ejpmr, 2016,3(12), 422-453

SJIF Impact Factor 3.628

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

A STUDY OF GAMMA GLUTAMYL TRANSFERASE AS A DIAGNOSTIC MARKER IN METABOLIC SYNDROME.

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Article Received on 14/10/2016 **Article Revised on 04/11/2016** **Article Accepted on 24/11/2016**

ABSTRACT

Introduction: Metabolic syndrome or syndrome X is a cluster of risk factors (diabetes, prediabetes, abdominal obesity, hypertension and dyslipidemias) for the development of cardiovascular disease. The prevalence of Metabolic Syndrome worldwide is 20-25%. Although GGT is a less specific marker of liver function, higher GGT levels have also been linked with obesity, physical inactivity, hypertension, dyslipidemias, and hyperinsulinemia, implying that elevated GGT belongs in the cluster of the metabolic syndrome. And it has been shown that risk for the individual metabolic syndrome components increased as the baseline GGT levels increased. It has been clearly demonstrated that serum GGT levels elevated even within normal range are associated with some atherosclerotic risk factors. Although the exact mechanism responsible for this association is unknown, several possible mechanisms have been proposed for the role of serum GGT in increasing cardiovascular risk. The most widely accepted mechanism is oxidative stress, followed by hepatic insulin resistance and subclinical inflammation.Raised liver enzymes, as relatively sensitive and easily obtained markers of non alcoholic fatty liver disease, reflect chronic ectopic fat deposition in the liver that may be useful in diagnosis of metabolic syndrome. High liver function tests, especially GGT levels, are associated with prevalent metabolic syndrome and in this aspect they may have a predictive value in diagnosis of metabolic syndrome. **Objectives**

1. To study the association of gamma glutamyl Transferase with metabolic syndrome.
2. To assess the sensitivity and specificity of GGT in the diagnosis of metabolic syndrome.

Methods: In a cross sectional study of 100 subjects, 50 were taken as cases and 50 as controls, after fulfilling necessary inclusion and exclusion criteria and relevant investigations were done including estimation of gamma glutamyl transferase in all.Results A total of 100 subjects were chosen in the study with 50 as study population and the other 50 as controls, investigations were done as mentioned and their gamma glutamyl transferase levels were assessed.The estimated GGT values were high in 35(70%) of cases showing moderate elevation and7(14%) cases showing severe elevation. The mean GGT among the cases is 48.18±14.68 and that among controls is 30.96±10.06 with a very significant p value of <0.001.The sensitivity and specificity of gamma glutamyl transferase in diagnosis of metabolic syndrome was found to be 92% and 88% respectively. **Conclusion:** Elevated levels of GGT were found to be associated with metabolic syndrome. GGT was found to be more specific than the other liver enzymes which are also raised in metabolic syndrome. Sensitivity of 92% and specificity of 88% makes gamma glutamyl transferase a good marker for diagnosis of metabolic syndrome.

KEYWORDS: metabolic syndrome, gamma glutamyl transferase.

INTRODUCTION

The metabolic syndrome (syndrome X, insulin resistance syndrome) is a syndrome consisting of a constellation of metabolic abnormalities that confer increased risk of cardiovascular disease (CVD) and cerebrovascular disease.[1] The criteria for the metabolic syndrome have evolved since the original definition by the World Health Organization in 1998, reflecting growing clinical evidence and analysis by a variety of consensus conferences and professional organizations. The major features of the metabolic syndrome include central obesity, hypertriglyceridemia, low high-density lipoprotein (HDL) cholesterol, hyperglycemia, and hypertension.[1] The rise in the prevalence of obesity in India is threatening to increase the burden of atherosclerotic cardiovascular (ASCVD). The prevalence of metabolic syndrome worldwide is 20-25% (IDF).[2,3] Among the complications, cardiovascular events produce the greatest morbidity and mortality. A significant portion

of the latter occurs in persons in whom obesity precedes type II diabetes. But diabetes is only one of several conditions that associate strongly with obesity. Others include dyslipidemia, hypertension, systemic inflammation, and thrombotic tendency.

Recently there has been a trend in the cardiovascular field to group all of these factors together under the heading of metabolic syndrome.[1] In this sense, metabolic syndrome can be taken to represent a multiplex cardiovascular risk factor. This syndrome does not include, but is strongly associated with, other complications of obesity, for example, fatty liver, cholesterol gallstones, obstructive sleep apnea, and polycystic ovarian syndrome.[4] The current definition generally regards hyperglycemia in the range of type II diabetes to be one of the components of metabolic syndrome. The clustering of CVD risk factors that typifies metabolic syndrome is considered to be the driving force behind a CVD epidemic.

There has been a consistent effort to evaluate biochemical markers to predict an early onset of metabolic syndrome and subsequently intervene appropriately by means of lifestyle changes and drug therapy and thereby reduce cardiovascular morbidity and mortality.Studies are lacking in the adult Indian population.Markers like adiponectin have been studied as a measure of increased adipose tissue but have not proven to be cost effective and easily available. Clearly a prompt, cost effective and easily available biochemical marker is required to predict an early onset of this syndrome. Gamma Glutamyl Transferase (GGT) is one such marker which is cost effective, easily available and performed as part of liver function tests.[4] High levels of GGT have been associated in populations with increased risk of atherosclerotic cardiovascular disease (ASCVD).[2,6] Several prospective studies reported that baseline serum GGT concentration was an independent risk factor for the development of coronary artery disease (CAD), diabetes mellitus, stroke and hypertension.[7] The purpose of this study is to evaluate the utility of GGT as an early diagnostic marker of metabolic syndrome.

AIMS AND OBJECTIVES:

1. To study the association of gamma glutamyl Transferase with metabolic syndrome.
2. To assess the sensitivity and specificity of GGT in the diagnosis of metabolic syndrome.

REVIEW OF LITERATURE: HISTORICAL ASPECT

The term metabolic syndrome dates back to at least the late 1950s, but came into common usage in the late 1970s to describe various associations of risk factors with diabetes that had been noted as early as the 1920s[8,9] The Marseilles physician Dr. Jean Vague, in 1947, observed that upper body obesity appeared to predispose to diabetes, atherosclerosis, gout and calculi.[10] Avogaro, Crepaldi and co-workers described six moderately obese patients with diabetes, hypercholesterolemia, and marked hypertriglyceridemia all of which improved when the patients were put on a hypocaloric, low-carbohydrate diet.[11] In 1977, Haller used the term "metabolic syndrome" for associations of obesity, diabetes, hyperlipoproteinemia, hyperuricemia, and Hepatic steatosis when describing the additive effects of risk factors on atherosclerosis.[12] The same year, Singer used the term for associations of obesity, gout, diabetes mellitus, and hypertension with hyperlipoprotenemia.[13] In 1977 and 1978, Gerald B. Phillips developed the concept that risk factors for myocardial infarction concur to form a "constellation of abnormalities" (i.e., glucose intolerance, hyperinsulinemia, hyperlipidemia and hypertriglyceridemia, and hypertension) that is associated not only with heart disease but also with aging, obesity and other clinical states.[14,15]

He suggested there must be an underlying linking factor, the identification of which could lead to the prevention of cardiovascular disease, he hypothesized that this factor was sex hormones.[16] In 1988, in his Banting lecture, Gerald M. Reaven proposed insulin resistance as the underlying factor and named the constellation of abnormalities Syndrome X. Reaven did not include abdominal obesity, which has also been hypothesized as the underlying factor, as part of the condition.

METABOLIC SYNDROME DEFINITION

Various groups have laid out criteria based on certain clinical, anthropometric and biochemical parameters to define the metabolic syndrome. The two generally accepted definitions are the ones defined by the international diabetes federation (IDF).[17] and national cholesterol education programme; adult treatment panel III (NCEP: ATPIII).[18] In this study definition as per IDF has been considered.

IDF CRITERIA.[17]

The essential presence of **central adiposity** defined as waist circumference of >/=90cm in males and >/=80 in females in the Indian population.

Along with central adiposity two of the following four factors should be present to define metabolic syndrome:

1. Fasting triglycerides >150 mg/dl or specific medication
2. HDL cholesterol <40 mg/dl and <50 mg/dl for men and women, respectively, or specific medication
3. Blood pressure >130 mm systolic or >85 mm diastolic or previous diagnosis or specific medication
4. Fasting plasma glucose 100 mg/dl or previously diagnosed Type 2 diabetes

NCEP: ATP III CRITERIA[18]

Three or more of the following criteria:

1. Central obesity: Waist circumference >102 cm (M), >88 cm (F)
2. Hypertriglyceridemia: Triglycerides 150 mg/dl or specific medication
3. Low HDL cholesterol: <40 mg/dl and <50 mg/dl, respectively, or specific medication
4. Hypertension: Blood pressure 130 mm systolic or 85 mm diastolic or specific medication
5. Fasting plasma glucose 100 mg/dl or specific medication or previously diagnosed Type 2 diabetes

The difference between the two criteria is that the IDF takes central adiposity as an essential factor for defining metabolic syndrome.

EPIDEMIOLOGY

The prevalence of metabolic syndrome varies around the world, in part reflecting the age and ethnicity of the populations studied and the diagnostic criteria applied. In general, the prevalence of metabolic syndrome increases with age.

The highest recorded prevalence worldwide is in Native Americans, with nearly 60% of women ages 45–49 and 45% of men ages 45–49 meeting National Cholesterol Education Program and Adult Treatment Panel III (NCEP:ATPIII) criteria[19] In the United States, metabolic syndrome is less common in African-American men and more common in Mexican-American women. Based on data from the National Health and Nutrition Examination Survey (NHANES) 1999–2000, the age-adjusted prevalence of the metabolic syndrome in United States adults who did not have diabetes is 28% for men and 30% for women. In France, a cohort 30 to 60 years old has shown a <10% prevalence for each sex, although 17.5% are affected in the age range 60–64.[19] Greater industrialization worldwide is associated with rising rates of obesity, which is anticipated to increase prevalence of the metabolic syndrome dramatically, especially as the population ages. Moreover, the rising prevalence and severity of obesity in children is initiating features of the metabolic syndrome in a younger population.[20]

In the Indian setting the prevalence of metabolic syndrome has been on the rise; with a prevalence of 45% in females and 22% in males and increases with increasing age and in the population belonging to the upper socio-economic strata. This has been the reason for the increased cardiovascular morbidity and mortality in the country.[21]

ETIOLOGY

OBESITY

The high prevalence of metabolic syndrome worldwide is secondary to a rising prevalence of obesity.[22,26] Metabolic Syndrome prevalence rises in parallel with increasing obesity.[27] Physical inactivity also is associated with a higher prevalence of metabolic syndrome.[28] Part of this association can be related to the greater obesity accompanying a sedentary lifestyle; nevertheless it is likely that physical activity provides a protective role against metabolic syndrome independently of the obesity.[29-35] Further, high-carbohydrate diets, particularly those rich in simple carbohydrates or high-glycemic index foods, have been claimed to worsen metabolic syndrome. The literature nonetheless is mixed on the ideal diet composition for prevention and treatment of the syndrome.[36-39]

The mechanisms whereby obesity results in metabolic syndrome are being increasingly Understood.[1] Adipose tissue releases several products that appear to worsen metabolic syndrome.[40] The most important is a key fuel source, nonesterified fatty acids (NEFA). During the fasting state, adipose tissue triglyceride undergoes lipolysis and releases NEFA.The major enzyme involved in lipolysis is hormone sensitive lipase (HSL); the activity of this enzyme is enhanced by catecholamines and suppressed by insulin. When insulin levels are low during fasting, lipolysis is high as is NEFA release. NEFA is the major energy source during fasting. But if NEFA supply exceeds needs for energy utilization, they accumulate in muscle and liver. This accumulation is called ectopic fat. When fat accumulates in muscle and the liver, insulin resistance is increased. This change plus other metabolic alterations predisposes to the metabolic syndrome.[40] Beyond excess fatty acids, other products of adipose tissue are released in abnormal

Amounts from adipose tissue. One category of products includes the inflammatory cytokines, for example, tumor necrosis factor alpha- TNF and IL-6.[41] This excess release of cytokines appears to be secondary to infiltration of adipose tissue with activated macrophages, which can produce these cytokines.[42] The result is a high level of circulating cytokines. These can have several systemic effects: enhancement of insulin resistance in muscle, production of acute phase reactants C-reactive protein (CRP) and fibrinogen by the liver, and exacerbation of inflammation in arteriosclerotic lesions. Both of the latter can predispose to major cardiovascular events. These cytokines play a key role in the causation of the pro-inflammatory state of metabolic syndrome.

The adipose tissue likewise can predispose to a pro-thrombotic state by release of excess amounts of PAI-1, which is released from adipose tissue in response to obesity[44]Adipose tissue further secretes leptin, an appetite suppressant. Leptin levels are high in obesity and seemingly do not suppress the appetite of obese individuals, a condition called leptin resistance. Leptin can have systemic actions as well as actions in the hypothalamus. One such systemic action is to enhance fatty-acid oxidation by the liver, preventing steatosis.[44]

Several other bioactive adipokines have been reported to be produced by adipose tissue: resistin, angiotensinogen, tissue factor, transforming growth factor- beta, nitric oxide synthase, acylation stimulating protein, adipophilin, adipoQ, adipsin, monobutyrin, and agouti protein. Their role in the causation of metabolic syndrome remains to be fully elucidated.

