2. REVIEW OF LITERATURE

A global transition in the disease pattern has been observed, where the relative impact of communicable diseases are decreasing while on the other hand, non-communicable diseases like cardiovascular disease (CVD), diabetes and hypertension are increasing at a faster rate. In addition, NCDs now account for nearly half of the overall global burden of disease. It is estimated currently that of every 10 deaths, 6 are attributable to non-communicable conditions (WHO, 2004).

The prevalence of the metabolic syndrome has dramatically increased over the last few decades and has become a major health challenge worldwide, increasing the risk of cardiovascular disease (CVD), Type 2 diabetes (T2D), non-alcoholic liver disease, renal disease, and some forms of cancer in adults (Steele et al, 2008). The metabolic syndrome is a constellation of interrelated risk factors of metabolic origin—metabolic risk factors—that appear to directly promote the development of atherosclerotic cardiovascular disease (ASCVD). Conditions such as dyslipidemia, high blood pressure, impaired glucose tolerance and abdominal fat accumulation fall into this category.

According to ATP III, underlying risk factors for CVD are obesity (especially abdominal obesity), physical inactivity, and atherogenic diet; the major risk factors are cigarette smoking, hypertension, elevated LDL cholesterol, low HDL cholesterol, family history of premature coronary heart disease (CHD), and aging; and the emerging risk factors include elevated triglycerides, small LDL particles, insulin resistance, glucose intolerance, proinflammatory state, and prothrombotic state.
2.1 DEFINITION OF METABOLIC SYNDROME

The metabolic syndrome is a widely prevalent and multi-factorial disorder. The syndrome has been given several names, including the insulin resistance syndrome, the plurimetabolic syndrome, and the deadly quartet. With the formulation of NCEP ATP III guidelines, some uniformity and standardization has occurred in the definition of metabolic syndrome and has been very useful for epidemiological purposes. It is rare to see type 2 diabetes, dyslipidemia, obesity or hypertension in isolation. Insulin resistance and resulting hyperinsulinemia have been implicated in the development of glucose intolerance (and progression to type 2 diabetes), hypertriglyceridemia, hypertension, polycystic ovary syndrome, hypercoagulability and vascular inflammation, as well as the eventual development of atherosclerotic cardiovascular disease manifested as myocardial infarction, stroke and myriad end organ diseases (Gogia et al 2006).

Fedorwski et al (2009) aimed to examine whether three main definitions of the metabolic syndrome (MetS)--WHO, NCEP ATP III and IDF--identify the same individuals and are able to predict incident myocardial infarction (MI) in families with essential hypertension. The tested definitions were prospectively related to data on MI in a cohort of approximately 1700 individuals with overt essential hypertension and their normotensive first-degree relatives. At baseline, 616 participants had MetS, yet only 209 of them (33.9%) were identified by all definitions, and compatibility rate for each pair of definitions was approximately 50%. During follow-up (Tmean approximately 6.6 years), 53 participants developed MI and they were generally older and more dysmetabolic than the rest of the cohort. There were also more men, smokers and diabetic individuals in this group. After adjustment for all conventional cardiovascular risk factors, including hypertension and diabetes, only the National Cholesterol Education Program definition could predict the increased risk of MI [odds ratio (OR) = 2.2, confidence interval (CI) = 1.2-4.0, P = 0.01]. It was found out that the presence of MetS in
hypertensive and genetically hypertension prone individuals may signal the increased risk of future MI. However, only the National Cholesterol Education Program criteria appear to have a sufficient predictive accuracy.

Simone et al (2007) analyzed which definition of the metabolic syndrome is more predictive of cardiovascular events in both diabetic and nondiabetic members of a population-based sample. A 10-year, longitudinal follow-up of the Strong Heart Study cohort has been evaluated. The analysis included 3,945 participants (2,384 female) with complete data (1,700 with diabetes and 1,468 with arterial hypertension) for evaluation of metabolic syndrome. Those with prevalent cardiovascular disease were excluded (n = 287, of whom 127 were female). Prevalence of metabolic syndrome was assessed based on the WHO, NCEP ATPIII, and IDF definitions. The main outcome was 10-year incidence of combined fatal and nonfatal cardiovascular events, including stroke, coronary heart disease, and congestive heart failure. It was found out that in individuals without diabetes, metabolic syndrome is associated with incident cardiovascular disease, especially with WHO and NCEP ATP III definitions. Metabolic syndrome also predicts higher cardiovascular event rates in diabetic participants, a prediction that is greatest using the WHO definition.

A population-based, cross-sectional study of a total of 4232 participants--2039 men and 2193 women, aged 60 years was employed. Three different metabolic syndrome definitions were compared: European Group for the Study of Insulin Resistance (EGIR), IDF, and NCEP ATPIII. Forty five percent of men and 30% of women met the criteria for the metabolic syndrome by any definition, but only 17% of men and 9% of women met the criteria of all three definitions. Depending on the definition used, different individuals were identified as having the metabolic syndrome, which affects the reliability of interpretations to be made from scientific studies of the metabolic syndrome. Unified criteria are warranted.
Physicians facing a physically inactive former smoker may consider diagnosing metabolic syndrome (Carlsson, 2009).

Lopez et al (2008) examined combinations for joint probabilities and heritabilities of MetS criteria from NCEP ATPIII, WHO, and IDF in a sample of Omani families. The study included 1277 subjects from 5 pedigrees. The likelihood ratio of diagnostic cluster dependence over clustering by chance was $L_{\text{Dep}} = \frac{P(\text{dependent})}{P(\text{independent})}$. Heritabilities were adjusted by sex and age. The highest $L_{\text{Dep}}$ were central obesity (CO) + high glucose level (HGl) + triglycerides (IDF, 3.08; NCEP, 4.38; WHO, 3.17; $P < 0.001$). The WHO criteria yielded the highest heritability for a MetS diagnosis ($h^2(2) = 0.9$), followed by NCEP (0.48) and IDF (0.38). The rationale of the metabolic syndrome diagnostics is based on insulin resistance. This base would be lost by continuing lowering cut-off points for diagnosis for increasing the sensitivity. The WHO showed the highest values for $L_{\text{Dep}}$ for all components because they used the highest cut-off points.

Vaidya et al (2007) quantified the agreement between the WHO and NCEP definitions and their association with subclinical atherosclerosis in the Multi-Ethnic Study of Atherosclerosis (MESA). The study analyzed 2601 Caucasian-Americans (C), 800 Chinese-Americans (Ch), 1864 African-Americans (A), and 1483 Hispanic-Americans (H) with complete data for MetS classification from the baseline of the population-based study MESA. It was concluded that metabolic risk factors that differ between the NCEP and WHO MetS definitions are useful in combination to assess the presence of subclinical atherosclerosis.

Churilla et al (2007) examined the relationships that various medical society definitions have on metabolic syndrome (MetS) prevalence and the likelihood of a MetS diagnosis among a national sample of the United States (US) adult population. The sample for this study included adults, 20 years and older, ($N = 5620$) who completed the mobile examination center (MEC) examination in the 1999-2004 National Health and Nutrition Examination Survey (NHANES).
overall age-adjusted MetS prevalence ranged from a high of 38.9% (ACE/AACE), to a low of 21.2% (EGIR). For most metabolic syndrome definitions, males, people in the eighth decade of life (70-79 years of age), Mexican-Americans, those without a high school education, and those living in poverty were found to have the greatest prevalence. It was concluded that metabolic syndrome prevalence and the likelihood of being diagnosed with the metabolic syndrome within populations are highly dependent on the requisite criteria and medical society definition used.

According to Dandona et al (2004), the metabolic syndrome, as described by Reaven, is a combination of obesity, insulin resistance, hypertension, hypertriglyceridemia, low HDL cholesterol, and hyperinsulinemia. The syndrome was recognized as a very high pro-atherogenic risk causing coronary heart disease. More recently, other features like an elevated plasma PAI-1 and CRP have been added to the syndrome. In view of the recent data demonstrating that insulin exerts an anti-inflammatory effect while macronutrients exert a pro-inflammatory effect, it was better explained not only why an insulin resistant state like the metabolic syndrome is pro-inflammatory but also how it develops. This review discussed the relevance of these recent observations and put into perspective the pathogenesis of various features of the metabolic syndrome and also predicted some features which may get incorporated into it in the future.

2.2 PREVALENCE OF METABOLIC SYNDROME

Guize et al (2006) evaluated the prevalence, risk factors and impact on all-cause mortality of the metabolic syndrome (MetS) and its components in a large French population. The study population consisted of subjects aged 40 years or more who volunteered for a free health check-up at the IPC Center (Investigations Préventives et Cliniques, Paris) between 1999 and 2002. There were 40,977
men (53.2 +/- 9.1 years) and 21,277 women (55.9 +/- 10.3 years). MetS was defined according to NCEP-ATP III criteria. MetS was present at baseline in 11.8% of men and 7.6% of women. The prevalence of MetS increased from 9% in men aged 40 to 49 years to 12.5% in men aged 70 years. In women, the prevalence rose from 4.9% to 11.3%, respectively. From 1999 to 2002, the prevalence of MetS increased from 11.0% to 12.8% in men and from 7.2% to 8.8% in women. The three-component combination most strongly associated with mortality was high waist circumference + elevated glucose + elevated triglycerides.

Mousavi et al (2009) assessed the effect of parity on the prevalence of metabolic syndrome in analyses controlling for socio demographic and reproductive variables as well as behavioral risk factors. They evaluated the relationship between number of children and metabolic syndrome in 6331 adult non-pregnant women above 20 years of age. The data source for this study was Isfahan Healthy Heart Program (IHHP). Metabolic syndrome was defined according to Adult Treatment Panel III (ATP III). Overall, 34.2% of women met the criteria for metabolic syndrome. The number of children born in women with metabolic syndrome was significantly higher than others. In logistic regression analyses, the odds of metabolic syndrome increased 24% (95% confidence interval [CI], 22-26%) with each additional child, but after adjustment for socio demographic, reproductive, and behavioral characteristics, the odds of metabolic syndrome was attenuated. It was concluded that a combination of lifestyle risk factors and/or biological changes associated with childbearing may explain the positive association between parity and increased risk of metabolic syndrome.

