"A ONE YEAR CROSS-SECTIONAL STUDY: TO STUDY THE ASSOCIATION OF SERUM GAMMA GLUTAMYL TRANSFERASE LEVELS WITH METABOLIC SYNDROME - DR.PRABHAKAR KORE'S K.L.E.S HOSPITAL, BELGAUM"

REG NO. BG0111009

Dissertation

Submitted to the
KLE University, Belgaum, Karnataka

In Partial Fulfillment
of the requirements for the degree of

M. D.
in
GENERAL MEDICINE

DEPARTMENT OF MEDICINE,
JAWAHARLAL NEHRU MEDICAL COLLEGE,
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ENDORSEMENT

This is to certify that the dissertation entitled **"A ONE YEAR CROSS-SECTIONAL STUDY: TO STUDY THE ASSOCIATION OF SERUM GAMMA GLUTAMYL TRANSFERASE LEVELS WITH METABOLIC SYNDROME - DR.PRABHAKAR KORE'S K.L.E.S HOSPITAL, BELGAUM"** is a bonafide research work done by **THE CANDIDATE REG NO. BG0111009**.

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LIST OF ABBREVIATIONS USED

˚C	-	Degree centrigrade
AACE	-	American Association of Clinical Endocrinologists
AIR	-	Acute insulin response
ALP	-	Alkaline phosphatase
ALT	-	Alanine aminotransferase
ANS	-	Autonomic nervous system
APC	-	Asia-Pacific criteria
apoB	-	Apolipoprotein B
AST	-	Aspartate aminotransferase
ATP	-	Adenosine triphosphate
BMI	-	Body mass index
BP	-	Blood pressure
CAD	-	Coronary artery disease
CHD	-	Coronary heart disease
CI	-	Confidence interval
cm	-	Centimeter
CRP	-	C-reactive protein
CVD	-	Cardiovascular atherosclerotic diseases
DBP	-	Diastolic blood pressure
DMT2	-	Diabetes mellitus type 2
DPP	-	Diabetes Prevention Program
DPS	-	Diabetes Prevention Study
EGIR	-	European Group for the Study of Insulin Resistance
FBS	-	Fasting blood sugar

GGT	-	Gamma-glutamyl transferase
H/O	-	History of
HbA1C	-	Hemoglobin-A1C
HDL	-	High-density lipoproteins
HOMA IR	-	Homoeostatic model assessment for insulin resistance
HPA	-	Hypothalamic-pituitary-adrenal
HR	-	Hazard ratio
Hs-CRP	-	High-sensitivity C-reactive protein
IDF	-	International Diabetes Federation
IFG	-	Impaired fasting glucose
IGR	-	Impaired glucose regulation
IGT	-	Impaired glucose tolerance
IR	-	Insulin resistance
kg/m^2	-	Kilogram per square meter
LDL	-	Low-density lipoprotein
LFT	-	Liver function test
MetS	-	Metabolic syndrome
mg/dL	-	Milligram per deciliter
mg/g	-	Milligram per gram
MI	-	Myocardial infarction
mmHg	-	Millimeters of mercury
mmol/l	-	Milli moles per liter
MONICA	-	Multinational Monitoring of trends and determinants in Cardiovascular disease
MS	-	Metabolic syndrome

n	-	Total number
NAFLD	-	Non-alcoholic fatty liver disease
NCEP	-	National Cholesterol Education Program
NHANES	-	National Health and Nutrition Examination Survey
OGTT	-	Oral glucose tolerance test
OPD	-	Out patient department
OR	-	Odds ratio
p	-	Probability value
PUFAs	-	Polyunsaturated fatty acids
RNA	-	Ribonucleic acid
rNCEP	-	Revised National Cholesterol Education Program
ROC	-	Received operating curve
RR	-	Relative risk
SAHS	-	San Antonio Heart Study
SAT	-	Subcutaneous abdominal tissue
SBP	-	Systolic blood pressure
SD	-	Standard deviation
SLE	-	Systemic lupus etythematosus
TG	-	Triglycerides
TV	-	Television
U.S.	-	United states
VAT	-	Visceral abdominal tissue
VLDL	-	Very-low-density lipoprotein
WC	-	Waist circumference
WHO	-	World Health Organization

WHR	-	Waist-to-hip ratio
α	-	Alpha
γ	-	Gamma
µg/min	-	Micro gram per min

ABSTRACT

Background and objectives

Serum Gamma-glutamyl transferase level is a promising diagnostic marker for early detection of metabolic syndrome. It has also been shown to be an independent risk factor for the mortality and morbidity of cardiovascular diseases. The present study was aimed to find the association of serum gamma glutamyl transferase levels in patients with metabolic syndrome and to correlate serum gamma glutamyl transferase levels with the different components of metabolic syndrome.

Methodology

This one year study was conducted from January 2012 to December 2012 in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on a total of 100 patients with metabolic syndrome based on IDF criteria.

Results

In this study, 59% patients were males and 41% were females. The commonest age group was 41 to 50 years comprised of 42% of patients. There were no significant gender differences in GGT levels. History of diabetes was present in 65% of the patients and 55% had hypertension. Diabetic complications e.g. retinopathy was noted in 46% of the patients, and 44% of the patients had nephropathy. In this study, of the 63% patients presented with all the five metabolic syndrome components.

Conclusion and interpretation

Raised serum GGT levels were noted in 65% of the patients, while 35% of the patients had normal serum GGT levels. Among patients with all the five component abnormality, the mean serum GGT levels were significantly high (87.62 ± 17.57) ($p<0.034$). Serum GGT levels were comparable in both the sexes and in all the age groups. Raised serum GGT levels correlated well with hypertension and HDL, whereas no correlation was found between waist circumference and diabetes mellitus. Raised serum GGT levels also correlated well with glycaemic control (HbA1c), insulin resistance, and body mass index.

Keywords

Insulin Resistance; Metabolic Syndrome; Serum Gamma Glutamyl Transferase;

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Chapter 1

Introduction

INTRODUCTION

Metabolic syndrome (MS) is a cluster of inter-connected factors that directly increase the risk of coronary heart disease (CHD), other forms of cardiovascular atherosclerotic diseases (CVD), and Type 2 Diabetes Mellitus (DM). It's main components are dyslipidemia (elevated triglycerides and apolipoprotein B (apoB)-containing lipoproteins, and low high-density lipoproteins (HDL)), elevation of arterial blood pressure (BP) and deregulated glucose homeostasis, while abdominal obesity and/or insulin resistance (IR) have gained increasing attention as the core manifestations of the syndrome. Recently, other abnormalities such as chronic pro-inflammatory and prothrombotic states, non-alcoholic fatty liver disease and sleep apnea have been added to the entity of to the syndrome, making its definition even more complex. Besides the many components and clinical implications of MS, there is still no universally accepted pathogenic mechanism or clearly defined diagnostic criteria[1].

Ever since the MS was described by Reaven in 1988[2], a number of definitions have been published by organizations including the National Cholesterol Education Program (NCEP)[3], the International Diabetes Federation[4], and the World Health Organization[5], among others. Of these, the 2001 Third Report of the NCEP's Adult Treatment Panel has emerged as the most widely used definition, primarily because it provides a relatively simple approach for diagnosing the MS by employing easily measurable risk factors [3,6].

Specifically, the NCEP defines the MS as having 3 or more of the following 5 cardiovascular risk factors: Central obesity (waist circumference:

men >102 cm; women >88 cm); Elevated triglycerides (≥150 mg/dl); Diminished high-density lipoprotein (HDL) cholesterol (men <40 mg/dl; women <50 mg/dl); Systemic hypertension (≥130/≥85 mm Hg); and 5) elevated fasting glucose (≥110 mg/dl). In 2004, this NCEP definition was revised (rNCEP) by lowering the threshold for fasting glucose to ≥100 mg/dl in concordance with American Diabetes Association criteria for impaired fasting glucose[7]. Also, thresholds for central obesity were lowered from strictly >102 cm in men and 88 cm in women to greater than or equal to these values. Finally, the rNCEP definition includes patients being treated for dyslipidemia, hyperglycemia, or systemic hypertension.

A main evolving aspect of MS is its increasing prevalence in both childhood and young adulthood and the future implications to the global health burden this may confer. Clearly, the prevalence of MS varies and depends on the criteria used in different definitions, as well as the composition (sex, age, race and ethnicity) of the population studied[8]. No matter which criteria are used, the prevalence of MS is high and rising in all western societies, probably as a result of the obesity epidemic[9-11]. According to National Health and Examination Survey (NHANES) 2003-2006,[12] approximately 34% of people studied met the NCEP:ATP III revised criteria for MS. In countries from areas other than Europe and Africa, the IDF guidelines also identify a greater prevalence of MS than the NCEP:ATPIII[13-17]. A similar prevalence of MS in the Iranian population was recently reported, applying both the IDF and ATPIII criteria (32.1% and 33.2% respectively)[18].

In a recently published review of MS in south Asians,[19]it has been reported that one-third of urban population in large cities in different parts of

India have MS, while the prevalence rates are lower in rural areas[19,20]. Employing the IDF 2005 guidelines, MS was reported to be 29.7% in semi-urban south Indian population of Mangalore[21], which is similar (24.9%) to the present study from Lucknow (situated in north India) and has mixed data from largely a semi-urban and rural setting.

The emergence of obesity and MS in developing countries is related to a number of factors. Demographic transition (shift to low fertility, low mortality, and higher life expectancy), and epidemiological transition (from widely prevalent infectious diseases to a pattern of a high prevalence of lifestyle related diseases) evolved in developing countries as they become economically more resourceful, leading to significant shifts in dietary and physical activity patterns. These changes cause significant effects on body composition and metabolism, often resulting in an increase in BMI, generalized and abdominal obesity, and an increase in dyslipidemia and DM[22].

Despite advances in pathophysiology and delineation of risk factors that predispose to MS, there are many key aspects that remain unclear. The great variation in susceptibility and age of onset in individuals with a very similar risk profile, suggests a major interaction between genetic and environmental factors[23]. Although obesity and IR remain at the core of the pathophysiology of MS, a number of other factors such as chronic stress and deregulation of the hypothalamic-pituitary-adrenal (HPA) axis and autonomic nervous system (ANS), increases in cellular oxidative stress, renin-angiotensin-aldosterone system activity, and intrinsic tissue glucocorticoid actions, as well as currently

discovered molecules such as micro RNAs can also be involved in its pathogenesis[1].

All the components of the various MS definitions are involved in conferring risk for CVD and DM. In particular, the three components of atherogenic dyslipidemia (increased low-density lipoprotein) (LDL), decreased HDL and high triglyceride levels) are individually associated with a cardiovascular risk, while IR significantly increases the risk of developing DM, although approximately 25% of insulin resistant patients have normal glucose tolerance. Central obesity has been shown in several studies to be associated with an increased risk of CVD and DM[1].

GGT is shown to be an independent risk factor for the mortality and morbidity of cardiovascular diseases in recent epidemiological and clinical studies.[24]

GGT is an enzyme found in cell membranes of many tissues mainly in the liver, kidney, and pancreas.It is also found in other tissues including intestine, spleen, heart, brain, and seminal vesicles. The highest concentration is in the kidney, but the liver is considered the source of normal enzyme activity.[1]

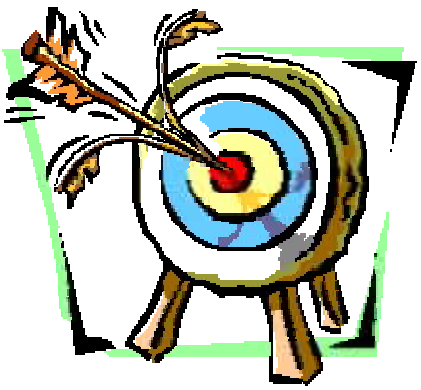
Prospective studies[25,26] have shown a significant relationship between serum GGT and the development of specific conditions including coronary heart disease (CHD) and stroke. In addition to alcohol, obesity has been found[27] to have a major effect on serum GGT, and there is increasing evidence linking raised serum GGT levels with other metabolic disturbances, such as glycemic disorder, hypertension, hypertriglyceridemia, and low HDL cholesterol. Excess

deposition of fat in liver, usually termed non-alcoholic fatty liver disease, is closely associated with elevated serum GGT, obesity, insulin resistance, and hyperinsulinemia[28]. These interrelations between serum GGT, obesity, other metabolic disturbances, and plasma insulin raise the possibility that elevated GGT levels can help predict the development of MS and DM. MS was found to be associated with increased GGT activity in a prospective study of Japanese men[28], in the Framingham Study and cross-sectionally among Turkish adults[30].