In adipose tissue, 11 β-hydroxysteroid dehydrogenase type 1 (11 β-HSD1) converts inactive cortisone to active cortisol. Over expression of 11 β-HSD1 induced in mice produces central obesity and insulin resistance.[45] It also has been reported that obesity in humans is accompanied by over expression of 11β-HSD1[46] Finally, the release of another substance, adiponectin, actually reduced with obesity.[47-50]

Adiponectin can protect against insulin resistance, metabolic risk factors and atherogenesis. The mechanism whereby adiponectin exerts this protective effect is a topic of intense research at present.

Only a portion of patients with obesity develop metabolic syndrome. It appears that an individual must be metabolically susceptible to developing the syndrome, and when obesity is acquired, the syndrome becomes manifest. Several factors seemingly contribute to endogenous susceptibility. Among these are dysfunctional adipose tissue, genetic forms of insulin resistance, various endocrine disorders, and other genetic factors. Of particular importance appears to be a dysfunction of adipose tissue.

There are at least four potential disorders that can contribute to dysfunctional adipose tissue, which in turn will accentuate metabolic syndrome. These include a deficiency of subcutaneous adipose tissue, genetic forms of insulin resistance, dysfunctional adipocytes, and inflammation of adipose tissue (Fig 1).

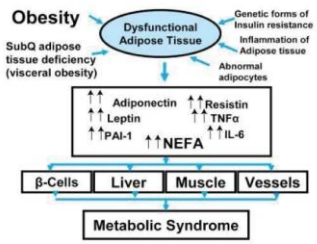


Figure 1: METABOLIC SYNDROME: DYSFUNCTIONAL ADIPOSE TISSUE

One of the most important of these is a deficiency of subcutaneous adipose tissue. This abnormality is seen in an extreme form in a condition called lipodystrophy. Several metabolic defects can cause lipodystrophy; a severe deficiency of adipose tissue[51] n patients with lipodystrophy, who have little adipose tissue for storage of extra energy, fat becomes deposited ectopically in the liver and muscle; the result is the development of severe metabolic syndrome. Less severe forms of adipose-tissue deficiency are manifest by an abnormal body fat distribution. Differences in body fat distribution can typically be seen between obese women and men.[52] Women normally have considerable quantities of subcutaneous adipose tissue in the lower body. Only when they are more severely obese does fat begin to accumulate in the upper body. It first enters upper body subcutaneous adipose tissue and only later does it accumulate in visceral adipose tissue beds. As a result, substantial ectopic fat accumulation is relatively rare. In contrast, men typically have a paucity of lower body subcutaneous adipose tissue; as a result, they tend to develop upper-body obesity including considerable amounts of visceral fat as well as ectopic fat.

This pattern of fat distribution is called abdominal obesity; it is complicated by larger amounts of ectopic fat, which predisposes to metabolic syndrome.[53] There is considerable variation in these trends in both men and women, and some individuals are particularly prone to development of ectopic fat and metabolic syndrome when they become obese.[52] The causes of a relative deficiency of subcutaneous adipose tissue are not known, although because of male/female differences, endocrine factors can contribute. The net result of adipose tissue deficiency is a shift of fat away from adipose tissue and into ectopic stores, which will worsen metabolic syndrome. In addition, the normal release of other adipokines appears to be impaired.[54]Dysfunctional forms of adipose tissue further can result from genetic forms of insulin resistance. Insulin is a major regulator of adipose tissue metabolism. When genetic defects occur in insulin-signaling in adipocytes, suppression of lipolysis and other products is impaired.[55] In addition, adiponectin release is reduced.[55] All of these will accentuate ectopic fat distribution and metabolic syndrome. Moreover, defective insulin signaling in other tissues such as muscle and liver most likely will accentuate metabolic syndrome.[56-57] A good example of a genetic form of insulin resistance is found in many persons of South Asian origin Insulin-resistant South Asians have multiple signs of dysfunctional adipose tissue; elevated NEFA levels, high CRP and leptin levels, and low adiponectin concentrations; even when they are not obese.[55] These persons are prone to metabolic syndrome and to premature type II diabetes and CVD.

It is likely dysfunction within adipocytes contributes to failure to store fat, to suppress lipolysis, or to suppress release of other adipokines. Defects in adipocyte function might occur at several levels including conversion of mesenchymal stem cells into preadipocyte,further conversion into various adipocyte populations, and to adipocyte cell death.[58] A variety of key pathways have been described in adipocytes in which defects potentially could lead to abnormalities in

product release.[59-64]

Finally, in obese persons, the adipose tissue is invaded with macrophages.[65-68] The possibility has been raised that activation of these macrophages will result in the production of cytokines that will derange the function of adipocytes. In particular, these cytokines can cause insulin resistance and the same defects are noted in persons with genetic forms of insulin resistance. Thus, inflammation of adipose tissue can be yet another factor contributing to dysfunctional adipose tissue and metabolic syndrome.

INSULIN RESISTANCE

The most accepted and unifying hypothesis to describe the pathophysiology of the metabolic syndrome is insulin resistance, which is caused by an incompletely understood defect in insulin action.[69] The onset of insulin resistance is heralded by postprandial hyperinsulinemia, followed by fasting hyperinsulinemia and, ultimately, hyperglycemia.[70]

An early major contributor to the development of insulin resistance is an overabundance of circulating fatty acids. Plasma albumin-bound free fatty acids (FFAs) are derived predominantly from adipose tissue triglyceride stores released by lipolytic enzymes lipase. Fatty acids are also derived from the lipolysis of triglyceride-rich lipoproteins in tissues by lipoprotein lipase (LPL). Insulin mediates both antilipolysis and the stimulation of LPL in adipose tissue. Of note, the inhibition of lipolysis in adipose tissue is the most sensitive pathway of insulin action. Thus, when insulin resistance develops, increased lipolysis produces more fatty acids, which further decrease the antilipolytic effect of insulin.

Excessive fatty acids enhance substrate availability and create insulin resistance by modifying downstream signaling. Fatty acids impair insulin-mediated glucose uptake and accumulate as triglycerides in both skeletal and cardiac muscle, whereas increased glucose production and triglyceride accumulation are seen in liver.

The oxidative stress hypothesis provides a unifying theory for aging and the predisposition to the metabolic syndrome. In studies carried out in insulin-resistant subjects with obesity or Type 2 diabetes, the offspring of patients with Type 2 diabetes, and the elderly, a defect has been identified in mitochondrial oxidative phosphorylation, leading to the accumulation of triglycerides and related lipid molecules in muscle. The accumulation of lipids in muscle is associated with insulin resistance. In the preceding discussion the effects of genetic forms of insulin resistance on adipose tissue were reviewed. One hypothesis holds that genetic forms of insulin resistance are the major cause of metabolic syndrome.[69-70] According to this hypothesis, resistance to the action of insulin is widespread and causes a gross metabolic disturbance in many tissues. This disturbance can account for the multiple metabolic risk factors characteristic of the syndrome. This hypothesis is provocative and has provided a basis for many studies the causation of metabolic syndrome.

The effects of insulin resistance in adipose tissue provides the most direct evidence for the mechanism linking resistance to insulin to metabolic syndrome. Nevertheless, it is certainly possible that widespread metabolic disturbance contributes beyond adipose tissue abnormalities.[69] Just how much of metabolic syndrome can be attributed to genetic forms of insulin resistance is uncertain. However, the close association between obesity and dysfunctional adipose tissue and the syndrome suggests that in the overall picture, genetic forms of insulin resistance are not dominant. Nonetheless, insulin resistance can be a particularly important contributor to the syndrome if it is present in conjunction with obesity.[70]

INCREASED WAIST CIRCUMFERENCE

Waist circumference is an important component of the most recent and frequently applied diagnostic criteria for the metabolic syndrome.[71] However, measuring waist circumference does not reliably distinguish increases in subcutaneous adipose tissue vs. visceral fat; this distinction requires CT or MRI. With increases in visceral adipose tissue, adipose tissue-derived FFAs are directed to the liver. In contrast, increases in abdominal subcutaneous fat release lipolysis products into the systemic circulation and avoid more direct effects on hepatic metabolism. Relative increases in visceral versus subcutaneous adipose tissue with increasing waist circumference in Asians and Asian Indians may explain the greater prevalence of the syndrome in those populations compared with African-American men in whom subcutaneous fat predominates. It is also possible that visceral fat is a marker for, but not the source of, excess postprandial FFAs in obesity.

DYSLIPIDEMIA

In general, FFA flux to the liver is associated with increased production of apoB-containing, triglyceride-rich very low density lipoproteins (VLDLs). The effect of insulin on this process is complex, but hypertriglyceridemia is an excellent marker of the insulin-resistant condition.[19] The other major lipoprotein disturbance in the metabolic syndrome is a reduction in HDL cholesterol. This reduction is a consequence of changes in HDL composition and metabolism. In the presence of hypertriglyceridemia, a decrease in the cholesterol content of HDL is a consequence of reduced cholesteryl ester content of the lipoprotein core in combination with cholesteryl ester transfer protein–mediated alterations in triglyceride, making the particle small and dense. This change in lipoprotein composition also results in

increased clearance of HDL from the circulation. The relationships of these changes in HDL to insulin resistance are probably indirect, occurring in concert with the changes in triglyceride-rich lipoprotein metabolism.

In addition to HDL, low-density lipoproteins (LDLs) are modified in composition. With fasting serum triglycerides >180 mg/dL, there is almost always a predominance of small dense LDLs[19] Small dense LDLs are thought to be more atherogenic. They may be toxic to the endothelium, and they are able to transit through the endothelial basement membrane and adhere to glycosaminoglycans. They also have increased susceptibility to oxidation and are selectively bound to scavenger receptors on monocyte-derived macrophages. Subjects with increased small dense LDL particles and hypertriglyceridemia also have increased cholesterol content of both VLDL1 and VLDL2 sub fractions. This relatively cholesterol- rich VLDL particle may contribute to the atherogenic risk in patients with metabolic syndrome.[75]

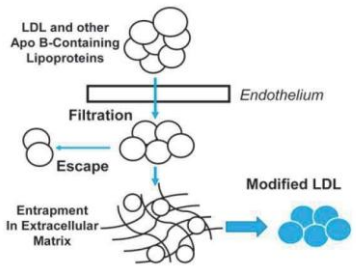


Figure 2: ARTERIAL INJURY PRODUCED BY LOW DENSITY LIPOPROTEIN (LDL)

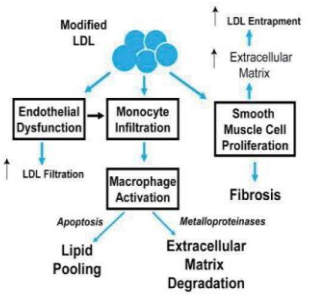


Figure 3: INFLAMMATORY PROCESS EVOKED BY MODIFIED LDL

The development of atherosclerosis can be considered to occur in two stages: injury and response to injury. The primary injurious agents include LDL and other apolipoprotein B (apo B)-containing lipoproteins. The response to injury makes up a process called inflammation. Metabolic syndrome exacerbates atherogenesis by enhancing the inflammatory response to LDL injury. The first step in the pathogenesis of atherosclerosis is the infiltration of plasma LDL into the arterial intima (Fig2). The rate of infiltration of LDL depends on two factors: (1) the concentration of LDL in the circulation and (2) the permeability of the arterial wall.[72]

Several mechanisms have been proposed for transport into the sub endothelium: vesicular ferrying through endothelial cells, passive sieving through endothelial-cell pores, and passage between cells. Not all that enters the arterial wall stays there. Some escapes by a reversal of the same process. However, a portion of the LDL becomes entrapped into the extracellular matrix.[73] When this occurs, LDL is ripe for modification. Several types of modification have been proposed: aggregation, fusion of lipoproteins, proteolysis, lipolytic degradation such as hydrolysis of cholesterol esters, phospholipids, and triglyceride, oxidation and glycation.[74] When LDL is modified in various ways, it acquires inflammatory potential. The consequences of LDL modification include the activation of various types of cells; endothelial cells, monocyte/macrophages, and smooth muscle cells.[73,75]

All of these changes come under the category of inflammation (Fig2). Key changes are endothelial dysfunction, which allows for a more rapid infiltration of LDL into the arterial wall and adherence to circulating monocytes, movement of monocytes into the arterial wall and their activation, proliferation of smooth muscle cells, and enhanced fibrosis. Macrophages are a key player in atherogenesis.[75] They first accumulate lipid and then undergo apoptosis; releasing their excess lipid into lipid pools. Macrophages further produce enzymes, such as metalloproteinases, that degrade the extracellular matrix. These latter twochanges seemingly create unstable plaques that are prone to rupture and to causation of acute ASCVD events.