Schultz et al (2009) conducted a study on a total of 4188 employees (83.4% male, 92.1% Caucasian, average age 40.8 years) of a midwestern U.S. manufacturing corporation participating in a health risk appraisal and biometric screening in 2006. Those with metabolic syndrome were compared to those
without metabolic syndrome in terms of their 2006 health risks. A total of 30.2% of employees met the criteria for metabolic syndrome and were more likely to also have a variety of additional health risks and health conditions compared to those without metabolic syndrome. It was concluded that because metabolic syndrome is prevalent among the employees of this manufacturing company and is associated with significant economic costs, employers would be wise to address the health risks of employees through health promotion programs and benefit plan designs that help individuals improve their health and receive appropriate health screenings and medical care.

Bener et al (2009) examined the prevalence of metabolic syndrome among adult Qatari population according to the revised criteria of NCEP ATP III and IDF to assess which component contributed to the increased risk of the metabolic syndrome, and identify the characteristics of the subjects with metabolic syndrome. The survey was carried out in urban and semi-urban primary health-care centres. The survey was conducted from January 2007 to July 2008 among Qatari nationals above 20 years of age. Of the 1496 subjects who were approached to participate in the study, the overall prevalence of metabolic syndrome was 26.5% and 33.7% according to ATP III and IDF criteria (P < 0.001) respectively. The current study found a high prevalence of metabolic syndrome among Qataris. There was a steady increase in the prevalence of metabolic syndrome through the decades, independent of the definition. Age and BMI were important significant predictors for metabolic syndrome.

Al et al (2008) estimated the prevalence of metabolic syndrome among pre-diabetic Omani adults. The study included 281 Omani pre-diabetic adults. In this study, the prevalence of metabolic syndrome was found to be 45.9%, and the gender-based distribution was 30.8% for men and 58.9% for women. This study showed that the prevalence of metabolic syndrome in this pre-diabetic study
population was higher than that in the general population. Certain health promotion and disease prevention measures were suggested.

Schumacher et al (2008) measured the prevalence of metabolic syndrome, as defined by the National Cholesterol Education Program, among four groups of American Indian and Alaska Native people, aged 20 years and older. One group was from the southwestern United States (Navajo Nation), and three groups resided within Alaska. Among participants from the southwestern United States, metabolic syndrome was found among 43.2% of men and 47.3% of women. Among Alaska Native people, metabolic syndrome was found among 26.5% of men and 31.2% of women. In Alaska, the prevalence rate varied by region, ranging among men from 18.9% (western Alaska) to 35.1% (southeast), and among women from 22.0% (western Alaska) to 38.4% (southeast). It was concluded that the prevalence rate of metabolic syndrome varies widely among different American Indian and Alaska Native populations. Differences paralleled differences in the prevalence rates of diabetes.

Villegas et al (2008) estimated the prevalence and lifestyle risk factors of metabolic syndrome according to three definitions of metabolic syndrome in urban Chinese men participating in the Shanghai Men's Health Study (SMHS). In this cross-sectional study, 3988 middle-aged, urban Chinese men 40-74 years of age who were free of type 2 diabetes at baseline were assessed. The three definitions of metabolic syndrome were from the International Diabetes Federation (IDF), the U.S. Third Report of the NCEP (ATP III), and a modified version of the ATP III criteria for Asian populations. The prevalence of metabolic syndrome was 18.63%, 18.36%, and 29.34% according to IDF, ATP III, and ATP III-modified criteria, respectively. Results from this representative sample of middle-aged, urban Chinese men showed that metabolic syndrome is highly prevalent in this population. The data supported the hypothesis that physical
activity decreases the risk of developing metabolic syndrome and that high alcohol consumption increases risk.

Hydrie et al (2009) determined the prevalence of metabolic syndrome in adults aged 25 years and older from an urban population of Karachi, Pakistan, according to the IDF definition and modified Adult Treatment Panel III (ATP III) criteria. Out of the 85,520 households, 532 households were randomly selected and 867 adults, 25 years or more of age, consented to take part in the survey; 363 of these subjects gave blood samples. The prevalence of diabetes was 9.4% whereas 5.6% had impaired fasting glucose (abnormal glucose tolerance 15%). The prevalence of metabolic syndrome according to the IDF definition and modified ATP III criteria was 34.8% and 49%, respectively. High prevalence of metabolic syndrome was identified irrespective of the definition applied in this population. This may call for immediate action to halt the accelerating risk of diabetes and CVD that would lead to a possible unparalleled rise in the cost of health care and human suffering.

Oh et al (2008) determined the prevalence and clinical characteristics of metabolic syndrome for an at-risk population in a rural community health-care center. Data were collected from 136 people who were defined as being at risk for metabolic syndrome by being over 40 years of age and being treated for hypertension, diabetes mellitus, dyslipidemia, or central obesity at a rural community health-care center in Korea. Prevalence and clinical characteristics were evaluated by the diagnostic guidelines of NCEP-ATP III and WHO-AP. It was found that the prevalence of metabolic syndrome among this group was 64.7% and 74.3% according to the NCEP-ATP III and WHO-AP criteria, respectively. The prevalence of metabolic syndrome increased with age and was higher in women. Of the five risk factors, fasting blood sugar and central obesity in women were the most prevalent (81.6%), followed by systolic hypertension (80.1%).
Al et al (2008) investigated causes of the prevalence of the metabolic syndrome in multiparous Omani Arab women using IDF. Of 392 married women (mean age 40 years), 354 (90%) were multiparous with an average parity of 8. They were divided into four parity groups: Para 0, Para 1-3, Para 4-6, and Para >6. In the whole cohort, the IDF definition identified 28% women with the metabolic syndrome, whereas it identified 48% in Para >6. In comparison, the National Cholesterol Education Program (NCEP) definition identified 21% and 39%, respectively. It was concluded that high prevalence of the metabolic syndrome in multiparous Omani Arab women appeared to be influenced by the parity-related large waist circumference. The high dependency of the IDF criteria on waist circumference for the definition of the metabolic syndrome in this population has led to the misclassification of such women.

Malik et al (2008) determined the prevalence of the metabolic syndrome using the NCEP ATPIII, and to compare this with the prevalence using IDF definitions in the United Arab Emirates (UAE). Data were collected on 4097 men and women aged 20 years or more, from the 2000 Emirates National Diabetes study and screening for risks factors for Coronary Artery Disease (ENDCAD) Study. The age-adjusted prevalence of metabolic syndrome using the NCEP definition was 39.6%, which was similar to 40.5% using the IDF definition. By either definition, the metabolic syndrome was found to be highly prevalent in the UAE. This would have important implications for the national health-care sector in the future.

Lee et al (2008) compared the prevalence of metabolic syndrome (MetS) by four MetS definitions in four Asia-Pacific populations, and compared the prevalence of individual metabolic components. Population-based cross-sectional studies from Australia, Japan, Korea, and Samoa were used to assess WHO, European Group for the Study of Insulin Resistance (EGIR), modified NCEP ATPIII, and IDF metabolic syndrome definitions. The study found that the highest prevalence
of metabolic syndrome was obtained with the IDF definition. The best overall agreement with IDF metabolic syndrome definition was for modified NCEP ATPIII, and the worst for EGIR. Marked differences in the prevalence of MetS between the sexes, with no systematic pattern, and between the prevalence of individual metabolic components, both within and between populations, indicate that caution is required when comparing studies from different countries.

Tonstad et al (2007) compared gender differences in the prevalence and determinants of the metabolic syndrome in subjects who were re-examined after a cardiovascular risk factor screening program. In a population-based cross-sectional study of 14,811 screened men and women aged 30, 40, 45, and 59 to 60 years, 1,491 subjects in the predetermined risk categories of high glucose (n = 64, 69% male), high cholesterol (n = 496, 66.3% male), and high blood pressure (n = 362, 63.5% male) or Framingham risk score (n = 253, 93.7% male) or low HDL cholesterol (n = 316, 79.1% male) underwent further examination. It was concluded that the metabolic syndrome was more prevalent and more strongly characterized by obesity and low grade inflammation in women than men. These findings underscore the need to study gender-specific approaches to screen for CHD risk.

Hightower et al (2007) assessed the reversal of metabolic syndrome characteristics. A retrospective analysis of clinical records for members participating in a university-based health assessment/fitness center between 1978 and 2003 was undertaken in 2005. First-year and second-year measures of body mass index, triglycerides, high-density lipoproteins, fasting blood glucose, and blood pressure were compared. Prevalence of individual metabolic syndrome risk markers, as well as deviation from cut-point levels, was compared in members with and without the syndrome and in subgroups of those whose metabolic syndrome status changed between the two examinations. This study found that while metabolic syndrome resolution was achieved within 2 years for
many participants in this study, it is likely that customized treatment interventions are necessary for those individuals with elevated triglycerides, the chief abnormality for those who did not resolve.

Baracco et al (2007) determined the prevalence of the metabolic syndrome on a population from the Andes Mountains of Peru and compared it to a sea-level population. A cross-sectional study of subjects aged 30 years old or more from the high-altitude population of San Pedro de Cajas (SPC) (13,450 feet) and the sea-level population of Rimac (331 feet) was done. The metabolic syndrome was identified according to the revised NCEP ATPIII definition. The study found an overwhelming predominance of females with the metabolic syndrome in both populations due to high prevalences of abdominal obesity and low high-density lipoprotein (HDL). Hypertriglyceridemia prevalence was elevated in both men and women of high altitude. Lower prevalence of high blood pressure and of high fasting glucose was found in the high-altitude natives. The prevalence and characteristics of the metabolic syndrome apparently varies among different population from the Andes Mountains of Peru and compared it to a sea-level population.

Fakhrzadeh et al (2006) determined prevalence of the metabolic syndrome and its underlying components in an urban population of Tehran. 1573 participants, 25-64 year-old, in the Population Laboratory of Tehran University of Medical Sciences were studied through a single-stage cluster sampling. The response rate was 94.08%. The study was designed according to the World Health Organization (WHO), MONICA (Multinational Monitoring of Trends and Determinants in Cardiovascular Disease) project using the Adult Treatment Panel III (ATPIII) criteria. The crude prevalence rate of the metabolic syndrome was 29.9% (age-adjusted: 27.5%). The prevalence was significantly higher in women than in men (35.9% vs. 20.3%). The study demonstrated high metabolic
syndrome rate among target population, especially in women. In view of correlation between metabolic syndrome and cardiovascular disease, it must be the priority for interventional preventive measures.