However to date, few studies have studies focused the relation between MS and GGT and the information is sparse on Indian population. Hence, the present study was undertaken to find the association of serum GGT levels in patients with MS and to correlate serum GGT levels with the different components of MS, so as to examine the relationship of serum GGT levels with each of the components of MS, which might provide clues to the preferential pathways operative in different cardio-metabolic risks.

Chapter 2

Objectives



OBJECTIVES

The objectives of the study were;

- To study the association of serum gamma glutamyl transferase levels in patients with metabolic syndrome.
- To correlate serum gamma glutamyl transferase levels with the different components of metabolic syndrome.

Chapter 3

Review of Literature

REVIEW OF LITERATURE

In 1923, Kylin first described the clustering of hypertension, hyperglycemia, and gout as a syndrome. In 1988, Reaven reintroduced the concept of "Syndrome X" for the clustering of cardiovascular risk factors, including resistance to insulin-stimulated glucose uptake, glucose intolerance, hyperinsulinemia, increased very-low-density lipoprotein (VLDL), and triglycerides, with decreased high-density lipoprotein (HDL) cholesterol, and hypertension.[31]

Subsequently, several other components to the syndrome, such as obesity and especially its central distribution, micro albuminuria, hyperuricemia, and abnormalities in haemostatic factors had been added.[32]

However, controversies still existed as to whether or not micro albuminuria is a component of the syndrome. In addition, the syndrome had been given several different names like the deadly quartet, the insulin resistance syndrome, the metabolic cardiovascular syndrome, the insulin resistance-dyslipidemia syndrome, and plurimetabolic syndrome.[33]

The name "insulin resistance syndrome" was been widely used and refers to insulin resistance as a common denominator of the syndrome. In 1999, the WHO proposed a unifying definition for the syndrome and chose it to call MS rather than the insulin resistance syndrome.[34]

The reason was mainly that it was not established that insulin resistance was the cause of all the components of the syndrome.

Definitions of MS

Despite abundant research on the subject of MS, the criteria used for diagnosing MS are different across studies, causing confusion when assessing prevalence rates across countries. To aid in the clinical practice and research of the syndrome, the WHO,[5] the EGIR,[35] the NCEP,[3] the AACE[36] and the IDF[4] have proposed different definitions.

The new IDF definition emphasizes the importance of central obesity defined by ethnic specific values. WHO,[5] EGIR,[35] NCEP,[3] AACE[36] and IDF[4] definitions of MS are as below.

WHO definition[5]

Diabetes (fasting plasma glucose ≥7.0 mmol/l and/or 2-hour plasma glucose ≥11.1 mmol/l), or impaired glucose regulation (fasting plasma glucose 6.1-6.9 mmol/l and/or 2-hour plasma glucose 7.8-11.0 mmol/l), and/or insulin resistance (below lowest quartile of glucose uptake in the euglycaemic), and two or more of the following:

- Raised triglycerides (≥1.7 mmol/l or > 150 mg/dL) and/or
- Low HDL-cholesterol (<0.9 mmol/l in men, < 1.0 mmol/l in women).
- Central obesity (waist-to-hip ratio >0.90 in men, >0.85 in women) and/or body mass index (BMI) >30 kg/m^2.
- Raised blood pressure (systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg).

- Micro albuminuria (urinary albumin excretion rate ≥20 μg/min or albumin/creatinine ratio ≥30 mg/g).

EGIR definition for non-diabetic individuals [35]

Hyperinsulinemia (fasting insulin concentrations in the highest quartile) and at least two of the following:

- Hyperglycemia (fasting plasma glucose ≥6.1 mmol/l or 110 mg/dL).
- Central obesity (waist circumference ≥94 cm in men, ≥80 cm in women).
- Hypertension (systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg or treated for hypertension).
- Dyslipidemia (triglycerides >2.0 mmol/l [>178 mg/dL] or low HDL-cholesterol < 1.0 mmol/l [<39 mg/dL] or treated for dyslipidemia).

NCEP definition[3]

Three or more of the following:

- Abdominal obesity (waist circumference >102 cm in men, >88 cm in women).
- Triglycerides ≥1.7 mmol/l (> 150 mg/dL).
- HDL-cholesterol < 1.03 mmol/l in men (< 40 mg/dL), <1.29 mmol/l in women (< 50 mg/dL).

- Systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥85 mmHg.

- Fasting plasma glucose ≥6.1mmol/l (≥ 110 mg/dL).

AACE definition for non-diabetic individuals[36]

Two or more of the following:

- Triglycerides ≥1.7 mmol/l (≥ 150 mg/dL).

- HDL-cholesterol < 1.03 mmol/l (< 40 mg/dL) in men, <1.29 mmol/l (< 50 mg/dL) in women.

- Systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥85 mmHg or current use of antihypertensive medications.

- 2-hour plasma glucose 7.8-11.0 mmol/l or fasting plasma glucose 6.1-6.9 mmol/l (IFG) (IFG was added in updated AACE criteria).

IDF definition[4]

Central obesity defined as ethnicity specific values of waist circumference (≥ 90cm for South Asian men and ≥80cm for South Asian women) and at least two of the following:

- Raised triglycerides levels (≥1.7 mmol/l or > 150 mg/dL), or specific treatment for this lipid abnormality.

- Reduced HDL-cholesterol (< 1.03 mmol/l or <40mg/dl in men, <1.29 mmol/l or <50mg/dl in women), or specific treatment for this lipid abnormality.

- Raised blood pressure (systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥85 mmHg), or treatment of previously diagnosed hypertension.

- Raised fasting plasma glucose (≥5.6 mmol/l or 100mg/dl), or previously diagnosed type 2 diabetes.

  If above 5.6 mmol/l, OGTT is strongly recommended but is not necessary to define presence of the syndrome.

Epidemiology

Prevalence

Applying the NCEP[13] definition of MS in a representative U.S. sample of 8,814 men and women aged 20 years and older from the Third National Health and Nutrition Examination Survey (1988-1994), the unadjusted and age-adjusted prevalence of MS was 21.8% and 23.7%, respectively. The prevalence increased from 6.7% among participants aged 20 through 29 years to 43.5% and 42.0% for participants aged 60 through 69 years and aged at least 70 years, respectively. Mexican Americans had the highest age-adjusted prevalence of MS (31.9%). The age-adjusted prevalence was similar for men (24.0%) and women (23.4%). However, African American women had a 57% higher prevalence than African American men did, and Mexican American women had a 26% higher prevalence

than Mexican American men did. Using 2000 census data, about 47 million U.S. residents have MS.[37]

The data from eight European studies, which included 8,200 men and 9,363 women, showed that in non-diabetic subjects, the frequency of the WHO-defined syndrome[28] varied between 7% and 36% for men aged 40 to 55 years, and for women of the same age, between 5% and 22%; the EGIR-defined syndrome was less frequent than the WHO-defined syndrome (1% to 22% in men, 1% to 14% in women 40-55 years).[38]

In another study based on 11 prospective European cohort studies comprising 6,156 men and 5,356 women without diabetes, and aged from 30 to 89 years, the age-standardized prevalence of MS defined by the modified WHO[28] definition was slightly higher in men (15.7%) than in women (14.2%). The overall prevalence of the WHO defined MS in non-diabetic adult Europeans is 15%.[39]

In Omani adults aged 20 years and over, living in the city of Nizwa, the age-adjusted prevalence of the NCEP-defined MS[13] was 21.0% (men: 19.5%, women: 23.0%).[40]

Among 40,698 Korean metropolitan subjects (26,528 men, 14,170 women) aged 20-82 years, the age-adjusted prevalence of the NCEP-defined MS[13] was 6.8% in total (5.2% male, 9.0% female). Using the Asia-Pacific criteria (APC) for abdominal obesity based on waist circumference (WC) (APC-WC: ≥ 90 cm in men, ≥ 80 cm in women), the prevalence rates of MS increased to 10.9% (9.8% male, 12.4% female). The subjects over 70 years of age had a 14-

fold increased risk for MS than those aged 20-29 years, and females had higher prevalence rates than males in age groups older than 50 years.[41]

The 1998 Singapore National Health Survey involving 4,723 men and women of Chinese, Malay, and Asian-Indian ethnicity aged 18-69 years, demonstrated that the age-adjusted prevalence rates of the NCEP-defined MS[13] were 9.4, 18.7, and 20.4% for Chinese, Malays, and Asian-Indians, respectively. Using the APC criteria, the analogous prevalence rates increased to 14.8, 24.2, and 28.8% for the three ethnic groups, respectively.[42]

The prevalence of the MS depends on age, ethnic background, and gender. It rises linearly from 20 to 50 years and plateaus thereafter. Looking at various studies around the world, which included population samples, aged from 20 to 25 and upwards, the prevalence varies from 8% (India) to 24% (United States) in men and from 7% (France) to 46% (India) in women.[43]

Two Indian studies, which differed in their definition of obesity, the first[44] used the obesity criteria suitable for Indians, while the second[45] used the standard ATP III definition of obesity. Both studies used population based samples within the age range but reported prevalence of 13% in Jaipur[45] and 41% in Chennai.[44] Although, the prevalence of obesity in the two study groups was quite similar (31% versus 33%), despite the different definitions used, far larger differences were observed between the two studies for the prevalence of elevated triglycerides (46% vs. 30%), hypertension (55% vs. 39%) and elevated fasting plasma glucose (27% vs. 5%); indicating a far larger impact of these risk factors than obesity alone.

Various Factors contributing to increasing prevalence of MS have been identified. These include, atherogenic dyslipidemia, Elevated Triglycerides, apolipoprotein B and small low-density lipoprotein, low HDL, elevated plasma glucose, blood pressure, pro-thrombotic and pro-inflammatory state.

Many studies[46-48] have reported that low socio-economic status is associated with a higher mortality rate due to cardiovascular disease. A low education level links cardiovascular disease with risk factors such as smoking, hypertension, impaired glucose tolerance, diabetes mellitus, physical inactivity and overweight associated with other metabolic abnormalities. The prevalence of MS increases with age, with about 40% of people older than 60 years meeting the criteria.[49] The MS affects 44% of the U.S. population older than age 50. A greater percentage of women older than age 50 have the syndrome than men. The age dependency of the syndrome's prevalence is seen in most populations around the world.

Components of MS and incident diabetes

There have been many prospective studies on the association between the components of MS, e.g. IFG, IGT, insulin resistance, overweight/obesity, hypertension, and dyslipidemia, and incident diabetes. Among these individual risk factors, the most important and consistent are impaired glucose regulation (IGR), obesity, and insulin resistance. However, studies in relation to prediction of other risk factors such as hypertension and dyslipidemia, to incident diabetes showed conflicting results due to differences in covariates or definition of

diabetes. Little information is available on whether or not micro albuminuria is an independent predictor of incident diabetes.

Impaired glucose regulation

Although, there is evidence that other factors such as age, family history of diabetes, waist-to-hip ratio (WHR), BMI, blood pressure (BP), and lipid levels are independently associated with the development of diabetes, none of the above, taken singly, is good at predicting as to who will progress to diabetes. IGT had been found to be a strong predictor of development of diabetes, before IFG was created as a new category of abnormal glucose metabolism.[50]

Since, the WHO approved new diagnostic criteria for the diagnosis of diabetes in 1999, the Hoorn Study has demonstrated that after adjustment for age, sex, and follow-up duration, the relative risks (RR) of incident diabetes were 10.0 and 10.9 for isolated IFG and isolated IGT, respectively, compared to normal glucose levels, while combined IFG and IGT were associated with a 39.5-fold increased risk of future diabetes.[51]

Obesity

Overweight, obesity, or weight gain has shown to be an important risk factor for the development of type 2 diabetes. In a cohort study of 51,529 U.S. male health professionals aged 40-75 years, a strong positive association between overall obesity as measured by BMI and risk of incident diabetes was observed during the 5-year follow-up.[52] In this study[52] men with a BMI of at least 35 kg/m2 had a multivariate RR of 42.1, compared to men with a BMI of less than

23 kg/m2 ($p<0.001$). Fat distribution, measured by WHR, was a good predictor of diabetes only among the top 5%, while WC was positively associated with the risk of diabetes among the top 20% of the cohort.

