to be included in studies to bridge the gap between social and biological determinants.

(iv) How gender determines the food allocation in a family, more specifically in resource constrain family, is another interesting area for study. While doing resource allocation In India, son preference is an ongoing social phenomenon. This age old phenomenon can hamper the growth and development of females compared to male siblings as a result of better food and care received by sons as compared to daughters. Gender specific follow up studies are required (both in rural and urban scenario) to know the probable lasting effect on the health outcomes due to this variation, particularly for metabolic disorders.

(v) Whether education impacts positively or negatively on the food plate diversity is another interesting topic that has not been given much focus. Education as either driving force or as resistant force for food diversity needs to be studied upon.

6.1.10 Stressors as important determinants of metabolic syndrome are poorly studied:

(i) Is obesity or adiposity always mandatory: The biological pathway of stress mechanism within human body has been quite extensively studied. We have substantial information on how the endocrine, neurological, and immune system are involved in stress cascade. We do have micro level information on release of chemicals in response to stressors and their effect on target organs; leading to obesity, adiposity

or insulin resistance. However we are deficient in knowing any mechanism, if any, where stressors can bypass the presumed to be mandatory phase of obesity/adiposity to give the ultimate outcome of metabolic syndrome. This point is very important because all persons with metabolic syndrome may not have obesity or adiposity. If we go back to the pioneer Reaven who first proposed the concept, he never included obesity as a feature of insulin resistance syndrome or metabolic syndrome (Despres *et al*., 2008). To support this statement we need to have extensive studies on non-obese cohort of people having metabolic syndrome. In west, very few studies were conducted on immigrants to show that stress actually takes the upper hand rather than obesity/adiposity in the pathway of metabolic syndrome. At present in India we do not have sufficient data to prove this phenomenon as initial screenings are done based on BMI value. As discussed already BMI is not sensitive enough as a tool and excludes potential candidates in Indian scenario. Once proved that obesity is not always mandatory for metabolic syndrome, we may have to give focus on wide range of social stressors as important determinants of metabolic syndrome. If studies can substantiate this in near future then we may be in a position to propose that chronic stressors can dominate over obesity to cause metabolic syndrome. This phenomenon is very much relevant in Indian scenario for that cohort where stressors are stronger determinants over obesity to cause metabolic syndrome. The marginalised section of society (rural or urban) has the probability of exposure to various stressors as a result of food scarcity, insufficient income, poor living condition, unemployment, migration, sleep deprivation etc. throughout their life course. As the chances of obesity in such population are comparatively low, hence we can propose that the pathway of metabolic syndrome will be primarily stressor driven. It is noteworthy that variations in adiposity may only account for 25% of the variable in insulin-mediated glucose clearance, but variations in physical fitness may account for an additional 25% of the variation (Reaven, 2006). In such scenario other determinants will be

accountable for remaining percentage and a list of determinants can be developed based on importance.

(ii) Stressor effect on foetus: How stressors affect on foetus is another area which requires more attention. We all know that the period of pregnancy is very crucial for future health of offspring. Expecting mothers if exposed to unavoidable stressors can have long term effect on self and next generation. Pregnancy period is expected ideally to have a stress free phase. However, in reality women of lower economic strata are found to perform labour intense work even in pregnancy to meet the family livelihood. Intensity of workload performed by expecting mother during pregnancy and its effect on developing foetus needs to be studied. Similarly, how stress caused by migration of expecting mother during pregnancy effects the health of developing foetus has been rarely studied.

(iii) Food as stressor: Food is indispensable for human life but can food itself become a stressor? Food as determinant of metabolic syndrome has been mostly studied either as positive energy balance or as change in dietary habit (nutrition transition). Apart from causing obesity can over nutrition be a stressor to act on vital organs and alter the physiological function? We need to study whether energy dense diet can be a stressor or not. Similarly, food scarcity can be a stressor and most importantly during crucial phases of pregnancy. How food scarcity causes developmental compromises in foetus have been studied well, but how food inadequacy acts as a stressor and fastens the progression of metabolic syndrome need to be studied.

It has been proved that over eating is a mechanism to overcome stress. However we need to look the other way around, where depression or sadness can act as loss of interest in cooking or eating food. Such situation can be seen most commonly in migrant population who are saddened by staying away from their native land. Disinterest

of eating or cooking usually leads to unhealthy food habits where both quantity and quality are compromised.

(iv) Migration as stressor: The process of migration and post migration phase in host place can be stressful due to various factors. Change in socio-economic status, cultural aspect, change in lifestyle, and food habit change are extensively studied on migrant population. However, the impact on health due to migration itself as a stressor is rarely studied. The process of migration (voluntary or forced) works as a stressor due to physical and emotional challenges. All age groups starting from foetus to adults are impacted by such stressors and increase the risk of metabolic syndrome. The process of migration may be of short duration but its impact can be of long term.

Stressors can have their impact at individual level, family level, or at community level. Depending on such levels same stressor can have different outcomes because of concentration or dilution of its impact. Chronic stressors are given more importance as determinant of metabolic syndrome but acute stressors can be equally important depending on its severity. There are studies which showed that exposure to short duration natural calamities, socio-economic or political events as stressors are enough to cause future metabolic syndrome. Exposure to acute stressors and their role as determinant of metabolic syndrome in long term need more studies.

(v) Sleep as stressor: Sleep deprivation has been considered as risk factor for obesity. We are not clear on what is the optimal amount of sleep a person should have to remain healthy. Sleep deprivation due to various factors like early school hours for kids, late night studies to do well in exams, habit of late going to bed, poor living conditions hampering sound sleep, shift work disturbing the sleep cycle etc. can act as stressors. These factors (mostly social) of sleep loss act as stressor which can further act as determinant of metabolic syndrome. Sleep deprivation and stress can be a vicious cycle with metabolic disorder

as an outcome. Sleep deprivation or sleep loss need more studies (experimental or interventional or long term social) in Indian situation. Another interesting fact is that most of the studies have related sleep deprivation and metabolic disorder through obesity/adiposity as essential phase. We need to look it from another angle in Indian situation because evidence has recently emerged that sleep loss need not cause obesity and hence closely related to insulin resistance and glucose intolerance (Wolk and Somers, 2006). It means a lean person with perfect weight or BMI may have metabolic syndrome due to chronic stress caused by sleep deprivation (ibid).

A definite link between chronic partial sleep deprivation and the risk of acquiring diabetes or obesity can be shown by epidemiologic research with large sample sizes. However, available studies have relied on self-reported measures of sleep and hence somehow fail to indicate the direction of causality (Knutson *et al*., 2007). Studies are required which can determine the direction of causality of metabolic syndrome due to sleep deprivation. There is a great need for more research on the possible impact of sleep deprivation and the tiredness and drowsiness it causes on lowering of energy expenditure (Knutson *et al*., 2007).

(vi) Smoking and alcohol consumption: As a consequence of stress, substance abuse has been most commonly rationalized as a way of pacifying both mind and body. Though smoking has a clear association with metabolic syndrome but this association is more complex in case of alcohol consumption. Factors like loneliness, social insecurity, work overburden, as a way of socializing, status symbol, tradition etc. needs to be given importance as root cause rather than only looking from substance dependence point. We need nationwide studies to reach at a conclusion on harmful dose of smoke and alcohol for Indian population. As like western studies whether low or moderate consumption of alcohol is beneficial for Indian phenotype (with more fat content in body) needs to be determined. How various adulterations

of alcoholic beverages can modulate the pathway of metabolic syndrome is another study area not explored till now. The harmful effects of smokeless products, which are now used more rampantly, are not being researched. The marginalized population with already compromised nutrition, low BMI, amidst stressors etc. may have another additional risk factor in the form of substance abuse.

6.1.11 Certain environmental factors can be dominant determinants of metabolic syndrome:

(i) Infections: Poor living condition like housing, problem of water and sanitation, and overall environmental degradation or pollution is a common sight in developing countries like India. Frequent infections in early life are almost every household's story in Asian Indians. Countless episodes of diarrhoea, pneumonia, seasonal respiratory tract infections etc. are witnessed by children irrespective of their social status. Such infections at frequent intervals in early life may trigger pro-inflammatory cytokines such as tumor necrosis factor-α and interleukein-6. Chapter III goes into great depth on how these factors link inflammation, obesity, and insulin resistance. Frequent episodes of infection in childhood as a factor to enhance the future progression of metabolic syndrome should be studied in Indian scenario.

(ii) Overcrowding: Overcrowding as a reason of water and sanitation crisis has been studied by various researchers. Overcrowding increases the chance of infection and can be a reason for space crisis too. This is very much relevant in urban settlements and also in areas of urban slums. In India, cities are growing very fast and most importantly without proper town planning. Numbers of inhabitants are out of proportion to open spaces available in most of Indian cities. Parks, playgrounds, recreational areas etc. are very limited to cater to the need of the citizen. Apartment culture is another story of every city. Unplanned apartments are mushrooming in cities where open space for dwelling is mostly ignored. Besides, apartment floor areas are such

that occupiers get very little chance to dwell freely. Traditional Indian houses used to have sufficient spaces around or in front (courtyard) to move around. People living in such used to burn substantial calorie while performing day to day tasks. With time such spaces in urban areas have been turned into apartments or multi-storied buildings. Similarly, people living in urban slums are forced to cramp into smaller living spaces with little scope of dwelling within the house or outside.

Studies which look into gradual constriction of dwelling spaces and its impact on physical activities, energy balance, obesity etc. are needed to know their role in causing metabolic syndrome for some specific cohorts.

(iii) Endocrine Disrupting Chemicals (EDCs) and other chemicals: Environmental chemicals or pollutants are considered inseparable as determinants of metabolic syndrome. EDCs particularly function as hormonal agonist and can be major obesity determinants in certain situations. Even after considering them as important determinants we do not have a continuous monitoring system in India to determine the safe levels in the environment. The latest guidelines on 'Hazard criteria' even negated the concept of 'tolerable daily intake' and slightest presence of side effects due to exposure to environmental chemicals have been considered as unsafe to human health, and the entire ecosystem (Solecki *et al*., 2017). In the wake of present situation when humans are surrounded by chemicals, endocrine disruption deserves more research with involvement of various streams of science to address issues like (a) the amount of exposure to the chemical under research on populations, (b) the dosage responses as a result of such exposure, (c) the cocktail effect of many chemicals, and (d) the degree to which health is influenced (disease attribution) as a result of exposure to EDCs (Solecki *et al*., 2017).

6.1.12 Occupation as determinant of metabolic syndrome:

Pattern of occupation and work environment can be important determinant as people used to spend a major portion of lifetime in earning. Only handful of studies has been conducted till date in order to assess the impact of one's occupation in the development of metabolic syndrome (Nair, 2010).

6.2 Determinants to inform policy:

The whole jigsaw of determinants for metabolic syndrome needs to be complete for policy interventions. How same causality can act differently in different situation and ultimately reach metabolic syndrome needs to be understood. We cannot compartmentalize biological and social factors but has to look them together. Knowing "what" is important so that health policy can address "when" to target and "where" to target the risk group. This will also help in relooking at the existing tools or reference values available for risk assessment. Any addition, omission, or modification can be proposed accordingly. From the above review a causality pattern for Indian population can be proposed for metabolic syndrome as in Fig 6.3.

The web of causation for metabolic syndrome helps us in targeting the at risk population. Causes start to build up from womb due to social situations and then reach disease condition through biological pathway or sometimes bypassing it. In India where there is high population density and determinants of metabolic syndrome start acting early; hence identifying the risk groups early will be the most apt strategy to delay the progression. Biological risk assessment has the tendency to detect the stage when disease progression has already occurred. On the contrary social risk assessment can be done at the earliest stage and will help in risk profiling. Hence proper preventive measures at proper time for proper risk group can delay the progress towards biological pathway and disease condition. Present policies are more inclined towards risk group having obesity/overweight. However policies to target the underprivileged is equally important because they have no lesser risk even without obesity/overweight. Health inequality due to pitfall in policy needs to be addressed.