Piche et al (2006) examined the metabolic risk profile in postmenopausal women characterized by either the metabolic syndrome (MS) as defined by the World Health Organization (WHO) or the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATPIII). One hundred and eight postmenopausal women (56.9 +/- 4.2 years; BMI 28.5 +/- 5.9 kg/m(2)) were examined. Each underwent an oral glucose tolerance test, an euglycemic-hyperinsulinemic clamp, an assessment of body fat distribution by computed tomography, a complete plasma lipid-lipoprotein profile, and standard measurements of inflammatory markers. The results suggested that, in postmenopausal women, the concordance in the identification of subjects with the metabolic syndrome using each of the proposed definitions is only moderate.

Seclen et al (2006) assessed the prevalence of the metabolic syndrome in urban Peruvian Mestizos, in the coastal districts of Lima, the capital of Peru. A cross-sectional, epidemiological survey was undertaken, including 612 unrelated subjects aged 30-92 years (68.3% females). Prevalence of the metabolic syndrome was defined by the National Cholesterol Education Program Expert Panel on Detection Evaluation, and Treatment of High Blood Cholesterol in Adults (ATPIII) criteria. In this Mestizo Peruvian population, prevalence of the metabolic syndrome was relatively low as compared to other ethnic groups; the higher prevalence in females was likely due to a higher prevalence of abdominal obesity. Overall, abdominal obesity and hypertriglyceridemia were the predominant combination of metabolic disorders in individuals fulfilling criteria for the diagnosis of the metabolic syndrome.

Al et al (2006) estimated the prevalence of metabolic syndrome in Saudi adult women aged 18 years and above using the criteria of IDF and modified NCEP-
ATPIII. A cross-sectional survey was performed involving a group of 2577 non-pregnant Saudi women subjects, aged 18-59 years, residing in a military city in northern Saudi Arabia, recruited from a primary care setting. 1922 subjects who attended the laboratory for investigations were assessed. Non-respondents were excluded from data analysis. Prevalence rates were estimated according to both definitions. Age-adjusted prevalence of metabolic syndrome was found to be 16.1% and 13.6% by IDF and modified NCEP-ATPIII definitions, respectively. High prevalence rates in this young sample predicted a sharp rise in the prevalence rates of this syndrome among Saudi women over the next few years.

Bonora et al (2003) evaluated the prevalence of the Metabolic Syndrome. Within a prospective population-based survey examining 888 subjects aged 40-79 years, subjects were identified fulfilling the WHO and NCEP-ATPIII criteria for diagnosing the Metabolic Syndrome. In these subjects and in the rest of the sample (controls), several metabolic and non metabolic biochemical parameters were compared. The prevalence of the Metabolic Syndrome by WHO criteria was 34.1% (95% CI 31.0-37.2) and by NCEP-ATPIII criteria 17.8% (15.5-20.3). The prevalence was significantly higher in older subjects and in those less physically active. It was concluded that the Metabolic Syndrome occurs very frequently in the general population aged 40-79 years, and is associated with several additional metabolic and non-metabolic abnormalities that likely contribute to an increased cardiovascular risk.

Ford et al (2002) estimated the prevalence of the metabolic syndrome in the United States as defined by the ATP III report. Analysis of data was done for 8814 men and women, aged 20 years or older from the Third National Health and Nutrition Examination Survey (1988-1994), a cross-sectional health survey of a nationally representative sample of the non institutionalized civilian US population. The results from a representative sample of US adults showed that
the metabolic syndrome is highly prevalent which may have important implications for the health care sector.

Kanjilal et al (2008) estimated metabolic syndrome prevalence in 531 Asian Indian families comprising of 2318 individuals. Metabolic syndrome prevalence was estimated using standard ATP-III and WHO criteria and modified definitions. ATP-III criteria identified a significantly higher proportion of people with MS (N = 933; 40.3%) compared with WHO (N = 708; 30.6%; p < 0.0001) while modified ATP-III showed maximum gain in percent prevalence among the revised criteria (17.3%; p = 0.0056). The IDF criteria identified similar proportion of subjects with MS (N = 809; 34.9%) as the revised WHO criteria (N = 792; 34.2%). The number of MS subjects was highest in the 50–59 years age group. In conclusion, the revision of definition criteria for MS with lowered cut-offs for WC and BMI is critical for the accurate assessment of MS among Asian Indians.

Bonora et al (2003) evaluated the prevalence of the Metabolic Syndrome and at identifying its additional clinical features. Within a prospective population-based survey examining 888 subjects aged 40-79 years, subjects were identified fulfilling the WHO and the NCEP-ATPIII criteria for diagnosing the Metabolic Syndrome. The prevalence of the Metabolic Syndrome by WHO criteria was 34.1% (95% CI 31.0-37.2) and by NCEP-ATPIII criteria 17.8% (15.5-20.3). The prevalence was significantly higher in older subjects and in those less physically active. It was concluded that the Metabolic Syndrome occurs very frequently in the general population aged 40-79 years, and is associated with several additional metabolic and nonmetabolic abnormalities that likely contribute to an increased cardiovascular risk. Insulin resistance seems to play a major role in classic and additional abnormalities featuring the Metabolic Syndrome.
2.3 COMPONENTS OF METABOLIC SYNDROME

According to Gerich (2006), the metabolic syndrome represents a cluster of cardiovascular risk factors that occur together more commonly than expected from the prevalence of their individual rates. Insulin resistance is widely believed to be the common denominator causing, in susceptible individuals, the development of various cardiovascular risk factor components of the syndrome (e.g., hyperlipidemia, hypertension, and hyperglycemia). The major cause of this insulin resistance appears to be obesity, especially the accumulation of visceral fat. This obesity is due to the combination of excessive caloric intake and inadequate physical activity rather than alterations in energy utilization. In individuals whose beta cells cannot increase their insulin secretion adequately to compensate for insulin resistance, hyperglycemia occurs.

2.3(a) Diabetes

Mancia et al (2008) conducted a study on long-term risk of diabetes, hypertension and left ventricular hypertrophy associated with the metabolic syndrome in a general population. In 1412 individuals representative of the population of Monza, plasma glucose, ambulatory blood pressure, and echocardiographic left ventricular mass index were measured between 1990 and 1992 and 10 years later. New onset diabetes mellitus, hypertension and left ventricular hypertrophy were much more frequent in individuals with metabolic syndrome than in those without. In patients with metabolic syndrome, the adjusted risk of new onset diabetes mellitus was five to six times greater (p < 0.001) as compared to others. It was concluded that in the general population, metabolic syndrome is associated with a marked increase in the risk not only of new onset diabetes mellitus but also of new onset office and daily-life hypertension, and left ventricular hypertrophy. This may account for the
increased rate of cardiovascular morbidity and mortality exhibited with this condition in long-term studies.

Luk et al (2008) conducted a research on metabolic syndrome which predicts new onset of chronic kidney disease in 5,829 patients with type 2 diabetes: a 5-year prospective analysis of the Hong Kong Diabetes Registry. Metabolic syndrome was defined by National Cholesterol Education Program Adult Treatment Panel III criteria with the Asian definition of obesity. Subjects with CKD at baseline were excluded from the analysis. After a median follow-up duration of 4.6 years, 741 patients developed CKD. The multivariable-adjusted hazard ratio (HR) of CKD was 1.31 (95% CI 1.12-1.54, P = 0.001) for subjects with metabolic syndrome compared with those without metabolic syndrome. Relative to subjects with no other components of metabolic syndrome except for diabetes, those with two, three, four, and five metabolic syndrome components had HRs of an increased risk of CKD of 1.15. It was found that the presence of metabolic syndrome independently predicts the development of CKD in subjects with type 2 diabetes.

Ford et al (2008) performed a quantitative review of prospective studies examining the association between the metabolic syndrome and incident diabetes. Based on the results from 16 cohorts, they performed a meta-analysis of estimates of relative risk (RR) and incident diabetes. Higher number of abnormal components was strongly related to incident diabetes. Compared with participants without an abnormality, estimates of RR for those with four or more abnormal components ranged from 10.88 to 24.4. Limited evidence suggested fasting glucose alone may be as good as metabolic syndrome for diabetes prediction. It was found out that the metabolic syndrome, however defined, has a stronger association with incident diabetes than that previously demonstrated for coronary heart disease. Its clinical value for diabetes prediction remains uncertain.
Ghani et al (2009) assessed the efficacy of 1-h plasma glucose concentration and the metabolic syndrome in predicting future risk of type 2 diabetes. A total of 1,611 subjects from the San Antonio Heart Study were assessed. Two models, based on glucose tolerance status, 1-h plasma glucose concentration, and presence of the metabolic syndrome, were tested in predicting the risk for type 2 diabetes at 7-8 years of follow-up. It was concluded that the plasma glucose concentration at 1 h during the OGTT is a strong predictor of future risk for type 2 diabetes. A plasma glucose cutoff point of 155 mg/dl and the ATP III criteria for the metabolic syndrome can be used to stratify non-diabetic subjects into three risk groups: low, intermediate, and high risk.

Cheung et al (2007) investigated the association of the metabolic syndrome with new-onset diabetes in the Hong Kong Cardiovascular Risk Factor Prevalence Study cohort. They followed up on 1,679 subjects without diabetes at baseline. Those with a previous diagnosis of diabetes or those who were receiving drug treatment were considered to be diabetic. The prevalence of the metabolic syndrome at baseline was 14.5% and 11.4%, respectively, according to U.S. National Cholesterol Education Program (NCEP) and International Diabetes Federation (IDF) criteria. After a median of 6.4 years, there were 66 and 54 new cases of diabetes in men and women, respectively. The study revealed that metabolic syndrome at baseline predicted incident diabetes. The metabolic syndrome, particularly its component, elevated FPG, predicted diabetes in Chinese. An individual without the metabolic syndrome is unlikely to develop diabetes, but one who has it should practice therapeutic lifestyle changes and have periodic FPG measurements to detect new-onset diabetes.

in South Africa. A total of 500 African and 254 White diabetic patients were evaluated for features of the metabolic syndrome (IDF definition). In men, the metabolic syndrome was present in 46.5% and 74.1% of African and White patients respectively ($p < 0.0001$). In women, frequencies of the metabolic syndrome were similar, but severe metabolic syndrome (4 or 5 criteria) was more frequent in the White group (73.1%) than in the Africans (52.9%) ($p = 0.0003$). It was found out that in diabetic Africans, in comparison with White patients, the lower prevalence of the metabolic syndrome in men and severe metabolic syndrome in women, and lesser insulin resistance, might contribute to their lower risk of CHD.