GLUCOSE INTOLERANCE

The defects in insulin action lead to impaired suppression of glucose production by the liver and kidney and reduced glucose uptake and metabolism in insulin-sensitive tissues, i.e., muscle and adipose tissue.[19] The relationship between impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) and insulin resistance is well supported by human, nonhuman primate, and rodent studies. To compensate for defects in insulin action, insulin secretion and/or clearance must be modified to sustain euglycemia. Ultimately, this compensatory mechanism fails, usually because of defects in insulin secretion, resulting in progress from IFG and/or IGT to DM.

HYPERTENSION

The relationship between insulin resistance and hypertension is well established.[76] Paradoxically, under normal physiologic conditions, insulin is a vasodilator with secondary effects on sodium reabsorption in the kidney. However, in the setting of insulin resistance, the vasodilatory effect of insulin is lost but the renal effect on sodium reabsorption is preserved. Sodium reabsorption is increased in whites

with the metabolic syndrome but not in Africans or Asians.

Insulin also increases the activity of the sympathetic nervous system, an effect that also may be preserved in the setting of the insulin resistance. Finally, insulin resistance is characterized by pathway-specific impairment in phosphatidylinositol-3-kinase signaling. In the endothelium, this may cause an imbalance between the production of nitric oxide and the secretion of endothelin 1, leading to decreased blood flow. Although these mechanisms are provocative, when insulin action is assessed by levels of fasting insulin or by the Homeostasis Model Assessment (HOMA), insulin resistance contributes only modestly to the increased prevalence of hypertension in the metabolic syndrome.

AGING

The metabolic syndrome affects 44% of the population older than age 50. A greater percentage of women over age 50 have the syndrome than men. The age dependency of the syndrome's prevalence is seen in most populations around the world.[19]

SEDENTARY LIFESTYLE

Physical inactivity is a predictor of CVD events and related mortality rate.[28] Many components of the metabolic syndrome are associated with a sedentary lifestyle, including increased adipose tissue (predominantly central), reduced HDL cholesterol, and a trend toward increased triglycerides, high blood pressure, and increased glucose in the genetically susceptible.[29]

Compared with individuals who watched television or videos or used the computer <1 h daily, those who carried out those behaviours for >4 h daily had a twofold increased risk of the metabolic syndrome.[30]

LIPODYSTROPHY

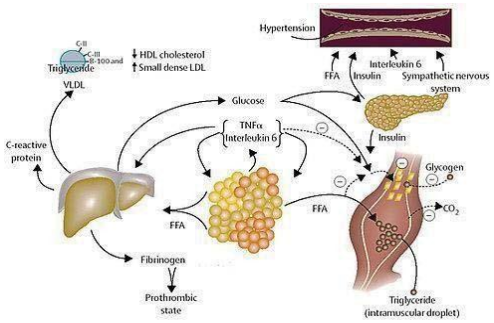
Lipodystrophic disorders in general are associated with the metabolic syndrome.[19] Both genetic.[51] (e.g., Berardinelli-Seip congenital lipodystrophy, Dunnigan familial partial lipodystrophy) and acquired (e.g., HIV-related lipodystrophy in patients treated with highly active antiretroviral therapy) forms of lipodystrophy may give rise to severe insulin resistance and many of the components of the metabolic syndrome.

PATHOPHYSIOLOGY

Free fatty acids (FFAs) are released in abundance from an expanded adipose tissue mass. In the liver, FFAs result in an increased production of glucose and triglycerides and secretion of very low density lipoproteins (VLDLs) .[19] Associated lipid/lipoprotein abnormalities include reductions in high-density lipoprotein (HDL) cholesterol and an increased density of low-density lipoproteins (LDLs). FFAs also reduce insulin sensitivity in muscle by inhibiting insulin-mediated glucose uptake. Associated defects include a reduction in glucose partitioning to glycogen and increased lipid accumulation in triglyceride (TG).

Increases in circulating glucose, and to some extent FFA, increase pancreatic insulin secretion, resulting in hyperinsulinemia. Hyperinsulinemia may result in enhanced sodium reabsorption and increased sympathetic nervous system (SNS) activity and contribute to the hypertension, as might increased levels of circulating FFAs.

The proinflammatory state is superimposed and contributory to the insulin resistance produced by excessive FFAs. The enhanced secretion of interleukin 6 (IL-6) and tumor necrosis factor (TNF-alpha) produced by adipocytes and monocyte- derived macrophages results in more insulin resistance and lipolysis of adipose tissue triglyceride stores to circulating FFAs. IL-6 and other cytokines also enhance hepatic glucose production, VLDL production by the liver, and insulin resistance in muscle. Cytokines and FFAs also increase the hepatic production of fibrinogen and adipocyte production of plasminogen activator inhibitor 1 (PAI-1), resulting in a prothrombotic state. Higher levels of circulating cytokines also stimulate the hepatic production of CRP.



PATHOGENESIS

A simple way to visualize the pathogenesis of metabolic syndrome is illustrated in Fig. This view identifies an interaction between exogenous and endogenous factors. Obesity is the major exogenous factor, but physical inactivity and excess dietary factors can play a role.[4] Endogenous factors include inherent insulin resistance, dysfunctional adipose tissue, endocrine disorders, and various genetic aberrations. The endogenous factors can be grouped together under the heading of metabolic susceptibility. To develop the syndrome, most individuals must be metabolically susceptible. But even in the presence of susceptibility, the full blown metabolic syndrome generally will not develop in the absence of obesity.

METABOLIC SYNDROME AND RISK OF CARDIOVASCULAR DISEASE

Long-Term (Lifetime) Risk

In populations at risk, metabolic syndrome is accompanied by an increase in relative risk for ASCVD.[77-79].In prospective epidemiologic studies, the relative risk for ASCVD events is essentially doubled. It is likely that the twofold increase in risk seen in short-term, prospective studies underestimates the long-term impact of the syndrome.

The reason is that metabolic risk factors tend to worsen with time. Lipid levels and blood pressure rise with advancing age, and normal glucose levels advance to prediabetes or frank diabetes. Consequently, the earlier metabolic syndrome can be detected and managed, the slower will be the progression.

Short-Term (10-Year) Risk

At present, more intense clinical intervention is driven by short-term risk for ASCVD.[80] This risk usually is identified as 10- year risk for coronary heart disease (CHD). According to ATP III guidelines, risk can be stratified into four categories.

1. High risk is a 10-year risk for CHD >20 percent and includes patients with clinically evident ASCVD, diabetes, or enough other major risk factors to raise the risk to this level.
2. Moderately high risk consists of two or more major risk factors and a 10-year risk of 10 to 20 percent.
3. Moderate risk exhibits two or more risk factors, but a 10-year risk <10 percent.
4. Lower-risk individuals have 0 to 1 risk factor and a 10-year risk <10 percent.

Most persons with metabolic syndrome can be considered to be at least a moderate risk; but many will have risk >10 percent.Framingham risk scoring should be used to estimate 10-year risk in metabolic syndrome patients without established ASCVD or type II diabetes mellitus (T2DM).[80] Because metabolic syndrome is only one part of overall risk assessment for ASCVD, it is not an adequate tool to estimate 10-year risk for CHD. These patients must be considered to be at higher lifetime risk for ASCVD, but metabolic syndrome alone is inadequate to guide clinical management for short-term risk reduction.

Although Framingham risk scoring provides a good first-step risk for estimating risk, other considerations can be brought into play both for confirmation of metabolic syndrome and for estimating 10-year risk in affected patients. Besides the simple clinical measures proposed by ATP III, other emerging risk factors are commonly present in patients with metabolic syndrome1.[80] Identification of abnormalities in these factors can help to confirm the presence of the syndrome. Although these emerging risk factors are not required for diagnosis, the presence of several of them will give strong confirmation of the presence of a systemic metabolic disorder. Therefore, their measurement is optional. In addition, confirmation of a higher risk status can be obtained by the finding of significant subclinical atherosclerosis.

ASSOCIATIONS

NON-ALCOHOLIC FATTY LIVER DISEASE

Fatty liver is relatively common. However, in NASH, both triglyceride accumulation and inflammation coexist.[81] NASH is now present in 2–3% of the population. As the prevalence of overweight/obesity and the metabolic syndrome increases, NASH may become one of the more common causes of end-stage liver disease and hepatocellular carcinoma.[82]

HYPERURICEMIA

Hyperuricemia reflects defects in insulin action on the renal tubular reabsorption of uric acid, whereas the increase in asymmetric dimethylarginine, an endogenous inhibitor of nitric oxide synthase, relates to endothelial dysfunction.[19] Microalbuminuria also may be caused by altered endothelial pathophysiology in the insulin-resistant state.

POLYCYSTIC OVARY SYNDROME

PCOS is highly associated with the metabolic syndrome, with prevalence between 40 and 50%. Women with PCOS are 2–4 times more likely to have the metabolic syndrome than are women without PCOS.[83]

OBSTRUCTIVE SLEEP APNEA

OSA is commonly associated with obesity, hypertension, increased circulating cytokines, IGT, and insulin resistance. With these associations, it is not surprising that the metabolic syndrome is frequently present.[19]. Moreover, when biomarkers of insulin resistance are compared between patients with OSA and weight-matched controls, insulin resistance is more severe in patients with OSA. Continuous positive airway pressure (CPAP) treatment in OSA patients improves insulinsensitivity.

DIAGNOSIS

The diagnosis of the metabolic syndrome relies on satisfying the criteria listed above by using tools at the bedside and in the laboratory. The medical history should include evaluation of symptoms for OSA in all patients and PCOS in premenopausal women. Family history will help determine risk for CVD and DM. Blood pressure and waist circumference measurements provide information necessary for the diagnosis.

LABORATORY EVALUATION

Fasting lipids and glucose are needed to determine if the metabolic syndrome is present. The measurement of additional biomarkers associated with insulin resistance can be individualized. Such tests might include apoB, high-sensitivity CRP, fibrinogen, uric acid, urinary microalbumin, and liver function tests. A

sleep study should be performed if symptoms of OSA are present. If PCOS is suspected on the basis of clinical features and anovulation, testosterone, luteinizing hormone, and follicle-stimulating hormone should be measured.

MANAGEMENT

LIFESTYLE MODIFICATIONS

Because obesity is the major driving force behind metabolic syndrome it is a reasonable primary target of therapy.[1,80] The initial goal for obesity management is to reduce the body weight by 10 percent per year; an ultimate goal is to achieve aBMI <25 kg/m2 over a longer period of time. Obesity guidelines.[84] recommend caloric intake and behavioural change as first-line therapies to achieve weight loss. Behavioural change should include increased physical activity as one of its components. The weight-reduction diet should not be a crash diet; they invariably fail in the long run. Extreme diets that allow for little variety in foods should be avoided. Many popular diets are of this type. Experience shows that they cannot be tolerated for a lifetime. Neither can their caloric adequacy be ensured. Instead, a heart- healthy diet of reduced caloric content can be recommended. A reduction of 500 to 1000 calories will achieve the desired 10 percent reduction in weight, depending on baseline weight.

Diet that is appropriate for long-term weight reduction should be consistent with current recommendations for a healthy diet in general. Emphasis should be given to reducing consumption of saturated and trans-fatty acids and cholesterol, reduced intake of simple sugars, and ample intakes of fruits, vegetables, and whole grains. Some investigators favour a relatively higher intake of unsaturated fatty acids at the expense of carbohydrates.[80]

Avoidance of high-carbohydrate intakes will improve atherogenic dyslipidemia and will reduce postprandial rises in glucose and insulin. As mentioned before, extremes of high-fat or low-fat intakes should be avoided. Behavioural change is the second major requirement for successful weight reduction. Without behavioural change, long-term weight loss will not be possible. It is rarely easyto reverse the lifetime of behaviour that resulted in obesity. The earlier in life that obesity (or overweight) can be identified, the more effective will be theintervention. Before a physical activity recommendation is provided to patients with the metabolic syndrome, it is important to ensure that the increased activity does not incur risk. Some high-risk patients should undergo formal cardiovascular evaluation before initiating an exercise program.[1] For an inactive participant, gradual increases in physical activity should be encouraged to enhance adherence and avoid injury. Although increases in physical activity can lead to modest weight reduction, 60–90 min of daily activity is required to achieve this goal.[1] Even if an overweight or obese adult is unable to achieve this level of activity, he or she will still derive a significant health benefit from at least 30 min of moderate-intensity dailyactivity.

DYSLIPIDEMIA

This condition is recognized clinically by an increase in serum triglyceride and a reduction in high-density lipoprotein- cholesterol (HDL-C). When triglycerides are elevated this is usually a sign of an increase in apo B-containing lipoproteins. The primary target of lipid-lowering therapy in all patients is low-density lipoprotein-cholesterol (LDL-C).[80-85] In patients with metabolic syndrome who have high triglycerides, a sizable portion of apo B can be present in very-low-density lipoprotein (VLDL). For this reason, it is useful to make VLDL a secondary target of therapy. The goals for non–HDL-C are 30 mg/dl higher than those for LDL-C. A low level of HDL-C can be considered a tertiary target.