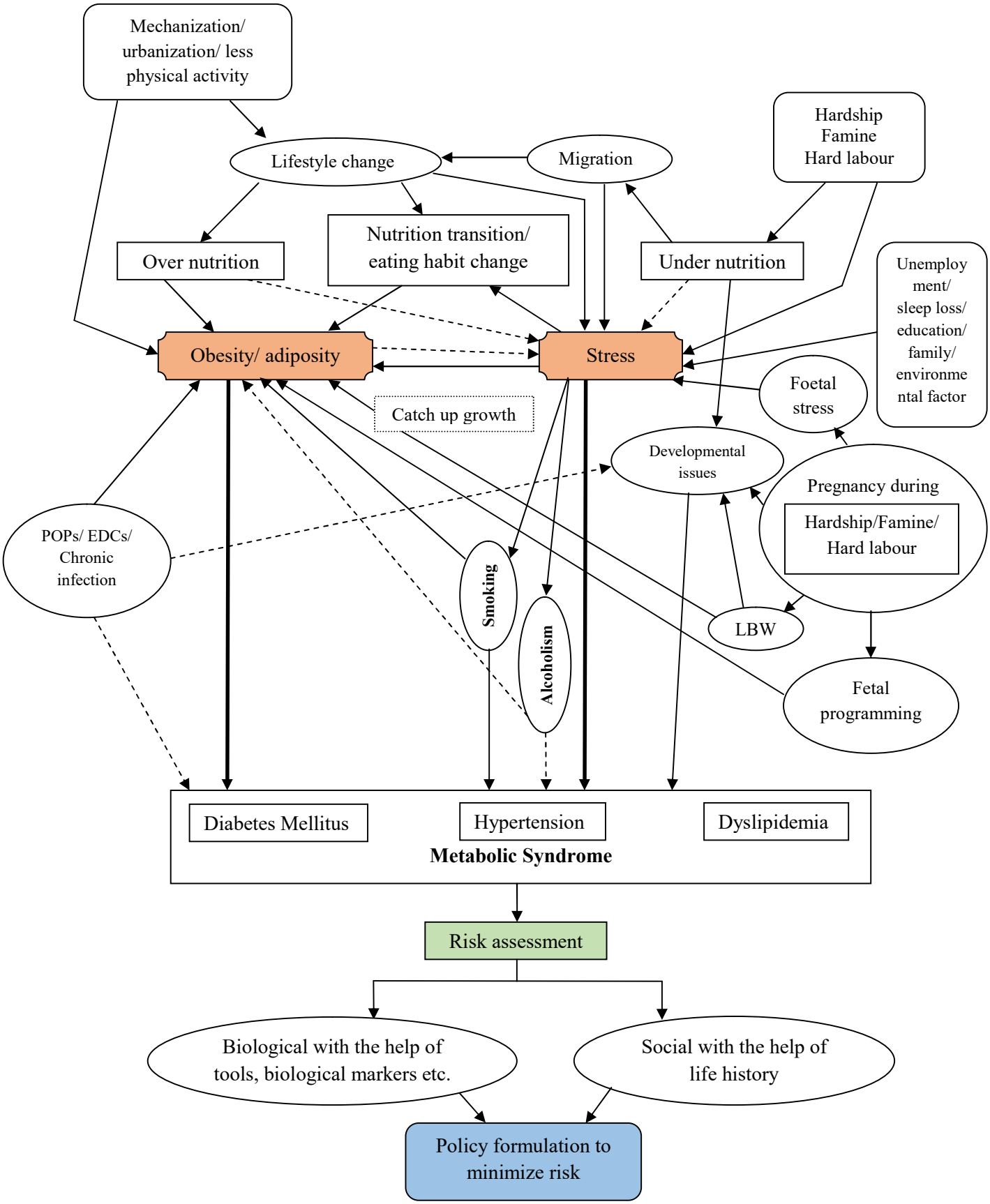


Fig 6.3: Author proposed web of causation leading to policy formulation for metabolic syndrome. Pathways requiring more study are shown as -------►

6.3 Conclusions:

While reviewing various domains of literature in determining social and biological factors of metabolic syndrome in India, several issues popped up and need further in depth analysis. A substantial number of India centric studies or reviews were published focusing on non-communicable diseases in and around the year 2010. The reason behind it might be due to introduction of National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS) in 2010 by Government of India. Now it is more than a decade and we should analyze on how much information we are able to gather to get the exact picture of the problem. This review is intentionally based on metabolic syndrome so that measures can be taken to prevent its components before reaching the disease state. We are aware that same determinants (biological or social) can give rise to components of metabolic syndrome or can have their permutation and combination.

Biological determinants of metabolic syndrome are studied well and we have almost clear knowledge regarding various pathways or mechanisms. The advancement of medical science has contributed to this knowledge and we do have scientific evidence on how our body response to various mediators to ultimately reach at metabolic syndrome. Though there is every scope of newer knowledge and latest findings are being updated with time, but still the basic medical concepts are already scientifically proven and established. Medical science has reached up to cellular and molecular level and has succeeded in building a strong knowledge of micro determinants. In other words we can say that biological determinants are relatively white areas of knowledge with sufficient evidences.

On the contrary, our knowledge on macro or social determinants of metabolic syndrome can be considered in either grey phase or in dark phase which need further enlightenment. The blurring of knowledge is quite evident between social and biological linkage due to insufficient studies on even established social determinants. To know macro level social determinants large scale and long follow up studies are required which covers the life course. Except few, most studies are small scale and of short duration keeping certain determinants at hypothetical state.

While going through various studies, reviews, data etc. it is evident that a good number of studies have been conducted on themes like weight gain, physical activity, BMI, excess diet, nutrition transition in relation to metabolic syndrome. These themes are relatively easy for researchers to conduct studies and hence can be found in abundance. However we lack studies on energy balance with respect to physical activity, change of food habit, under nutrition or food scarcity, various stressors in relation to metabolic syndrome.

We should try to develop a scaling or scoring system by including both biological and social determinants which will indicate the contribution of each factor as per characteristic of the cohort. Such listing of determinants according to importance will help in deciding which determinant we will have to target to reduce risk or to prevent the final disease condition. For example, this scoring system will help in deciding which cohort we will target for obesity reduction and which we will target for hunger management or under nutrition. Moreover such scoring system will guide the researcher in which determinant focus should be given for study purposes. In line with Indian Diabetes Risk Score (IDRS) other important factors like birth weight and later growth rate, diet habit, occupational history, migration history, living condition, and stress history can be considered to be included.

Finally, let me quote this line "understanding what factors are predictive of metabolic syndrome and how these risk factors are distributed and interrelated within different populations is important for identifying and targeting populations at risk, thus helping in the development and implementation of public health interventions" (Buckland *et al*., 2008).

6.4 Policy recommendations:

The review pointed out certain gaps in our knowledge regarding determinants of metabolic syndrome whether biological or social. Addressing these gaps is very important from policy perspective or implementation of health programmes in India. Following recommendations are cited below which may not be the conclusive ones and there are obvious scopes for future exploration.

(i) The definition of metabolic syndrome needs to be more inclusive in Indian scenario with scope to address determinants like physical activity, calorie consumption, weight age on stress, migration, exposure to obesogenic agents etc. In other words it should be more ethnic or Asian Indian specific and should be customised based on the evidences gathered following nationwide epidemiological survey.

(ii) Tools of risk assessment like BMI, waist hip ratio etc. needs to be studied for sensitivity and specificity, and their usefulness in field situation. Moreover, reference value for them and also for serum glucose, serum lipid, and blood pressure should be customised according to Indian population through national level surveys. We need to conduct such studies for children also to get age specific references. Inclusion of such references in the policy document will help in identifying population with metabolic syndrome or at future risk. Small scale epidemiological studies (very few) in India have already shown different ranges of prevalence of metabolic syndrome in same population while following the most accepted criteria set up by WHO, ATPIII, and IDF. Criteria standardization is mandatory to avoid such kind of variations.

(iii) We need to relook into the existing nutrition supplementation programs in India. The blanket policy to supplement each and every child without calculating calorie requirement in NRCs, Anganwadi Centers, mid day meals in schools etc. need to be revalidated through proper studies. The calorie supplementation should be calculated keeping in mind the socio-economic background of the child and other important indicators like low birth weight, physical activity, maternal under-nutrition, presence of stressors etc.

At present maternal nutrition mainly give emphasis on iron and folic acid supplementation for adolescents and pregnant women. The existing policy has to address the calorie and protein deficiency in women to minimise the future risk in foetus. PDS has to be strengthened and food basket needs to more wide with inclusion of fibre rich food items.

(iv) Unregulated use of vegetable oils or fats, sugar, and salt are established as important nutrition factors in causing metabolic syndrome. Limited studies have also established that Indians are consuming more than the recommended quantity of these items. No strict policy level regulations have been observed at food related businesses on adherence to the recommended value. It is a matter of doubt on how much unorganized fast food sellers or packaging food industries are adhering to the recommended norms. The underprivileged and vulnerable populations have the higher chances of consuming such type of foods. Such groups are already exposed to various socio-economic factors of metabolic syndrome and this will definitely add another one to fasten the process.

(v) The idea of giving over emphasis on overweight or obesity or waist-hip ratio as risk factors of metabolic syndrome will exclude a large cohort in Asian Indians. The underprivileged group is equally vulnerable due to developmental origin of disease or due to stress induced foetal programming. Equal importance should be given on past history (not only clinical but also social) of such population to ascertain the risk associated with. Major life events which indicate towards adversities should be included in the history. We cannot nullify the possibility of including only well offs as risk group for metabolic syndrome if overweight or obesity or waist-hip ratio are kept as parameters.

(vi) Stressors are never included as parameters to determine the risk of metabolic syndrome in programme guidelines. Stressors cannot be quantified directly but we may consider them indirectly depending on their mere presence or absence.

(vii) Urban migrants are exposed to most of the determinants of metabolic syndrome in Indian situation. More studies and subsequent policies are required to target them so that the risk of the disease can be minimized at the early stage.

(viii) Smoking, tobacco or alcohol consumption should not be looked only from addiction point with de-addiction as the solution. Policy should look into the underlying stressors which lead to such behaviour for long term remedial. Eliminating the stressors will not only help in preventing such behaviour but will also decrease the risk of metabolic syndrome.

(ix) Developing a risk scoring system to determine the type of factors associated with an individual and incorporation of the same in the program guideline as tools of risk assessment will be apt for Asian Indians. Such scoring system will also help in determining the areas where thrush has to be given to reduce the risk or in highlighting the areas where we need more research.

References:

1) Ala'a, A., Michel, B., Michel, V. *et al*., 2009. Alcohol consumption and the prevalence of metabolic syndrome: A meta-analysis of observational studies, *Atherosclerosis*, 204, pp.624-635.

2) Alberti, G., Eckel, R. H., Grundy, S. M., Zimmet, P. Z. *et al*., 2009. Harmonizing the metabolic syndrome: A joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation*, 120(16), pp.1640-1645. doi: 10.1161/circulationaha.109.192644.

3) Alberti, G., Zimmet, P. and Shaw, J., 2006. Metabolic syndrome- a new world-wide definition: A consensus statement from the International Diabetes Federation. *Diabetic Medicine, 23*(5), 469-480. doi: 10.1111/j.1464-5491.2006.01858.

4) Alberti, K. G. M. M. and Zimmet, P. Z., 1998. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus. Provisional report of a WHO Consultation. *Diabetic Medicine*, 15(7), pp.539–553.

5) AlDabal, L. and BaHammam, A.S., 2011. Metabolic, endocrine, and immune consequences of sleep deprivation, *The Open Respiratory Medicine Journal*, 5, pp.31-43.

6) Ali, O., Tan, T.T., Sakinah, O. *et al*., 1993. Prevalence of NIDDM and impaired glucose tolerance in aborigines and Malays in Malaysia and their relationship to socio demographic, health and nutritional factors, *Diabetes Care*, 16(1), January 1993, pp.68–75.

7) Aneja, J., Basu, D., Mattoo, S.K. *et al*., 2013. Metabolic syndrome in alcohol-dependent men: A cross sectional study, *Indian Journal of Psychological Medicine*, Vol. 35, Issue 2, Apr-Jun 2013, pp.190-196.

8) Anitharaj, M.S., 2018. Global fast food retailing in India- a way ahead, *IOSR Journal of Business and Management*, Vol. 20, Issue 2, February 2018, pp.38-43.

9) Anjana, R.M., Pradeepa, R., Deepa, M. *et al*., 2011. Prevalence of diabetes and prediabetes (impaired fasting glucose and/or impaired glucose tolerance) in urban and rural India: phase I results of the Indian Council of Medical Research-India DIABetes (ICMR-INDIAB) study, *Diabetologia* (2011), 54, pp.3022-3027.

10) Ardeshna, D.R., Bob-Manuel, T., Nanda, T. *et al*., 2017. Asian-Indians: a review of coronary artery disease in this understudied cohort in the United States, *Ann Transl Med*, 6(1): 12.

11) Armitage, J.A., Khan, I.Y., Taylor, P.D. *et al*., 2004. Developmental programming of the metabolic syndrome by maternal nutritional imbalance: how strong is the evidence from experimental models in mammals? *J Physiol*, Vol. 561, Issue 2, December 2004, pp.355-377.

12) Arora, N.K., Pillai, R., Dasgupta, R. *et al*. 2014. Whole of society monitoring framework for sugar, salt and fat consumption and non-communicable diseases in India, *Ann. N.Y. Acad. Sci.* 1331, pp. 157-173.

13) Bagchi Bhattacharjee, G. and Paul Khurana, S.M., 2014. In vitro reporter assays for screening of chemicals that disrupt androgen signalling, *Journal of Toxicology*, Vol. 2014, Article ID 701752.

14) Baig, U., Belsare, P., Watve, M. *et al*., 2011. Can thrifty gene(s) or predictive fetal programming for thriftiness lead to obesity, *Journal of Obesity*, Vol. 2011, Article ID 861049.

15) Balhara, Y.P.S., 2012. Tobacco and metabolic syndrome, *Indian Journal of Endocrinology and Metabolism*, Vol. 16, Issue 1, Jan-Feb 2012, pp.81-87.

16) Balhara, Y.P.S., Kalra, S., Bajaj, S. *et al*., 2017. Uttar Pradesh Association of Physicians of India position statement: tobacco use and metabolic syndrome, *Journal of The Association of Physicians of India*, Vol. 65, December 2017, pp.66-72.

17) Bang, H.O., Dyerberg, J. And Nielsen, A.B., 1971. Plasma lipid and lipoprotein pattern in Greenlandic West-Coast Eskimos, *The Lancet*, Vol. 297, Issue 7710, June 1972, pp.1143-1146.

18) Bansal, D., Satija, A., Khandpur, N. *et al*., 2010. Effects of migration on food consumption patterns in a sample of Indian factory workers and their families, *Public Health Nutrition*, Vol. 13, Issue 12, December 2010, pp.1982-1989.

19) Barker, D.J.P., 1997. Fetal Nutrition and Cardiovascular Disease in Later Life, *British Medical Bulletin*, 53(No.1), pp.96-108.

20) Barker, D.J.P., Bull, A.R., Osmond, C. *et al*., 1990. Fetal and placental size and risk of hypertension in adult life, *BMJ*, 4th August 1990, Vol. 301, pp.259-262.

21) Barouki, R., Gluckman, P.D., Grandjean, P. *et al*., 2012. Developmental origins of non-communicable disease: implications for research and public health, *Environmental Health*, 11:42, June 2012.