Janghorbani et al (2007) estimated the prevalence and risk factors of metabolic syndrome in people with type 2 diabetes mellitus (T2DM) using routinely collected data from a clinical information system at Isfahan Endocrinology and Metabolism Research Centre, Iran. A total of 9889 consecutive diabetic patients, 4164 males and 5725 females were examined. The mean (SD) age of participants was 52.0 (10.9) years with a mean (standard deviation) duration of diabetes of 6.4 (6.4) years at initial registration. A modified National Cholesterol Education Program-Adult Treatment Panel III definition with body mass index instead of waist circumference was used for the metabolic syndrome. The data suggests that metabolic syndrome in this population of Iranian type 2 diabetic patients is common, and with an estimated prevalence of 65%, metabolic syndrome clearly poses a formidable health threat to Iranian diabetic patients. Lifestyle interventions in T2DM subjects are needed in Iran to halt the burden of macro- and micro-vascular complications in T2DM.

Bo et al (2006) conducted a study on mild gestational hyperglycemia and the metabolic syndrome in later life. Fifty women with previous positive oral glucose challenge test and negative oral glucose tolerance test (pOGCT+OGTT-), 161 with previous normal glucose tolerance (pNGT), and 182 pGDM were studied
after 6.5 years from the index pregnancy. It was concluded that women who failed the OGCT, but not the OGTT, showed a subsequent worse metabolic pattern than pNGT subjects, independently of confounding factors. In the presence of obesity, the prevalence of the metabolic syndrome was similar to that of obese pGDM women, and almost twofold higher than in obese pNGT controls.

2.3(b) Hypertension

Mule et al (2006) conducted a study on influence of metabolic syndrome on hypertension-related target organ damage. The aim of the study was to analyse, in a wide group of essential hypertensive patients without diabetes mellitus, the influence of metabolic syndrome on markers of preclinical cardiac, renal and retinal damage. It was a cross-sectional study. A total of 353 young and middle-aged hypertensives, free from cardiovascular and renal diseases (and 37% of whom had MS), underwent echocardiographic examination, microalbuminuria determination and non-mydriatic retinography. It was concluded that metabolic syndrome may amplify hypertension-related cardiac and renal changes, over and above the potential contribution of each single component of this syndrome. As these markers of target organ damage are well-known predictors of cardiovascular events, the results may partly explain the enhanced cardiovascular risk associated with metabolic syndrome.

According to Kjeldsen et al (2008), the Global Cardio-metabolic Risk Profile in Patients with hypertension disease survey investigated the cardio-metabolic risk profile in adult outpatients with hypertension in Europe. Data on BP control and cardio-metabolic risk factors were collected for 3370 patients with hypertension in 12 European countries. Prevalence was analyzed according to BP status and ATP III criteria for metabolic syndrome. BP was controlled in 28.1% of patients.
Patients with uncontrolled BP had significantly higher mean weight, BMI, waist circumference, fasting blood glucose, total cholesterol and triglycerides and high-density lipoprotein cholesterol levels were significantly lower (women only) compared with patients with controlled BP ($p < 0.05$). The prevalence of metabolic syndrome and type 2 diabetes was also significantly higher in patients with uncontrolled BP compared with controlled BP ($p < 0.001$) (metabolic syndrome: 66.5 versus 35.5%; diabetes 41.1 versus 9.8%, respectively). 95.3% of patients with both metabolic syndrome and type 2 diabetes had uncontrolled BP. According to this European study, fewer than one third of treated hypertensive patients had controlled BP. Metabolic syndrome and diabetes were important characteristics associated with poor BP control. Thus, more focus is needed on controlling hypertension in people with high cardio-metabolic risk and diabetes.

Nita et al (2009) analyzed the ability of hypertensive waist to predict the presence of the metabolic syndrome. A total of 1294 women and men, randomly selected from general population, aged 18 years and above were included in this study. Hypertensive waist was defined as the presence of the systolic blood pressure 130 mmHg and higher or a diastolic blood pressure 85 mmHg and higher or history of treated hypertension plus a waist circumference of 80 cm or higher for women and 94 cm or higher for men. International Diabetes Federation criteria were used for the diagnosis of the metabolic syndrome. The prevalence of hypertensive waist was 43.3% and the prevalence of the metabolic syndrome was 45.7%. It was concluded that on the basis of the easy-to-determine clinical parameters and on high predictive value, the clinical couple of hypertensive waist could be used as a starting point to screen for metabolic syndrome in Romanian population.

McCaffery et al (2007) examined the extent to which measures of ambulatory blood pressure, reflecting blood pressure variability throughout the day and night,
may strengthen the association between blood pressure and the other components of the syndrome. Participants were a community sample of 358 men (248 with hypertension), aged 40-70 years, not receiving antihypertensive medications. Confirmatory factor analysis was employed to examine model fit and the strength of association between clinic and ambulatory blood pressure and the metabolic syndrome. It was concluded that both clinic and ambulatory measures of blood pressure are significantly associated with the underlying metabolic syndrome using confirmatory factor analytic methods. However, the strength of association appears greater for the clinic measures relative to the ambulatory measures in this study.

According to Franklin (2006), increased blood pressure is considered an important component of metabolic syndrome. More than 85% of those with metabolic syndrome, even in the absence of diabetes, have elevated blood pressure (BP) or hypertension. The association of elevated BP with the metabolic syndrome is strongly linked through the causative pathway of obesity. Hypertension is the leading metabolic syndrome risk factor that predisposes to increased cardiovascular morbidity and mortality, and is additionally an important risk factor for development of chronic kidney disease.

Hermida et al (2009) investigated the association between metabolic syndrome and impaired nocturnal BP decline in 1,770 non-diabetic, untreated hypertensive patients (824 men and 946 women), 48.7 +/- 13.2 years of age. BP was measured by ambulatory monitoring for 48 h to increase reproducibility of the dipping pattern. Physical activity was simultaneously monitored every minute by wrist actigraphy. Metabolic syndrome was present in 42.4% of the patients. The prevalence of a nondipper BP profile was significantly higher in patients with metabolic syndrome (46.1% vs. 37.5% in patients without metabolic syndrome, p < 0.001). This study documented a significant increase of a blunted nocturnal BP decline in patients with metabolic syndrome. Patients with metabolic syndrome
were also characterized by elevated values of relevant markers of cardiovascular risk, including fibrinogen and globular sedimentation rate.

Cheung et al (2008) conducted a study on relationship between the metabolic syndrome and the development of hypertension in the Hong Kong Cardiovascular Risk Factor Prevalence Study-2 (CRISPS2). A total of 1,944 subjects (901 men and 1,043 women; age 46 +/- 12 years) from the Hong Kong Cardiovascular Risk Factor Prevalence Survey were recruited in 1995-1996 and restudied in 2000-2004. In 2000-2004, hypertension was found in 23.2% of the men and 17.2% of the women. Of the 1,602 subjects who were normotensive at baseline, 258 subjects developed hypertension after a median interval of 6.4 years. According to the National Cholesterol Education Program (NCEP) and International Diabetes Federation (IDF) criteria, the hazard ratios associated with the metabolic syndrome were 1.89 (95% confidence interval (CI): 1.41-2.54) and 1.72 (95% CI: 1.24-2.39), respectively. It was concluded that blood pressure, when not optimal, is the predominant predictor of hypertension. The metabolic syndrome contributes to the risk, especially when blood pressure is optimal.

Cuspidi et al (2007) investigated the association of the metabolic syndrome (MS) with cardiovascular alterations in essential hypertensives in relation to age. A total of 3266 untreated and treated hypertensive patients categorized in three age groups (I: 17 to 40 years; II: 41 to 64 years; III: >64 years) were considered for this analysis. All patients underwent extensive investigations searching for target organ damage (TOD). The metabolic syndrome was defined according to Advanced Technology Laboratories (ATP) III criteria. The study demonstrated that in hypertensive patients, the metabolic syndrome amplifies TOD regardless of patient's age, thus increasing cardiovascular risk. This synergistic effect may accelerate the early development of TOD in young hypertensives and enhance the age-associated cardiovascular alterations in the elderly.
Mule et al (2005) analyzed in a group of patients with essential hypertension and without diabetes mellitus, the influence of metabolic syndrome on clinic and 24-h pulse pressures. A total of 528 hypertensive subjects, aged 18 to 72 years, who were free of cardiovascular and renal diseases were enrolled. Of the subjects, 41% had metabolic syndrome. In all subjects, routine blood chemistry, echocardiographic examination, and 24-h ambulatory blood pressure monitoring were performed. It was concluded that the elevated levels of clinic and 24-h pulse pressure observed in hypertensive patients with metabolic syndrome may reflect increased large arteries stiffness and may therefore contribute to explain the enhanced cardiovascular risk associated with metabolic syndrome.

Chen et al (2000) conducted a study on different association of hypertension and insulin-related metabolic syndrome between men and women in 8437 non-diabetic Chinese. They examined fasting insulin, glucose, triglyceride and high-density lipoprotein (HDL)-cholesterol levels, systolic blood pressure, body mass index, and waist-to-hip ratio in a dataset from 8437 non-diabetic residents (age range, 30 to 89 years) in Kinmen. Factor analysis, a multivariate correlation statistical technique, was used to investigate the clustering and interdependence of these risk variables. It was concluded that a distinct insulin-resistance-related metabolic syndrome characterized by hyperinsulinemia, dyslipidemia, and obesity was observed for both men and women in this Chinese population. However, hypertension was linked to the metabolic syndrome in women only.