Of an age- and sex-stratified random sample of 1,000 individuals aged 40-79 years, the Bruneck Study confirmed that BMI was a predictor of incident diabetes, independently of other components of MS such as IFG, IGT, insulin resistance, hypertension, and dyslipidemia.[53]

Insulin resistance

In a prospective study of Pima Indians the 90th percentile of fasting insulin level was associated with a 15.8-fold increased risk of incident diabetes compared with the 10th percentile adjusted only for gender.[54]

The San Antonio Heart Study[55] (SAHS) of Mexican Americans and non-Hispanic whites reported that after adjustment for age, sex, ethnicity, BMI, and centrality, the top quartile of fasting insulin levels were significantly associated with a 2.3-fold increased risk of the development of diabetes over an 8-year follow-up.

Dyslipidemia

The results from the Norwegian population-based Finnmark Study showed that HDL cholesterol was inversely related to incident diabetes in women, but not in men, controlling for other risk factors such as BMI, diastolic blood pressure (DBP), glucose and ethnicity. However, triglycerides were

positively related to the incidence of diabetes in men and women adjusted for age.[56]

The MONICA (Monitoring of Trends and Determinants in Cardiovascular Disease) Augsburg Cohort Study[57] also displayed an inverse association between HDL-cholesterol and incident diabetes in both genders.

Hypertension

A questionnaire survey in the Netherlands among 5,700 men and women aged 20 to 65 showed that after adjusting for age and BMI, SBP and DBP were still associated with the incidence of diabetes (defined as the current use of oral hypoglycemic drugs and /or insulin) in men. For women, only the relative risk associated with the use of diuretics remained statistically significant.[58] The MONICA Augsburg Cohort Study[57] demonstrated that in multivariate analysis (controlling for age, BMI, HDL cholesterol, uric acid, alcohol intake, physical activity and survey), SBP predicted the development of diabetes in men also.[57]

A study[59] reported that the Swedish women whose SBP was at least 145 mm Hg had a risk to diabetes over 2.2 times that of women with a SBP of less than 145 mmHg, after adjusting for age, BMI, physical activity, TG, and total cholesterol.

Microalbuminuria

Microalbuminuria is a well-established marker for incipient nephropathy in patients with diabetes.[60]

In addition, micro albuminuria is associated with increased CVD in both diabetic and non-diabetic subjects.[61]

Previous studies reported that micro albuminuria in non-diabetic subjects was associated with MS, and suggested that micro albuminuria might be a feature of MS.[62]

However, multiple logistic regression analyses in diabetic and non-diabetic subjects separately showed that micro albuminuria was independently associated only with hypertension, diabetes and WHR, but not with other variables of MS in a Caucasian population. It is therefore likely that micro albuminuria is a complication of hypertension and diabetes, and not an integral part of MS.[63]

Mechanism of MS

Although the underlying mechanism of the syndrome is not completely understood, environmental factors such as obesity, sedentary lifestyle and inadequate diet, together with unknown genetic triggers, increase susceptibility to the syndrome.[64] The environmental factors in the mechanism of MS include birth weight, childhood obesity, smoking, alcohol, coffee, tea, social status and age.

Birth weight

Low birth weight and inadequate nutrition after birth are correlated with abnormal glucose tolerance, dyslipidemia and hyperinsulinemia in later adulthood.[64]

Of 64-year-old men whose birth weights were 2.95 kg or less, 22% had MS. Their risk of developing MS was more than 10 times greater than that of men whose birth weights were more than 4.31 kg.[65]

Childhood obesity

It has been suggested that the origins of adulthood risk of CVD and type 2 diabetes can be related to somatic growth as a child, not necessarily to intrauterine growth. In westernized countries, the relative proportion of underweight newborn children is decreasing; thus, considering the entire population's low birth weight has lost its theoretical role in the etiology of type 2 diabetes and CVD.[66]

Conversely, as obesity is known to be increasing in the industrialized countries among all age groups, the association between weight gain in childhood and MS in adulthood is more than noteworthy. The risk of MS was lower amongst obese adults, who had not been obese as children, compared to obese adults who had also been obese as children.[67]

A population study[66] in Finland found that among obese children at the age of seven (BMI in the highest quartile), the OR for MS in adulthood was 4.4 (95% CI 2.1-9.5) as compared to the other children (the three other quartiles combined). After adjustment for age, sex and current obesity, the risk of the syndrome still was 2.4 (95% CI 2.1-9.5).

Smoking

The results of 54 published studies displayed that overall, smokers had significantly higher serum concentrations of cholesterol, TG, VLDL cholesterol, and low-density lipoprotein (LDL) cholesterol, and lower serum concentrations of HDL cholesterol and apolipoprotein AI compared with non-smokers.[68]

It was shown that the measures of insulin sensitivity were significantly lower in smokers when the degree of insulin-mediated glucose uptake (insulin sensitivity) was compared in smoking and non-smoking men.[69]

Among those who smoked at least two packs per day at baseline, men had a 45% higher diabetes rate than men who had never smoked; the comparable increase for women was 74%. Quitting smoking reduced the rate of diabetes to that of non-smokers after five years in women and after ten years in men.[70]

Recently, a study on Koreans reported that smoking (more than 20 pack-years) was associated with a 1.4-fold and 1.9-fold increased risk of high triglycerides and low HDL-cholesterol. The relative risk of developing NCEP-defined MS in smokers (more than 20 pack-years) was 1.9-fold higher compared with non-smokers although there was no significant difference in blood pressure in the smoking group.[71]

Alcohol

Epidemiological studies have shown an association between light to moderate alcohol consumption and reduced risk of MS and developing type 2 diabetes. Some of the biological mechanisms reported to explain this observation

include an improvement of the lipid profile, especially HDL cholesterol and increasing insulin sensitivity.[71]

Recently, a cross-sectional analysis on data from 8,125 participants in the U.S. showed that after adjustment for age, sex, race/ethnicity, education, income, tobacco use, physical activity, and diet, subjects who consumed 1-19 and >20 drinks of alcohol per month had ORs for the prevalence of the NCEP defined-MS of 0.65 and 0.34, respectively ($P < 0.05$), compared with current nondrinkers. These findings were particularly noteworthy for beer and wine drinkers. Alcohol consumption was significantly and inversely associated with the prevalence of the following four components of MS: low serum HDL cholesterol, elevated serum triglycerides, high WC and hyperinsulinemia.[79]

Although, alcohol consumption had a significant inverse relation with the OR for low HDL cholesterol in all alcohol groups, and lower alcohol consumption had a favorable effect on MS, an increasing dose-response relation was found between alcohol consumption and the OR for MS in a Korean population. In this population, heavy alcohol consumption of at least 30 g per day was associated with significantly higher ORs for high blood pressure, and high triglycerides in men and high fasting blood glucose and high triglycerides in women. ORs for the NCEP-defined MS and its components tended to increase with increasing alcohol consumption.[74]

Coffee

Intake of coffee is often reported as a cardiovascular risk factor. However, no clear association between coffee and the risk of hypertension, total cholesterol,

LDL-C levels, myocardial infarction, or other cardiovascular diseases has been demonstrated.[75] Furthermore; coffee consumption was related to improved insulin sensitivity.[76]

Several studies[77,78] on Dutch, Japanese, American, and Swedish population have shown that coffee consumption was associated with a substantially lower risk of clinical type 2 diabetes, although the reasons for this risk reduction remain unclear.

A Finnish study[79] reported that in 6,974 Finnish men and 7,655 women aged 35 to 64 years during a mean follow-up of 12 years, after adjustment for confounding factors (age, study year, BMI, SBP, education, occupation, commuting, leisure-time physical activity, alcohol and tea consumption, and smoking), the hazard ratios of diabetes associated with the amount of coffee consumed daily (0-2, 3-4, 5-6, 7-9, >10 cups) were 1.00, 0.71 (95% CI, 0.48-1.05), 0.39 (0.25-0.60), 0.39 (0.20-0.74), and 0.21 (0.06-0.69) in women, and 1.00, 0.73 (0.47-1.13), 0.70 (0.45-1.05), 0.67 (0.40-1.12), and 0.45 (0.25-0.81) in men, respectively. In both sexes combined, the multivariate-adjusted inverse association was significant and persisted when stratified by younger and older than 50 years; smokers and non-smokers; healthy weight, overweight, and obese participants; alcohol drinkers and non-drinkers; and participants drinking filtered and non-filtered coffee.

Tea

The results of experimental studies[80,81] have shown the protective effect of tea in improving lipid and glucose metabolism and enhancing insulin sensitivity.

A study[82] from Taiwan showed that Oolong tea significantly decreased plasma glucose (from an initial concentration of 229±53.9 to 162.2±29.7 mg/dl), whereas water did not (from 208.7± 61.0 to 232.3±63.1 mg/dl). Fructosamine concentration decreased significantly (from 409.9± 96.1 to 323.3±56.4 µmol/l with the tea treatment) but did not change significantly with water treatment (from 368.4±85.0 to 340.0±76.1 µmol/l). This study supports the concept that Oolong tea is effective in lowering the plasma glucose levels of subjects who have type 2 diabetes.

However, the epidemiological evidence, data released from recent the cohort study[77-79] of diverse countries (the Netherland, the U.S., Sweden and Finland), failed to show the same association as coffee on the risk of type 2 diabetes.

Diet

Dramatic changes in the prevalence or incidence of type 2 diabetes have been observed in communities where there have been major changes in the type of diet consumed, from a traditional indigenous diet to a typical 'Western' diet, e.g. Pima Indians in Arizona, Micronestans in Nauru and Aborigines in Australia.[83-95]

For Pima Indians in Arizona, the transition from an agrarian to a modern society was associated with the consumption of increasing amounts of dietary fat, decreasing amounts of dietary carbohydrates, and deterioration in insulin sensitivity.[86]

Most developing countries have experienced a shift in the overall structure of its dietary pattern with related disease patterns over the last few decades. Major dietary change includes a large increase in the consumption of fat and added sugar in the diet, often a dramatic increase in animal food products contrasted with a fall in total cereal and fiber intake.[87]

The traditional lifestyle of Chinese has changed markedly over two decades with rapid development of its economy. According to 4th CNHS, fat consumption in the diet increased from 28% in 1992 to 35 % of total energy intake in 2002 in urban areas, while carbohydrate consumption decreased from 57% in 1992 to 47% of total energy intake in 2002. In contrast, the analogous values of fat intake were 19%, 28% (carbohydrate: 72%, 61%), respectively, in rural areas. In developed countries, i.e. in the U.S., a demographic shift toward an overall positive energy balance that has increased over the past few decades has been observed. It has been estimated that Americans consumed an average of 340 kcal/day more in 1994 than in 1984 and 500 kcal/day more than in 1977.[88]

In humans, intakes high in total fat and saturated fat, and intakes low in carbohydrates or starches and fiber, correlated with higher fasting insulin concentrations.[89]

High total fat intake has also been associated with a lower insulin sensitivity index. In both Pima Indians and Caucasians, glucose-mediated glucose disposal, beta-cell function, and glucose tolerance deteriorated in the modern diet (carbohydrate, 30%; fat, 50%; protein, 20%).[90]

A high fat intake has been shown to predict development of IGT in a group of healthy subjects and progression from IGT to type 2 diabetes in a group of subjects with IGT.[91]

Higher proportions of saturated fatty acids in serum lipids/muscle phospholipids have been associated with higher fasting insulin levels, lower insulin sensitivity, and a higher risk of developing type 2 diabetes.[92]