22) Bartley, M., Ferrie, J. and Montgomery, S.M., 2006. Health and labour market disadvantage: unemployment, non-employment, and job insecurity, in *Social Determinants of Health* edited by Marmot, M. and Wilkinson, R.G., Second edition, OUP, 2006, pp.78-96.

23) Bastarrachea, R.A., Kent Jr. J.W., Williams, J.T. *et al*., 2006. The genetic contribution of obesity, in *Overweight and the Metabolic Syndrome: From Bench to Bedside* edited by Bray, G.A. and Ryan, D.H., Springer, 2006, pp.55-81.

24) Baumgartner, R.N., Heymsfield, S.B. and Roche, A.F., 1995. Human body composition and the epidemiology of chronic diseases, *Obesity Research*, Vol.3, No.1, Jan 1995, pp.73-95.

25) Bawazeer, N.M., Al-Daghri, N.M., Valsamakis, G. *et al*., 2009. Sleep duration and quality associated with obesity among Arab children, *Obesity*, Vol. 17, No. 12, December 2009, pp.2251-2253.

26) Bell, A.C., Ge, K. and Popkin, G.M., 2002. The road to obesity or the path to prevention: motorized transportation and obesity in China, *Obesity Research*, Vol. 10, No. 4, April 2002, pp.277-283.

27) Ben-Shlomo, Y. and Kuh, D., 2002. A life course approach to chronic disease epidemiology: conceptual models, empirical challenges and interdisciplinary perspectives, *International Journal of Epidemiology*, 31, pp.285-293.

28) Berlin, I., Lin, S., Lima, J.A.C. *et al*., 2012. Smoking status and metabolic syndrome in the multi-ethnic study of atherosclerosis: a cross-sectional study, *Tobacco Induced Diseases*, 10:9.

29) Bhati, R.K., 2015. A study of rural to urban migration in India, *ASM' s International E-Journal on Ongoing Research in Management and IT*, January 2015, conference paper uploaded on 14th February 2019.

30) Borisova, A.M. and Georgieva, R., 1991. Tobacco smoking and beta-cell secretion, *Vutr Boles*, 30, pp.58-60.

31) Bray, G.A. and Ryan, D.H., 2006. Evaluation of the overweight and obese patient, in *Overweight and the Metabolic Syndrome: From Bench to Bedside* edited by Bray, G.A. and Ryan, D.H., Springer, 2006, pp.169-186.

32) Bray, G.A., 2007. Definitions and prevalence, in *The Metabolic Syndrome and Obesity* edited by Bray, G.A., Humana Press, 2007, pp.3-29.

33) Bray, G.A., 2007. Evaluation, prevention, and introduction to treatment, in *The Metabolic Syndrome and Obesity* edited by Bray, G.A., Humana Press, 2007, pp.123-145.

34) Bray, G.A., 2007. How do we get fat? An epidemiological and metabolic approach, in *The Metabolic Syndrome and Obesity* edited by Bray, G.A., Humana Press, 2007, pp.31-66.

35) Bray, G.A., Paeratakul, S., and Popkin, B.M., 2004. Dietary fat and obesity: a review of animal, clinical and epidemiological studies, *Physiology & Behavior*, 83(4), pp.549-555.

36) Brunner, E. and Marmot, M., 2006. Social organization, stress, and health, in *Social Determinants of Health* edited by Marmot, M. and Wilkinson, R.G., Second edition, OUP, 2006, pp.6-30.

37) Buckland, G., Salas-Salvado, J., Roure, E. *et al*., 2008. Socio-demographic risk factors associated with metabolic syndrome in a Mediterranean population, *Public Health Nutr*, 11(12), pp.1372-1378.

38) Butler, A.A., Trevaskis, J.L. and Morrison, C.D., 2006. Neuroendocrine control of food intake, in *Overweight and the Metabolic Syndrome: From Bench to Bedside* edited by Bray, G.A. and Ryan, D.H., Springer, 2006, pp.1-22.

39) Buxton, O.M., Chang, A.N., Spilsbury, J.C. *et al*., 2015. Sleep in the modern family: protective family routines for child and adolescent sleep, *Sleep Health*, May 2015, 1(1), pp.15-27.

40) Cain, N., and Gradisar, M., 2010. Electronic media use and sleep in school-aged children and adolescents: a review, *Sleep Medicine*, 11, pp.735–742.

41) Caleyachetty, A., Krishnaveni, G.V., Veena, S.R. *et al*., 2013. Breastfeeding duration, age of starting solids and high BMI risk and adiposity in Indian children, *Maternal and Child Nutrition*, Vol. 9, Issue 2, April 2013, pp.199-216.

42) Calo, W.A., Ortiz, A.P., Suarez, E. *et al*., 2013. Association of cigarette smoking and metabolic syndrome in a Puerto Rican adult population, *J Immigrant Minority Health*, 15, pp.810-816.

43) Cappuccio, F.P., and Miller, M.A., 2017. Sleep and cardio-metabolic disease, *Current Cardiology Reports*, 19(11).

44) Cappuccio, F.P., Cooper, D., D'Elia, L. *et al*., 2011. Sleep duration predicts cardiovascular outcomes: a systematic review and meta-analysis of prospective studies, *European Heart Journal*, 32(12), pp.1484–1492.

45) Carballo, M. and Siem, F., 2006. Migration and diabetes: the emerging challenge, *Diabetes Voice*, Vol. 51, Issue 2, June 2006.

46) Cassel, J., 1974. An epidemiological perspective of psychosocial factors in disease etiology, *AJPH*, Vol. 64, No. 11, November 1974, pp.1040-1043.

47) Cena, H., Fonte, M.L. and Turconi, G., 2011. Relationship between smoking and metabolic syndrome, *Nutrition Reviews*, Vol. 69, Issue 12, December 2011, pp.745-753.

48) Census of India 1901, 1951, 1961, 1971, 1981, 1991, 2001, 2011.

49) Chan, J.C.N., Malik, V., Jia, W. *et al*., 2009. Diabetes in Asia- Epidemiology, Risk Factors, and Pathophysiology, *JAMA*, Vol. 301, No. 20, May 27, 2009, pp.2129-2140.

50) Chandalia, M., Abate, N., Garg, A. *et al*., 1999. Relationship between generalized and upper body obesity to insulin resistance in Asian Indian men, *The Journal of Clinical Endocrinology and Metabolism*, Vol. 84, No. 7, July 1999, pp.2329-2335.

51) Chemicals as an Emerging Risk Factor in Developing Type-2 Diabetes: A Short History, available at www.healthandenvironmentonline.com/2011/02/21/chemicals-and-diabetes-a-short-history as accessed on 08-08-2012.

52) Chen, C. and Lu, F.C., 2006. The guidelines for prevention and control of overweight and obesity in Chinese adults, *Biomedical and Environmental Sciences*, Vol. 176, 2006, pp.1-35.

53) Chen, C.C., Li, T.C., Chang, P.C. *et al*., 2008. Association among cigarette smoking, metabolic syndrome, and its individual components: the metabolic

syndrome study in Taiwan, *Metabolism Clinical and Experimental*, 57, pp.544-548.

54) Chen, X., Beydoun, M.A., and Wang, Y., 2008. Is sleep duration associated with childhood obesity? A systematic review and meta-analysis, *Obesity*, Vol. 16, No.2, February 2008, pp.265-274.

55) Chitnis, S.P., 2019. A study on scenario of fast food industry in India, *International Journal of Trend in Scientific Research and Development*, March 2019, pp.88-90.

56) Chockalingam, R., Raghavan, R., Agrawal, J. *et al*., 2011. Understanding geographic variations in BMI in India, *Center for Social Development Washington University in St. Louis*, CSD Working Papers, No.11-13.

57) Chrousos, G.P. and Gold, P.W., 1992. The concepts of stress and stress system disorders, *JAMA*, 267, pp.1244–1252.

58) Chrousos, G.P., 2009. Stress and disorders of the stress system, *Nat Rev Endocrinol*, July 2009, 5(7), pp.374-381.

59) Chumlea, W.C., 2006. Body composition assessment of obesity, in *Overweight and the Metabolic Syndrome: From Bench to Bedside* edited by Bray, G.A. and Ryan, D.H., Springer, 2006, pp.23-35.

60) Cockram, C.S., 2000. The epidemiology of diabetes mellitus in the Asia-Pacific region, *HKMJ*, Vol. 6, No. 1, March 2000, pp.43-52.

61) Colten, H.R. and Altevogt, B.M. 2006. Sleep physiology in *Sleep disorders and sleep deprivation: an unmet public health problem* edited by Colten, H.R. and Altevogt, B.M., The National Academies Press, Washington DC.

62) Cota, D., Vicennati, V., Ceroni, L. *et al*., 2001. Relationship between socio-economic and cultural status, psychological factors and body fat distribution in middle-aged women living in Northern Italy, *Eating and Weight Disorders*, 6(4), December 2001, pp.205-213.

63) CSDH, 2008. Closing the Gap in a Generation: Health Equity through Action on the Social Determinants of Health, *Final Report of Commission on Social Determinants of Health*, WHO, Geneva, 2008.

64) Das, U.N., 2003. Metabolic syndrome X is common in Indians: But, why and how, *JAPI*, Vol. 51, October 2003, pp.987-998.

65) Das, U.N., 2005. Pathophysiology of metabolic syndrome X and its links to the perinatal period, *Nutrition*, 21, pp.762-773.

66) Das, U.N., 2010. Metabolic syndrome is low-grade systemic inflammatory condition, *Expert Rev. Endocrinol. Metab.*, 5(4), pp.577-592.

67) Dasgupta, R., 2003. Cholera in Delhi: A Study of Time Trend and its Determinants, PhD Thesis, CSMCH/JNU, 2003.

68) Dasgupta, R., Pillai, R., Kumar, R. *et al*. 2015. Sugar, salt, fat, and chronic disease epidemic in India: Is there need for policy interventions? *Indian Journal of Community Medicine*, Vol. 40, Issue 2, April 2015, pp.71-74.

69) De Boo, H.A. and Harding, J.E., 2006. The Developmental Origin of Adult Disease (Barker) Hypothesis, *Australian and New Zealand Journal of Obstetrics and Gynaecology* 2006; 46, pp.4-14.

70) de Ferranti, S. and Mozaffarian, D., 2008. The perfect storm: obesity, adipocyte dysfunction, and metabolic consequences, *Clinical Chemistry*, 54:6, pp.945-955.

71) de Franca, G.V.A., Restrepo-Mendez, M.C., de Mola, C.L. *et al*., 2014. Size at birth and abdominal adiposity in adults: A systematic review and meta analysis, *Obesity Reviews*, 15, pp.77-91.

72) de Oliveira, E. P., McLellan, K.C.P., de Arruda Silveira, L.V. *et al*., 2012. Dietary factors associated with metabolic syndrome in Brazilian adults, *Nutrition Journal*, 11:13, pp.1-7.

73) Deepa, M., Farooq, S., Datta, M. *et al*., 2007. Prevalence of metabolic syndrome using WHO, ATPIII, and IDF definitions in Asian Indians: The Chennai Urban

Rural Epidemiology Study (CURES-34), *Diabetes Metab Res Rev*, 23, pp.127-134.

74) Denova-Gutierrez, E., Castanon, S., Talavera, J.O. *et al*., 2010. Dietary patterns are associated with metabolic syndrome in an urban Mexican population, *The Journal of Nutrition*, Vol. 140, Issue 10, October 2010, pp.1855-1863.

75) Deshmukh, P.R., Kamble, P., Goswami, K. *et al*., 2013. Metabolic syndrome in the rural population of Wardha, Central India: An exploratory factor analysis, *Indian Journal of Community Medicine*, Vol. 38, Issue 1, January 2013, pp33-38.

76) Despres, J.P., Lemieux, I., Bergeron, J. *et al*., 2008. Abdominal obesity and the metabolic syndrome: contribution to global cardio-metabolic risk, *Arterioscler Thromb Vasc Biol*, June 2008, pp.1039-1049.

77) Dettoni, J.L., Consolim-Colombo, F.M., Drager, L.F. *et al*., 2012. Cardiovascular effects of partial sleep deprivation in healthy volunteers, *Journal of Applied Physiology*, 113(2), pp.232–236.

78) Deurenberg, P., Durenberg-Yap, M. and Guricci, S., 2002. Asians are different from Caucasians and from each other in their body mass index/body fat percent relationship, *Obesity Reviews*, 3, pp.141-146.

79) Dhingra, R., Sullivan, L., Jacques, P.F. *et al*., 2007. Soft drink consumption and risk of developing cardiometabolic risk factors and the metabolic syndrome in middle-aged adults in the community, *Circulation*, 116(5), pp.480-488.

80) Di Lorenzo, L., De Pergola, G., Zocchetti, C. *et al*., 2003. Effect of shift work on body mass index: results of a study performed in 319 glucose-tolerant men working in a Southern Italian industry, *Int J Obes Relat Metab Disord*, 27, pp.1353-1358.

81) Diabetes and the Environment- Persistent Organic Pollutants, available at https://www.diabetesandenvironment.org/home/environmental-chemicals/persistent-organic-pollutants as accessed on 16-02-2022.

82) Dinges, D.F., 2006. The state of sleep deprivation: from functional biology to functional consequences, *Sleep Medicine Review*, 10, pp.303-305.

83) Dulloo, A.G., Jacquet, J., Solinas, G. *et al*., 2010. Body composition phenotype in pathways to obesity and metabolic syndrome, *International Journal of Obesity*, December 2010, 34, pp.4-17.

84) Dwivedi, S., Aggarwal, R., and Vohra, N., 2020. Is migration stress related to increased cardiovascular disease? *MGM Journal of Medical Sciences*, Vol. 7, Issue 4, Oct-Dec 2020, pp.184-188.