Mazza et al (2007) conducted a study on pulse hypertension: a new component of the metabolic syndrome in elderly women. They evaluated the categorization of arterial hypertension (HT) most qualified to define metabolic syndrome in relationship with coronary heart disease (CHD) mortality at a population level. A total of 3257 subjects aged 65 years or more were followed up for 12 years. Metabolic syndrome was defined according to the criteria of the National Education Cholesterol Program. Gender-specific adjusted hazard ratio (HR) with
95% confidence intervals (CI) for CHD mortality was derived from Cox analysis in the three metabolic syndrome groups, both including and excluding antihypertensive treatment. It was concluded that MS can predict CHD mortality in elderly women with untreated HT but not in those with treated HT; in the latter, pulse pressure is the most predictive BP value.

2.3(c) Obesity / Waist Circumference

Mombelli et al (2009) conducted a research on waist-to-height ratio(WHtR) - a highly sensitive index for the metabolic syndrome in a mediterranean population. WHtR, BMI and WC were determined in 552 males and 552 females, together with the evaluation of associated metabolic syndrome variables Results revealed that WHtR >/= 0.5, the most frequently suggested threshold value, when added to any two non-anthropometric variables, gave a sensitivity for the identification of a metabolic syndrome of, respectively, 92.0% for males and 87.4% for females. Sensitivities for elevated WC (American Heart Association [AHA] criteria) and BMI >/= 25 proved lower. The study concluded that WHtR >/= 0.5 may be the most effective anthropometric index for screening high-risk patients in the diagnosis of metabolic syndrome, with the advantage of the opportunity of direct comparisons with other populations.

Okosum (2008) determined the impact of abdominal obesity (AO) on the association of C-reactive protein (CRP) with metabolic syndrome. Data (n = 6270) from the 2005-2006 U.S. National Health and Nutrition Examination Survey were used in this investigation. It was concluded that in multivariate logistic regression analysis, C-reactive protein was associated with reduced risk of metabolic syndrome adjusting for abdominal obesity independently of potential confounders, thus confirming once again the importance of weight reduction for the management of metabolic syndrome. Weight reduction programs or other interventions targeted specifically at abdominal regions may help to alleviate risk of metabolic syndrome.
According to Basit et al (2008), over the past two decades, there has been a striking increase in the number of people with metabolic syndrome. Considering the increased cardiovascular risk among Asian people, a lower cutoff for waist circumference is defined. Obesity in terms of waist circumference is found to be present in 46-68% of the Pakistani population, with a strong association found between arm fat and insulin insensitivity. In studying dyslipidemia, hypertriglyceridemia is found in 27-54% of the population, whereas 68-81% has low levels of high-density lipoprotein (HDL). Fifty percent were found to be at high risk of metabolic syndrome and as being hypertensive. With the high prevalence of all of these metabolic risk factors, the prevalence of metabolic syndrome in Pakistan according to different definitions is reported to be from 18% to 46%, comparable to the data from other South Asian countries. Thus, metabolic syndrome should be considered as a prime target for preventive medicine.

Yan et al (2008) assessed which specific adipose tissue factors would discriminate the presence of metabolic syndrome (MS) in a strictly obese population meeting waist circumference (WC) criteria for the MS. This was a cross-sectional study of 148 subjects recruited from a university-based weight loss program prior to starting the program. Of the total population, 33.8% satisfied criteria for the metabolic syndrome. It was concluded that in a population where an excess amount of adipose tissue exists, insulin is the only reliable biomarker to differentiate metabolic syndrome status.

Chang et al (2007) determined the pattern of metabolic risk factors in very obese women who were considered candidates for bariatric surgery. Twenty-eight women of this type were compared to 28 non-obese women. Among the former, 11 had categorical hyperglycemia (type 2 diabetes), and 26 had metabolic syndrome by current criteria. Both those with and without diabetes had higher triglycerides and lower high-density lipoprotein (HDL) cholesterol levels than
nonobese, but their levels were not categorically abnormal. In addition, they had very high C-reactive protein levels. Thus, the metabolic syndrome, which appears to be typical of very obese women, is characterized by insulin resistance, glucose intolerance and a proinflammatory state. Atherogenic dyslipidemia as a metabolic risk factor in contrast is relatively mild. This pattern is more likely to lead to type 2 diabetes prior to development of clinically evident cardiovascular disease.

Kumagai et al (2005) examined the contribution of endurance fitness and visceral fat accumulation on the prevalence of metabolic syndrome in Japanese male patients with either an impaired glucose tolerance (IGT) or type 2 diabetes mellitus (DM). The subjects of this cross-sectional study consisted of 135 Japanese male patients with either IGT or type 2 DM who had not taken any medication or intervention. Metabolic syndrome was defined based on the WHO criteria. The visceral fat area (VFA) was determined using a computed tomography scan. The results indicate that a high degree of cardiorespiratory fitness positively contributed to the low prevalence of metabolic syndrome in Japanese male patients with IGT and type 2 DM.

Ebrahimpour et al (2006) conducted a study on metabolic syndrome and related insulin levels in obese children. A total of 535 obese 7-11 year-old students of all the primary schools of the 6th district of Tehran were screened according to their waist circumference and then confirmed according to the International Obesity Task Force (IOTF) criteria. Waist circumference, fasting serum triglycerides, high-density lipoprotein (HDL) cholesterol, blood pressure, fasting plasma glucose, and insulin levels were measured. The crude prevalence rate of metabolic syndrome in these children was 20.6%. It was concluded that the prevalence of metabolic syndrome is high in Iranian obese children. Early intervention in this population who will become future obese adults is needed, not
only to increase their life quality, but also to decrease the future burden of diabetes and cardiovascular diseases on the society.

Anderson et al (2001) evaluated whether there is one central abnormality contributing to the conditions associated with the metabolic syndrome (MS), or whether one abnormality is contributing on multiple levels. 145 Chinese subjects aged 17-68 years with varying degrees of insulin-sensitivity (IS): 33 healthy, 59 with type 2 diabetes mellitus, 32 essential hypertensives and 21 dyslipidaemics were included. This study suggested that the clustering of variables in metabolic syndrome is a result of multiple factors linked by adiposity and not a single aetiology. Furthermore, increases in blood pressure are related to obesity in these Chinese subjects rather than decreased IS per se.

Forouhi et al (2001) investigated the association between circulating C-reactive protein (CRP) concentrations and indices of body fat distribution and the insulin resistance syndrome in 113 healthy South Asian and European men and women in West London (age 40-55 years with body mass index (BMI) 17-34 kg/m2. The study suggested that adiposity and in particular visceral adipose tissue is a key promoter of low-grade chronic inflammation. This observation may in part account for the association of CRP with markers of the metabolic syndrome. Future studies should confirm whether CRP concentrations are elevated in South Asians and whether losing weight by exercise or diet, or reduction in visceral fat mass, is associated with reduction in plasma CRP concentrations.

Vanhala et al (1999) examined whether birth weight, weight gain from birth to the age of seven or body-mass index at the age of seven have any association with metabolic syndrome as an adult in a population study on 210 men and 218 women aged 36, 41 or 46 years in Pieksämäki town, Finland. The study could not replicate the close association between low birth weight and the metabolic syndrome in adulthood as has been shown in some earlier studies. Obesity at the age of seven predicts the metabolic syndrome in adulthood.
Lin et al (2006) investigated the relationship between the metabolic syndrome and its related factors among non-diabetic pre- and post-menopausal women in a cross-sectional study in North Taiwan. Five hundred and ninety-four, non-diabetic middle-aged women (age range 40-64 years, mean 48.9+-5.4 years) were recruited. Metabolic syndrome was defined by using the National Cholesterol Education Panel (NCEP) criteria and modified NCEP criteria (waist circumference >80 cm). It was concluded that the prevalence of metabolic syndrome was higher in post-menopausal than pre-menopausal women. Both obesity and insulin resistance may play an important role in the development of metabolic syndrome among the middle-aged women in North Taiwan.

Santos et al (2005) conducted a study on central obesity as a major determinant of increased high-sensitivity C-reactive protein in metabolic syndrome. Using random digit dialing, 1022 participants, aged 18-92 years were selected. Metabolic syndrome was defined, according to the Third Report of the Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults. High-sensitivity CRP was assessed by immunonephelometric assay. The study showed that increasing severity of metabolic syndrome is associated with increasing CRP. Additionally, it was found that central obesity and high blood pressure are the most important determinants of the low-grade chronic inflammation present in metabolic syndrome.

Wannamethee et al (1998) investigated the prevalence of the metabolic syndrome and its component variables and their relationship to body mass index (BMI) and non-fasting insulin levels in a general population; and the distribution and clustering of metabolic variables in normotensives and hypertensives in a cross-sectional study of 5222 men, aged 40-59 years, with no history of coronary heart disease (CHD), diabetes mellitus or stroke drawn from general practices in
18 British towns. The men were a subgroup of the 7735 men in the British Regional Heart Study (BRHS) cohort whose baseline non-fasting serum was analysed for insulin, using a specific ELISA method. It was concluded that hypertensives were more likely to have lipid abnormalities and clustering of risk factors than normotensives even after adjustment for BMI. The metabolic syndrome is more strongly associated with hyperinsulinaemia than with obesity but it is relatively uncommon in men with no history of cardiovascular disease or diabetes. Given the weak relationship between hypertension and hyperinsulinaemia, the latter is unlikely to explain the higher levels of lipid abnormalities and clustering seen in hypertensives. Overweight/obesity may be primarily involved in the pathways to hypertension and lipid abnormalities but the unravelling of these relationships requires more specific measures of adipose tissue distribution, composition and function.

2.3(d) Cardiovascular Disease

Isomaa et al (2001) estimated the prevalence and the cardiovascular risk associated with the metabolic syndrome using the new definition proposed by the World Health Organization (WHO). A total of 4,483 subjects aged 35-70 years participating in a large family study of type 2 diabetes in Finland and Sweden (the Botnia study) were included in the analysis of cardiovascular risk associated with the metabolic syndrome. In women and men, respectively, the metabolic syndrome was seen in 10 and 15% of subjects with NGT, 42 and 64% of those with IFG/IGT, and 78 and 84% of those with type 2 diabetes. The risk for coronary heart disease and stroke was increased threefold in subjects with the metabolic syndrome \( (p < 0.001) \). Cardiovascular mortality was markedly increased in subjects with the metabolic syndrome \( (12.0 \text{ vs. } 2.2\%, \ p < 0.001) \). The study concluded that the WHO definition of the metabolic syndrome
identifies subjects with increased cardiovascular morbidity and mortality and offers a tool for comparison of results from different studies.