A high intake of trans-fatty acids was also associated a higher risk of diabetes. However, higher vegetable fat (unsaturated fat) and polyunsaturated fatty acids (PUFAs) intake have been associated with a lower risk of type 2 diabetes, as well as lower fasting and 2-hour glucose concentrations.[93]

A whole-grain diet resulted in higher concentrations of insulin sensitivity and lower concentrations of fasting insulin than did a refined-grain diet, while increasing intakes of refined carbohydrates (corn syrup) concomitant with decreasing intakes of fiber paralleled the upward trend in the prevalence of type 2 diabetes.[94]

Physical inactivity

Low levels of physical activity are associated with most components of MS, especially with an increased risk of obesity. Advances in technology and

transportation have reduced the need for physical activity in daily life. Labor-saving devices have eliminated many of back-breaking tasks of agricultural- and industrial-sector occupations and reduced the time it takes to complete them. The appeal of television, electronic games, and computers has increased the time spent in sedentary pursuits among children and adults.[95]

A cohort study (1989 to 1997) from 2,485 adults aged 20 to 45 years from eight provinces in China found that after adjustment of age, work, leisure activity, energy intake, smoking status, alcohol consumption, income, education, household ownership of a computer and TV, and urban residence, the odds of being obese were 70% higher for men and 85% higher for women in households who owned a motorized vehicle compared with those who did not own a vehicle.[96]

Insulin resistance plays a central role in MS, being associated with most of the other metabolic abnormalities in the syndrome.[97]

Physical training has mostly been shown to improve insulin sensitivity in healthy humans regardless of age, in obese non-diabetic subjects, and in patients with type 2 diabetes.[98] Exercise also has pronounced effects upon the metabolism of glucose because exercising muscle may increase glucose uptake 7- to 20-fold.[99]

The Finnish Diabetes Prevention Study (DPS)[100] and the Diabetes Prevention Program (DPP)[101] in the United States revealed a 58% reduction in the risk of diabetes in high-risk subjects who enhanced physical activity.

The DPS[100] also found that the intervention group had a significant decrease in serum concentrations of 2-h post-load insulin and TG, and a marked increase in HDL cholesterol levels compared with the control group.

A cross-sectional survey[102] in an urban area of the city of Tianjin, China, found that daily walking or cycling to and from work was inversely associated with serum total cholesterol, LDL cholesterol, and TG concentrations among men, and was positively associated with HDL cholesterol concentrations among women as compared to traveling to and from work by bus.

A meta-analysis[103] of 25 longitudinal studies examining the antihypertensive effect of exercise showed reductions in resting SBP and DBP of 11 and 8 mmHg, respectively. However, the decrement in BP evoked by exercise was not sufficient to produce normotension in many studies.

Obesity

Obesity is becoming increasingly common worldwide due to adoption of a more sedentary lifestyle and an increased intake of energy-rich diets. It is well accepted that obesity, as the core of MS, promotes glucose intolerance, insulin resistance, hypertension, and dyslipidemia, and is associated with the development of type 2 diabetes and coronary heart disease.[104]

The 4th CNHS[105] showed that the prevalence of obesity (BMI >30) and overweight (BMI >25) has increased by 97% and doubled, respectively, between 1992 and 2002 in Chinese adults.

Obesity and weight gain are important determinants of clustering of the individual traits of MS. A study in Hong Kong Chinese men showed, after adjustment for age, smoking, and insulin resistance, increasing BMI and WHR remained closely associated with increased concentrations of TG and apo B, increased ratios between LDL and HDL (LDL/HDL) cholesterol, and between apo B and LDL (apo B/LDL), increased fasting and 2-h plasma glucose and insulin, as well as decreased concentrations of HDL, and apolipoprotein A-I (apo A-I).[106]

The relationship between insulin sensitivity and overall obesity is well established. Furthermore, visceral abdominal tissue (VAT) and subcutaneous abdominal tissue (SAT), which were measured from computed tomography scans performed at the L4/L5 vertebral region, and their joint interactions were each inversely and significantly associated with ISI, adjusting for age, sex, ethnicity, and BMI. SAT, but not VAT, was positively associated with acute insulin response (AIR). Thus, fat distribution is an important determinant of both insulin resistance and insulin secretion.[107]

The NHANES II (National Health and Nutrition Examination Survey II) study[108] found obese women to be four times more likely to develop diastolic hypertension than non-obese women.

In the Framingham population,[109] weight gain had a stronger relationship with blood pressure in males than in females.

There appears to be a consensus that obesity is an important risk factor of type 2 diabetes.[110]

Presentation

History

As with other diseases, careful history taking is important in MS. Even though the condition is diagnosed based on physical and laboratory features, it may be suspected if symptoms of any of the component disorders are present, such as the increased hunger, thirst, or urination that may accompany hyperglycemia. Patients reporting a history of hypertension, dyslipidemia warrant screening for MS. Symptoms suggesting the rise of cardiovascular and other complications, such as chest pain or shortness of breath, must be investigated carefully. As lifestyle changes can ameliorate the condition, attention should be paid to the patient's dietary habits and exercise routines so that areas for improvement can be identified.

The social history is important for identifying additional risks, such as tobacco use, which may exacerbate the increased cardiovascular complications associated with MS. A family history should be obtained because genetics may play an important role in MS. This feature of the disease is under active investigation; however, currently no gene or group of genes has been implicated consistently, suggesting that the environment exerts substantial influence.[111] Finally, a thorough review of systems may help identify related problems, such as menstrual irregularities that can be seen in polycystic ovarian syndrome.

Physical examination

The physical examination is crucial in patients with MS as the findings of elevated blood pressure and abdominal obesity are 2 of the 5 diagnostic criteria. Measurement and documentation of waist circumference are important routines when screening for MS. Additionally, the examination may reveal findings reflective of the other criteria. For example, patients with insulin resistance and hyperglycemia or diabetes mellitus may have acanthosis nigricans, hirsutism, peripheral neuropathy, and retinopathy. Patients with severe dyslipidemia may have xanthomas or xanthelasmas. The presence of arterial bruits may portend a higher risk of cardiovascular complications.

Diagnosis

Initial laboratory studies in patients suspected of having MS should include standard chemistries to assess for hyperglycemia and renal dysfunction and lipid studies to assess for hypertriglyceridemia or low HDL levels.

If a family history of early coronary or other atherosclerotic disease is present, consider including, in addition to HDL-C and low-density lipoprotein cholesterol (LDL-C), studies of lipoprotein(a), apolipoprotein-B100, high-sensitivity C-reactive protein (CRP), and (if the patient does not already merit the lowest LDL-C target [< 70]), homocysteine and fractionated LDL-C.

In view of the various associations between MS and other conditions discussed, additional helpful blood tests may include thyroid and liver studies, hemoglobin-A1C levels, and uric acid. Hyperuricemia appears to be much more

common in patients with MS than in the general population, and this is attributed to the inflammatory effects of MS.[112]

A significant relationship is postulated between serum GGT and the development of specific conditions including coronary heart disease (CHD) and stroke. In addition to alcohol, obesity has been found to have a major effect on serum GGT, and there is increasing evidence linking raised serum GGT levels with other metabolic disturbances, such as glycemic disorder, hypertension, hypertriglyceridemia, and low HDL cholesterol. Excess deposition of fat in liver, usually termed nonalcoholic fatty liver disease, is closely associated with elevated serum GGT, obesity, insulin resistance, and hyperinsulinemia. These interrelations between serum GGT, obesity, other metabolic disturbances, and plasma insulin raise the possibility that elevated GGT levels can help predict the development of MS and type 2 diabetes.[28]

Non-alcoholic fatty liver disease (NAFLD), accounting for asymptomatic elevation of aminotransferase levels in up to 90% of cases, is the most frequent cause of abnormal liver function tests results.[24]

NAFLD covers a wide spectrum of hepatic lesions including simple fatty infiltration of the liver, steatohepatitis with necroinflammatory changes and a variable degree of fibrosis which may finally progress to liver cirrhosis. Fatty liver is now believed to be an integral part of the MS, since it has been shown to be independently related to insulin resistance independent of obesity and abdominal adiposity.[24]

GGT is shown to be an independent risk factor for the mortality and morbidity of cardiovascular diseases in recent epidemiological and clinical studies. In addition, 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[113,114]

Hence it is postulated that, raised liver enzymes, as relatively sensitive and easily obtained markers of NAFLD, reflect chronic ectopic fat deposition in the liver that may be useful in MS diagnosis.[24]

GAMMA-GLUTAMYL TRANSFERASE (GGT)

It is a peptidase that catalyzes the transfer of the γ-glutamyl group from a peptide gamma-glutamyl-peptide to an acceptor peptide or an L-amino acid. It is equally effective at removing the γ-glutamyl group from simpler compounds such as N- γ-glutamyl naphthylamide and N- γ-glutamyl-p-nitroanilide.[10]

$$\text{Glutathione + Amino acid} \xrightarrow{\text{GGT}} \text{glutamyl peptide + L-cysteinyl glycine}$$

It is a microsomal glycoprotein enzyme, first recognized by Hanes et al. in 1952. In most biological systems, glutathione serves as γ-glutamyl donor. This enzyme was originally termed as transpeptidase but the more appropriate term is transferase.

GGT in the serum has a molecular weight of 90,000 daltons, as measured by electrophoresis. The main fraction of normal serum migrates with the fast α2-globulins, while two minor bands of activity are found with the slow α2-globulins. The activity of the minor band is considerably increased in hepatitis

and biliary obstruction, but the diagnostic value of GGT isoenzymes remains to be established.

Tissue distribution

The enzyme was first identified in kidney tissue where its concentration is very high but significant amounts occur in the liver and pancreas and only minor quantities in the intestine, heart and other tissues. It has thus proved useful in the investigation of disease of liver and biliary system.[115]

Functions of GGT

It has been suggested that GGT is involved in;

1) The transport of amino acids and peptides into the cell across the cell membrane in the form of γ-glutamyl peptides as the larger fraction of the enzyme is located in the cell membrane.

2) Peptide and protein biosynthesis.

3) Regulation of tissue glutathione levels and its metabolism.[116]

Clinical Significance

Even though, renal tissue has the highest level of GGT, the enzyme present in serum appears to originate primarily from the hepatobiliary system, and GGT activity is elevated in any and all forms of liver diseases.

In the liver, GGT is located in the canaliculi of the hepatic cells, and particularly in the epithelial cells lining the biliary ductules. In the liver cell, the

enzyme exists in two forms, a minor soluble form of low molecular weight in the cell, and a high molecular weight membrane bound microsomal component. Higher levels are generally observed in biliary tract obstruction. It is highest in cases of intrahepatic or post hepatic biliary obstruction, reaching levels five to 30 times normal. It is more sensitive than alkaline phosphatase (ALP), arylamidase and the transaminases in detection of obstructive jaundice, cholangitis and cholecystitis. The rise in GGT activity occurs earlier in these diseases than do these other enzymes and persists longer. Moderate elevations (two to five times normal) occur in infectious hepatitis.

Elevated levels of GGT are noted in the sera of individuals with alcoholic cirrhosis and in the majority of sera from those who drink heavily and in individuals receiving drugs such as phenytoin, Phenobarbital. The release of GGT into serum reflects the toxic effects of alcohol and other drugs on microsomal structures in liver cells, as within the hepatic parenchyma, GGT exists to a large extent in the smooth endoplasmic reticulum and is therefore subjected to hepatic microsomal induction. Hepatic complications occurring in cases of cystic fibrosis (mucoviscoidosis) also lead to elevations of GGT.

Patients with primary or secondary hepatic malignancy with jaundice almost invariably have raised GGT activities with levels averaging fifteen times the upper limit of normal.

GGT activity in serum can be elevated in some non-hepatic disorders such as acute pancreatitis, carcinoma head of the pancreas, congestive cardiac failure, myocardial infarction (MI) and diabetes mellitus (DM).

In cases of acute and chronic pancreatitis, and in some pancreatic malignancies (especially those associated with hepatobiliary obstruction), enzyme activity may be five to 15 times the upper limit of normal. Normal levels of the enzyme are found in cases of skeletal disease (Paget's disease, bone neoplasms), children older than one year, and healthy pregnant women, and in all conditions in which ALP is elevated. Thus, measurement of GGT levels in serum helps ascertain whether observed elevations of ALP are caused by skeletal disease or reflect the presence of hepatobiliary disease.