85) Ebrahim, S., Kinra, S., Bowen, L. *et al*., 2010. The effect of rural-to-urban migration on obesity and diabetes in India: A cross-sectional study, *PLoS Med*, Vol. 7, Issue 4, April 27, 2010.

86) Eckel, R.H., Grundy, S.M. and Zimmet, P.Z., 2005. The metabolic syndrome, *Lancet*, April 2005, 365, pp.1415-1428.

87) Edwardson, C.L., Gorely, T., Davies, M.J. *et al*., 2012. Association of sedentary behaviour with metabolic syndrome: A meta-analysis, *PLoS ONE*, 7(4), 2012, e34916.

88) Elmadhun, N.Y. and Sellke, F.W., 2013. Is there a link between alcohol consumption and metabolic syndrome? *Clinical Lipidology*, 8(1), pp.5-8.

89) Epstein, L.H., Roemmich, J.N., Robinson, M.A. *et al*., 2008. A randomized trail of the effects of reducing television viewing and computer use on body mass index in young children, *Arch Pediatr Adolesc Med*, March 2008, 162(3), pp.239-245.

90) Everett, C.J., Frithsen, I. and Player, M., 2011. Relationship of Polychlorinated Biphenyl with type 2 diabetes and hypertension, *Journal of Environmental Monitoring*, 2011, 13, pp.241-251.

91) Exworthy, M., 2008. Policy to tackle the social determinants of health: using conceptual models to understand the policy process, *Health Policy and Planning*, 23, pp.318-327.

92) Eze, I.C., Schaffner, E., Foraster, M. *et al*., 2015. Long term exposure to ambient air pollution and metabolic syndrome in adults, *PLoS ONE*, 10(6), June 23, 2015, e0130337.

93) Fall, C.H.D., 2013. Fetal programming and risk of non-communicable disease, *Indian J Pediatr*, 80, Suppl 1, March 2013, S13-S20.

94) Fall, C.H.D., Sachdev, H.S., Osmond, C. *et al*., 2008. Adult metabolic syndrome and impaired glucose tolerance are associated with different patterns of BMI gain during infancy: data from the New Delhi birth cohort, *Diabetes Care*, Vol. 31, No. 12, December 2008, pp.2349-2356.

95) Fan, A.Z., Russell, M., Naimi, T. *et al*., 2008. Patterns of alcohol consumption and the metabolic syndrome, *J Clin Endocrinol Metab*, 93(10), October 2008, pp.3833-3838.

96) FAO/WHO, 1994. Fats and oils in human nutrition: report of a joint expert consultation, *FAO Food & Nutrition Papers*, Vol. 57, Rome FAO, pp.1-147.

97) FAO/WHO., 2019. Guidelines for the determination of pesticides as endocrine disruptors and harmonized risk management approach in respect of their presence in foods, Joint FAO/WHO Food Standards Programme, Codex Committee on Pesticide Residues, 5^{1st} session, China 8-13 April 2019.

98) Farin, H.M.F., Abbasi, F. and Reaven, G.M., 2005. Body mass index and waist circumference correlate to the same degree with insulin-mediated glucose uptake, *Metabolism Clinical and Experimental*, 54, pp.1323-1328.

99) Fauci, A.S., Braunwald, E., Kasper, D.L. *et al*., 2008. The metabolic syndrome in *Harrison's Principles of Internal Medicine*, 17th edition, McGraw-Hill Medical Publishing division.

100) Feingold, B.J., Vegosen, L., Davis, M. *et al*., 2010. A niche for infectious disease in environmental health: rethinking the toxicological paradigm, *Environmental Health Perspectives*, Vol. 118, No. 8, August 2010, pp.1165-1172.

101) FICCI (Federation of Indian Chambers of Commerce and Industry) PwC (PricewaterhouseCoopers) report. 2018. The changing landscape of the retail food service industry, December 2018.

102) Finkelstein, E. A., Ruhm, C.J. and Kosa, K.M., 2005. Economic causes and consequences of obesity, *Annu Rev Public Health*, 26, April 2005, pp.239-257.

103) Fisher, B.E., 1999. Most unwanted, *Environmental Health Perspectives*, Vol. 107, No. 1, January 1999, pp.A18-A23.

104) Forouhi, N.G., 2005. Ethnicity and the metabolic syndrome, in *The Metabolic Syndrome*, edited by Byrne, C.D. and Wild, S.H., John Wiley & Sons Ltd., 2005, pp.43-84.

105) Friedman, A.J., Ravnikar, V.A. and Barbieri, R.L., 1987. Serum steroid hormone profiles in postmenopausal smokers and non-smokers, *Fertility and Sterility*, Vol. 47, Issue 3, March 1987, pp.398-401.

106) Gangwisch, J.E., Malaspina, D., Boden-Albala, B. *et al*., 2005. Inadequate sleep as a risk factor for obesity: analyses of the NHANES I, *Sleep*, Vol. 28, No. 10, pp.1289-1296.

107) Gee, G.C., Ro, A., Shariff-Marco, S. *et al*., 2009. Racial discrimination and health among Asian Americans: evidence, assessment, and directions for future research, *Epidemiologic Review*, 31, pp.130-151.

108) Gholap, N., Davies, M., Patel, K. *et al*., 2011. Type 2 diabetes and cardiovascular disease in South Asians, *Primary Care Diabetes*, 5, pp.45-56.

109) Gillman, M.W., Rifas-Shiman, S., Berkey, C.S. *et al*., 2003. Maternal gestational diabetes, birth weight, and adolescent obesity, *Pediatrics*, Vol. 111, No. 3, March 2003, pp.e221-e226.

110) Gluckman, P.D. and Hanson, M.A., 2004. The developmental origins of the metabolic syndrome, *Trends in Endocrinology and Metabolism*, Vol. 15, No. 4, May 2004, pp.183-187.

111) Gonzalez-Ortiz, M., Martinez-Abundis, E., Balcazar-Munoz, B.R. *et al*., 2000. Effect of sleep deprivation on insulin sensitivity and cortisol concentration in healthy subjects, *Diabetes Nutr Metab*, 13, pp.80-83.

112) Gouveia, T.S., Trevisan, I.B., Santos, C.P. *et al*., 2020. Smoking history: relationships with inflammatory markers, metabolic markers, body composition, muscle strength, and cardiopulmonary capacity in current smokers, *J Bras Pneumol.*, 46(5).

113) Grant Thornton India LLP & FICCI, 2015. Transforming agriculture through mechanization: A knowledge paper on Indian farm equipment sector.

114) Grant, M.J. and Booth, A. 2009. A typology of review: an analysis of 14 review types and associated methodologies, *Health Information and Libraries Journal*, 26, pp.91-108.

115) Gregory, A.M., Caspi, A., Eley, T.C. *et al*., 2005. Prospective longitudinal associations between persistent sleep problems in childhood and anxiety and depression disorders in adulthood, *Journal of Abnormal Child Psychology*, Vol. 33, No. 2, April 2005, pp.157-163.

116) Groop, L., 2000. Genetics of the metabolic syndrome, *British Journal of Nutrition*, 83, Suppl. 1, pp.39-48.

117) Grundy, S., Brewer, B., Cleeman, J. *et al*., 2004. Definition of metabolic syndrome: Report of the National Heart, Lung and Blood Institute/American Heart Association Conference on scientific issues related to definition. *Circulation*, 109, pp.433-438.

118) Guilliams, T.G. and Edwards, L., 2010. Chronic stress and the HPA axis: Clinical assessment and therapeutic consideration, *The Standard*, Vol. 9, No. 2, 2010, pp.1-12.

119) Gupta, A., Kapil, U. and Singh, G., 2018. Consumption of junk foods by school aged children in rural Himachal Pradesh, India, *Indian J Public Health*, January-March 2018, Vol. 62, Issue 1, pp.65-67.

120) Gupta, R., Bhatia, M.S., Chhabra, V. *et al*., 2008. Sleep pattern of urban school going adolescents, *Indian Pediatrics*, Vol. 45, March 2008, pp.183-189.

121) Gupta, R., Gurm, H. and Bartholomew, J.R., 2004. Smokeless tobacco and cardiovascular risk, *Arch Intern Med*, 164, September 2004, pp.1845-1849.

122) Gupta, V., n.d. Type 2 diabetes mellitus in India, *South Asian Network for Chronic Disease*, New Delhi.

123) Hadewijch, V., Deboosere, P., Stibu, I. *et al*., 2012. Migrant mortality from deabetes millitus across Europe: the importance of socio-economic change, *Eur J Epidemiol*, 27, pp.109-117.

124) Hall, J.E. and Hall, M.E., 2021. Guyton and Hall Textbook of Medical Physiology 14th edition, *Elsevier*, 2021.

125) Hallqvist, J., Diderichsen, F, Theorell, T. *et al*., 1998. Is the effect of job strain on myocardial infarction due to interaction between high psychological demand and low decision latitude: results from the Stockholm Heart Epidemiology Program (SHEEP), *Social Science & Medicine*, 46(11), pp.1405-15.

126) Hansen, B.C., Jen K.L., Schwartz, J., 1988. Changes in insulin responses and binding in adipocytes from monkeys with obesity progressing to diabetes, *Int J Obes,* 1988, 12, pp.433-443.

127) Hansen, M., Janssen, I., Schiff, A. *et al*., 2005. The impact of school daily schedule on adolescent sleep, *Pediatrics*, Vol. 115, No. 6, June 2005, pp.1555-1561.

128) Havel, P. J., 2002. Control of energy homeostasis and insulin action by adipocyte hormones: Leptin, acylation stimulating protein, and Adiponectin, *Curr Opin Lipidol*, 13(1), pp.51–59.

129) Hemalatha, R., Laxmaiah, A., Sriswan, M.R. *et al*., 2020. What India Eats, *ICMR-National Institute of Nutrition*, Department of Health Research, MoH&FW, GoI, Hyderabad, Telangana.

130) Hensrud, D. D., 2004. Diet and obesity, *Current Opinion in Gastroenterology*, 20(2), pp.119-124.

131) Herman, J.P., McKlveen, J.M., Ghosal, S. *et al*., 2016. Regulation of the hypothalamic-pituitary-adrenocortical stress response, *Compr Physiol*, 6(2), May 2016, pp.603-621.

132) Holmboe-Ottesen, G. and Wandel, M., 2012. Changes in dietary habits after migration and consequences for health: a focus on South Asians in Europe, *Food and Nutrition Research*, 56.

133) Hoskote, S.S. and Joshi, S.R., 2008. Are Indians destined to be diabetic? *JAPI* (Editorial), Vol. 56, April 2008, pp.225-226.

134) Hossain, P., Kawar, B. and El Nahas, M., 2007. Obesity and diabetes in developing world- A growing challenge, *New England Journal of Medicine*, 356;3, January 18, 2007, pp.213-215.

135) https://www.globalhungerindex.org as accessed on 21st October 2021.

136) Hu, G., Lakka, T.A., Lakka, H.M. *et al*., 2007. Obesity, physical activity, and nutrition in the metabolic syndrome, in *Metabolic Syndrome and Cardiovascular Disease Epidemiology, Assessment and Management* edited by Krentz, A.J. and Wong, N.D., Informa Healthcare USA, 2007, pp.241-277.

137) Hwang, G.Y., Cho, Y.J., Chung, R.H. *et al*., 2014. The relationship between smoking level and metabolic syndrome in male health check up examinees over 40 years of age, *Korean J Fam Med.*, Vol. 35, No. 5, September 2014, pp.219-226.

138) ICMR, 2009. Nutrient requirements and recommended dietary allowances for Indians, *A Report of the Expert Group of the ICMR*, National Institute of Nutrition ICMR, 2009.

139) ICMR-MRC, 2009. ICMR-MRC workshop on chronic diseases: Building Indo-UK collaboration in chronic diseases, 4-5 November 2009, New Delhi.

140) IDF, 2006. The IDF consensus worldwide definition of the metabolic syndrome, *IDF*.

141) IDF, 2011. Annual report 2010, *IDF*.

142) IDF, 2012. IDF diabetes atlas, *IDF*, 5th edition, 2012 update.

143) Ikeda, M., Zhang, Z.W., Shimbo, S. *et al*., 2000. Urban population exposure to Lead and Cadmium in East and South-East Asia, *The Science of the Total Environment*, 249, pp.373-384.

144) Iyer, S.R., 2003. Type 2 diabetes express highway, where is the 'U' Turn? *JAPI*, Vol.51, May 2003, pp.495-500.

145) Jacob, S. and Chattopadhyay, S., 2016. Marriage dissolution in India: Evidence from census 2011, *EPW*, Vol. 51, No. 33, August 2016, pp.25-27.

146) Johanson, S., Sahu, R., and Saxena, S., 2012. Nutritional analysis of junk food, Report published by *Centre for Science and Environment* (CSE/PML/PR-41), pp.1-23.

147) Joshi, R., Cardona, M., Iyengar, S. *et al*., 2006. Chronic diseases now a leading cause of death in rural India- mortality data from the Andhra Pradesh Rural Health Initiative, *International Journal of Epidemiology*, 35, September 2006, pp1522-1529.

148) Joshi, S.R. and Parikh, R.M., 2007. India-diabetes capital of the world: now heading towards hypertension, *JAPI*, Vol. 55, May 2007, pp.323-324.

149) Joshi, S.R., 2003. Metabolic syndrome-emerging clusters of the Indian phenotype, *JAPI*, May 2003, Vol. 51, pp.445-446.

150) Kanjilal, S., Rao, V.S., Mukherjee, M. *et al*., 2008. Application of cardiovascular disease risk prediction models and the relevance of novel biomarkers to risk stratification in Asian Indians, *Vasc Health Risk Manag*, 2008, 4(1), pp.199-211.