Redon (2008) stated that the metabolic syndrome considerably increases the risk of cardiovascular and renal events in hypertension. Obesity and insulin resistance, besides a constellation of independent factors, which include molecules of hepatic, vascular, and immunologic origin with proinflammatory properties, have been implicated in the pathogenesis. The close relationships among the different components of the syndrome and their associated disturbances make it difficult to understand what the underlying causes and consequences are. At each of these key points, insulin resistance and obesity/proinflammatory molecules, and interaction of demographics, lifestyle, genetic factors, and environmental fetal programming results in the final phenotype. High prevalence of end-organ damage and poor prognosis has been demonstrated in a large number of cross-sectional and a few number of prospective studies.

Ninomiyo et al (2009) conducted a research on Association of the metabolic syndrome with history of myocardial infarction and stroke in the Third National Health and Nutrition Examination Survey. Applying National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) criteria, they evaluated 10,357 NHANES III subjects. The syndrome was significantly associated with MI/stroke in both women and men. Among the component conditions, insulin resistance, low HDL-C, hypertension, and hypertriglyceridemia were independently and significantly related to MI/stroke. These results indicate a strong, consistent relationship of the metabolic syndrome with prevalent MI and stroke.

Regitz et al (2007) reviewed on gender aspects of the role of the metabolic syndrome as a risk factor for cardiovascular disease. Using the search terms-
women, men, sex, gender, sex differences, and gender differences in combination with the metabolic syndrome, they conducted a systematic review of the available literature on sex differences in the metabolic syndrome. It was concluded that in recent years, metabolic syndrome has been more prevalent in men than in women but has risen particularly in young women, where it is mainly driven by obesity. Hypertension is a strong risk factor in both sexes, but the prevalence of hypertension increases more rapidly in aging women than in men.

Ninomiyo et al (2007) assessed the impact of metabolic syndrome on the development of cardiovascular disease in a general Japanese population: the Hisayama study. They prospectively evaluated a total of 2452 community-dwelling Japanese individuals aged 40 years or older from 1988 to 2002 and examined the effects of metabolic syndrome defined by the modified National Cholesterol Education Program Adult Treatment Panel III criteria on incident CVD. The prevalence of the metabolic syndrome was 21% in men and 30% in women at baseline. The risk of incident CVD was found to increase with the number of components of metabolic syndrome and became significantly predictive when the number of components reached 3. Similar associations were also observed when CVD was divided into coronary heart disease and stroke. The findings suggested that metabolic syndrome is a significant risk factor for the development of CVD in the Japanese middle-aged population.

Pannier et al (2006) designed a SYMFONIE study to analyze the clinical and biological characteristics, and the cardiovascular risk markers, in men and women with the metabolic syndrome compared to control subjects. The study population included 101,697 men and women, 18 to 80 years of age, who had a health checkup at the Centre d'Investigations Preventives et Cliniques (Paris, France) between 1997 to 2002. The metabolic syndrome was defined according to the ATPIII-NCEP 2001 criteria. Out of the 66,202 men (47.4+-11.8 years) and 35,495 women (48.5+-13.6 years) included in this population, 6761 men (10.2%)
and 2155 women (6.1%) presented the metabolic syndrome. Among subjects less and equal to 40 years of age, the prevalence of the metabolic syndrome was 5.0% in men and 2.2% in women, and rose to 14.1% and 12.0%, respectively, among men and women more than 70 years of age. It was concluded that in this large French population, the prevalence of the metabolic syndrome is lower than in North American and northern European populations. Patients with the metabolic syndrome present several additional hemodynamic, inflammatory and psychological risk markers which could contribute to the poor cardiovascular prognosis of these subjects.

Church et al (2009) examined cardiovascular disease (CVD) mortality risk in men with diabetes only, metabolic syndrome only and concurrent metabolic syndrome and diabetes. They examined CVD mortality risk by metabolic syndrome and diabetes status in men from the Aerobics Center Longitudinal Study (mean age [SD]: 45.1 [10.2] years). The mean duration of follow-up was 14.6 (7.0) years with a total of 483,079 man-years of exposure and 1,085 CVD deaths. CVD mortality was higher in men with metabolic syndrome only, diabetes only and both compared to men with neither. The presence of diabetes was associated with a 3-fold higher CVD mortality risk, and metabolic syndrome status did not modify this risk. The findings supported that physicians should be aggressive in utilizing CVD risk reducing therapies in all diabetic patients regardless of metabolic syndrome status.

Thorn et al (2009) conducted a study on metabolic syndrome as a risk factor for cardiovascular disease, mortality, and progression of diabetic nephropathy in type 1 diabetes. Patients were from the prospective Finnish Diabetic Nephropathy (FinnDiane) Study (n = 3,783): mean age 37 +/- 12 years and diabetes duration 23 +/- 12 years. Metabolic syndrome was defined according to World Health Organization (WHO), National Cholesterol Education Program
(NCEP), and International Diabetes Federation (IDF) definitions. Follow-up time was median 5.5 years (interquartile range 3.7-6.7). The WHO definition was associated with a 2.1-fold increased risk of cardiovascular events and a 2.5-fold increased risk of cardiovascular- and diabetes-related mortality, after adjustment for traditional risk factors and diabetic nephropathy. The NCEP definition did not predict outcomes when adjusted for nephropathy but markedly added to the risk associated with elevated albuminuria alone (P < 0.001). The IDF definition did not predict outcomes. It was concluded that the metabolic syndrome is a risk factor, beyond albuminuria, for cardiovascular morbidity and diabetes-related mortality in type 1 diabetes.

According to Kawada et al (2009), the Framingham Risk Score (FRS) has frequently been used in the United States to predict the 10-year risk of coronary heart disease (CHD). They conducted a cross-sectional study of 2619 Japanese male workers, ranging in age from 40 to 64 years, at a single workplace. Although the estimation by the Framingham Risk Score and metabolic syndrome involved some different factors, significant association of the risk estimated by the two methods was observed. In conclusion, the Framingham Risk Score and insulin were found to be significantly associated with the risk of likelihood of metabolic syndrome, even after controlling for weight change.

According to Davidson et al (2006), trials have revealed that cardiovascular risk is not uniform in the population, but is distributed in a "risk pyramid." Diabetic patients with prior cardiovascular disease (CVD) are at greatest risk. Non-diabetic patients with CVD, diabetic patients without CVD, and subjects with the metabolic syndrome form the next three risk categories. The presence of insulin resistance-related metabolic abnormalities is a common denominator in this risk pyramid. Statin therapy has demonstrated clinical benefits in insulin-resistant patients but residual cardiovascular risk remains elevated. Fibrates also improve the lipid profile and reduce cardiovascular risk in a variety of insulin-resistant
populations. Patients with atherogenic dyslipidemia who have developed insulin resistance, the metabolic syndrome, or type 2 diabetes should receive more intensive interventions including, where appropriate, statin-fibrate combination therapy, to comprehensively modify the lipid profile together with aggressive control of blood pressure and glucose to minimize risk in this very high-risk population.

According to Campbell et al (2006), the metabolic syndrome is a constellation of cardiovascular disease risk factors predisposing to future cardiovascular disease events as well as the development of type 2 diabetes mellitus. This syndrome is closely linked to both subclinical atherosclerosis and vascular inflammation. The extent of vascular inflammation can be estimated by a number of biomarkers, such as high-sensitivity C-reactive protein, that are associated with the presence of the metabolic syndrome. Evaluating for the presence of subclinical atherosclerosis and inflammatory biomarkers may help to risk stratify patients with the metabolic syndrome.

Larsson et al (2005) studied the three definitions of the metabolic syndrome: relations to mortality and atherosclerotic morbidity. A total of 1135 men and women, aged 37-61 years, were randomly selected from the populations of Mölndal and Orebro, Sweden. Mortality rate and incidence of cardiovascular morbidity were analyzed in subjects with and without the metabolic syndrome according to the definitions of WHO (World Health Organization), EGIR (European Group for the study of Insulin Resistance), and ATPIII (Adult Treatment Panel-III Guidelines). It was concluded that inclusion of glucose intolerance and/or insulin resistance as obligatory criteria in the definition of the metabolic syndrome seems to be important for the ability to predict all-cause mortality and incident cardiovascular morbidity.

According to Wofford et al (2006), metabolic syndrome is a cluster of risk factors associated with an increased risk for cardiovascular disease and type 2 diabetes.
Based on data from 1988 to 1994, it is estimated that 24% of adults in the United States meet the criteria for diagnosis of metabolic syndrome. The use of certain medications increases the risk for metabolic syndrome by either promoting weight gain or the development of changes in lipid or glucose metabolism. Diuretics and beta-blockers are among the agents recommended for first-line therapy for hypertension, yet these medications increase the risk of metabolic syndrome. Careful attention to drug choices should be given with patients who are overweight or have other risk factors for diabetes or cardiovascular disease.

Mishra et al (2004) ascertained presence and severity of coronary artery lesions in patients of Type 2 diabetic mellitus (DM) with coronary artery disease (CAD) by using scoring system analysis of the coronary angiography. 147 consecutive patients with Type 2 DM of chronic stable angina (CSA) were enrolled in the study with 147 age- and sex-matched patients of CSA who did not have diabetes to serve as control. All of them underwent coronary angiography and were evaluated by using four scores to quantify the coronary artery lesions. The scores analyzed were coronary score, extent score, severity score, and atherosclerosis score. Other major risk factors such as smoking and hypertension lipid profile were also evaluated. It was concluded that in the population, diabetics suffer from higher prevalence of diffuse and extensive coronary atherosclerosis. The grades of stenosis in coronary arteries are also higher in diabetic patients when compared with non-diabetics with CAD, as was the prevalence of other components of the metabolic syndrome.