Serum GGT levels and MS

A study on 3451 Framingham Study participants (mean age 44 years, 52% women) examined the relations of GGT with CVD risk factors, and prospectively determined the risk of new-onset MS, incident CVD, and death. GGT was positively associated with body mass index, blood pressure, LDL cholesterol, triglycerides, and blood glucose in cross-sectional analysis ($P<0.005$). On follow-up (mean 19 years), 968 participants developed MS, 535 developed incident CVD, and 362 died. The risk of MS increased with higher GGT (multivariable-adjusted hazard ratio [HR] per SD increment log-GGT, 1.26 [95%CI; 1.18 to 1.35]). Adjusting for established CVD risk factors (as time-dependent covariates updated quadriennially) and baseline CRP, a 1-SD increase in log-GGT conferred a 13% increase in CVD risk ($P=0.007$) and 26% increased risk of death ($P<0.001$). Individuals in the highest GGT quartile experienced a 67% increase in CVD incidence (multivariable-adjusted HR 1.67, 95%CI; 1.25 to 2.22). The study concluded an increase in serum GGT predicts onset of MS,

incident CVD, and death suggesting that GGT is a marker of metabolic and cardiovascular risk.[29]

A study from Turkey on 754 men and 802 women reported doubling in GGT activity and found to be associated with a rise of 74% in MS (MS) likelihood-independent of salient confounders ($p<0.001$). This association was mediated by waist circumference. Individuals in the top versus the bottom tertile exhibited an odds ratio for CHD likelihood of 1.81 (95% CI 1.09; 3.02)-independent of age, sex, total cholesterol, systolic blood pressure, impaired fasting glucose, smoking status, alcohol usage and, notably, of waist circumference. This indicated that a doubling in serum GGT activity corresponded to a 45% excess in CHD likelihood, after adjustment for standard risk factors. In conclusion, waist circumference was a major determinant of serum GGT activity among Turkish adults. Doubling in activity was associated with a (largely waist girth mediated) rise by over one-half in the multi-adjusted MS likelihood, and by nearly one-half in the CHD likelihood, independent of waist girth and major risk factors.[30]

A cross-sectional study from Japan recruited 793 men (mean age, 60+/-14 years), and 1,073 women (62+/-12 years), free from any history relating to cardiovascular disease during their annual health examination, from a single community to examine whether serum GGT was associated with MS. The levels of most confounding characteristics varied with increasing GGT activity. After adjustment for age, smoking status, drinking status, low-density lipoprotein cholesterol, uric acid, estimated glomerular filtration rate and alanine aminotransferase, the odds ratios (95% confidence interval) for MS increased

across serum GGT tertiles (1, 2.23 (1.224.07), and 2.32 (1.184.56) in men; and 1, 1.43 (0.812.51), and 2.64 (1.504.64) in women). After additional adjustment for insulin resistance markers (immuno-reactive insulin or homoeostasis model assessment of insulin resistance index), the association was attenuated and the linear relation no longer significant in both genders. Furthermore, serum GGT was significantly associated with the presence of individual components of MS in both genders, except for dyslipidemia in men and hypertension in women. Study concluded that, higher serum GGT was significantly associated with MS and its components in the general population. This association was related with insulin resistance but was independent of other confounding factors.[117]

A cross-sectional, single-center study to know if the liver function tests (LFT), especially GGT, have a predictive value in diagnosis of MS was carried out with 908 subjects. Four hundred and forty two of these subjects were diagnosed with MS with IDF criteria; while other 466 were sex and age matched healthy control subjects. Blood pressure, liver function tests, fasting blood glucose levels and lipid profile of the subjects were recorded. The mean values of alanine amino transferase (ALT), aspartate aminotransferase (AST) and GGT levels were statistically significantly higher in MSMS group. The mean values of liver enzymes, for female/ male subjects in MSMS group, AST; ALT and GGT respectively, were; 20.5/19.7 U/l; 25.9/28.5 U/l; 35.9/42.1 U/l. When the sample is divided into quartiles of the GGT levels, increase in GGT is positively correlated with increased MS prevalence. In ROC analysis GGT is as strongly associated with the IDF diagnostic components as is each individual IDF component, except elevated systolic blood pressure. In covariance analysis, there

was significant relationship between elevated GGT levels and MS presence after adjustment for age, sex and MS diagnostic criteria; but not AST and ALT levels. In multivariance analysis, in MS group, a high GGT was positively associated with CVD prevalance (odds ratio: 2.011, 95% CI 1.10-4.57) compared to low GGT group independent of age, sex and smoking habits. Overall, elevated liver enzymes, although in normal ranges, especially at upper quartiles, played a central role in early diagnosis of fat overflow to the liver. Authors recommended that, regarding the availability and simplicity of these tests in routine clinical practice, they, especially GGT, have potential to be considered in algorithms for MS.[24]

Another study to investigate the association between serum GGT and risk of MS and type 2 diabetes in Japanese male office workers included 2,957 MS free men and 3,260 non-diabetic men aged 35–59 years who did not have medication for hepatitis, ALT levels higher than three times the upper limit of the reference range, or a history of cardiovascular disease at study entry. Subjects were re-examined at periodic annual health examinations over a 7-year period. A modified National Cholesterol Education Program definition of MS with BMI instead of waist circumference was used and the revised criteria of the American Diabetes Association for type 2 diabetes. With adjustment for age, family history of diabetes, BMI, alcohol intake, cigarette smoking, regular physical activity (fasting plasma glucose for the risk of type 2 diabetes), and white blood cell (WBC) count, the risk of MS and type 2 diabetes increased in correlation with the levels of serum GGT, ALT, aspartate aminotransferase (AST), and alkaline phosphatase. Additional adjustment for all of the other liver enzymes attenuated

these associations, but serum GGT remained a significant risk factor for the risk of both MS and type 2 diabetes (*P* for trend_0.001 for both). Top one-fifth versus bottom one-fifth relative risks of MS and type 2 diabetes were 2.23 (95% CI 1.51–3.30) and 2.44 (1.34–4.46), respectively. Study concluded that, serum GGT may be an important predictor for developing MS and type 2 diabetes in middle-aged Japanese men.[28]

A study examined the association between serum GGT levels and the incidence of the MS in Korean male office workers. The study population consisted of 32,692 office workers who underwent health checkups in both 2005 and 2009. A total of 17,583 with elevated GGT levels, the presence of MS, medication history at baseline, and female office workers were excluded. Finally, 15,109 subjects were included in the final analysis. As a quartile of serum GGT increased, 4-year follow-up incidence of the MS increased. After adjustment for age, alcohol drinking status and smoking status in 2005, logistic regression analysis showed that the odds ratios (95% confidence interval) for incident MS in 2009 compared to the lowest quartile and upper quartiles were 1.00 (reference), 1.57 (1.24-2.00), 2.73 (2.17-3.43), 3.78 (3.02-4.74), and statistically significant ($p<0.001$), respectively. Authors concluded that, the higher serum GGT predicted the future development of MS.[118]

A cohort of 1,667 adults of a general population (age 52 ±11 years) was evaluated prospectively at 4 year's follow-up using partly Cox proportional hazard regressions in Turkey. GGT activity was measured kinetically, and values were log-transformed for analyses. MS was identified by Adult Treatment Panel-III criteria modified for male abdominal obesity. Median (interquartile range)

GGT activity was 24.9 (17.0; 35.05) U/l in men, 17.0 (12.3; 24.0) U/l in women. In linear regression analysis, while smoking status was not associated, (male) sex, sex dependent age, alcohol usage, BMI, fasting triglycerides and C-reactive protein (CRP) were significant independent determinants of circulating GGT. Each 1-s.d. increment in (= 0.53 ln GGT) GGT activity significantly predicted in each sex incident hypertension (hazard ratio (HR) 1.20 (95% confidence interval (CI) 1.10; 1.31)), and similarly MS, after adjustment for age, alcohol usage, smoking status, BMI and menopause. Strongest independent association existed with diabetes (HR 1.3 (95% CI 1.1; 1.5)) whereas GGT activity tended to marginally predict CHD independent of total bilirubin but not of BMI. Higher serum total bilirubin levels were protective against CHD risk in women. Study concluded that, elevated serum GGT confers, additively to BMI, risk of hypertension, MS, and type 2 diabetes but only mediates adiposity against CHD risk.[119]

Another study sought to evaluate serum GGT activity in patients with MS (MS) enrolled 232 patients (mean age 60.4 years) from outpatient cardiology clinic, 117 with and 115 without MS (control group) as defined by the ATP-III criteria. The results of serum liver function tests including serum GGT and C-reactive protein (CRP) levels were compared between the two groups. The two groups were similar with regard to age, sex, smoking, and family history of coronary artery disease ($p>0.05$). The prevalences of hypertension and dyslipidemia were significantly higher in patients with MS. Compared with controls, patients with MS had significantly higher serum GGT [(median 21, interquartile range (16-33) vs. 19 (14-26) U/l; $p=0.008$] and C-reactive protein

levels [6.2 (3.6-9.4) vs. 5.0 (3.1-7.0) U/l; p=0.044]. A high GGT activity (>40 U/l) was determined in 14.5% of the patients with MS and in 4.4% of the control subjects (p=0.012). Serum GGT level showed significant correlations with MS (r=0.24, p=0.001), CRP (r=0.20, p=0.003), triglyceride (r=0.18, p=0.006), HDL cholesterol (r=-0.19, p=0.004), aspartate aminotransferase (r=0.15, p=0.02), alanine aminotransferase (r=0.32, p=0.001), and alkaline phosphatase (r=0.16, p=0.01). This significant association continued only for MS (β=-0.25, p=0.03), HDL cholesterol (β=-0.18, p=0.03), and alkaline phosphatase (β=0.17, p=0.01) in multivariate regression analysis. The study findings suggested that, patients with MS have higher serum GGT and CRP levels compared with controls. This increased GGT level might be a marker of increased oxidative stress and premature atherosclerosis.[120]

Chapter 4

Methodology

METHODOLOGY

This study was conducted in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on patients with metabolic syndrome during the period of January 2012 to December 2013.

Study design

The study design was cross sectional study.

Study period and duration

The present one year study was conducted from January 2012 to December 2012.

Source of Data

Patients admitted in the wards of Medicine Department or attending the Medicine OPD/executive health check-up schemes, Wednesdays and Fridays at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum were enrolled.

Sample size

A total of 100 patients with metabolic syndrome were selected for the study.

Sampling procedure

The sample size was calculated based on the formula as mentioned below.

$n = 4 \times p \times q / d^2$

Where, p = Prevalence of the disease was considered as 50% due to scarcity of data on metabolic syndrome from hospital records

q = 100 – p

d = Absolute error taken as 10%

Therefore, $n = 4 \text{ X } 50 \text{ X } 50 / 10^2$

n = 100

Sampling method

Every third patient fulfilling the inclusion criteria will be included in the study.

Selection criteria

Inclusion Criteria

- Age above 18 years.
- All in-patients/patients attending Medicine OPDs/executive health check-up schemes who fulfill the IDF criteria[4] for the diagnosis of metabolic syndrome that is;
    - Waist Circumference
        - Men >90 cm
        - Women >80 cm
    - Fasting triglycerides - >150 or on specific medication
    - HDL cholesterol levels
        - Men < 40 mg/dL

- Women <50mg/dL

- Blood pressure
  - Systolic >130 mm Hg
  - Diastolic >85 mmHg or
  - On specific medication or previously diagnosed
- Fasting plasma glucose levels
  - >100 mg/dL or
  - Previously diagnosed type 2 diabetes

Exclusion Criteria

- Patients with abnormal AST/ ALT/ raised bilirubin.
- Patients with history of alcohol consumption.
- Patients with past H/O Jaundice, viral hepatitis.
- Known history of chronic inflammatory conditions like RA, SLE, Scleroderma.
- Drugs like phenytoin and Benzodiazepines

Ethical clearance

Prior to the commencement, the study was approved by the Institutional Ethics Committee of Jawaharlal Nehru Medical College, Belgaum.