The most effective drugs for reducing these lipoproteins are statins; most of the trials have used statins as the therapeutic intervention. Two clinical trials with statin therapy have specifically targeted type II diabetes. In the Collaborative Atorvastatin Diabetes Study(CARDS) trial.[86] statin treatment showed a 37 percent reduction in major coronary events by reduction of apo B-containing lipoproteins with a statin. In the Atorvastatin Study for Prevention of Coronary Heart Disease Endpoints in Noninsulin-Dependent Diabetes Mellitus (ASPEN) trial.[87]statin therapy showed a trend toward benefit in reduction of ASCVD events. Two other classes of drugs have been used for treatment of atherogenic dyslipidemia. These are nicotinic acid and fibrates. Their primary actions are to reduce triglyceride-rich lipoproteins and to raise HDL[80]. Both lowertriglycerides similarly, whereas nicotinic acid raises HDL more than do fibrates.

For secondary prevention, that is, in patients with established ASCVD, the first goal of therapy is to reduce LDL-C to <100 mg/dl and non–HDL-C to <130 mg/dl. These goals are strongly supported by clinical trial evidence.[80,85] For primary prevention, the therapeutic goals for lipids depend on the absolute risk of patients. Any patient who has metabolic syndrome with type II diabetes deserves to have the LDL-C reduced to <100 mg/dl (non– HDL-C <130 mg/dl).[88] It is possible to increase the intensity of statin therapy from standard doses to high doses.

The efficacy of this approach has recently been shown for the TNT trials in patients with metabolic syndrome with or without type II diabetes.[89,90]. Besides increasing statin therapy, lower LDL levels can be obtained by combining a standard dose of statins with either ezetimibe or bile acid sequestrants. Another alternative is to combine a standard dose of statin with either nicotinic acid or fibrates.[85,91]

ELEVATED BLOOD PRESSURE

The Eighth Report of the Joint National Committee (JNC 8) provides useful guidelines for management of blood pressure.[92] JNC 8 emphasized lifestyle therapy as first-line therapy. When lifestyle changes do not reduce the blood pressure to <140/90 mmHg, drug therapy must be considered.

Angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin-receptor blockers (ARBs) should be first-line therapy in patients with metabolic syndrome β-blockers and diuretics may be used but high doses of these drugs can increase insulin resistance and raise the plasma glucose. Because of the latter, they can convert prediabetes into categorical diabetes. These side effects must be taken into account when diuretics and β-blockers are used in patients with metabolic syndrome and diabetes.

Doses of these drugs should be kept as low as possible. The combination of ACEI (or ARB) plus low-dose thiazide is especially efficacious and appears to be preferable to a high dose of diuretic. In patients with metabolic syndrome, but without type II diabetes or chronic renal failure, the goal is to reduce blood pressure to <140/90 mmHg.[92] When type II diabetes or renal failure is present, lowering the pressure to <130/80 mmHg appears to provide added risk reduction.

ELEVATED PLASMA GLUCOSE

There is a high prevalence of dysglycemia in patients with metabolic syndrome. Choice of hypoglycemic drugs should be individualized according to available therapies and clinical judgment.

In patients with IFG without a diagnosis of diabetes, a lifestyle intervention that includes weight reduction, dietary fat restriction, and increased physical activity has been shown to reduce the incidence of Type 2 diabetes. Metformin has also been shown to reduce the incidence of diabetes, although the effect was less than that seen with lifestyle intervention. Several drug classes [biguanides, thiazolidinediones (TZDs)] increase insulin sensitivity.[93] Because insulin resistance is the primary pathophysiological mechanism for the metabolic syndrome, representative drugs in these classes reduce its prevalence. Both Metformin and TZDs enhance insulin action in the liver and suppress endogenous glucose production.[94] TZDs, but not Metformin, also improve insulin-mediated glucose uptake in muscle and adipose tissue. Benefits of both drugs have also been seen in patients with NAFLD and PCOS, and the drugs have been shown to reduce markers of inflammation and small dense LDL.

GGT AND ITS ROLE IN METABOLIC SYNDROME

Gamma-glutamyl transferase (GGT) is a cell-surface protein contributing to the extracellular catabolism of glutathione (GSH).[95] The enzyme is produced in many tissues, but most GGT in serum is derived from the liver. In the serum, GGT is carried primarily with lipoproteins and albumin.[96] Serum levels of GGT are determined by several factors: alcohol intake, body fat content, plasma lipid/lipoproteins and glucose levels, and various medications.[97,98] High levels of GGT have been associated in populations with increased risk of atherosclerotic cardiovascular disease (CVD).[99,100] Lee et al.[101] report that in 3451 Framingham Study participants (mean age 44 years, 52% women) an increased serum GGT predicted the onset of metabolic syndrome and the occurrence of CVD and death; moreover, the highest GGT quartile experienced a 67% increase in CVD incidence. In this study the association of GGT concentrations with CVD and mortality remained significant after adjustment for traditional cardiac risk factors and C-reactive protein (CRP).

One hypothesis for the relation of GGT levels and CVD holds that GGT itself is proatherogenic.[95] GGT has been reported to occur in atherosclerotic plaques.[102] which might support this hypothesis. The origins of GGT in plaques could be through influx of lipoproteins that carry it into lesions. One of the products of GSH hydrolysis produced by GGT is cysteinyl-glyceine, which can generate superoxide anion radicals through its interaction with free iron.[103] This effect could promote atherogenesis via LDL oxidation. At present the postulated pathogenic pathways remain hypothetical and are yet to be substantiated.

An alternative hypothesis that appears to be consistent with the findings of Lee et al.[101] is that elevations of GGT are a marker of the presence of the metabolic syndrome. Other workers have reported that high levels of GGT are associated with fatty liver, insulin resistance, type 2 diabetes, obesity and other metabolic risk factors. There is growing evidence that the liver, which is the primary source of circulating GGT, is a key target organ for the development of the metabolic syndrome.

An elevation of GGT is seemingly closely related to hepatic steatosis.[104] the latter in turn is strongly associated with the metabolic syndrome.[105] The mechanisms whereby elevated GGT is related to hepatic steatosis have not been determined, but several possibilities have been proposed by Ortega et al.[106] Fatty liver could cause hepatocellular damage that would simulate the synthesis of GGT. Alternatively, excess fat in the liver could enhance oxidative stress, leading to overconsumption of GSH with a compensatory increase in GGT synthesis.

Finally, a higher GGT production could be secondary to a low grade hepatic inflammation induced by hepatic steatosis. It must be noted that high levels of GGT are not the only hepatic biomarker of hepatic steatosis.

Elevations of transaminases are common in patients with fatty liver with or without histological evidence of inflammation.[107] In addition, higher levels of serum transaminases in populations have been associated with the metabolic syndrome and a higher risk for CVD.[108] Other lines of evidence support a relationship between elevated serum GGT and the metabolic syndrome.[76] Thus the higher GGT levels are accompanied by more insulin resistance and greater risk for developing type 2 diabetes.[109] Another important association between GGT and the metabolic syndrome is the finding that higher GGT levels occur in obese persons, particularly those with abdominal obesity.[110] The connection between GGT and the metabolic syndrome extends to an association of higher GGT levels with hypertension.[111] Thus, it appears that all of the major components of the metabolic syndrome are linked to elevations of serum GGT.

MATERIALS AND METHODS

Source of data

Patients attending the medicine, diabetic clinic and gastroenterology outpatient & inpatient services at Victoria and Bowring hospitals, BMCRI, Bangalore.

Methods of collection of data

A. Study design: cross-sectional, case control study

B. Study period: October 2013- May-2015.

C. Place of study: medicine, diabetic clinic and gastroenterology outpatient & inpatient departments at Victoria and Bowring hospitals, BMCRI, Bangalore

D. Sample size: 100 outpatients.

E. Inclusion Criteria

Criteria for metabolic syndrome as per IDF criteria: waist circumference of:
>/=90cm in males
>/=80 in females in the Indian population.

Along with central adiposity two of the following four factors should be present to define metabolic syndrome:

1. Fasting triglycerides >150 mg/dl or specific medication
2. HDL cholesterol <40 mg/dl and <50 mg/dl for men and women, respectively, or specific medication
3. Blood pressure >130 mm systolic or >85 mm diastolic or previous diagnosis or specific medication
4. Fasting plasma glucose 100 mg/dl or previously diagnosed Type 2 diabetes

F.Exclusion Criteria

1. Hypothyroidism
2. Malignant diseases
3. Severe renal insufficiency
4. Acute and chronic liver disease
5. Chronic alcohol consumption
6. Drugs - antiepileptics, OCPs, trimethoprim, sulphamethoxazole, erythromycin, cimetidine

Methodology

After obtaining clearance and approval from the Institutional Ethics Committee of BMCRI, Written informed consent will be taken from the patients. Data will be collected by pretested semi structured questionnaire, clinical examination and investigations. An estimation of gamma glutamyl Transferase will be done for all the patients satisfying the inclusion and exclusion criteria. An estimation of gamma glutamyl Transferase will be done for an equal number of controls. The two groups will be compared to fulfill the study objective For the purpose of the study the following operational standard criteria/definitions will be used:

1. Questionnaire
2. BMI calculated as : - wt in kg/ht in m2
3. Blood pressures will be recorded after at least 5 minutes of rest in both arms sitting/supine position
4. Waist circumference- measured in a horizontal plane midway between the inferior margin of the ribs and superior border of the iliac crest.

INVESTIGATIONS DONE

The following investigations are done.

1. profile
2. Renal function Liver function tests (including GGT)
3. Fasting lipid profile
4. Fasting plasma glucose
5. Thyroid tests (creatinine clearance as required)
6. USG Abdomen

STATISTICAL ANALYSIS

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance.

The following assumptions on data is made,

Assumptions

1. Dependent variables should be normally distributed,
2. Samples drawn from the population should be random, Cases of the samples should be independent.

Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters.

Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

Hypotheses
The null hypothesis will be that all population means are equal, the alternative hypothesis is that at least one mean is different.In the following, lower case letters apply to the individual samples and capital letters apply to the entire set collectively. That is, n is one of many sample sizes, but N is the total sample size.

Grand Mean
The grand mean of a set of samples is the total of all the data values divided by the total sample size. This requires that you have all of the sample data available to you, which is usually the case, but not always. It turns out that all that is necessary to find perform a one-way analysis of variances are the number of samples, the sample means, the sample variances, and the sample sizes. Another way to find the grand mean is to find the weighted average of the sample means. The weight applied is the sample size.

Total Variation
The total variation (not variance) is comprised the sum of the squares of the differences of each mean with the grand mean. There is the between group variation and the within group variation. The whole idea behind the analysis of variance is to compare the ratio of between group variance to within group variance. If the variance caused by the interaction between the samples is much larger when compared to the variance that appears within each group, then it is because the means aren't the same.

Between Group Variation
The variation due to the interaction between the samples is denoted SS(B) for Sum of Squares between groups. If the sample means are close to each other (and therefore the Grand Mean) this will be small. There are k samples involved with one data value for each sample (the sample mean), so there are k-1 degrees of freedom.

The variance due to the interaction between the samples is denoted MS(B) for Mean Square between groups. This is the between group variation divided by its degrees of freedom.

Within Group Variation
The variation due to differences within individual samples, denoted SS(W) for Sum of Squares Within groups. Each sample is considered independently, no interaction between samples is involved. The degrees of freedom is equal to the sum of the individual degrees of freedom for each sample. Since each sample has degrees of freedom equal to one less than their sample sizes, and there are k samples, the total degree of freedom is k less than the total sample size:df =N- k. The variance due to the differences within individual samples is denoted MS(W) for Mean Square Within groups. This is the within group variation divided by its degrees of freedom.

It is the weighted average of the variances (weighted with the degrees of freedom).

F test statistic
F variable is the ratio of two independent chi-square variables divided by their respective degrees of freedom. F test statistic is the ratio of two sample variances, well, it turns out that's exactly what we have here. The F test statistic is found by dividing the between group variance by the within group variance. The degrees of freedom for the numerator are the degrees of freedom for the between group (k-1) and the degrees of freedom for the denominator are the degrees of freedom for the within group (N-k).

Decision Rule
The decision will be to reject the null hypothesis if the test statistic from the table is greater than the F critical value with k-1 numerator and N-k denominator degrees of freedom. If the decision is to reject the null, then at least one of the means is different. However, the ANOVA does not tell you where the difference lies. For this, you need another test, either the Scheffe' or Tukey test.

Fisher LSD
The Fisher LSD test stands for the Least Significant Difference test (rather than what you might have guessed). The LSD test is simply the rationale that if an omnibus test is conducted and is significant, the null hypothesis is incorrect. (If the omnibus test is nonsignificant, no post hoc tests are conducted.)

The reasoning is based on the assumption that if the null hypothesis is incorrect, as indicated by a significant omnibus F-test, Type I errors are not really possible (or less likely), because they only occur when the null is true. So, by conducting an omnibus test first, one is screening out group differences that exist due to sampling error, and thus reducing the likelihood that a Type I error is present among the means.