151) Karlsson, B., Knutsson, A., and Lindahl, B., 2001. Is there an association between shift work and having a metabolic syndrome? Results from a population based study of 27485 people, *Occup Environ Med*, 58, pp.747–752.

152) Karlsson, B.H., Knutsson, A.K., Lindahl, B.O. *et al*., 2003. Metabolic disturbances in male workers with rotating three-shift work. Results of the WOLF study, *Int Arch Occup Environ Health*, 76, pp.424–430.

153) Katulanda, P., Ranasinghe, P., Jayawardana, R. *et al*., 2012. Metabolic syndrome among Sri Lankan adults: prevalence, patterns and co-relates, *Diabetology and Metabolic Syndrome*, 4:24, May 2012, pp.1-10.

154) Kaur, J., 2014. A comprehensive review on metabolic syndrome, *Cardiology Research and Practice*, Vol. 2014, ID 943162.

155) Kawada, T., Otsuka, T., Inagaki, H. *et al*., 2010. Association of smoking status, insulin resistance, body mass index, and metabolic syndrome in workers: A 1-year follow-up study, *Obes Res Clin Pract*, 4, pp.e163-e169.

156) Keen, H., Thomas, B.J., Jarrett, R.J. *et al*. 1979. Nutrient intake, adiposity, and diabetes, *BMJ*, 1, pp.655-658.

157) Keshari, P. and Mishra, C.P., 2016. Growing menace of fast food consumption in India: time to act, *International Journal of Community Medicine and Public Health*, Vol. 3, Issue 6, June 2016, pp.1355-1362.

158) Khadilkar, V., Yadav, S., Agrawal, K.K. *et al*., 2015. Revised IAP growth charts for height, weight and body mass index for 5 to 18 year old Indian children, *Indian Pediatrics*, Vol. 52, January 2015, pp.47-55.

159) Khadilkar, V.V., Khadilkar, A.V., Cole, T.J. *et al*., 2009. Crosssectional growth curves for height, weight and body mass index for affluent Indian children 2007, *Indian Pediatr*, 46, June 2009, pp.477–489.

160) Kim, S.W., Kim, H.J., Min, K. *et al*., 2021. The relationship between smoking cigarettes and metabolic syndrome: a cross-sectional study with non-single residents of Seoul under 40 years old, *PLoS ONE*, 16(8).

161) King, H., and Rewers, M., 1993. Global estimates for prevalence of diabetes mellitus and impaired glucose tolerance in adults. *Diabetes Care*, Vol. 16, No. 1, pp.157–177.

162) Kinra, S., Bowen, L.J., Lyngdoh, T. *et al*., 2010. Sociodemographic patterning of non-communicable disease risk factors in rural India: A cross sectional study, *BMJ*, September 2010, 341:c4974.

163) Kiranmala, N., Das, M.K. and Arora, N.K., 2013. Determinants of childhood obesity: need for a trans-sectoral convergent approach, *Indian Journal of Pediatrics*, 80 (Suppl 1), March 2013, pp.S38-S47.

164) Kitamura, T., Onishi, K., Dohi, K. *et al*., 2002. Circadian rhythm of blood pressure is transformed from a dipper to a non-dipper pattern in shift workers with hypertension, *J Hum Hypertens*, 16, pp.193–197.

165) Knutson, K.L., Spiegel, K., Penev, P. *et al*., 2007. The metabolic consequences of sleep deprivation, *Sleep Medicine Reviews*, 11, pp.163-178.

166) Kockturk-Runefors, T., 1991. A model for adaption to a new food pattern: the case of immigrants, in Furst, L., Prattala, R., Ekstrom, M. *et al*. edited *Palatable Worlds*, Oslo: Solum Forlag, pp.185-93.

167) Koski, M. and Naukkarinen, H., 2017. The relationship between stress and severe obesity: A case control study, *Biomedicine Hub*, 2:458771, pp.1-13.

168) Koupil, I., Shestov, D.B., Sparen, P. *et al*., 2007. Blood pressure, hypertension, and mortality from circulatory disease in men and women who survived the Siege of Leningrad, *European Journal of Epidemiology*, 22, pp.223-234.

169) Krieger, N., 2008. Proximal, distal, and politics of causation: what's level got to do with it? *American Journal of Public Health*, 2008, 98, pp.221-230.

170) Krishnaswamy, K., 2012. Evolutionary aspects of diets in the context of current chronic diseases, *NFI Bulletin*, Vol. 33, No. 1, January 2012, pp.1-7.

171) Krueger, J.M., Frank, M.G., Winsor, J.P. *et al*., 2016. Sleep function: toward elucidating an enigma, *Sleep Medicine Reviews*, 28, pp.46-54.

172) Krueger, P.M. and Friedman, E.M., 2009. Sleep duration in the United States: A cross-sectional population-based study, *Am J Epidemiol*, 169(9), pp.1052-1063.

173) Kuntson, K.L. and Cauter, E.V., 2008. Associations between sleep loss and increased risk of obesity and diabetes, *Ann N Y Acad Sci*, 1129, pp.287-304.

174) Kuriyan, R., Bhat, S., Thomas, T. *et al*., 2013. Television viewing and sleep are associated with overweight among urban and semi-urban south Indian children, *Nutr J*, 6:25, September 2007.

175) Laaksonen, D.E., Niskanen, L., Lakka, H.M. *et al*., 2004. Epidemiology and treatment of metabolic syndrome, *Ann Med*, Vol. 36, Issue 5, pp.332-346.

176) Lakshmy, R., Fall, C.H.D., Sachdev, H.S. *et al*., 2011. Childhood body mass index and adult pro-inflammatory and pro-thrombotic risk factors: data from the New Delhi birth cohort, *International Journal of Epidemiology*, Vol. 40, Issue 1, February 2011, pp.102-111.

177) Landhuis, C.E., Poulton, R., Welch, D. *et al*., 2008. Childhood sleep time and long-term risk for obesity: A 32-year prospective birth cohort study, *Pediatrics*, Vol. 122, No. 5, November 2008, pp.955-960.

178) Landsberg, L., 2008. The sympatho-adrenal system in the metabolic syndrome, in *The Metabolic Syndrome Epidemiology, Clinical Treatment, and Underlying Mechanisms* edited by Hansen, B.A. and Bray, G.A., Humana Press, 2008, pp.91.

179) Law, C., Fraser, I., and Piracha, M., 2020. Nutrition transition and changing food preferences in India, *Journal of Agricultural Economics*, Vol. 71, No. 1, pp.118-143.

180) Laxmaiah, A., Nagalla, B., Vijayaraghavan, K. *et al*., 2007. Factors affecting prevalence of overweight among 12- to 17-years old urban adolescents in Hyderabad India, *Obesity*, Vol. 15, No. 6, June 2007, pp.1384-1390.

181) Lee, B.K. and Kim, Y., 2016. Association of blood Cadmium level with metabolic syndrome after adjustment for confounding by serum ferritin and other factors: 2008–2012 Korean National Health and Nutrition Examination Survey, *Biol Trace Elem Res*, 171, pp.6-16.

182) Lee, D.H., Lee, I.K., Song, K. *et al*., 2006. A strong dose-response relation between serum concentration of persistent organic pollutants and diabetes: results from National Health and Examination Survey 1999-2002, *Diabetes Care*, Vol. 29, No. 7, July 2006, pp.1638-1644.

183) Lee, J.W., Brancati, F.L. and Yeh, H.C., 2011. Trends in the prevalence of type 2 diabetes in Asians versus whites: results from the United States National Health Interview Survey 1997–2008, *Diabetes Care*, Vol. 34, February 2011, pp.353–357.

184) Lee, S.W. and Jang, S.I., 2021. Association of alcohol drinking patterns with metabolic syndrome and its components in Korean adults: The Korea National Health and Nutrition Examination Survey 2016–2018, *Int. J Environ Res Public Health***,** 18, 6433.

185) Li, J.B., Wang, X. and Zhang, J.X. *et al*., 2010. Metabolic syndrome: prevalence and risk factors in Southern China, *The Journal of International Medical Research*, Vol. 38, Issue 3, June 2010, pp.1142-1148.

186) Lip, G.Y.H., Malik, I., Luscombe, C. *et al*., 1995. Dietary fat purchasing habits in whites, blacks and Asian peoples in England: implications for heart disease prevention, *Int J Cardiol*, 48, pp.287-293.

187) Lissner, L. and Heitmann, B.L., 1995. Dietary fat and obesity: evidence from epidemiology, *European Journal of Clinical Nutrition*, 49(2), pp.79-90.

188) Llyod, L.J., Langley-Evans, S.C. and McMullen, S., 2012. Childhood obesity and risk of the adult metabolic syndrome: A systematic review, *Internation Journal of Obesity*, 36, pp.1-11.

189) Lubrano, C., Genovesi, G., Specchia, P. *et al*., 2013. Obesity and metabolic comorbidities: environmental diseases? *Oxidative Medicine and Cellular Longevity*, Vol. 2013, Article ID 640673.

190) Lucas, A., 1991. Programming by early nutrition in man, in *The Childhood Environment and Adult Disease*, edited by Bock, G.R. and Whelan, J., John Wiley, pp.38-55.

191) Lyngdoh, T., Kinra, S., Ben Shlomo, Y. *et al*., 2006. Sib-recruitment for studying migration and its impact on obesity and diabetes, *Emerging Themes in Epidemiology*, 3:2, March 2006.

192) Magliano, D.J., Cameron, A., Shaw, J.E. *et al*., 2008. Epidemiology of metabolic syndrome, in *The Epidemiology of Diabetes Mellitus* edited by Ekoe, J.M., Rewers, M., Williams, R. *et al*., Second edition, Wiley-Blackwell, UK.

193) Mahal, A., Karan, A. and Engelgau, M., 2010. The economic implications of non-communicable disease for India, *HNP Discussion Paper*, The International Bank for Reconstruction and Development/ The World Bank, Washington, DC, January 2010.

194) Mahanta, B.N. and Mahanta, T.G., 2009. Clinical profile of persons with family history of diabetes mellitus with special reference to body fat percentage, *JAPI*, Vol. 57, October 2009, pp.703-705.

195) Malik, V.S., Popkin, B.M., Bray, G.A. *et al*., 2010. Sugar sweetened beverages and risk of metabolic syndrome and T2D, *Diabetes Care*, Vol. 33, No. 11, November 2011, pp.2477-2483.

196) Manson, J.E., Ajani, U.A., Liu, S. *et al*., 2000. A prospective study of cigarette smoking and the incidence of diabetes mellitus among US male physicians, *The American Journal of Medicine*, Vol. 109, November 2000, pp.539-542.

197) Marmot, M., Siegrist, J. and Theorell, T., 2006. Health and the psychosocial environment at work, in *Social Determinants of Health* edited by Marmot, M. and Wilkinson, R.G., Second edition, OUP, 2006, pp.97-130.

198) Martins, L., Whittle, A.J., Nogueiras, R. *et al*., 2014. The central nervous system in metabolic syndrome, in *A System Biology Approach to Study Metabolic Syndrome*, edited by Oresic, M. and Vidal-Puig, A., Springer, 2014, pp.137-156.

199) Mathias, R. A., 2009. Heritability of quantitative traits associated with type 2 diabetes mellitus in large multiplex families from South India, *Metabolism Clinical and Experimental*, 58, pp.1439-1445.

200) Mattoo, S.K., Chakraborty, K., Basu, D. *et al*., 2011. Prevalence & correlates of metabolic syndrome in alcohol & opioid dependent inpatients, *Indian J Med Res*, 134, September 2011, pp.341-348.

201) Maty, S.C., Everson-Rose, S.A., Haan, M.N. *et al*., 2005. Education, income, occupation, and the 34 year incidence (1965-99) of type 2 diabetes in the Alameda country study, *International Journal of Epidemiology*, 34, pp.1274-1281.

202) McKeigue, P.M., 1997. Cardiovascular disease and diabetes in migrants-interactions between nutritional changes and genetic background, in Shetty, P.S. and McPherson, K. edited *Diet, Nutrition and Chronic Disease: Lessons from Contrasting Worlds*, John Wiley & Sons, 1997, pp.59-70.

203) McMillen, C. and Robinson, J.S., 2005. Developmental origin of metabolic syndrome: prediction, plasticity, and programming, *Physiol Rev*, 85, pp.571-633.

204) Meigs, J.B., 2008. The role of obesity in insulin resistance: epidemiological and metabolic aspects, in *The Metabolic Syndrome: Epidemiology, Clinical Treatment, and Underlying Mechanisms*, edited by Hansen, B.C. and Bray, G.A., Humana Press, 2008, pp.37-55.

205) Mikolajczyk, R.T., El Ansari, W., and Maxwell, A.E., 2009. Food consumption frequency and perceived stress and depressive symptoms among students in three European countries, *Nutrition Journal*, 8:31, July 2009.

206) Ministry of Agriculture and Farmers Welfare, Department of Agriculture Cooperation and Farmers Welfare, Directorate of Economics and Statistics, GoI. 2020. Agricultural statistics at a glance 2020, *GoI*, May 2021.

207) Ministry of Agriculture and Farmers Welfare, GoI., 2019. Pocket book of agricultural statistics 2019.

208) Ministry of Education, GoI, 2006. Guidelines: National Programme of Nutritional Support to Primary Education, 2006 (Mid-Day Meal Scheme).

209) Ministry of Health and Family Welfare (MoHFW), Government of India, UNICEF and Population Council, 2019. Comprehensive National Nutrition Survey (CNNS) report 2016-18.

210) Ministry of Health and Family Welfare GoI, 2017. National multi-sectoral action plan for prevention and control of common non-communicable diseases 2017-2022, October 2017.