Informed consent

Patients admitted in the wards of Medicine Department or attending the Medicine OPD/executive health check-up schemes on Mondays, Wednesdays and Fridays at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre,

Belgaum were evaluated based on selection criteria. The selected patients were briefed about the nature of the study and a written informed consent was obtained (Annexure–I).

Data collection

Demographic data like gender and age were collected along with relevant history and recorded on predesigned and pretested proforma (Annexure-II). A thorough clinical examination was conducted and the findings were also recorded.

Investigations

Under aseptic precautions fasting blood sample was collected and following investigations were carried out.

- Estimation of Serum Gamma glutamyl Transferase
- Estimation of hs-CRP
- Blood glucose
- Lipid profile (total cholesterol, triglycerides, HDL, LDL)
- Insulin levels
- HbA1c
- Total leucocyte count
- Fasting blood sugar

Study variables

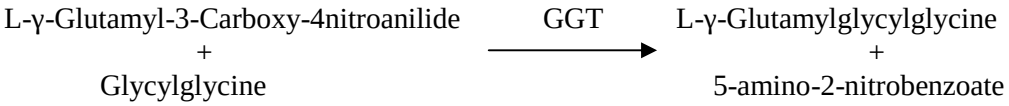
Estimation of gamma glutamyl transferase in serum by carboxy substrate method[121]

Collection of Blood Samples

About five ml of venous blood was collected from antecubital vein under aseptic precautionary measures using sterile disposable syringe. The blood was allowed to clot and serum was separated by centrifugation and stored at 4°C. The estimation of parameters were carried out immediately. Serum GGT was estimated using Carboxy substrate method.[121]

Principle

Gamma glutamyl transferase catalyzes the transfer of amino group between L-γ-Glutamyl-3-carboxy-4 nitroanilide and glycylglycine to form L-γ-glutamylglycyl glycine and 5-amino-2-nitrobenzoate. The rate of formation of 5-amino-2-nitrobenzoate is measured as an increase in absorbance which is proportional to the GGT activity in the sample.



The estimation of GGT was done using Automatic analyzer Flex reagent cartridge manufactured by Siemens Dimension Clinical Chemistry System.[121]

Reference values

Normal reference range: 5 to 85 U/L

Body mass index

Body mass index was calculated based on formula;

$$\text{Body Mass Index} = \frac{\text{Weight (Kg)}}{\text{Height}^2 \text{ (m)}}$$

Body mass index in the range of less than 18.5 kg/m^2 were considered as underweight, 18.5 to 24.9 kg/m^2 were considered as normal, 25.0 to 29.9 kg/m^2 were considered as overweight and more than 30 kg/m^2 were considered as obese.[122]

Waist circumference

The waist circumference was measured using a standard measuring tape in cms and interpreted based on IDF criteria[4] for the diagnosis of metabolic syndrome.

Blood pressure

Blood pressure was recorded in the sitting position after five minutes of rest using standard mercury manometer. Three readings were taken at an interval of one minute and mean BP was calculated. The interpretation was done according to IDF criteria[4] for the diagnosis of metabolic syndrome.

Fasting blood sugar and lipid profile

Fasting blood samples were drawn for investigations and interpretation of fasting blood sugar, HDL and triglycerides was done based on IDF criteria[9] for the diagnosis of metabolic syndrome while values > 200 for total cholesterol and > 100 for LDL were interpreted as abnormal based on NCEP (National Cholesterol Education Program) guidelines[123] normal values of lipid parameters.

hs-CRP

The hs-CRP values less than 3.0 were interpreted as normal.

HOMA IR[124,125]

Insulin resistance was calculated by HOMA;

$$\frac{\text{Fasting Insulin } \mu\text{U/L X Fasting plasma glucose mmol/L}}{22.5}$$

Patients were considered as insulin resistant if HOMA IR was > 3.8.

Statistical analysis

The data obtained was tabulated on Microsoft Excel spreadsheet. Categorical data was expressed as rates, ratios and percentages. Chi-square test was used to assess the level of significance between serum GGT and categorical variables. Continuous data was expressed as mean ± standard deviation (SD) and the comparison was done using two sample 't' test with unequal distribution. Pearsons correlation coefficient was used to find the correlation between MS components and GGT. A probability value ('p' value) of less than or equal to 0.050 was considered as statistically significant.

Chapter 5

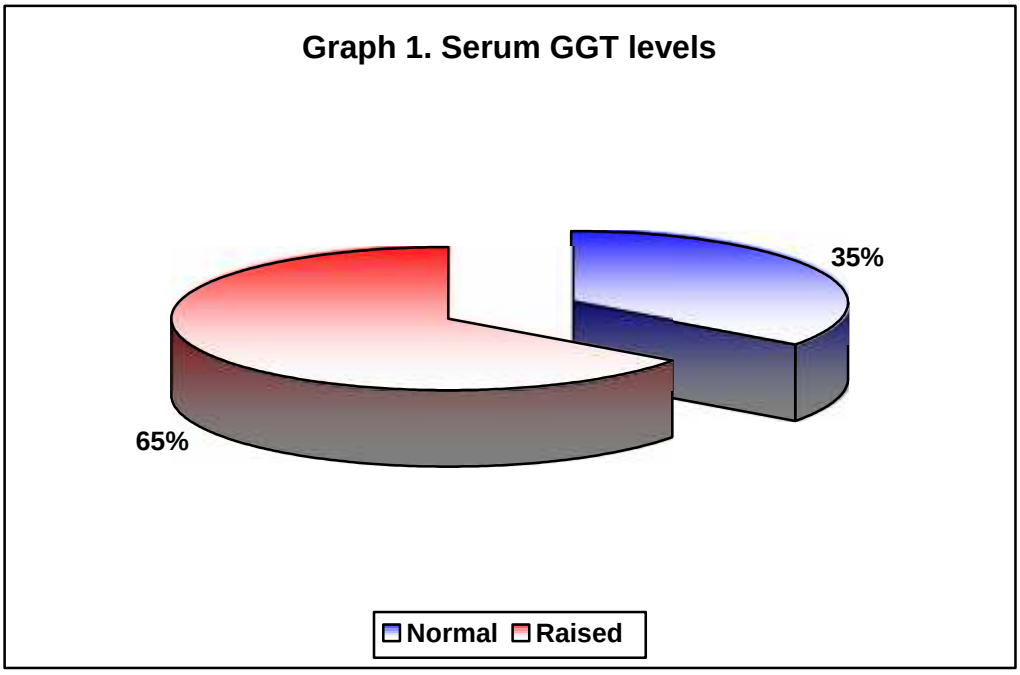
Results

RESULTS

Careful statistical analysis was performed on the obtained raw data, and following explanatory tables and charts were constructed for better insight into the topic.

Table 1. Observed Serum GGT levels in aggregate subject cohort

Serum GGT Levels	Distribution (n=100)	
	Number	Percentage
Normal	35	35.00
Raised	65	65.00
Total	**100**	**100.00**



In the present study, 65% of the patients presented with raised serum GGT levels, while 35% of the patients had normal serum GGT levels.

Table 2. Distribution of Patients presenting with 3 or more components of MS.

Components	Distribution (n=100)	
	Number	Percentage
3	10	10.00
4	27	27.00
5	63	63.00
Total	**100**	**100.00**

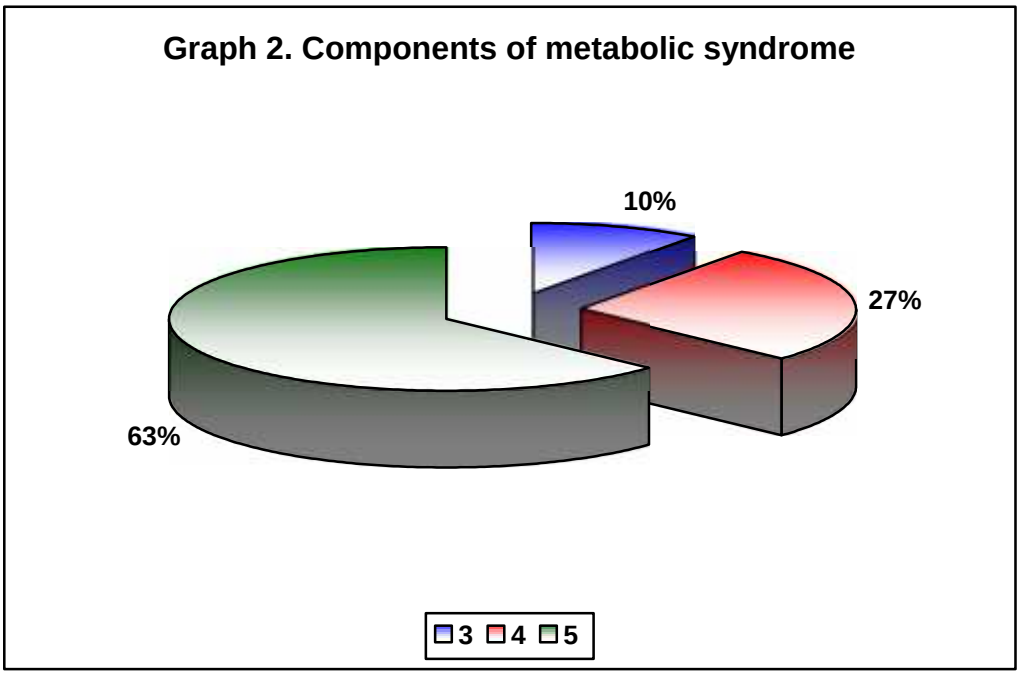


Table 3. Distribution of serum GGT levels in patients with 3 or more components of MS.

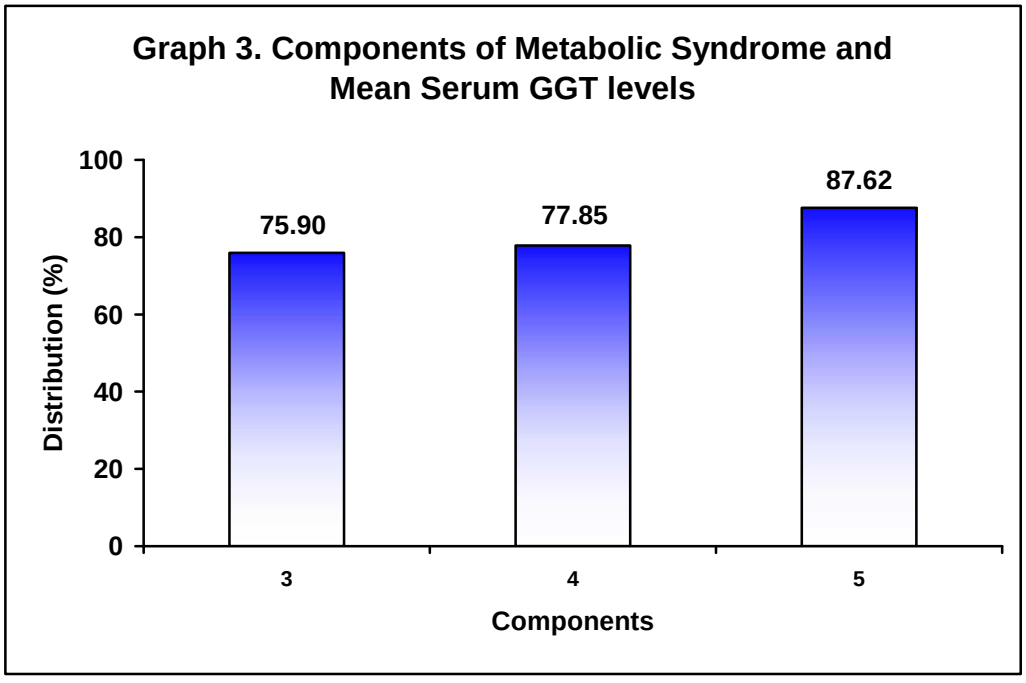
Components of MS	Serum GGT levels				Total	
	Normal		Raised			
	No	%	No	%	No	%
3	9	90.00	1	10.00	10	100.00
4	12	44.44	15	55.56	27	100.00
5	14	22.22	49	77.78	63	100.00
Total	**35**	**35.00**	**65**	**65.00**	**100**	**100.00**

$p < 0.001$

In this study, of the 63 patients who presented with all the five component abnormalities, 77.78% of the patients had raised serum GGT levels, compared to 22.22% of patients with normal serum GGT levels. This difference was statistically significant ($p<0.001$).