Fishers LSD test has been criticized for not sufficiently controlling for Type I error. Still, the Fisher LSD is sometimes found in the literature.

Statistical software
The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

ETHICAL CLEARANCE
This study was approved by ethical committee of Bangalore Medical College and Research Institute, Bangalore

RESULTS

Study design: A Comparative case-Control study Table 1: Age distribution of patients studied.

Age in years	Cases		Controls	
	No	%	No	%
31-40	11	22.0	11	22.0
41-50	16	32.0	16	32.0
51-60	13	26.0	13	26.0
61-70	10	20.0	10	20.0
Total	50	100.0	50	100.0
Mean ± SD	50.76±10.36		50.78±10.58	

Sample are age matched with P=0.992

Number of cases and controls were age matched with highest number in 41-50 age group.

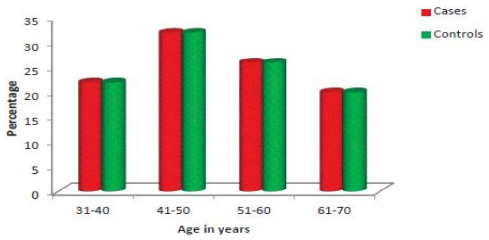


Figure 1

Table 2: Gender distribution of patients studied

Gender	Cases		Controls	
	No	%	No	%
Female	28	56.0	28	56.0
Male	22	44.0	22	44.0
Total	50	100.0	50	100.0

Samples are gender matched with P=1.000.

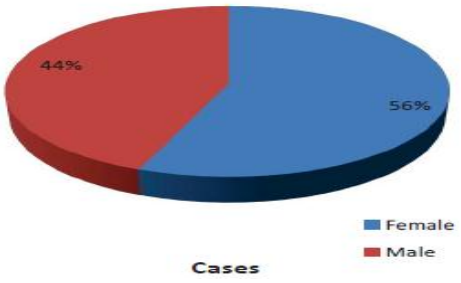


Figure 2

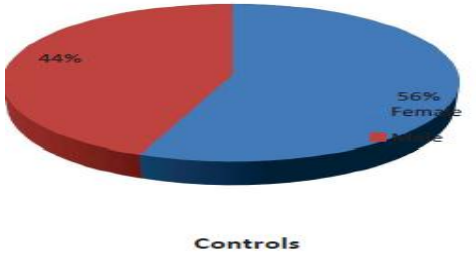


Figure 3

Table 3: Diabetes mellitus of patients studied

Diabetes mellitus	Cases		Controls	
	No	%	No	%
No	6	12.0	50	100.0
Yes	44	88.0	0	0.0
Total	50	100.0	50	100.0

P<0.001**, Significant, Fisher Exact test.

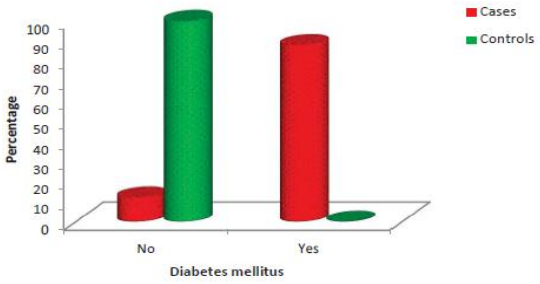


Figure 4

Table 4: Duration of DM (yrs) of patients studied

Duration of DM (yrs)		Cases (n=50)	
		No	%
No		6	12.0
Yes		44	88.0
•	<1	11	22.0
•	1-2	11	22.0
•	2-5	11	22.0
•	5-10	5	10.0
•	>10	6	12.0

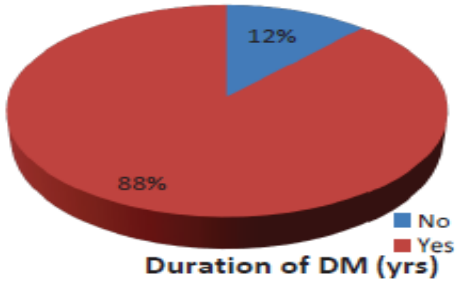


Figure 5

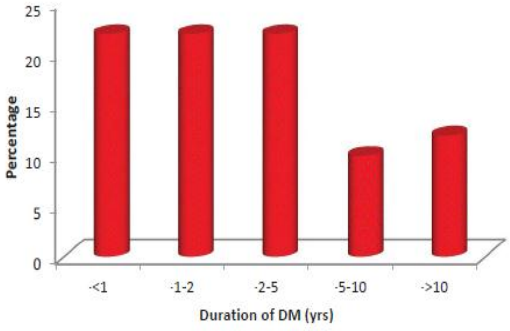


Figure 6

Table 5: Hypertension of patients studied

Hypertension	Cases	
	No	%
No	15	30.0
Yes	35	70.0
Total	50	100.0

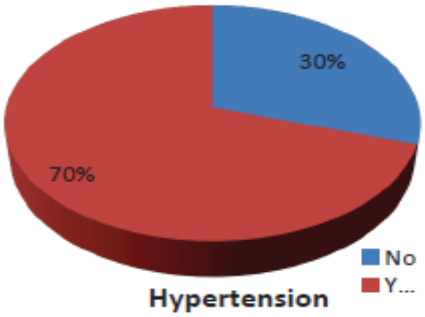


Figure 7

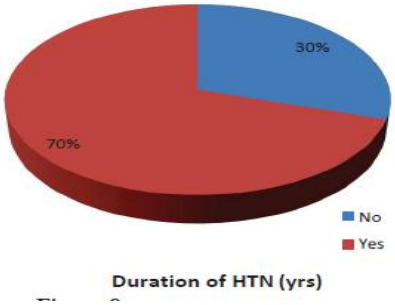


Figure 8

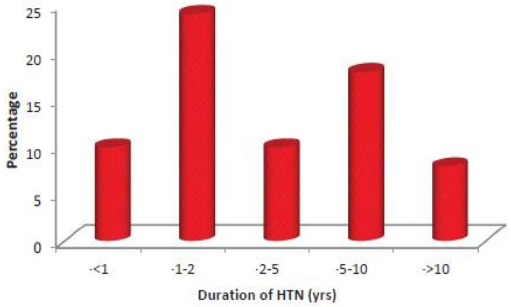


Figure 9

Table 6: Duration of HTN (yrs) of patients studied

Duration of HTN (yrs)		Cases (n=50)	
		No	%
No		15	30.0
Yes		35	70.0
•	<1	5	10.0
•	1-2	12	24.0
•	2-5	5	10.0
•	5-10	9	18.0
•	>10	4	8.0

Table 7: Waist Circumference (cm) of patients studied

Waist Circumference (cm)		Cases		Controls		P value
		No	%	No	%	
Female						
•	<80	0	0.0	24	85.7	<0.001**
•	80-100	14	50.0	4	14.3	
•	>100	14	50.0	0	0.0	
∉	Total	28	100.0	28	100.0	
Male						
•	<80	0	0.0	2	9.1	<0.001**
•	80-100	12	54.5	20	90.9	
•	>100	10	45.5	0	0.0	
∉	Total	22	100.0	22	100.0	

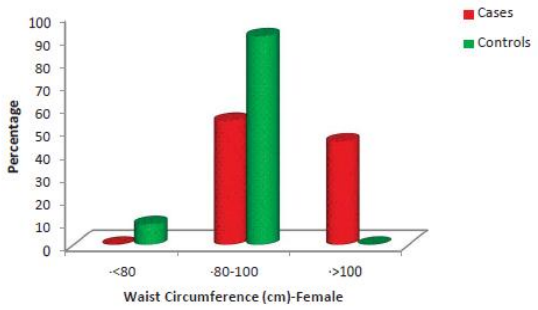


Figure 10

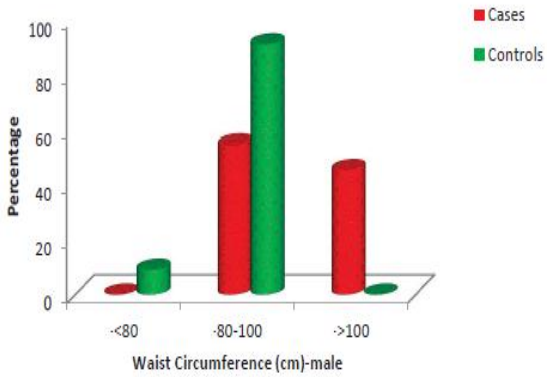


Figure 11

Table 8: Body mass index (kg/m^2) of patients studied

Body mass index (kg/m^2)	Cases		Controls	
	No	%	No	%
<18.5	0	0.0	5	10.0
18.5-25	5	10.0	44	88.0
25-30	25	50.0	1	2.0
>30	20	40.0	0	0.0
Total	50	100.0	50	100.0

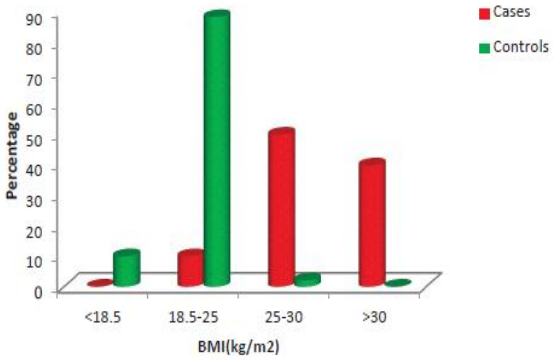


Figure 12

Table 9: Comparison of Baseline information in case-controls study

	Cases	Controls	P value
Age in years	50.76±10.36	50.78±10.58	0.992
Height (cm)	1.56±0.08	1.63±0.09	<0.001**
Weight (kg)	73.26±12.04	55.32±7.54	<0.001**
Waist Circumference (cm)	101.88±10.74	80.28±5.94	<0.001**
Body mass index (kg/m^2)	29.94±4.29	20.79±2.08	<0.001**

Student t test.

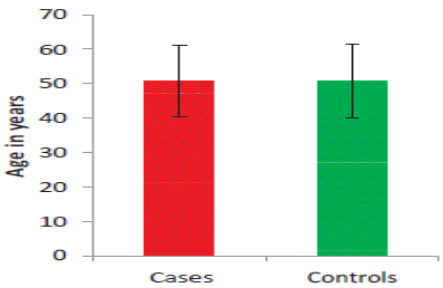


Figure13

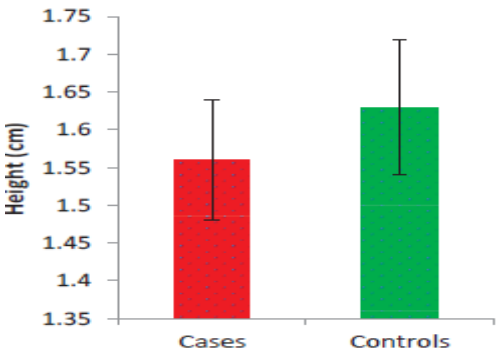


Figure 14

Table 10: Comparison of Vital parameters in cases and controls studied

Vitals		Cases (n=50)		Controls (n=50)		P value
		No	%	No	%	
Pulse rate (bpm)						
•	<70	9	18.0	7	14.0	

•	70-90	40	80.0	43	86.0	0.595
•	>90	1	2.0	0	0.0	
SBP (mm Hg)						
•	<120	7	14.0	41	82.0	<0.001**
•	120-140	28	56.0	8	16.0	
•	>140	15	30.0	1	2.0	
DBP (mm Hg)						
•	<80	8	16.0	43	86.0	<0.001**
•	80-100	40	80.0	7	14.0	
•	>100	2	4.0	0	0.0	

Chi-Square test/Fisher Exact test.

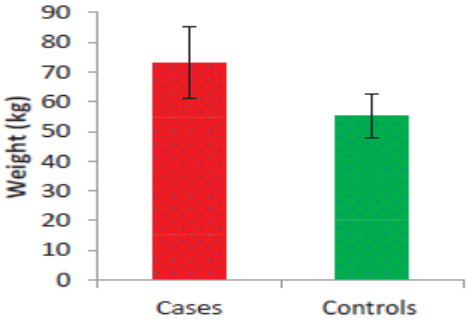


Figure 15

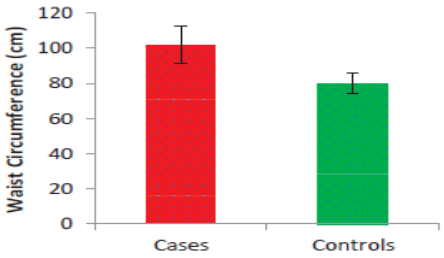


Figure 16

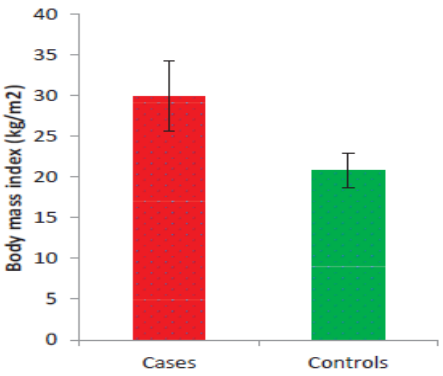


Figure 17

Table 17: Levels of Blood investigations in two groups studied

Investigations		Cases (n=50)		Controls (n=50)		P value
		No	%	No	%	
Hemoglobin %						
∉	<12	8	16.0	16	32.0	0.143
∉	12-16	40	80.0	31	62.0	
∉	>16	2	4.0	3	6.0	
White Blood Cells (cumm)						
∉	<4000	1	2.0	0	0.0	0.056+
∉	4000-11000	45	90.0	50	100.0	
∉	>11000	3	6.0	0	0.0	
Platelet Count (lakhs/cumm)						
∉	<1.5	0	0.0	0	0.0	0.023*
∉	1.5-3.5	38	76.0	47	94.0	
∉	>3.5	12	24.0	3	6.0	

Chi-Square test/Fisher Exact test.