211) Ministry of Health and Family Welfare, GoI, 2011. Operational guidelines on facility based management of children with severe acute malnutrition, 2011.

212) Ministry of Labour & Employment, GoI. 2017. Employment Exchange Statistics, 2017.

213) Ministry of Labour & Employment, GoI. 2018. Employment Exchange Statistics, 2018.

214) Ministry of Statistics and Programme Implementation, GoI. Annual survey of industries, 2015-16, 2016-17, 2017-18, and 2018-19.

215) Ministry of Statistics and Programme Implementation, GoI., 2018. Statistical year book India 2018, http://mospi.nic.in/statistical-year-book-india/2018/ as accessed on 05-04-2020.

216) Ministry of Statistics and Programme Implementation, GoI., 2019. Drinking water, sanitation, hygiene and housing condition in India, *NSS 76th Round*, NSS report number 584.

217) Misra, A. and Ganda, O.P., 2007. Migration and its impact on adiposity and type 2 diabetes, *Nutrition*, 23 (2007), pp.696-708.

218) Misra, A. and Khurana, L., 2008. Obesity and the metabolic syndrome in developing countries, *J Clin Endocrinol Metab*, November 2008, 93(11), pp.S9-S30.

219) Misra, A. and Vikram, N.K., 2004. Insulin resistance syndrome (metabolic syndrome) and obesity in Asian Indians: evidence and implications, *Nutrition*, 20, pp.482-491.

220) Misra, A., 2003. Body composition and the metabolic syndrome in Asian Indians: A saga of multiple adversities, *The National Med Journal of India*, Vol. 16, No. 1, pp.1-4.

221) Misra, A., Chowbey, P., Makkar, B.M. *et al*., 2009. Consensus statement for diagnosis of obesity, abdominal obesity and the metabolic syndrome for Asian Indians and recommendations for physical activity, medical and surgical Management, *JAPI*, Vol. 57, February 2009, pp163-170.

222) Misra, A., Singhal, N., Sivakumar, B. *et al*., 2011. Nutrition transition in India: secular trends in dietary intake and their relationship to diet related non-communicable diseases, *Journal of Diabetes*, 3, pp.278-292.

223) Mitchell, E.A., Stewart, A.W., Braithwaite, R. *et al*., 2017. Birth weight and subsequent body mass index in children: An international cross sectional study, *Pediatric Obesity*, 12, August 2017, pp.280-285.

224) Mitra, A., Basu, B. and Mukhejee, S., 2009. Significance of different dietary habits in sections of Indian diabetics, *J Hum Ecol*, 26(2), 2009, pp.89-98.

225) Mitra, A., Bhattacharya, D. and Roy, S., 2007. Dietary influence on type 2 diabetes (NIIDM), *J Hum. Ecol*., 2007, Vol. 21, Issue 2, pp.139-147.

226) MoH&FW, GoI., 2007. National Family Health Survey (NFHS-3) 2005-06, *International Institute for Population Sciences Mumbai*, Vol. 1, September 2007.

227) MoH&FW, GoI., 2017. National Family Health Survey (NFHS-4) India Report 2015-16, *International Institute for Population Sciences Mumbai*, December 2017.

228) MoH&FW, GoI., 2022. National Family Health Survey (NFHS-5) India Report 2019-2021, *International Institute for Population Sciences Mumbai*, March 2022.

229) Mohan, V. and Pradeepa, R., 2009. Epidemiology of diabetes in different regions of India, *Health Administrator*, Vol.XXII, No 1&2, pp.1-18.

230) Mohan, V., Madan, Z., Jha, R., *et al*., 2004. Diabetes- social and economic perspectives in the new millenium, *Int. J. Diab. Dev. Countries*, Vol. 24, pp.29-35.

231) Mohan, V., Sandeep, S., Deepa, R. *et al*., 2007. Epidemiology of type 2 diabetes: Indian scenario, *Indian J Med Res*, 125, March 2007, pp.217-230.

232) Mohan, V., Shanthirani, C.S., and Deepa, R., 2003. Glucose intolerance (diabetes and IGT) in a selected South Indian population with special reference to family history, obesity and lifestyle factors- the Chennai Urban Population Study (CUPS-14), *JAPI*, Vol. 51, August 2003, pp.771-777.

233) Mohan, V., Shanthirani, S., Deepa, R. *et al*., 2001. Intra-urban differences in the prevalence of the metabolic syndrome in southern India- the Chennai Urban Population Survey (CUPS No. 4), *Diabetic Medicine*, 18, pp.280-287.

234) MoHousing and Urban Affairs, GoI. 2018-19. Annual report 2018-19.

235) MoUrban Development, GoI. 2016. Handbook of urban statistics 2016.

236) Mozaffarian, Hao, T., Rimm, E.B. *et al*., 2011. Changes in diet and lifestyle and long-term weight gain in women and men, *New England Journal of Medicine*, 364(25), pp.2392-2404.

237) Mullington, J.M., Simpson, N.S., Meier-Ewert, H.K. *et al*., 2010. Sleep loss and inflammation, *Best Pract Res Clin Endocrinol Metab*, 24(5), October 2010, pp.775-784.

238) NABARD, 2018. Sectoral paper on farm mechanization, *NABARD*, December 2018.

239) Nagaya, T., Yoshida, H., Takahashi, H. *et al*., 2002. Markers of insulin resistance in day and shift workers aged 30–59 years, *Int Arch Occup Environ Health*, 75, pp.562-568.

240) Nair, C.V., 2010. Metabolic syndrome: An occupational perspective, *Indian Journal of Community Medicine*, Vol. 35, Issue. 1, January 2010, pp.122-124.

241) Nakanishi, N., Takatorige, T. and Suzuki, K., 2005. Cigarette smoking and the risk of the metabolic syndrome in middle-aged Japanese male office workers, *Industrial Health*, 43, pp.295-301.

242) National Family Health Survey 3 (2005-06), Ministry of Health and Family Welfare, GoI.

243) National Family Health Survey 4 (2015-16), Ministry of Health and Family Welfare, GoI.

244) National Family Health Survey 5 (2019-21) factsheet, Ministry of Health and Family Welfare, GoI.

245) National Transport Development Policy Committee, GoI. 2014. India transport report: moving India to 2032, *Routledge*, New Delhi.

246) Neels, J.G. and Olefsky, J.M., 2006. Inflamed fat: what starts the fire? *J Clin Invest.*, Vol. 116, No. 1, January 2006, pp.33-35.

247) Nethan, S., Sinha, D. and Mehrotra, R., 2017. Non-communicable disease risk factors and their trends in India, *Asian Pacific Journal of Cancer Prevention*, 18(7), pp.2005-2010.

248) Newsome, C.A., Shiell, A.W., Fall, C.H.D. *et al*., 2003. Is birth weight related to later glucose and insulin metabolism? A systematic review, *Diabetic Medicine*, 20, April 2003, pp.339-348.

249) Ng, D.M., and Jeffery, R.W., 2003. Relationships between perceived stress and health behaviours in a sample of working adults, *Health Psychology*, 22(6), pp.638–642.

250) Noll, J.G., Zeller, M.H., Trickett, P.K. *et al*., 2007. Obesity risk for female victims of childhood sexual abuse: A prospective study, *Pediatrics*, Vol. 120, No.1, July 2007, pp.e61-e67.

251) Norris, S.A., Osmond, C., Gigante, D. *et al*., 2012. Size at birth, weight gain in infancy and childhood, and adult diabetes risk in five low- or middle-income country birth cohorts, *Diabetes Care*, Vol. 35, January 2012, pp.72-79.

252) NSS 2018. Drinking water, sanitation, hygiene, and housing condition in India, *Ministry of Statistics and Programme Implementation GoI*, NSS report No.584.

253) NSSO, 2014. NSS report No.560: Nutrition intake in India 2011-12, NSS 68th Round, Ministry of Statistics and Program Implementation, GoI, October 2014.

254) Oken, E. and Gillman, M.W., 2003. Fetal origins of obesity, *Obesity Research*, Vol. 11, No. 4, April 2003, pp.496-506.

255) Palaniappan, L.P., Wong, E.C., Shin, J.J. *et al*., 2011. Asian Americans have greater prevalence of metabolic syndrome despite lower body mass index, *Int J Obes (Lond)*, 35(3), March 2011, pp.393-400.

256) Pandey, B., Reba, M., Joshi, P.K. *et al*., 2020. Urbanization and food consumption in India, *Nature Research*, 10:17241.

257) Parikh, R.M. and Mohan, V., 2012. Changing definitions of metabolic syndrome, *Indian Journal of Endocrinology and Metabolism*, Vol. 16, Issue 1, pp.7-12.

258) Pasquali, R., 2008. Sex dependent role of Glucocorticoids and Androgens in the pathophysiology of human obesity, *International Journal of Obesity*, 32, pp.1764-1779.

259) Pasquali, R., 2012. The Hypothalamic-Pituitary-Adrenal axis and sex hormones in chronic stress and obesity: pathophysiological and clinical aspects, *Ann. N.Y. Acad. Sci.*, pp.1-16.

260) Peeters, A., Barendregt, J.J., Willekens, F. *et al*., 2003. Obesity in adulthood and its consequences for life expectancy: a life-table analysis, *Ann Intern Med*, Vol. 138, No. 1, January 2003, pp.24-32.

261) Pereira, M.A., Kartashov, A.I., Ebbeling, C.B. *et al*., 2005. Fast food habits, weight gain, and insulin resistance (The CARDIA study): 15 year prospective analysis, *Lancet*, Vol. 365, January 1, pp.36-42.

262) Pervanidou, P. and Chrousos, G.P., 2011. Stress and obesity/metabolic syndrome in childhood and adolescence, *International Journal of Pediatric Obesity*, 6(S1), pp.21-28.

263) Pervanidou, P. and Chrousos, G.P., 2012. Metabolic consequences of stress during childhood and adolescence, *Metabolism Clinical and Experimental*, 61, pp.611-619.

264) Pickett, K.E. and Wilkinson, R.G., 2008. People like us: ethnic group density effects on health, *Ethnicity and Health*, Vol. 13, No. 4, September 2008, pp.321–334.

265) Pillai, S.M., Jones, A.K., Hoffman, M.L. *et al*., 2017. Fetal and organ development at gestational days 45, 90, 135 and at birth of lambs exposed to under or over nutriton during gestation, *Transl. Anim. Sci.*, Vol. 1, Issue 1, February 2017, pp.16-25.

266) Plotsky, P.M., Cunningham, E.T. and Widmaier, E.P., 1989. Catecholaminergic modulation of Corticotropin-Releasing Factor and Adrenocorticotropin Secretion, *Endocrine Review*, Vol. 10, No. 5, November 1989, pp.437-458.

267) Popkin, B.M., 2003. The nutrition transition in the developing World, *Development Policy Review*, 21(5-6), pp.581-597.

268) Popkin, B.M., 2010. The implication of nutrition transition for obesity in the developing world, in *Obesity Epidemiology: From Aetiology to Public Health* edited by Crawford, D., Jeffery, R.W., Ball, K., and Brug, J., OUP, pp.136-158.

269) Power, C. and Thomas, C., 2011. Change in BMI, duration of overweight and obesity, and glucose metabolism: 45 years of follow-up of a birth cohort, *Diabetes Care*, Vol. 34, September 2011, pp.1986-1991.

270) Pradeepa, R., Deepa, R., Rani, S.S. *et al*., 2003. Socio-economic status and dyslipidaemia in a South Indian Population: the Chennai Urban Population Study (CUPS 11), *The National Medical Journal of India*, Vol. 16, No. 2, pp.64-69.

271) Prasad, D.S., Kabir, Z., Dash, A.K. *et al*., 2012. Prevalence and risk factors for metabolic syndrome in Asian Indians: A community study from urban eastern India, *J Cardiovasc Dis Res*, 2012, 3, pp204-11.

272) Raj, M. and Kumar, R.K., 2010. Obesity in children and adolescent, *Indian J. of Medical Research*, 132, November 2010, pp.598-607.

273) Rajala, M.W. and Scherer, P.E., 2003. Minireview: The adipocyte- at the crossroads of energy homeostasis, inflammation, and atherosclerosis, *Endocrinology,* 2003, Vol. 144, Issue 9, pp.3765–3773.

274) Rajankar, P., 2018. Endocrine disruptor: review of Indian research, *Toxics Link*, 2018.

275) Ramachandran, A., 2007. Socio-economic burden of diabetes in India, *JAPI (Supplement)*, July 2007, Vol. 55, pp.9-12.

276) Ramachandran, A., Snehalatha, C. and Viswanathan, V., 2002. Burden of type 2 diabetes and its complications- the Indian scenario, *Current Science*, Vol. 83, No. 12, 25 December 2002, pp.1471-1476.

277) Ramachandran, A., Snehalatha, C., Baskar, A.D.S. *et al*., 2004. Temporal changes in prevalence of diabetes and impaired glucose tolerance associated with lifestyle transition occurring in the rural population in India, *Diabetologia*, 47, pp.860-865.

278) Ramachandran, A., Snehalatha, C., Latha, E. *et al*., 1997. Rising prevalence of NIDDM in an urban population in India, *Diabetologia*, 40, pp.232-237.

279) Ramachandran, A., Snehalatha, C., Yamuna, A. *et al*., 2006. Stress and undetected hyperglycemia in Southern Indian coastal population affected by tsunami, *JAPI*, Vol. 54, February 2006, pp.109-112.

280) Rampal, S., Mahadeva, S., Guallar, E. *et al*., 2012. Ethnic differences in the prevalence of metabolic syndrome: results from a multi-ethnic population based survey in Malaysia, *PLoS ONE*, Vol. 7, Issue 9, e46365.