Table 4. Distribution of mean serum GGT levels in patients with 3 or more components of MS.

Components	Distribution (n=100)	
	Mean	**SD**
3	75.90	14.22
4	77.85	22.93
5	87.62	17.57
F value	3.50	
p value	0.034	

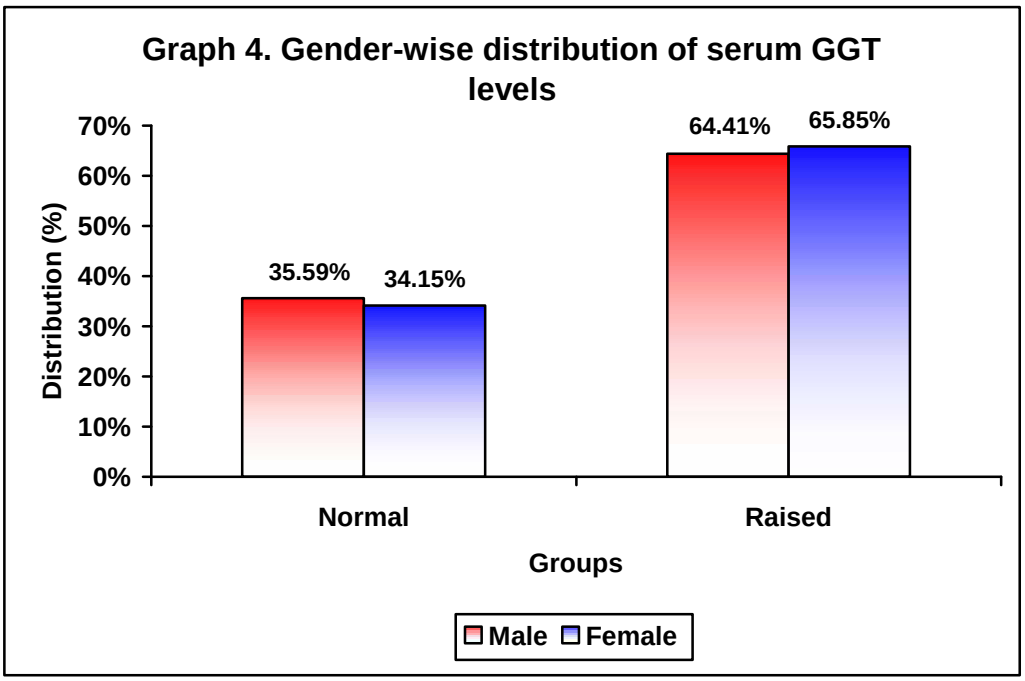


In the present study, amongst patients with all the five component abnormality, the mean serum GGT levels were significantly high (87.62 ± 17.57) compared to four component (77.85 ± 22.93) and three component (75.90 ± 14.22) abnormalities ($p<0.034$).

Table 5. Gender-wise distribution of serum GGT levels.

Sex	Serum GGT levels				Total	
	Normal		Raised			
	No	%	No	%	No	%
Male	21	35.59	38	64.41	59	100.00
Female	14	34.15	27	65.85	41	100.00
Total	**35**	**35.00**	**65**	**65.00**	**100**	**100.00**

p = 0.881



In this study, 59% patients were males, and 41% were females. Among the males, 64.41% of patients, and in females 65.85% of patients, had raised serum GGT levels. (p=0.881).

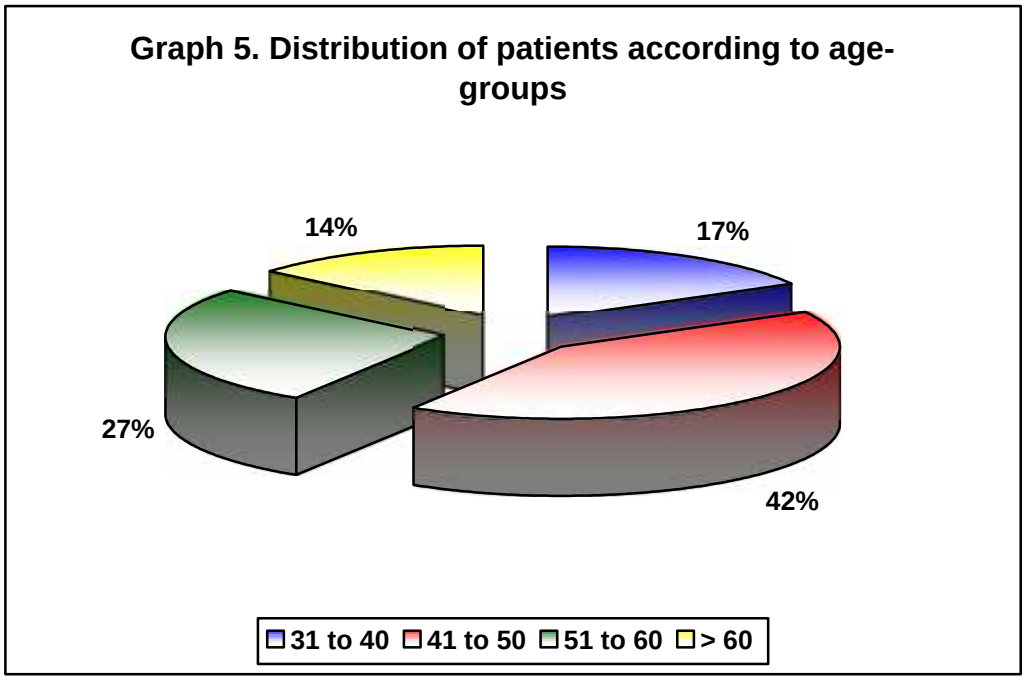
Table 6. Gender-wise mean serum GGT levels

Sex	Distribution (n=100)	
	Mean	**SD**
Male	83.74	18.30
Female	83.90	21.02
p value	**0.969**	

In the present study, mean serum GGT levels among males were 83.74 ± 18.30, while among females, the same were found to be 83.90 ± 21.02 (p=0.969).

Table 7. Distribution of patients according to their age-groups

Age group (Years)	Distribution (n=100)	
	Number	**Percentage**
31 to 40	17	17.00
41 to 50	42	42.00
51 to 60	27	27.00
> 60	14	14.00
Total	**100**	**100.00**



In this study, the commonest age group was 41 to 50 years, which comprised of 42% of the patients, followed by 27% with 51 to 60 years, and 17% between 31 to 40 years.

Table 8. Association of age-groups with serum GGT levels

Age group (years)	Serum GGT levels				Total	
	Normal		Raised			
	No	%	No	%	No	%
31 to 40	8	47.06	9	52.94	17	100.00
41 to 50	13	30.95	29	69.05	42	100.00
51 to 60	9	33.33	18	66.67	27	100.00
> 60	5	35.71	9	64.29	14	100.00
Total	**35**	**35.00**	**65**	**65.00**	**100**	**100.00**

p = 0.700

In this study, of the 42 patients aged between 41 to 50 years, 69.05% had raised serum GGT levels while 30.95% of the patients had normal serum GGT levels. However this difference was statistically not significant (p=0.700).

Table 9. Comparison of mean age in patients with normal and raised serum GGT levels

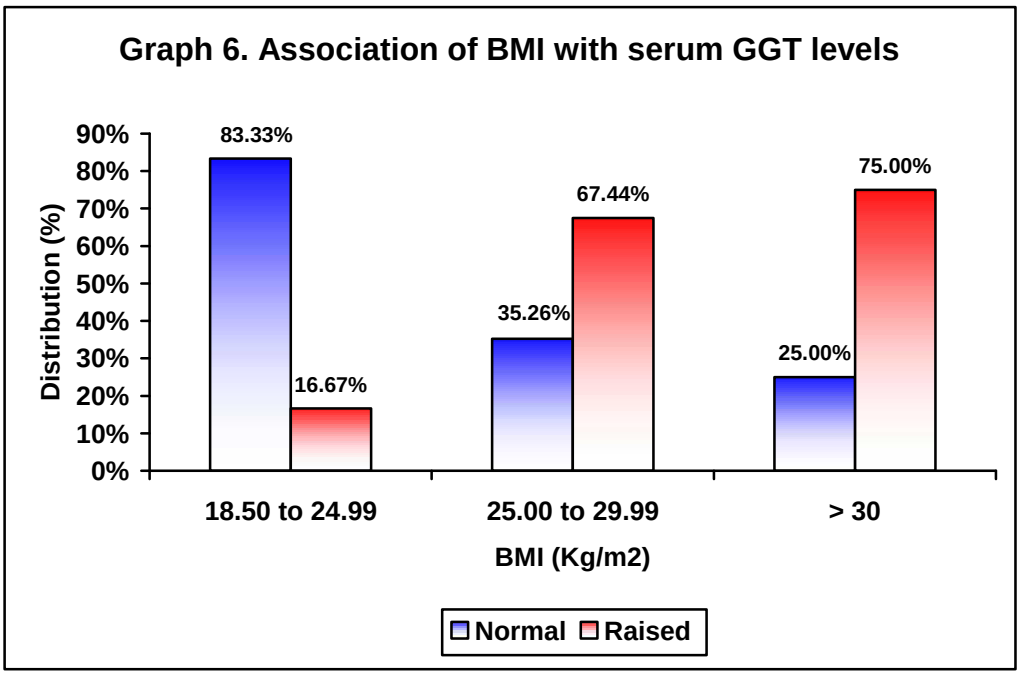
Serum GGT levels	Mean age (n=100)	
	Mean	SD
Normal	50.88	12.69
Raised	50.35	8.70
p value	**0.825**	

In the present study, the mean age in patients with normal GGT levels was 50.88 ± 12.69 years compared to 50.35 ± 8.70 years among the patients with raised GGT levels.

Table 10. Association of BMI with serum GGT levels

BMI (Kg/m^2)	Serum GGT levels				Total	
	Normal		Raised			
	No	%	No	%	No	%
18.50-24.99	5	83.33	1	16.67	6	100.00
25.00-29.99	28	32.56	58	67.44	86	100.00
> 30	2	25.00	6	75.00	8	100.00
Total	**35**	**35.00**	**65**	**65.00**	**100**	**100.00**

p = 0.034



In this study, majority (86%) of the patients had BMI between 25.00 to 29.99 Kg/m^2. Among these 67.44% had raised serum GGT levels compared to 32.56% of the patients with normal serum GGT levels and this difference was statistically significant (p=0.034).