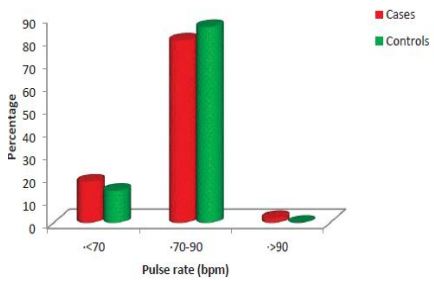


Figure 18

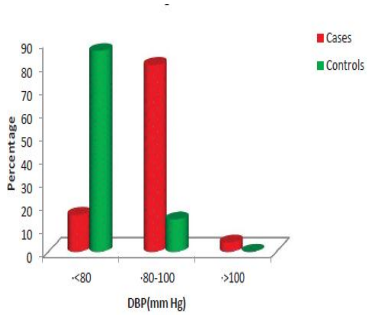


Figure 20

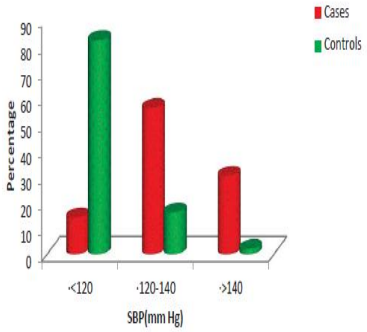


Figure 19

Table 11: Comparison of Vital parameters in cases and controls studied

	Cases	Controls	P value
Pulse rate (bpm)	77.40±6.87	75.66±6.19	0.186
SBP (mm Hg)	135.36±14.93	112.96±11.13	<0.001**
DBP (mm Hg)	85.24±10.49	70.88±7.04	<0.001**-

Student t test.

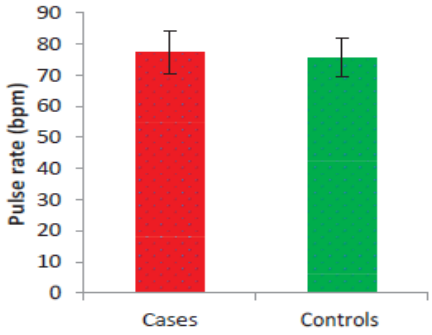


Figure 21

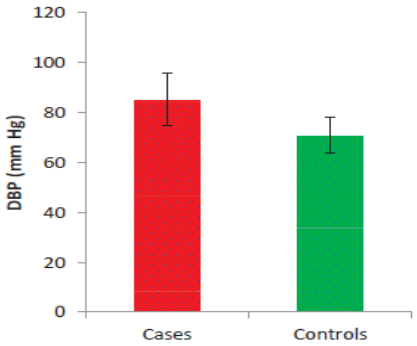


Figure 23

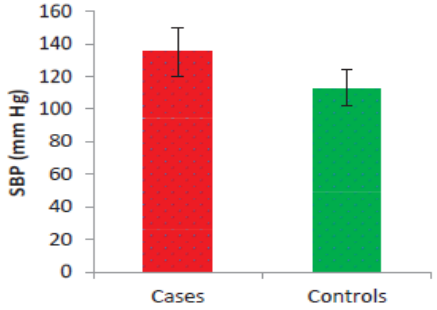


Figure 22

Table 12: Fasting Blood Sugar (mg/dl) in two groups studied

Fasting Blood Sugar (mg/dl)	Cases		Controls	
	No	%	No	%
<100	3	6.0	49	98.0
100-126	14	28.0	1	2.0
>126	33	66.0	0	0.0
Total	50	100.0	50	100.0
Mean ± SD	166.22±72.32		85.22±8.67	

P<0.001**, Significant, Student t test.

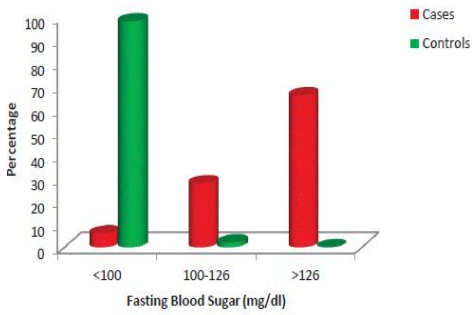


Figure 24

Table 13: RENAL parameters in two groups studied

Renal Parameters		Cases (n=50)		Controls (n=50)		P value
		No	%	No	%	
Urea (mg/dl)						
•	<20	19	38.0	16	32.0	0.365
•	20-40	29	58.0	34	68.0	
•	>40	2	4.0	0	0.0	
Serum Creatinine (mg/dl)						
•	<1.1	38	78.0	41	82.0	0.461
•	>1.1	12	24.0	9	18.0	

Chi-Square test/Fisher Exact test

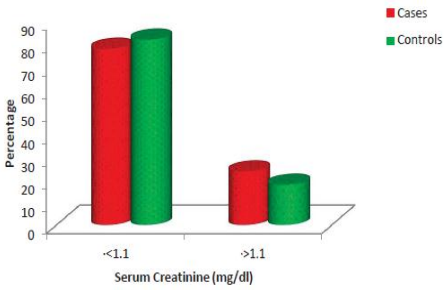
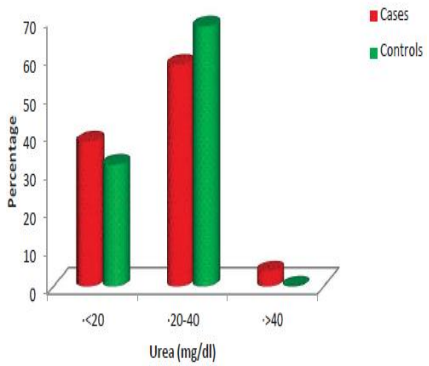


Figure 25



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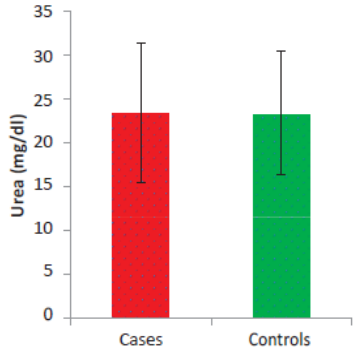


Figure 27

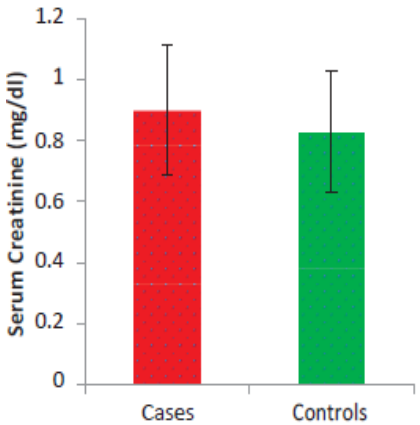


figure 28

Table 14: Comparison of Urea/Creatinine in two groups studied

	Cases	Controls	P value
Urea (mg/dl)	23.45±7.97	23.36±7.03	0.954
Serum Creatinine	0.90±0.21	0.83±0.20	0.118

Student t test.

Table 15: Levels of Lipids in two groups studied

Lipids		Cases (n=50)		Controls (n=50)		P value
		No	%	No	%	
Total Cholesterol (mg/dl)						
•	<200	25	50.0	50	100.0	<0.001**
•	200-280	20	40.0	0	0.0	
•	>280	5	10.0	0	0.0	
High density lipoprotein (mg/dl)						
•	<35	19	38.0	2	4.0	<0.001**
•	35-60	31	62.0	47	94.0	
•	>60	0	0.0	1	2.0	
Low density lipoprotein (mg/dl)						
•	<70	7	14.0	18	36.0	0.020*
•	70-190	42	84.0	32	64.0	
•	>190	1	2.0	0	0.0	
Triglycerides (mg/dl)						
•	<150	9	18.0	48	56.0	<0.001**
•	150-500	40	80.0	2	4.0	
•	>500	1	2.0	0	0.0	
Very low density lipoprotein (mg/dl)						
•	<35	17	34.0	49	58.0	<0.001**
•	35-60	21	42.0	1	2.0	
•	>60	12	24.0	0	0.0	

Chi-Square test/Fisher Exact test

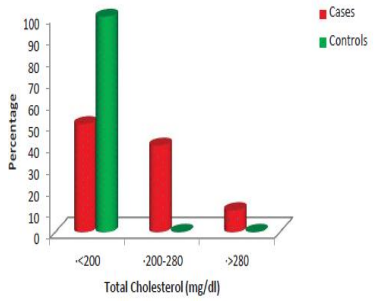


Figure 29

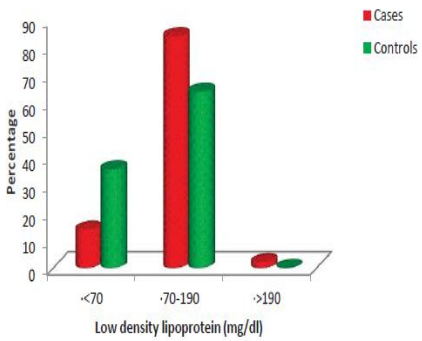


Figure 31

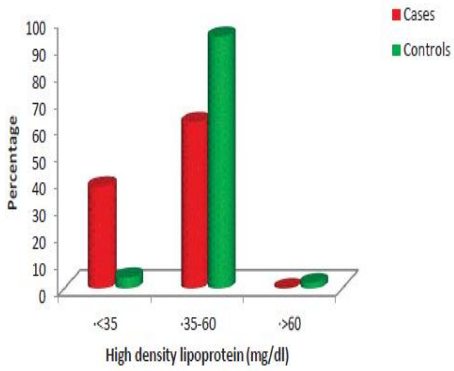


Figure 30

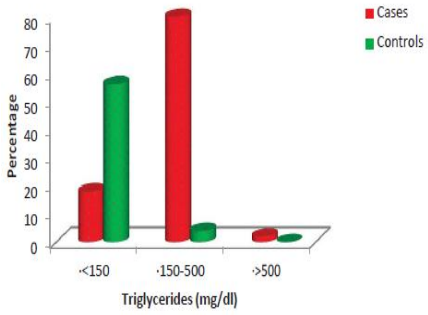


Figure 32

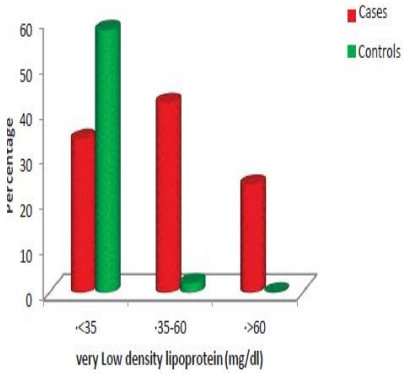


Figure 33

Table 16: Comparison of Lipids in two groups studied

Lipids	Cases	Controls	P value
Total Cholesterol (mg/dl)	204.00±42.77	153.18±23.91	<0.001**
High density lipoprotein (mg/dl)	39.01±9.78	49.48±7.11	<0.001**
Low density lipoprotein (mg/dl)	114.74±40.15	79.16±20.83	<0.001**
Triglycerides (mg/dl)	238.64±139.45	121.88±20.90	<0.001**
Very low density lipoprotein (mg/dl)	49.80±30.20	23.82±6.04	<0.001**

Student t test

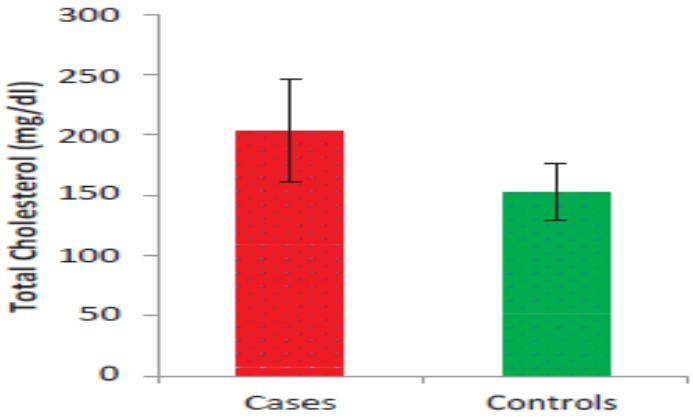


Figure 34

Table 17: Levels of Blood investigations in two groups studied

Investigations		Cases (n=50)		Controls (n=50)		P value
		No	%	No	%	
Hemoglobin %						
•	<12	8	16.0	16	32.0	0.143
•	12-16	40	80.0	31	62.0	
•	>16	2	4.0	3	6.0	
White Blood Cells (cumm)						
•	<4000	1	2.0	0	0.0	0.056+
•	4000-11000	45	90.0	50	100.0	
•	>11000	3	6.0	0	0.0	
Platelet Count (lakhs/cumm)						
•	<1.5	0	0.0	0	0.0	0.023*
•	1.5-3.5	38	76.0	47	94.0	
•	>3.5	12	24.0	3	6.0	

Chi-Square test/Fisher Exact test.