281) Ranjani, H., Mahreen, T.S., Pradeepa, R. *et al*., 2016. Epidemiology of childhood overweight and obesity in India: A systematic review, *Indian J Med Res*, February 2016, 143(2), pp.160-174.

282) Ravikiran, M., Bhansali, A., Ravikumar, P. *et al*., 2010. Prevalence and risk factors of metabolic syndrome among Asian Indians: A community survey, *Diabetes Res Clin Pract*, 89(2), August 2010, pp269-73.

283) Reaven, G.M., 1988. Banting lecture 1988: Role of insulin resistance in human disease, *Diabetes*, Vol. 37, December 1988, pp.1595-1607.

284) Reaven, G.M., 2006. The metabolic syndrome: is this diagnosis necessary? *Am J Clin Nutr*, 83, pp.1237-1247.

285) Rizzo, N.S., Sabate, J., Jaceldo-Siegl, K. *et al*., 2011. Vegetarian dietary patterns are associated with a lower risk of metabolic syndrome, *Diabetes* Care, Vol. 34, May 2011, pp.1225-1227.

286) Robinson, T., 1999. Reducing children's television viewing to prevent obesity: A randomized controlled trial, *JAMA*, Vol. 282, No. 16, October 27, 1999, pp.1561-1567.

287) Roglic, G. and Unwin, N., 2010. Mortality attributable to diabetes: estimates for the year 2010, *Diabetes Research and Clinical Practice*, 87(2010), pp.15-19.

288) Rosell, M., Faire, U.D. and Hellenius, M., 2003. Low prevalence of the metabolic syndrome in wine drinkers is it the alcohol beverage or the lifestyle? *Eur J ClinNutr*, 57, pp.227-234.

289) Rosmond, R., 2005. Role of stress in the pathogenesis of metabolic syndrome, *Psychoneuroendocrinology*, 30, pp.1-10.

290) Rothman, K.J., 1976. Causes, *American Journal of Epidemiology*, Vol. 104, No. 6, pp.587-592.

291) Ruzzin, J., Petersen, R., Meugnier, E. *et al*., 2010. Persistent organic pollutant exposure leads to insulin resistance syndrome, *Environmental Health Perspectives*, Vol. 118, No. 4, April 2010, pp.465-471.

292) Sachdev, H.P.S., Osmond, C., Fall, C.H.D. *et al*., 2009. Predicting adult metabolic syndrome from childhood body mass index: follow-up of the New Delhi birth cohort, *Arch Dis Child.*, October 2009, 94(10), pp.768-774.

293) Saiyadali, A., Manovijay, K., Chandrashekar, H. *et al*., 2020. Prevalence of metabolic syndrome in alcohol dependence: a cross sectional study at a tertiary care hospital, *Clin Psychiatry*, Vol. 6, No. 6:74.

294) Saklayen, M.G., 2018. The global epidemic of the metabolic syndrome, *Current Hypertension Reports*, 20, 12, pp.1-8.

295) Saleh, A., Amanatidis, S. and Samman, S., 2002. The effect of migration on dietary intake, type 2 diabetes and obesity: The Ghanaian health and nutrition analysis in Sydney, Australia (GHANAISA), *Ecology of Food and Nutrition*, 41:3, pp.255-270.

296) Sanchez-Infantes, D. and Stephens, J.M., 2014. Role of adipose tissue in the pathogenesis and treatment of metabolic syndrome, in *A System Biology Approach to Study Metabolic Syndrome*, edited by Oresic, M. and Vidal-Puig, A., Springer, 2014, pp.63-83.

297) Sandeep, S., Gokulakrishnan, K., Velmurugan, K. *et al*., 2010. Visceral & subcutaneous abdominal fat in relation to insulin resistance & metabolic syndrome in non-diabetic South Indians, *Indian J Med Res*, 131, May 2010, pp.629-635.

298) Satia-Abouta, J., Patterson, R.E., Neuhouser, M.L. *et al*., 2002. Dietary acculturation: applications to nutrition research and dietetics, *Journal of the American Dietetic Association*, 102(8), pp.1105–1118.

299) Sayeed, M.A., Ali, L., Hussain, M.Z. *et al*., 1997. Effect of socioeconomic risk factors on the difference in prevalence of diabetes between rural and urban population in Bangladesh, *Diabetes Care*, 20(4), April 1997, pp.551–555.

300) Schmidhuber, J. and Shetty, P., 2005.The Nutrition transition to 2030: why developing countries are likely to bear the major burden, *Acta Agric Scand*, 2005, 2, pp.150-166.

301) Schulze, M.B., Manson, J.E., Ludwig, D.S. *et al*., 2004. Sugar-sweetened beverages, weight gain, and incidence of type 2 diabetes in young and middle-aged women, *Journal of the American Medical Association*, 292(8), pp.927-934.

302) Sekine, M., Yamagami, T., Handa, K. *et al*., 2002. A dose-response relationship between short sleeping hours and childhood obesity: results of the Toyama Birth Cohort Study, *Child Care Health Dev*, 28, pp.163-170.

303) Selye, H., 1976. History and general outline of the stress concept, in *Stress in Health and Disease* edited by Selye, H., Butterworth, 1976, pp.3-34.

304) Shankar, A., Koh, W.P., Yuan, J.M. *et al*., 2008. Sleep duration and coronary heart disease mortality among Chinese adults in Singapore: a population-based cohort study, *Am J Epidemiol*, 2008, Vol. 168, No. 12, pp.1367-1373.

305) Sharifian, A., Farahani, S., Pasalar, P. *et al*., 2005. Shift work as an oxidative stressor, *Journal of Circadian Rhythms*, 3:15.

306) Sharma, D.K., 2018. Physiology of stress and its management, *J Med Stud Res*, Vol. 1, Issue 1.

307) Shelgikar, K.M., Yajnik, C.S. and Hockaday, T.D.R., 1991. Central rather than generalised obesity is associated with hyperglycemia in Indians, *Diabetic Medicine*, October 1991, 8, pp.712-717.

308) Shen, J., Goyal, A. and Sperling, L., 2011. The emerging epidemic of obesity, diabetes, and the metabolic syndrome in China, *Cardiology Reseach and Practice*, Vol. 2012, September 2011, pp.1-5.

309) Shetty, P. 2013. Nutrition transition and its health outcomes, *Indian J Pediatr*, March 2013, 80(Suppl 1), pp.S21-S27.

310) Shetty, P.S., 2002. Nutrition transition in India. *Public Health Nutrition*, 5(1A), pp.175-182.

311) Shigeta, H., Shigeta, M., Nakazawa, A. *et al*., 2001. Lifestyle, obesity, and insulin resistance, *Diabetes Care*, Vol. 24, No. 3, March 2001, pp.608–608.

312) Shobhana, R., Rama Rao, P., Lavanya, A., *et al*. 2000. Expenditure on health care incurred by diabetic subjects in a developing country- A study from Southern India, *Diabetes Research and Clinical Practice*, 48(1), pp.37-42.

313) Siddiqui, M.Z., Donato, R. and Jumrani, J., 2019. Looking past the Indian calorie debate: what is happening to the nutrition transition of India, *The Journal of Development Studies*, Vol. 55, No. 11, pp.2440-2459.

314) Siddiqui, N.I. and Bose, S., 2012. Prevalence and trends of obesity in Indian school children of different socioeconomic class, *Indian Journal of Basic & Applied Medical Research*, Vol. 2, Issue 5, December 2012, pp.393-398.

315) Singh, D.P., 1998. Internal migration in India: 1961-1991, *Demography India*, 27(1), pp.245-261.

316) Singh, H., 2016. Increasing rural to urban migration in India: A challenge or an opportunity, *International Journal of Applied Research*, 2(4), pp.447-450.

317) Sinha, R. and Jastreboff, A.M., 2013. Stress as a common risk factor for obesity and addiction, *Biol Psychiatry*, 73(9), May 2013, pp.827-835.

318) Skilton, M.R., Moulin, P., Terra, J.L. *et al*., 2007. Associations between anxiety, depression, and the metabolic syndrome, *Biological Psychiatry*, 62(11), pp.1251-1257.

319) Slagter, S.N., van Vliet-Ostaptchouk, J.V., Vonk, J.M. *et al*., 2013. Association between smoking, components of metabolic syndrome and lipoprotein particle size, *BMC Medicine*, 11:195.

320) Slagter, S.N., van Vliet-Ostaptchouk, J.V., Vonk, J.M. *et al*., 2014. Combined effects of smoking and alcohol on metabolic syndrome: the LifeLines Cohort Study, *PLoS ONE*, 9(4): e96406.

321) Smith, G.D., Ben-Shlomo, Y., Beswick. *et al*., 2005. Cortisol, testosterone, and coronary heart disease: prospective evidence from the Caerphilly Study, *Circulation*, 112, July 2005, pp.332-340.

322) Smith, R. and Mill, J., 2011. Epigenetics and chronic diseases: An overview, in *Epigenetic Aspects of Chronic Diseases* edited by Roach, H.I., Bronner, F, and Oreffo, R.O.C., Springer 2011, pp.1-20.

323) Smith, U. and Yang, X., 2005. Adipocytokines and the pathogenesis of the metabolic syndrome, in *The Metabolic Syndrome*, edited by Byrne, C.D. and Wild, S.H., John Wiley & Sons Ltd., 2005, pp.239-262.

324) Solecki, R., Kortenkamp, A., Bergman, A. *et al*., 2017. Scientific principles for the identification of endocrine-disrupting chemicals: a consensus statement, *Arch Toxicol*, 91, pp.1001-1006.

325) Speakman, J.R., 2006. Thrifty genes for obesity and metabolic syndrome- time to call off the search, *Diabetes and Vascular Disease Research*, Vol. 3, Issue 1, May 2006, pp.7-11.

326) Spiegel, K., Leproult, R. and Van Cauter, E., 1999. Impact of sleep debt on metabolic and endocrine function, *Lancet*, 354, pp.1435–1439.

327) Spitzer, D.L., n.d. Stress, migration, gender and type 2 diabetes, Department of Anthropology, University of Alberta, available at http://sancd.org/uploads/pdf/factsheet_diabetes.pdf as accessed on 17-10-2011.

328) Sridhar, G.R. and Madhu, K., 2002. Psychosocial and cultural issues in diabetes mellitus, *Current Science*, Vol. 83, No. 12, 25 December 2002, pp.1556-1564.

329) Stanner, S.A., Bulmer, K., Andres, C. *et al*., 1997. Does malnutrition in utero determine diabetes and coronary heart disease in adulthood? results from the Leningrad siege study, a cross sectional study. *BMJ*, 315, August 1997, pp.1342–1348.

330) Stansfeld, S.A., 2006. Social support and social cohesion, in *Social Determinants of Health* edited by Marmot, M. and Wilkinson, R.G., Second edition, OUP, 2006, pp.148-171.

331) Stene, L.C., Magnus, P., Lie, R.T. *et al*., 2001. Birth weight and childhood onset type 1 diabetes: population based cohort study, *BMJ*, Vol. 322, 14th April 2001, pp.889-892.

332) Sun, K., Liu, J. and Ning, G., 2012. Active smoking and risk of metabolic syndrome: A meta-analysis of prospective studies, *PLoS ONE*, Vol. 7, Issue 10, October 2012.

333) Sun, K., Ren, M., Liu, D. *et al*., 2013. Alcohol consumption and risk of metabolic syndrome: A meta-analysis of prospective studies, *Clinical Nutrition*, pp.1-7.

334) Sun, Q., Yue, P., Deiuliis, J.A. *et al*., 2009. Ambient air pollution exaggerates adipose inflammation and insulin resistance in a mouse model of diet induced obesity, *Circulation*, Vol. 119, Issue 4, February 2009, pp.538-546.

335) Sun, Y., Zhang, L., Duan, W. *et al*., 2018. Association between famine exposure in early life and type 2 diabetes mellitus and hyperglycemia in adulthood: results from the China Health and Retirement Longitudinal Study (CHARLS), *Journal of Diabetes*, 10, February 2018, pp.724-733.

336) Suriyaprom, A., Namjuntra, P., Thawnasom, K. *et al*., 2010. Association between cigarette smoking and metabolic syndrome in Thais, *Int J Health Res.*, 3(4), December 2010, pp.207-212.

337) Susser, M. and Stein, Z., 1994. Timing in prenatal nutrition: A reprise of the Dutch famine study, *Nutrition Reviews*, Vol. 52, No. 3, pp.84-94.

338) Swaminathan, S. and Vaz, M., 2013. Childhood physical activity, sports and exercise and non-communnicable disease: A special focus on India, *Indian J Pediatr*, 80 (Suppl 1), March 2013, S63-S70.

339) Tamakoshi, A. and Ohno, Y., 2004. Self-reported sleep duration as a predictor of all-cause mortality: results from the JACC study, Japan, *SLEEP*, Vol. 27, No. 1, pp.51-54.

340) Tata Institute of Social Sciences (TISS), Mumbai and Ministry of Health and Family Welfare, Government of India. 2016-17. Global Adult Tobacco Survey (GATS 2) India 2016-17.

341) Taveras, E.M., Rifas-Shiman, S.L., Oken, E. *et al*., 2008. Short sleep duration in infancy and risk of childhood overweight, *Arch Pediatr Adolesc Med*, April 2008, Vol. 162, No. 4, pp.305-311.

342) Taylor, S.E., Welch, W.T., Kim, H.S. *et al*., 2007. Cultural differences in the impact of social support on psychological and biological stress responses, *Psychological Science*, Vol. 18, No. 9, pp.831–837.

343) Tchernof, A. and Despres, J.P., 2013. Pathophysiology of human visceral obesity: an update, *Physiol Rev*, Vol. 93, January 2013, pp.359-404.