According to Sparks et al (2008), excessive production of triglyceride-rich VLDL, which can result from dietary overindulgence, underlies metabolic syndrome a combination of disorders including high blood pressure, obesity, high triglyceride, and insulin resistance and places individuals at increased risk of developing cardiovascular disease and type 2 diabetes.
Holvoet et al (2008) established the relation of oxidized LDL with metabolic syndrome in the general community. The Coronary Artery Risk Development in Young Adults (CARDIA) study is a population-based, prospective, observational study. They studied 1889 participants who were between the ages of 18 and 30 years at the time of recruitment in 1985 and 1986 and living in 1 of 4 US metropolitan areas (41% African American; 56% women) and were seen both at year 15 (2000-2001, ages 33-45 years) and year 20 examinations (2005-2006). The metabolic syndrome was defined according to the Adult Treatment Panel III of the National Cholesterol Education Program. It was concluded that higher concentration of oxidized LDL was associated with increased incidence of metabolic syndrome overall, as well as its components of abdominal obesity, hyperglycemia, and hypertriglyceridemia.

Lakka et al (2002) assessed the association of the metabolic syndrome with cardiovascular and overall mortality using recently proposed definitions and factor analysis. The Kuopio Ischaemic Heart Disease Risk Factor Study was a population-based, prospective cohort study of 1209 Finnish men, aged 42 to 60 years at baseline (1984-1989) who were initially without CVD, cancer, or diabetes. Follow-up continued through December 1998. The results found that cardiovascular disease and all-cause mortality are increased in men with the metabolic syndrome, even in the absence of baseline CVD and diabetes. Early identification, treatment, and prevention of the metabolic syndrome present a major challenge for health care professionals facing an epidemic of overweight and sedentary lifestyle.

2.4 METABOLIC SYNDROME AND DIET

According to Wasir (2004), rapid pace of economic and demographic changes in India has ushered marked nutritional and lifestyle changes. The diets in the
urban and semi-urban areas contain more calories and saturated fats, and less fibre as compared to the traditional frugal diets, and have become similar to diets consumed by the people living in the developed countries. Increasing urbanization and mechanization have also resulted in increase in sedentary lifestyle. Overall, obesity and the metabolic syndrome are becoming increasingly prevalent in adults in the urban areas of India. These changes are conducive to development of early-onset type 2 diabetes mellitus and accelerated atherosclerosis.

According to Cacciapuoti (2008), several experimental studies and some clinical experience have shown that metabolic syndrome and caloric restriction exert opposite effects on thrombosis, because these two nourishing conditions are at extreme ends of the same spectrum.

Esposito et al (2007) documented those nutritional factors that may affect the prevalence of the metabolic syndrome. They state that beyond weight control and reduction of total calories, the diet should be low in saturated fats, trans fats, cholesterol, sodium, and simple sugars. In addition, there should be ample intake of fruits, vegetables, whole grains, and monounsaturated fat; fish intake should be encouraged. The high fiber content, n-3 fatty acids, and antioxidants, as well as phytochemicals from olive oil, legumes, whole grains, fruits, and vegetables, might be responsible for beneficial effect on the health of metabolic syndrome patients. This may occur through the reduction of systemic vascular inflammation and endothelium dysfunction without having a drastic effect on body weight. They concluded that the choice of healthy sources of carbohydrates, fat, and proteins, associated with regular physical activity and avoidance of smoking is critical to fighting the war against chronic disease.

Melchionda et al (2006) conducted a study on disease management of the metabolic syndrome in a community. They worked on study design and process analysis on baseline data. After initial visits by general practitioners for clinical
assessments and motivation to treatment, patients were randomly assigned to: (a) prescriptive diet, managed by general practitioners; (b) counseling (four group lessons); (c) cognitive-behavioral treatment (12 group lessons), both managed by specialist center. Data of the first 503 subjects were compared with those of 139 cases self-referring to the specialist center for the treatment of obesity. It was concluded that an integrated approach to lifestyle changes between general practitioners and a specialist center is feasible in the metabolic syndrome and may be cost-effective, considering the high burden of disease.

Vernon et al (2004) analyzed a restricted carbohydrate dietary approach compared to a standard low-fat diet plus medication plan as treatment for weight loss and the metabolic syndrome. This was a retrospective analysis of patients attending an outpatient weight and metabolism management program. Clinical data were maintained on standardized flow sheets. It was concluded that in this outpatient program, a carbohydrate-restricted diet and a low-fat/low-calorie diet + medication led to weight loss, but the carbohydrate-restricted diet had a more favorable effect on triglycerides and HDL. Because of the effects on weight, triglycerides, and HDL, a carbohydrate-restricted diet may be useful for the treatment of metabolic syndrome.

Hickey et al (2003) assessed the effect of a carbohydrate-restricted diet on the dyslipidemia of the metabolic syndrome in a clinical setting. If present, patients were counseled to begin a carbohydrate-restricted diet (< 20 g/day). Patients already on statin therapy were included only if the medication dose was not changed. The outcomes were changes in body weight, fasting serum lipid profiles and serum lipoprotein subclasses. It was concluded that a carbohydrate-restricted diet recommendation led to improvements in lipid profiles and lipoprotein subclass traits of the metabolic syndrome in a clinical outpatient setting, and should be considered as a treatment for the metabolic syndrome.
Brunner et al (2001) conducted a study on what is an optimal diet and relationship of macronutrient intake to obesity, glucose tolerance, lipoprotein cholesterol levels and the metabolic syndrome in a cross-sectional analysis of 4497 men and 1865 women aged 39-62 years in the Whitehall II study. In men, higher intakes of both polyunsaturated fats and carbohydrates were linked to lower waist-hip ratio, triglycerides and LDL-cholesterol. Higher carbohydrate intake alone was linked to decreased body mass index and lower HDL-cholesterol. In normoglycaemic men, higher carbohydrate intakes were associated with higher 2 h insulin and glucose levels. Dietary effects among women were similar. The observational data provide evidence that both polyunsaturated fatty acids and carbohydrates offer small metabolic benefits with few adverse effects compared with saturated fats.

Nettleton et al (2009) determined associations between diet soda consumption and risk of incident metabolic syndrome, its components, and type 2 diabetes in the Multi-Ethnic Study of Atherosclerosis. Diet soda consumption was assessed by food frequency questionnaire at baseline (2000-2002). Incident type 2 diabetes was identified at three follow-up examinations (2002-2003, 2004-2005, and 2005-2007) as fasting glucose >126 mg/dl, self-reported type 2 diabetes, or use of diabetes medication. Metabolic syndrome (and components) was defined by National Cholesterol Education Program Adult Treatment Panel III criteria. Daily consumption of diet soda was associated with a 36% greater relative risk of incident metabolic syndrome and a 67% greater relative risk of incident type 2 diabetes compared with non consumption. Of metabolic syndrome components, only high waist circumference and high fasting glucose were prospectively associated with diet soda consumption. It was concluded that consumption of diet soda at least daily was associated with significantly greater risks of select incident metabolic syndrome components and type 2 diabetes.
Esposito et al (2004) assessed the effect of a Mediterranean-style diet on endothelial function and vascular inflammatory markers in patients with the metabolic syndrome. Randomized, single-blind trial was conducted from June 2001 to January 2004 at a university hospital in Italy among 180 patients (99 men and 81 women) with the metabolic syndrome, as defined by the Adult Treatment Panel III. Patients in the intervention group (n = 90) were instructed to follow a Mediterranean-style diet and received detailed advice about how to increase daily consumption of whole grains, fruits, vegetables, nuts, and olive oil; patients in the control group (n = 90) followed a prudent diet (carbohydrates, 50%-60%; proteins, 15%-20%; total fat, <30%). It was concluded that mediterranean-style diet might be effective in reducing the prevalence of the metabolic syndrome and its associated cardiovascular risk factors.

2.5 METABOLIC SYNDROME AND PHYSICAL ACTIVITY

Physical inactivity is an independent risk factor for chronic diseases and overall is estimated to cause 1.9 million deaths globally (WHO, 2008). Physical inactivity has been identified as the fourth leading risk factor for global mortality (6% of deaths globally). This follows high blood pressure (13%), tobacco use (9%) and high blood glucose (6%). Levels of physical inactivity are rising in many countries with major implications for the general health of people worldwide and for the prevalence of NCDs such as cardiovascular disease, diabetes and cancer and their risk factors such as raised blood pressure, raised blood sugar and overweight. Physical inactivity is estimated as being the principal cause for approximately 21–25% of breast and colon cancer burden, 27% of diabetes and approximately 30% of ischaemic heart disease burden (WHO, 2009).

Regular physical activity reduces the risk of obesity, blood lipid abnormalities, hypertension and non insulin dependent diabetes mellitus and has been shown to reduce substantially the risk of coronary heart disease. Conversely, a measure
of sedentary lifestyle or physical inactivity has been associated with a 1.5 – 2.5 fold elevation in cardiovascular disease risk. It is estimated that 2.4% of the US Health Care expenditure is directly related to a lack of physical activity. As a result of economic changes and increased mechanization, the prevalence of physical inactivity is increasing in India, particularly in urban areas, to levels compared with west (Rastogi et al, 2004).

According to Hu et al (2006), Type 2 diabetes and metabolic syndrome are two of the fastest growing public health problems in both developed and developing countries. Cardiovascular disease is the most prevalent complication of type 2 diabetes and the metabolic syndrome. Data from prospective studies have shown that at least 30 min/day of moderate to vigorous physical activity can prevent type 2 diabetes. Results from clinical trials have indicated that lifestyle changes, including dietary modification and increase in physical activity, can prevent type 2 diabetes. Analyses from prospective studies have confirmed that healthy diets are effective and safe ways to prevent type 2 diabetes and the metabolic syndrome. He concluded that health care professionals, and the health care system should aggressively promote physical activity and responsible nutritional habits during occupation, leisure time, and daily life and prevent overweight and obesity.

Ilanne et al (2008) conducted a study on effect of lifestyle intervention on the occurrence of metabolic syndrome and its components in the Finnish Diabetes Prevention Study. A total of 522 middle-aged overweight men and women with impaired glucose tolerance were randomized into an individualized lifestyle intervention group or a standard care control group. National Cholesterol Education Program criteria were used for the definition of metabolic syndrome. At the end of the study, with a mean follow-up of 3.9 years, a significant reduction was found in the prevalence of metabolic syndrome in the intervention group compared with the control group (odds ratio [OR] 0.62 [95% CI 0.40-0.95]) and in
the prevalence of abdominal obesity (0.48 [0.28-0.81]). The results suggest that lifestyle intervention may also reduce risk of cardiovascular disease in the long run.