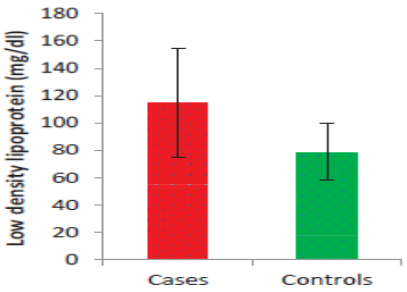


Figure 36

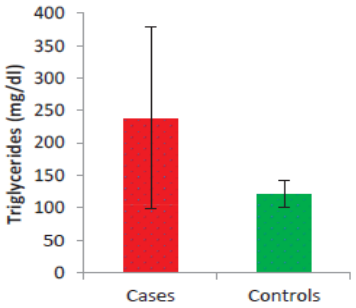


Figure 37

Table 17: Levels of Blood investigations in two groups studied

Investigations		Cases (n=50)		Controls (n=50)		P value
		No	%	No	%	
Hemoglobin %						
•	<12	8	16.0	16	32.0	0.143
•	12-16	40	80.0	31	62.0	
•	>16	2	4.0	3	6.0	
White Blood Cells (cumm)						
•	<4000	1	2.0	0	0.0	0.056+
•	4000-11000	45	90.0	50	100.0	
•	>11000	3	6.0	0	0.0	
Platelet Count (lakhs/cumm)						
•	<1.5	0	0.0	0	0.0	0.023*
•	1.5-3.5	38	76.0	47	94.0	
•	>3.5	12	24.0	3	6.0	

Chi-Square test/Fisher Exact test

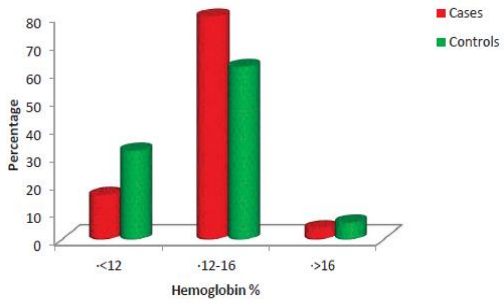


Figure 38

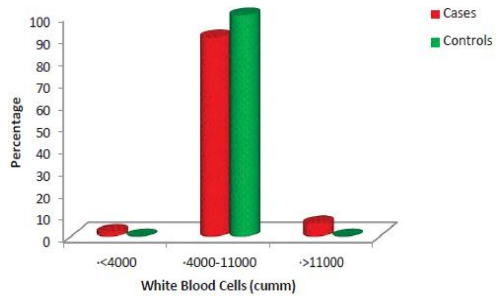


Figure 39

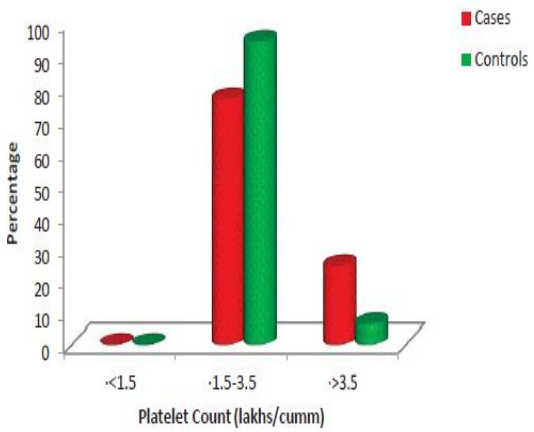


Figure 40

Table 18: Comparison of Hematological parameters in two groups studied

Variables	Cases	Controls	P value
Hemoglobin %	13.55±1.53	13.34±1.88	0.538
White Blood Cells (cumm)	8987.35±2100.68	8060.00±1851.86	0.022*
Platelet Count (lakhs/cumm)	17.04±69.79	2.60±0.77	0.147

Student t test

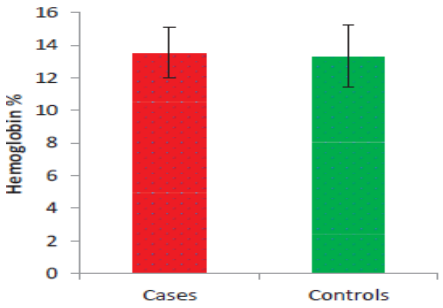
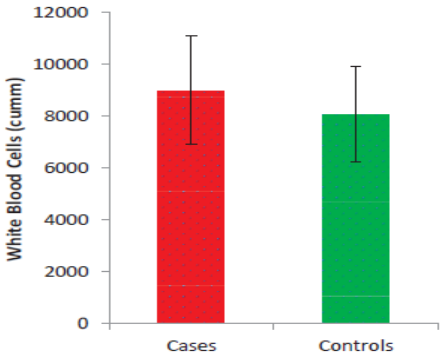


Figure 41

Table 19: Thyroid stimulating hormone in two groups studied

Thyroid stimulating hormone	Cases		Controls	
	No	%	No	%
<5	50	100.0	50	100.0
5-6	0	0.0	0	0.0
>6	0	0.0	0	0.0
Total	50	100.0	50	100.0

P=1.000, Not significant, Fisher Exact test



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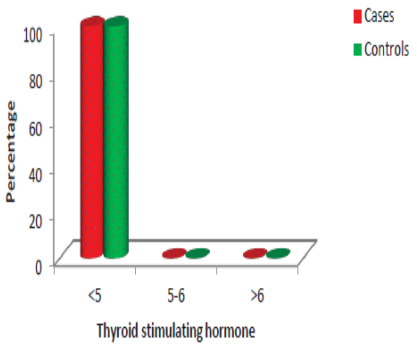

Figure 44

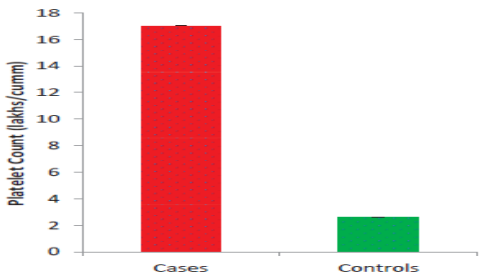

Figure 43

Table 20: Alkaline phosphatase in two groups studied

Alkaline phosphatase	Cases		Controls	
	No	%	No	%
<20	0	0.0	0	0.0
20-125	37	74.0	37	74.0
>125	13	26.0	13	26.0
Total	50	100.0	50	100.0

P=1.000, Not significant, Chi-Square test

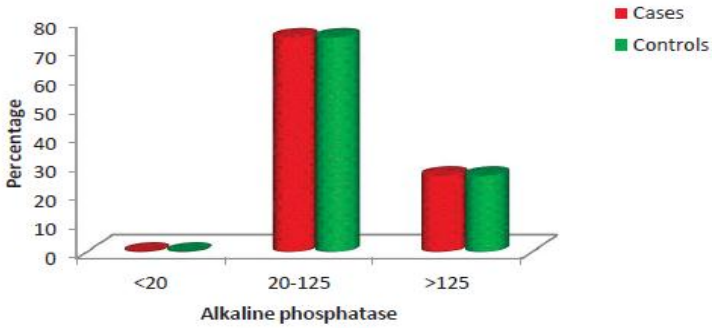

Figure 45

Table 21: Serum glutamic oxaloacetic transaminase/ Serum glutamic pyruvic transaminase in two groups studied

Variables		Cases		Controls		P value
		No	%	No	%	
Serum glutamic oxaloacetic transaminase						
•	0	0	0.0	0	0.0	0.009**
•	0-42	18	36.0	32	64.0	
•	>42	32	64.0	18	36.0	
Serum glutamic pyruvic transaminase						
•	0	0	0.0	0	0.0	0.027*
•	0-48	30	60.0	41	82.0	
•	>48	20	40.0	9	18.0	

Chi-Square test/ Fisher Exact test

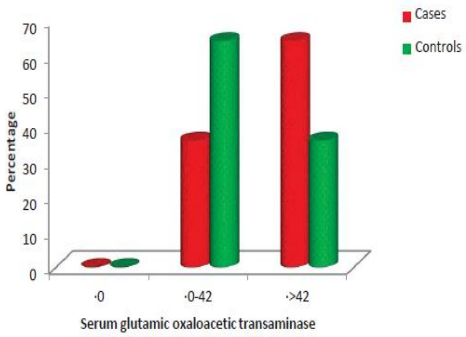

Figure 46

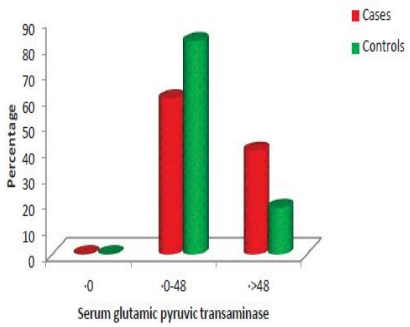

Figure 47

Table 22: Gamma glutamyl transferase

Gamma glutamyl transferase	Cases		Controls	
	No	%	No	%
<30	8	16.0	22	44.0
30-60	35	70.0	27	54.0
>60	7	14.0	1	2.0
Total	50	100.0	50	100.0

=0.002**, significant, Fisher

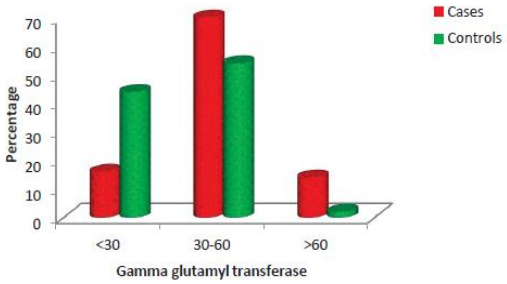

Figure 48

Table 23: Comparison of study variables in two groups studied

Variables	Cases	Controls	P value
Thyroid stimulating hormone	2.69±0.59	2.09±0.82	<0.001**
Alkaline phosphatase	117.52±43.48	102.44±45.18	0.092+

Serum glutamic oxaloacetic transaminase	50.56±24.42	38.74±16.24	0.005**
Serum glutamic pyruvic transaminase	51.16±23.69	38.46±15.47	0.002**
Gamma glutamyl transferase	48.18±14.68	30.96±10.06	<0.001**

Student t test

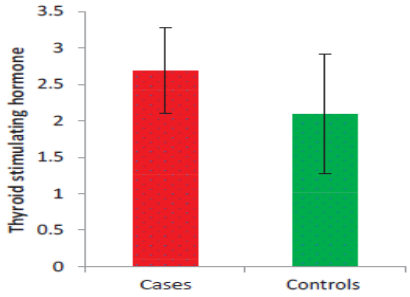

Figure 49

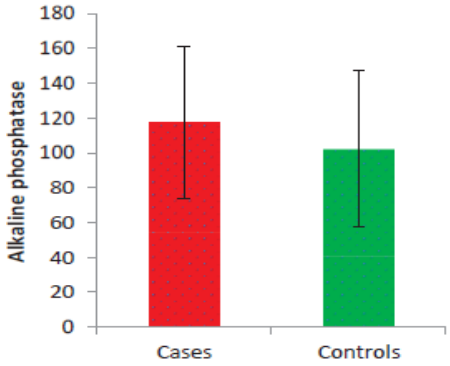

Figure 50

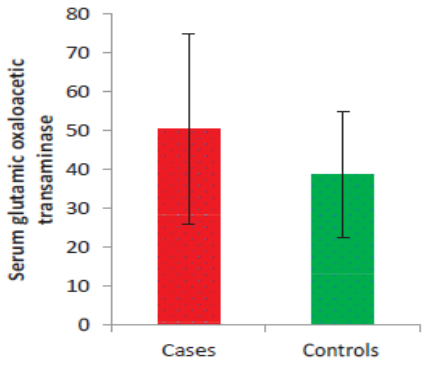

Figure 51

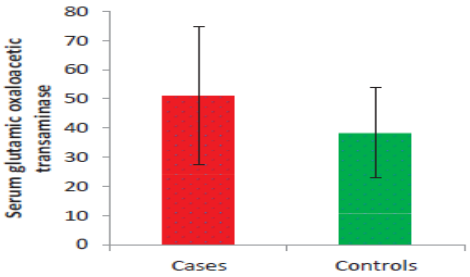

Figure 52

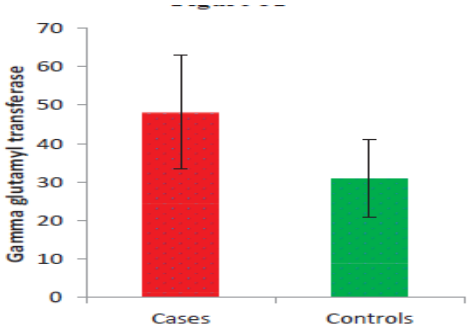

Figure 53

Table 24: USG Abdomen

USG Abdomen	Cases (n=50)		Controls (n=50)	
	No	%	No	%
Normal	34	74.0	49	58.0
Abnormal	16	32.0	1	2.0
Hepatic steatosis	15	30.0	1	2.0
Grade 2 fatty liver	1	2.0	0	0.0