344) Tharkar, S. and Viswanathan, V., 2009. Impact of socioeconomic status on prevalence of overweight and obesity among children and adolescents in urban India, *The Open Obesity Journal*, 1, pp.9-14.

345) The Global Health Policy Summit, 2012. Countering non-communicable disease through innovation: report of the Non Communicable Disease Woking Group 2012.

346) Thomas, G.N., Ho, S.Y., Janus, E.D. *et al*., 2005. The US national cholesterol education programme adult treatment panel III (NCEP ATP III) prevalence of the metabolic syndrome in a Chinese population, *Diabetes Research and Clinical Practice*, Vol. 67, No. 3, March 2005, pp. 251–257.

347) Trisrivirat, K., Jiraporncharoen, W. and Angkurawaranon, C., 2021. Association between metabolic syndrome and alcohol consumption: A cross-sectional study, *J Health Sci Med Res*, 39(2), pp.145-155.

348) Tsigos, C., Kyrou, I., Kassi, E. *et al*., 2020. Stress: endocrine physiology and pathophysiology, in *Endotext* edited by Feingold, K.R., Anawalt, B., Boyce, A., *et al*., South Dartmouth (MA): MDText.com, Inc., 2000. Available from https://www.ncbi.nlm.nih.gov/books/NBK278995.

349) UNDP and OPHI, 2021. Global Multidimensional Poverty Index 2021: Unmasking disparities by ethnicity, caste and gender, *UNDP and OPHI*.

350) UNDP, 2010. Human Development Report 2010- the real wealth of nations: pathways of human development, *UNDP*, November 2010, New York, USA.

351) van Dam, R.M., 2003. The epidemiology of lifestyle and risk for type 2 diabetes, *European Journal of Epidemiology*, Vol. 18, No. 12 (2003), pp.1115-1125.

352) Vancampfort, D., Hallgren, M., Mugisha, J. *et al*., 2016. The prevalence of metabolic syndrome in alcohol use disorders: a systematic review and meta-analysis, *Alcohol and Alcoholism*, Vol. 51, No. 5, June 2016, pp.515-521.

353) Vepa, S.S., 2010. Impact of globalization on food consumption of urban India, in *Globalization in India: New Frontiers and Emerging Challenges* edited by Pramanick, S.K. and Ganguly, R., PHI Learning Pvt. Ltd., 2010, pp.95-113.

354) Vidal-Puig, A., 2014. The metabolic syndrome and its complex pathophysiology, in *A System Biology Approach to Study Metabolic Syndrome*, edited by Oresic, M. and Vidal-Puig, A., Springer, 2014, pp.3-16.

355) Vieira, B.A., Luft, V.C., Schmidt, M.I. *et al*., 2016. Timing and type of alcohol consumption and the metabolic syndrome - ELSA-Brasil, *PLoS ONE*, 11(9).

356) Vijaya Krishna V., 2011. Metabolic syndrome: the genetic aspect, *Endocrinol Metabol Syndrome*, S1:e001, December 2011.

357) Vincent, P. and D'Mello, L., 2018. Changing trends of divorce in India: issues and concerns, *International Journal of Management Technology and Social Sciences*, Vol. 3, No. 2, December 2018, pp.151-157.

358) Vonnahme, K.A., Hess, B.W., Hansen, T.R. *et al*., 2003. Maternal under-nutrition from early to mid gestation leads to growth retardation, cardiac ventricular hypertrophy, and increased liver weight in foetal sheep, *Biology of Reproduction,* Vol. 69, Issue 1, July 2003, pp.133-140.

359) Vorona, R.D., Winn, M.P., Babineau, T.W. *et al*., 2005. Overweight and obese patients in a primary care population report less sleep than patients with a normal body mass index, *Arch Intern Med*, 165, January 2005, pp.25-30.

360) Wandel, M., Raberg, M., Kumar, B. *et al*., 2008. Changes in food habits after migration among South Asians settled in Oslo: the effect of demographic, socio-economic and integration factors, *Appetite*, 50, pp.376-385.

361) Wang, W., Kong, J., Sun, J. *et al*., 2010. Epidemiological investigation of metabolic syndrome and analysis of relevant factors in North Eastern China, *The Journal of International Medical Research*, 38, 2010, pp.150-159.

362) Ward, A.M.V., Fall, C.H.D., Stein, C.E. *et al*., 2003. Corticol and the metabolic syndrome in South Asians, *Clinical Endrocrinology*, Vol. 58, Issue 4, April 2003, pp.500-505.

363) Webber, J., 2009. Changing epidemiology of obesity- implications for diabetes, in *Obesity and Diabetes, Second Edition* edited by Barnett, A.H. and Kumar, S., John Wiley & Sons Ltd., pp.1-12.

364) Wei, Y., Zhang, J., Li, Z. *et al*., 2016. Chronic exposure to air pollution particles increases the risk of obesity and metabolic syndrome: findings from a natural experiment in Beijing, *The FASEB Journal*, Vol. 30, Issue 6, June 2016, pp.2115-2122.

365) Weisberg, S.P., McCann, D., Desai, M. *et al*., 2003. Obesity is associated with macrophage accumulation in adipose tissue, *J Clin Invest.*, Vol. 112, No. 12, December 2003, pp.1796-1808.

366) Weiss, R., Dziura, J., Burgert, T. S. *et al*., 2004. Obesity and the metabolic syndrome in children and adolescents, *N Engl J Med*., 350 (23), pp.2362–2374.

367) Weitzman, M., Cook, S., Auinger, P. *et al*., 2005. Tobacco smoke exposure is associated with the metabolic syndrome in adolescents, *Circulation*, 112, pp.862-869.

368) Wheaton, A.G., Chapman, D.P., and Croft, J.B., 2016. School start times, sleep, behavioral, health, and academic outcomes: a review of the literature, *Journal of School Health*, Vol. 86, No. 5, May 2016, pp.363–381.

369) Whitlock, G., 2009. Body mass index and cause specific mortality in 900000 adults: collaborative analyses of 57 prospective studies, *Lancet*, 373, March 2009, pp.1083-1096.

370) WHO expert consultation, 2004. Appropriate body mass index for Asian populations and its implications for policy and intervention strategies, *The Lancet*, Vol. 363, January 2004, pp.157-163.

371) WHO, 1996. The global burden of disease: A comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020, *WHO*, The Havard School of Public Health.

372) WHO, 2005. Preventing chronic diseases: A vital investment. *WHO*.

373) WHO, 2011. Global Status Report on Non-communicable Diseases 2010, *WHO*.

374) WHO, 2014. Global Status Report on Non-communicable Diseases 2014, *WHO*.

375) WHO, 2000. Obesity: Preventing and managing the global epidemic, *WHO*, WHO technical report series 894.

376) Wieser, V., Moschen, A.R. and Tilg, H., 2014. Adipose tissue inflammation, in *Adipose Tissue and Adipokines in Health and Disease*, edited by Fantuzzi, G. and Braunschweig, C., Humana Press, 2nd Edition, 2014, pp.93-103.

377) Wild, S., Roglic, G., Green, A. *et al*., 2004. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030, *Diabetes Care*, Vol. 27, No. 5, May 2004, pp.1047-1053.

378) Wild, S.H. and Byrne, C.D. 2005. The global burden of the metabolic syndrome and its consequences for diabetes and cardiovascular disease, in *The Metabolic Syndrome* edited by Byrne, C.D. and Wild, S.H., Wiley, 2005, pp.1-41.

379) Wolk, R. and Somers, V.K., 2006. Sleep and the metabolic syndrome, *Exp Physiol*, 92.1, pp.67-78.

380) Woo Oh, S., Sook Yoon, Y., Sook Lee, E. *et al*., 2005. Association between cigarette smoking and metabolic syndrome: The Korea National Health and Nutrition Examination Survey, *Diabetes Care*, Vol. 28, No. 8, August 2005, pp.2064-2066.

381) Xiao, X., Zhang, Z.X., Li, W.H. *et al*., 2010. Low birth weight is associated with components of the metabolic syndrome, *Metabolism*, 59(9), September 2010, pp.1282-1286.

382) Xita, N. and Tsatsoulis, A., 2010. Fetal origins of metabolic syndrome, *Ann. N.Y. Acad. Sci.*, 1205, pp.148-155.

383) Yach, D., Stuckler, D., and Brownell, K.D., 2006. Epidemiologic and economic consequences of the global epidemics of obesity and diabetes, *Nature Medicine*, Vol. 12, No. 1, January 2006, pp.62-66.

384) Yadav, K. and Krishnan, A., 2008. National prevalence of obesity- changing pattern of diet, physical activity and obesity among urban, rural and slum populations in North India, *Obesity Reviews* (2008), 9, pp.400-408.

385) Yajnik, C.S., 2001. The insulin resistance epidemic in India: fetal origins, later lifestyle, or both? *Nutrition Reviews*, Vol. 59, No. 1, January 2001, pp.1-9.

386) Yajnik, C.S., 2004. Early life origins of insulin resistance and type 2 diabetes in India and other Asian Countries, *The Journal of Nutrition*, 134, pp.205-210.

387) Yamasaki, F., Schwartz, J.E., Gerber, L.M. *et al*., 1998. Impact of shift work and race/ethnicity on the diurnal rhythm of blood pressure and catecholamines. *Hypertension*, 32, pp.417–423.

388) Zavaroni, I., Mazza, S., Dall'Aglio, E. *et al*., 1992. Prevalence of hyperinsulinaemia in patients with high blood pressure, *Journal of Internal Medicine*, 231(3), pp.235-240.

389) Zhang, W., Hong, S., Takeuchi, D.T. *et al*., 2012. Limited English proficiency and psychological distress among Latinos and Asian Americans, *Soc. Sci. Med.*, 75 (6), pp.1006–1014.

Bibliography:

1) Abraham, N., Mahalingaiah, T., Balagopal, P. *et al*. 2002. Indian foods: AAPI's guide to nutrition, health and diabetes, *Allied Publishers Pvt. Ltd.*, *Chennai*.

2) Ahima, R.S. 2016. Metabolic syndrome: A comprehensive textbook, *Springer Reference, Philadelphia*.

3) Gillman, M.W. 2002. Epidemiological challenges in studying the fetal origins of adult chronic disease, *International Journal of Epidemiology*, 31, pp.294-299.

4) Hardman, J.E. and Stensel, D.J. 2009. Physical activity and health: The evidence explained, *Routledge*, Second edition.

5) Jimenez-Chillaron, J.C., Diaz, R., Martinez, D. *et al*. 2012. The role of nutrition on epigenetic modification and their implications on health, *Biochimie*, 94, pp.2242-2263.

6) Joshi, S.R., Anjana, R.M., Deepa, M. et al. 2014. Prevalence of dyslipidemia in urban and rural India: The ICMR-INDIAB study, *PLoS ONE*, Vol. 9, Issue 5.

7) Kalra, S. and Unnikrishnan, A.G. 2012. Obesity in India: The weight of the nation, *Journal of Medical Nutrition and Nutraceuticals*, Vol. 1, Issue 1, Jan-Jun 2012, pp.37-41.

8) Kim, Y.A., Park, J.B., Woo, M.S. *et al*. 2019. Persistent organic pollutant mediated insulin resistance, *Int. J. Environ. Res. Public Health*, 16, 448, February 2019.

9) Levine, T.B. and Levine, A.B. 2006. Metabolic syndrome and cardiovascular diseases, *Saunders Elsevier, Philadelphia*.

10) Moss, M. 2013. Salt sugar fat: how the food giants hooked us, *Random House*, New York.

11) NABARD, 2018. Sectoral paper on farm mechanization, *Farm sector policy department NABARD*, December 2018.

12) Sathya, R.M. 2007. Dietary patterns in an urban South Indian population and their association with diabetes, obesity, hypertension, dyslipidemia and the metabolic syndrome, PhD Thesis, University of Madras, Chennai.

13) Sears, M.E. and Genuis, S.J. 2012. Environmental determinants of chronic disease and medical approaches: recognition, avoidance, supportive therapy, and detoxification, *Journal of Environmental and Public Health*, Vol. 2012.

14) Sridhar, G.R., Putcha, V. and Lakshmi, G. 2010. Time trends in the prevalence of diabetes mellitus: ten year analysis from Southern India (1994-2004) on 19,072 on subjects with diabetes, *JAPI*, Vol. 58, pp.290-294.

15) Street, M.E., Angelini, S., Bernasconi, S. *et al*. 2018. Current knowledge on endocrine disrupting chemicals (EDCs) from animal biology to humans, from pregnancy to adulthood: highlights from a national Italian meeting, *Int. J. Mol. Sci.*, 19, 1647, June 2018.

16) Subramanian, S.V. and Kawachi, I. 2004. Income inequality and health: what have we learned so far? *Epidemiologic Review*, Vol. 26, pp.78-91.

17) Tchernof, A. and Despres, J.P. 2013. Pathophysiology of human visceral obesity: An update, *Physiol Rev*, 93, pp.359-404.

18) Toxics Link, 2018. Endocrine disruptor: review of Indian research, *Toxics Link*, New Delhi.

19) Tsigos, C. and Chrousos, G.P. 2002. Hypothalamic-pituitary-adrenal axis, neuroendocrine factors and stress, *Journal of Psychosomatic Research*, 53, pp.865-871.

20) Varshney, V., Sachan, D. and Matharu, S. 2012. The new obesity, *Down to Earth*, http://www.downtoearth.org.in/print/38434 as accessed on 24-08-2012.

21) Yajnik, C.S. 2004. Obesity epidemic in India: intrauterine origins? *Proceedings of the Nutrition Society*, 63, pp.387-396.

22) Zimering, M.B. 2011. Recent advances in the pathogenesis, prevention and management of type 2 diabetes and its complications, *InTech, Croatia*.

***