Kim et al (2009) assessed the exercise training-induced changes in heart rate recovery in obese men with metabolic syndrome. Middle-aged obese men (metabolic syndrome, n = 20; non-metabolic syndrome, n = 22) classified on the basis of Adult Treatment Panel III criteria were investigated in this study. Postexercise heart rate recovery (HRR) and the HRR decay constant following a symptom-limited bicycle exercise test were evaluated before and after a 12-week exercise training program (60-70% of maximal heart rate; 60 minutes per day; 3 days per week). Although the peak HR remained unchanged, HR at anaerobic threshold significantly decreased for both groups after exercise training; HR at rest was significantly decreased in the metabolic syndrome group after training. HRR significantly improved in the metabolic syndrome group with no change for the non-metabolic syndrome group (P > 0.05). This study demonstrated that moderate-intensity physical training without caloric restrictions improves HRR in obese men with metabolic syndrome, possibly due to a reduction in the resting HR. Therefore, weight loss-induced exercise training would help in improving the resting HR, and the responsiveness of the autonomic nervous system in obese men with metabolic syndrome.

Cohen et al (2008) worked on restorative yoga in adults with metabolic syndrome: a randomized, controlled pilot trial. Twenty six underactive, overweight adult men and women with metabolic syndrome were randomized to attend 15 yoga sessions of 90 minutes each over 10 weeks or to a wait-list control group. A total of 280 people were screened by phone, and 93 with high likelihood of metabolic syndrome were invited to a screening visit. Of the 68 who attended screening visits, 26 (38%) were randomized, and 24 (92%) completed the trial. Attendance at yoga classes and adherence to home practice exceeded
the goals. It was concluded that restorative yoga was a feasible and acceptable intervention in overweight adults with metabolic syndrome.

Kawada et al (2008) studied the effects of exercise on the metabolic syndrome. The study subjects were 1792 Japanese male workers, aged 21 to 60 years, who were employees of a manufacturing company of electrical products. The standard Japanese criteria for the diagnosis of MetS were used. The body mass index (BMI) was used as an obesity-related overweight index; BMI 25 kg/m(2) or more was defined as overweight. Age, smoking habit and frequency of drinking were used for the adjustment of significance. It was concluded that although subjects with no habitual exercise have risk of MetS, the situation of physical activity should precisely be evaluated.

Maxwell et al (2008) examined the effects of changes in cardiorespiratory fitness level on metabolic syndrome status. Male and female participants in a health enhancement program (n = 212) were clinically examined for changes in their metabolic syndrome status and estimated aerobic capacity over a 3-year period. Two physical examinations, each including a maximal treadmill stress test, occurred within this time frame. Participants were divided into three groups: Group 1 (n = 103) was composed of individuals who presented with MetS at exam 1 and reversed their metabolic syndrome disease status by exam 2; Group 2 (n = 75) members presented with metabolic syndrome at both exams; and Group 3 (n = 34) individuals were metabolic syndrome-free at exam 1 but acquired MetS by exam 2. The relationships between MetS clinical characteristics at exam 1 and exam 2 and changes in graded exercise test (GXT) duration were contrasted for the three groups. This study demonstrated that increases in GXT duration accompanied MetS reversal while declines in GXT duration occurred with MetS acquisition. On an individual basis, these changes in GXT duration may be an indicator of disease status.
Thompson et al (2007) investigated the baseline associations between body composition, cardiorespiratory fitness, physical activity, family history of type 2 diabetes, metabolic syndrome and impaired fasting glucose (IFG) among 200 asymptomatic urban Native American women, aged 18-40 years, participating in a diabetes prevention intervention. Participants without diabetes who self-identified as Native American were recruited from the general urban community into a randomized controlled trial. It was concluded that BMI, cardiorespiratory fitness, and physical activity levels are important variables to modify when attempting to reduce the prevalence of metabolic syndrome and IFG among young, asymptomatic Native American women. This information can be used to design effective diabetes prevention interventions.

Kawada et al (2008) examined the relation of lifestyles to components of the metabolic syndrome in Japanese male workers. The associations of six lifestyle factors with each of the components of the metabolic syndrome, as defined by the modified International Diabetes Federation (IDF) criteria for Japanese people, were evaluated in 4941 men at a workplace participating in the annual health examination; the subjects ranged in age from 36 to 60 years. The overall prevalence of the metabolic syndrome in the male workers was 9.1%. The odds ratios (ORs; 95% confidence interval) of three components of the metabolic syndrome such as high blood pressure, dyslipidemia, and glucose intolerance in body mass index (BMI) less than 25 were 0.51 (0.44, 0.59), 0.40 (0.35, 0.46), and 0.55 (0.45, 0.66), respectively. In contrast, eating breakfast everyday, not snacking frequently, and sleeping 6 hours or more did not relate to the occurrence of any components of the metabolic syndrome.
2.6 METABOLIC SYNDROME AND FAMILY HISTORY

Nelson et al (2007) examined effect modifiers of the relationship between family history of diabetes, a proxy for genetic predisposition, and the metabolic syndrome. A cross-sectional sample of 205 Mexican-Americans patients of the San Ysidro Health Center in San Diego County were taken. Self-reported parental history of diabetes was examined as a risk factor for individual metabolic syndrome traits and a composite phenotype, defined both by standard modified NCEP-ATPIII criteria and using principal components analysis, in age and sex-adjusted multiple logistic and linear regression models. The results of this study support a common etiology for at least some components of the metabolic syndrome, especially hyperglycemia and low HDL-cholesterol, the basis of which may be genetic. Moreover, the effect of genes on these traits may be modified by longer duration in the United States, supporting the concept of gene-environment interaction in the development of the metabolic syndrome.

Bosy et al (2007) examined the common genetic background that contributes to the clustering between the two main features (insulin resistance, central obesity) and different metabolic syndrome component traits. In all, 492 individuals from 90 families were investigated in a three-generation family path study as part of the Kiel Obesity Prevention Study. Overall heritability was estimated and common familial (genetic and environmental) influences on insulin resistance (HOMA-IR) or central obesity (elevated waist circumference, WC), respectively, and different metabolic syndrome traits were compared in a bivariate cross-trait correlation model. It was concluded that a common genetic background contributes to the clustering of different metabolic syndrome component traits and central obesity or insulin resistance. Common genetic influences favour central obesity as a major characteristic linking these traits.

Sarkar et al (2006) examined the role of environmental and genetic factors in metabolic syndrome. They conducted a study in two sub-Himalayan tribal
populations with shared ancestry (Toto and Bhutia). The Toto live exclusively in a rural area, whereas a section of the Bhutia has adopted a modern lifestyle. Fasting (12 h) blood samples of Toto (n=258); rural Bhutia (n=75) and urban Bhutia (n=230) were collected, with written informed consent. Criteria suggested by NCEP ATP III were used for assessment of metabolic syndrome. The study suggested that metabolic syndrome and its correlates could be a major health problem even in traditional societies, indicating that this syndrome was not necessarily a result of modernization. Further, the study indicated that genetic factors that adversely affect the levels of such variables have long antiquities in Indian ethnic groups.

2.7 METABOLIC SYNDROME AND STRESS

Raikkonen et al (2007) evaluated whether psychosocial factors that are related to cardiovascular disease and type 2 diabetes predict prospectively the risk for the metabolic syndrome using the different clinical criteria available for defining the syndrome. Women were enrolled in a population-based prospective cohort study called the Healthy Women Study and were followed for an average of 15 years after baseline. Metabolic syndrome was defined via the World Health Organization, the National Cholesterol Education Program Adult Treatment Panel III, and the International Diabetes Foundation clinical criteria. Among women who did not have the metabolic syndrome at the baseline, the risk for the metabolic syndrome defined in multiple ways varied from 1.21- to 2.12-fold for more severe depressive symptoms or very stressful life event. These associations were largely the same, regardless of the clinical criteria used to define the metabolic syndrome. Those who at the baseline reported feeling frequently and intensely angry, tense, or stressed also had an increased risk for developing the metabolic syndrome at least by one definition. These are the first data to demonstrate that psychosocial factors predict the risk for developing the metabolic syndrome by
multiple definitions. Psychosocial factors may play a causal role in the chain of events leading to the metabolic syndrome.

Calugi et al (2009) investigated the relationship of metabolic disorders and psychological features with the night eating syndrome (NES) in individuals with moderate-to-severe obesity. It was a design cross-sectional observation on a total of 266 consecutive participants with class II-III obesity, entering an inpatient weight loss program. Participants who reported consuming either a large amount of their caloric intake after the evening meal (roughly self-assessed as 25% and more of daily calories) or the presence of nocturnal feeding at the Night Eating Questionnaire (NEQ) (N=49) were interviewed by the Night Eating Syndrome History and Inventory (NESHI). Night eating syndrome was diagnosed by Night Eating Syndrome History and Inventory criteria (evening hyperphagia (25% and more of daily food intake after the evening meal) and/or waking at night to eat at least three times a week) in the last 3 months. The study found that diagnosing night eating syndrome does not help identify obese individuals with specific medical complications, but indicates more severe psychological distress and depression.

Corica et al (2008) investigated the association of the clinical variables of the metabolic syndrome (MS) and psychological parameters on health-related quality of life (HRQL) in obesity. In particular, the aim was to investigate the relative impact of physical symptoms, somatic diseases and psychological distress on both the physical and the mental domains of HRQL. It was a cross-sectional study of a cohort of 1822 obese outpatients seeking treatment in medical centers. It was concluded that psychological well-being is the most important correlate of HRQL in obesity, both in the physical and in the mental domains, whereas the features of metabolic syndrome correlate only to some extent with the physical domain of HRQL.
According to Mishra et al (2006), the metabolic syndrome is a crucial factor in causation of type 2 diabetes mellitus (T2DM) and coronary heart disease (CHD) in South Asians. Approximately 20-25 per cent of urban South Asians have evidence of the metabolic syndrome. Furthermore, insulin resistance was reported to be present in nearly 30 per cent of children and adolescents in India, more so in girls. Rapid nutritional and lifestyle transition in urbanized areas in various countries in South Asia are prime reasons for increasing prevalence of obesity and the metabolic syndrome. The lifestyle factor modification to prevent the metabolic syndrome and T2DM in South Asians should start in early childhood. Finally, there is an urgent need to conduct research studies regarding the correct definitions of the metabolic syndrome and genetic and perinatal factors related to insulin resistance in South Asians.