P<0.001**, significant, Fisher Exact test

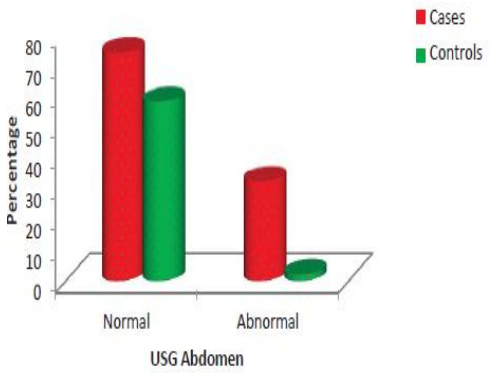

Figure 54

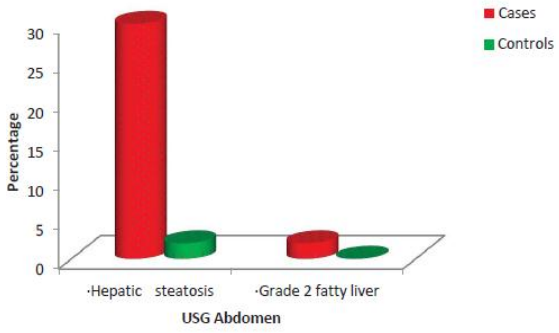

Figure 55

Table 25: Correlations GGT vs all other variables

Pair for correlation	Cases		Controls	
	r value	P value	r value	P value
GGT **vs** Age in years	-0.026	0.857	0.172	0.233
GGT **vs** Waist Circumfernce	0.057	0.693	0.234	0.102
GGT **vs** BMI (kg/m^2)	-0.065	0.654	-0.088	0.543
GGT **vs** FBS (mg/dl)	-0.069	0.632	0.207	0.150
GGT **vs** Urea (mg/dl)	-0.016	0.911	0.061	0.675
GGT **vs** Serum Creatinine	0.027	0.851	-0.036	0.804
GGT **vs** Total cholesterol (mg/dl)	0.004	0.979	-0.165	0.254
GGT **vs** HDL (mg/dl)	-0.186	0.197	-0.175	0.225
GGT **vs** LDL (mg/dl)	0.025	0.864	-0.112	0.436
GGT **vs** TGL (mg/dl)	0.048	0.739	-0.059	0.685
GGT **vs** VLDL (mg/dl)	0.048	0.742	0.011	0.942
GGT **vs** Hemoglobin (g/dl)	-0.014	0.923	0.255	0.074+
GGT **vs** WBC	-0.010	0.946	0.257	0.072+
GGT **vs** Platelet count	0.117	0.420	-0.035	0.812
GGT **vs** TSH	0.027	0.851	0.154	0.284
GGT **vs** ALP	0.156	0.279	0.488	<0.001**
GGT **vs** SGOT	0.343	0.015*	-0.205	0.153
GGT **vs** SGPT	0.353	0.012*	-0.139	0.336
GGT **vs** Pulse (bpm)	0.137	0.344	-0.080	0.581
GGT **vs** SBP (mm Hg)	0.103	0.476	-0.215	0.133
GGT **vs** DBP (mm Hg)	0.130	0.367	-0.126	0.384

Table 26: Sensitivity and specificity of GGT in diagnosis of metabolic syndrome

GGT result	Patients with metabolic syndrome (IDF criteria)	Patients without metabolic syndrome	Total
Positive(≥55/38 IU/L)	46	6	52
Negative(<55/38 IU/L)	4	44	48
Total	50	50	100

Sensitivity= 92%
Specificity= 88%
Positive predictive value=88.46% Negative predictive value=91.67%

DISCUSSION

Metabolic syndrome is important to be recognized at the earliest because of the cardiovascular risks and to decrease morbidity and mortality related to it, especially so the studies to identify it at the earliest is lacking in Indian population. This study has been done to critically evaluate Gamma Glutamyl transferase as a diagnostic marker in diagnosis of metabolic syndrome. In our study, 50 cases and 50 controls were studied, the mean age of the studied population is 50.76±10.36 of cases and 50.78±10.58 of controls. Clustered around the 5th decade The slight preponderance of female population is noted in cases where in 28 (56%) are females compared to 22 (44%) are males, this is matched in controls.

Out of the cases studied 44(88%) were diabetics and 6(12%) were non diabetics. All the controls were non diabetics. The mean fasting blood sugars of cases is 166.22±72.32, with 33(66%) of cases with blood sugars >126 and 14(28%) with blood sugars between 100-126. The control population has a mean of 85.22±8.67, with 1(2%) with a blood sugar between 100-126.Shows that the prevalence of diabetics is high in cases of metabolic syndrome with a p value of < 0.001.

The number of hypertensives in cases is 35(70%) the mean duration of hypertension is 1.5 years. Measured blood pressure has a very significant increase with a p value of <0.001 when compared to cases and controls with a mean of 135.36±14.93 of SBP in cases and 112.96±11.13 in controls.

The waist circumference of the cases was studied in 28 females and 22 males. It was between 80- 100 in 14(50%) of females and >100 in 14(50%) of the female cases. Whereas in out of the 22 males studied, 12(54.5%) had waist circumference between 80-100

and 10(45.5%) had waist circumference >100. This shows slight female preponderance for increase in waist circumference among the cases. The reference study by kasapagolu et al also showed female preponderance in increased waist circumference.[5]

The mean weight of the control population is 55.32±7.54, whereas that of cases is 73.26±12.04, which is very significant with a p value of <0.001. The mean BMI of the control population was 20.79±2.08 and that of case population was 29.94±4.29. The waist circumference had a very significant p value of <0.001 with a mean of 101.88±10.74 in the study population and 80.28±5.94 in the control population. This shows the high prevalence of central adiposity in cases of metabolic syndrome.

Renal parameters studied showed no difference among cases and controls without any significant variation. Of the Serum lipid profile studied in cases total cholesterol was a mean of 204.00±42.77, HDL a mean of 39.01±9.78, LDL 114.74±40.15, VLDL 49.80±30.20, and triglycerides 238.64±139.45 as opposed to controls with total mean cholesterol 153.18±23.91, HDL 49.48±7.11, LDL 79.16±20.83, VLDL 23.82±6.04 and triglycerides of 121.88±20.90. This difference was very significant with a p value of <0.001. shows the association of dyslipidemia as a predominant factor in metabolic syndrome. In the evaluation of liver function tests all the enzymes were assessed i.e, SGOT, SGPT and GGT SGOT showed increased levels in cases. Out of the 50 cases studied, 18(36%) had normal values while 32(64%) had elevated values. Even in controls 18(36%) had elevated values. However the difference is significant with a p value of 0.009. Mean SGOT in cases being 50.56±24.42 and in controls being 38.74±16.24.

SGPT had a similar raise in cases, with 30(60%) of them having normal values and 20 (40%) with raised values. Mean in cases was 51.16±23.69 and in controls was 38.46±15.47. ALP however had raised in 13(26%) of cases as well as 13(26%) of controls and there was no difference. The highest significance among the liver enzymes was that of the GGT with 35(70%) of cases showing moderate elevation and 7(14%) cases showing severe elevation.

This in contrast to controls where 22(44%) were normal levels and 27(54%) showed moderate elevation and 1(2%) showed severe elevation.

The mean GGT among the cases is 48.18±14.68 and that among controls is 30.96±10.06 with a very Significant p value of <0.001.Validity measures were computed taking the reference values of GGT as ≥55 for males and ≥38 for females, in general the sensitivity and specificity of GGT to diagnose patients with metabolic syndrome was found to be 92% and 88% respectively.

An interesting observation noted in the study group with respect to GGT was that most of the subjects with values less than 55/38 IU/L although in the normal range were clustered in the upper limit of normal values for GGT (>50 IU/L for males and >35 IU/L for females). This therefore suggests that GGT values even in the upper limit of normal may have a predictive value in diagnosing patients with metabolic syndrome.

USG abdomen done in the control group shows hepatic steatosis in 1(2%) whereas in study group it is hepatic steatosis in 15(30%) and grade 2 fatty liver in 1(2%). Which is again very significant with a p value <0.001 In the study done by B Kasapgolu et al.[5], transaminases were in normal ranges in 91.2 per centand GGT was in normal range in 83.4 per cent of MS patients. Especially ALT and GGT values were significantly higher than control group but still remain in normal ranges. They therefore conclude that normal liver enzymes values could coexist with metabolic syndrome. In a study of Balogun et al.[113] on 90 patients with type 2 diabetes and 90 non- diabetic controls the GGT and ALT values were significantly higher (52.9 IU/l and 24.3 U/l respectively) in the diabetic group compared to the controls (34.4 IU/l and9.2 IU/l respectively). Moreover, the most predominant LFT abnormality in diabetic group was found to be isolated elevation of GGT. C Meisinger et al.[114] stated that GGT is an important predictor for incident type 2 diabetes in men and women from the general population.

In some other studies, done by Bruckert E et al.[115] and Onat A et a[116], it has been demonstrated that circulating GGT and transaminases activities are elevated in patients with metabolic syndrome.

Nannipieri et al[117] revealed an association with mild elevations in liver function tests and metabolic syndrome.

Moreover, Wannamethee et al[100] revealed that; elevated levels of ALT and GGT within the normal ranges are found to be the independent predictors of type 2 diabetes mellitus. Rantala et al.[76] investigated the relationship between GGT and MS and revealed a highly significant relationship between GGT and the components of the metabolic syndrome even after adjustment for age, body mass index and alcohol consumption. In another study of Sakugawa et al.[118] the serum GGT level was found to be correlated with components ofMS.

SUMMARY

A total of 100 subjects were chosen in the study with 50 as study population and the other 50 as controls, investigations were done as mentioned and their gamma glutamyl transferase levels were assessed.

The age of the population was clustered around 41-50 yrs with a slight female preponderance of 56% Out of the cases studied 44(88%) were diabetics and 6(12%) were non diabetics. All the controls were non diabetics. The mean fasting blood sugars of cases was 166.22±72.32, with 33(66%) of cases with blood sugars >126 and 14(28%) with blood sugars between 100-126.

The number of hypertensives in cases is 35(70%) and the mean duration of hypertension is 1.5 years. Measured blood pressure has a very significant increase with a p value of<0.001. with a mean of 135.36±14.93 of SBP in cases and 112.96±11.13 in controls respectively.

The central adiposity in cases of metabolic syndrome is well illustrated in this study by, the mean weight of the control population which is 55.32±7.54, whereas that of cases is 73.26±12.04, which is very significant with a p value of <0.001. The mean BMI of the control population was 20.79±2.08 and that of case population was 29.94±4.29.

The waist circumference was studied in 28 females and 22 males. It was between 80- 100 in 14(50%) of females and >100 in 14(50%) of the female cases. Whereas in out of the 22 males studied 12(54.5%) had waist circumference between 80-100 and 10(45.5%) had waist circumference >100. This shows slight female preponderance for increase in waist circumference among the cases.

The waist circumference had a very significant p value of <0.001 with a mean of 101.88±10.74 in the study population and 80.28±5.94 in the control population. Of the Serum lipid profile studied in cases total cholesterol was a mean of 204.00±42.77, HDL a mean of 39.01±9.78, LDL 114.74±40.15, VLDL 49.80±30.20, and triglycerides 238.64±139. shows the association of dyslipidemia as a predominant factor in metabolic syndrome. SGOT showed increased levels in cases. Out of the 50 cases studied, 18(36%) had normal values while 32(64%) had elevated values. Mean SGOT in cases being 50.56±24.42.

SGPT had a similar raise in cases, with 30(60%) of them having normal values and 20 (40%) with raised values. Mean in cases was 51.16±23.69 and in controls was 38.46±15.47.

The highest significance among the liver enzymes was that of the GGT with 35(70%) of cases showing moderate elevation and 7(14%) cases showing severe elevation. The mean GGT among the cases is 48.18±14.68 and that among controls is 30.96±10.06 with a very significant p value of <0.001.

The sensitivity and specificity of gamma glutamyl transferase in diagnosis of metabolic syndrome was found to be 92% and 88% respectively.

CONCLUSION

Elevated levels of GGT were found to be associated with metabolic syndrome.

GGT was found to be more specific than the other liver enzymes which are also raised in metabolic syndrome. Sensitivity of 92% and specificity of 88% makes gamma glutamyl transferase a good marker for diagnosis of metabolic syndrome. Considering all the observations made in the study GGT values should probably find a position in algorithms for evaluation of patients with metabolic syndrome.

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