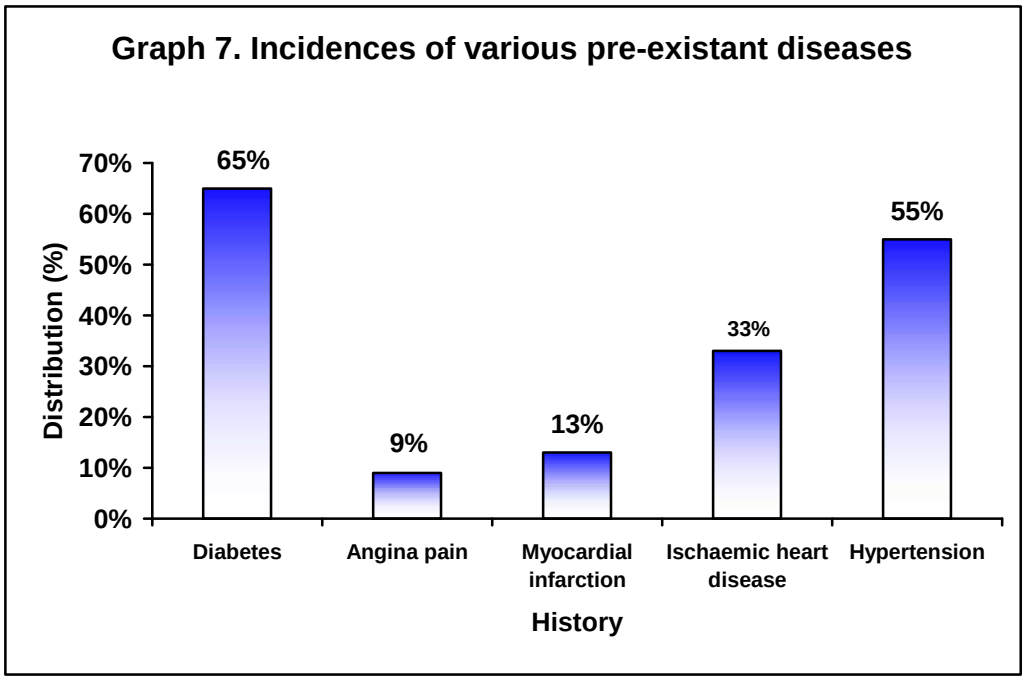
Table 11. Comparison of BMI groups and mean serum GGT levels

BMI (Kg/m^2)	Distribution (n=100)	
	Mean GGT	**SD**
18.50-24.99	92.33	13.57
25.00-29.99	82.96	20.18
> 30	90.00	6.67
F value	0.780	
p value	**0.461**	

In the present study, the mean serum GGT levels in patients with BMI > 30 Kg/m2 were high (90.00 ± 6.67) compared to those with BMI between 25 to 29.99 Kg/m2 (82.96 ± 20.18) and 18.50 to 24.99 (92.33 ± 13.57) but, this difference was statistically not significant (p=0.461).

Table 12. Incidences of various pre-existing diseases in subjects

History	Distribution (n=100)	
	Number	Percentage
Diabetes	65	65.00
Angina pain	9	9.00
Myocardial infarction	13	13.00
Ischaemic heart disease	33	33.00
Hypertension	55	55.00



In the present study, 65% of the patients presented with history of diabetes, and 55% with hypertension. In the remaining, history of ischaemic heart disease was noted in 33%, myocardial infarction in 13%, and angina pain in 9% of the patients.

Table 13. Duration of Pre-existent diabetes in patients

Duration (Years)	Distribution (n=65)	
	Number	Percentage
≤ 5	50	76.92
> 5 to 10	13	20.00
> 10	2	3.08
Total	**65**	**100.00**

In this study, the duration of diabetes was less than 5 years in 76.92% of the patients. Among the others, 20% reported duration of DM between 5 to 10 years and 3.08% with more than 10 years.

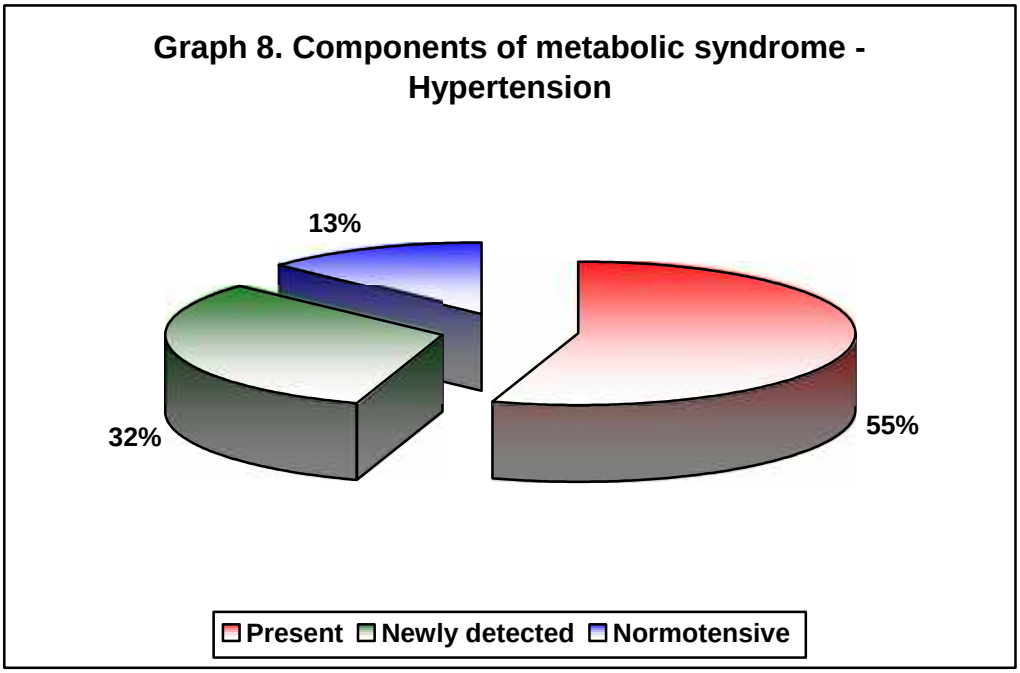
Table 14. Duration of Hypertension

Duration (Years)	Distribution (n=55)	
	Number	Percentage
≤ 5	38	69.09
< 5 to 10	14	25.45
> 10	3	5.45
Total	**55**	**100.00**

In the present study, the duration of hypertension was less than 5 years in 69.09% of the patients. In the remaining, 25.45% reported duration between 5 to 10 years and 5.45% with more than 10 years.

Table 15. Components of MS - Hypertension

Hypertension	Distribution (n=100)	
	Number	Percentage
Present	55	55.00
Newly detected	32	32.00
Normotensive	13	13.00
Total	**100**	**100.00**



In this study, history of hypertension was reported by 55% of the patients. On clinical examination, 32% of the patients were detected as hypertensive while 13% had normal blood pressure.

Table 16. Association of hypertension with serum GGT levels

Hypertension	Serum GGT levels				Total	
	Normal		Raised			
	No	%	No	%	No	%
Hypertensive	25	28.74	62	71.26	87	100.00
Normotensive	10	76.92	3	23.08	13	100.00
Total	**35**	**35.00**	**65**	**65.00**	**100**	**100.00**

p = 0.001

In this study, majority (87%) of the patients were hypertensive. Among them, 71.26% of the patients had raised serum GGT levels, while 28.74% of the patients had normal serum GGT levels. This difference was statistically significant ($p<0.001$).

Table 17. Association of waist circumference with serum GGT levels

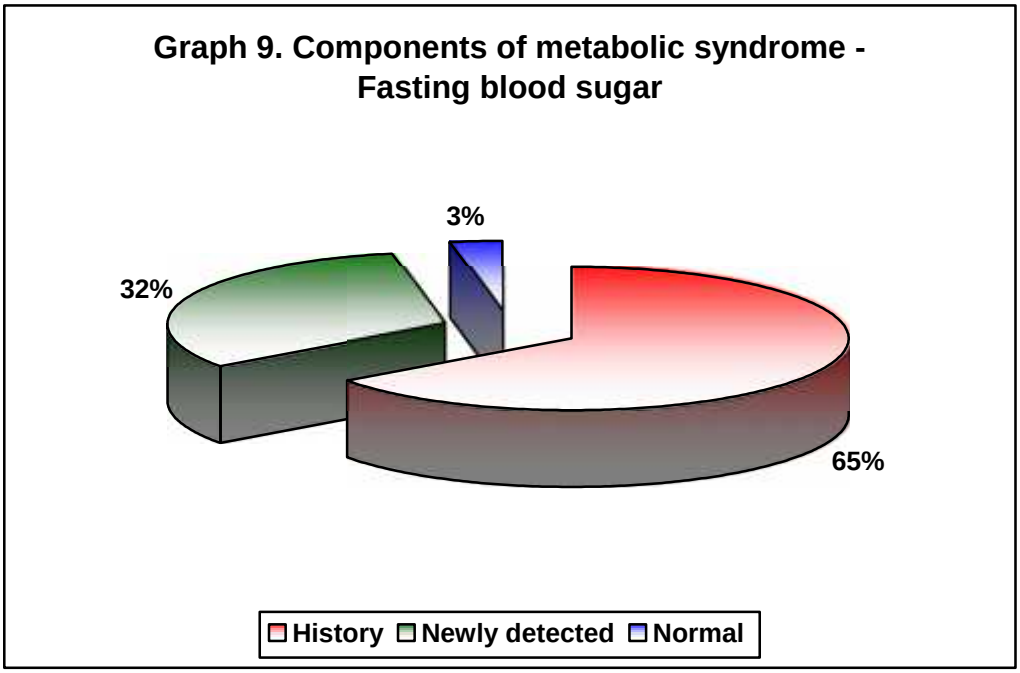
Waist circumference	Serum GGT levels				Total	
	Normal		Raised			
	No	%	No	%	No	%
Normal	1	100.00	0	0.00	1	100.00
Abnormal	34	34.34	65	65.66	99	100.00
Total	**35**	**35.00**	**65**	**65.00**	**100**	**100.00**

p = 0.171

In this study 99% of the patients had abnormal waist circumference, and of these, 65.66% had raised serum GGT levels, while 34.34% of the patients had normal serum GGT levels. However, this difference was statistically not significant (p=0.171).

Table 18. Components of MS - Fasting blood sugar

FBS	Distribution (n=100)	
	Number	**Percentage**
History	65	65.00
Newly detected	32	32.00
Normal	3	3.00
Total	**100**	**100.00**



In this study, history diabetes was reported by 65% of the patients. On fasting blood sugar, 32% of the patients were detected as diabetic while 3% had normal fasting blood sugar levels.

Table 19. Association of fasting blood sugar with serum GGT levels

FBS	Serum GGT levels				Total	
	Normal		Raised			
	No	%	No	%	No	%
Normal	1	33.33	2	66.67	3	100.00
Abnormal	34	35.05	63	64.95	97	100.00
Total	**35**	**35.00**	**65**	**65.00**	**100**	**100.00**

p = 0.951

In this study, majority (97%) of the patients were diabetics. Among them, 64.95% of the patients had raised serum GGT levels and 35.05% had normal serum GGT levels but, this difference was statistically not significant (p=0.951).

Table 20. Association of high density lipoprotein with serum GGT levels

HDL	Serum GGT levels				Total	
	Normal		Raised			
	No	%	No	%	No	%
Normal	10	71.43	4	28.57	14	100.00
Abnormal	25	29.07	61	70.93	86	100.00
Total	**35**	**35.00**	**65**	**65.00**	**100**	**100.00**

p = 0.002

In the present study, 86% of the patients had abnormal HDL levels. Of these, 70.93% had raised serum GGT levels and 29.07% had normal serum GGT levels. This difference was statistically significant (p=0.002).

Table 21. Association of triglycerides with serum GGT levels

Triglycerides	Serum GGT levels				Total	
	Normal		Raised			
	No	%	No	%	No	%
Normal	8	50.00	8	50.00	16	100.00
Abnormal	27	32.14	57	67.86	84	100.00
Total	**35**	**35.00**	**65**	**65.00**	**100**	**100.00**

p = 0.170

In this study, majority (84%) of the patients had raised triglycerides. Of these, 67.86% had raised serum GGT levels and 32.14% had normal serum GGT levels. However, this difference was statistically not significant (p=0.170).

Table 22. Association of HbA1c and serum GGT levels

Diabetic control	Serum GGT levels				Total	
	Normal		Raised			
	No	%	No	%	No	%
Normal	7	41.18	10	58.82	17	100.00
Well controlled	1	12.50	7	87.50	8	100.00
Moderate	13	52.00	12	48.00	25	100.00
Poor	14	28.00	36	72.00	50	100.00
Total	**35**	**35.00**	**65**	**65.00**	**100**	**100.00**

p = 0.039

In this study, of the 50 patients with poor diabetic control, 72% had raised serum GGT levels, while 28% had normal serum GGT levels. This difference was statistically significant (p=0.039).

Table 23. Association of total cholesterol with serum GGT levels

Total cholesterol	Serum GGT levels				Total	
	Normal		Raised			
	No	%	No	%	No	%
Normal	32	39.02	50	60.98	82	100.00
Abnormal	3	16.67	15	83.33	18	100.00
Total	**35**	**35.00**	**65**	**65.00**	**100**	**100.00**

p = 0.072

In the present study, 70% of the patients had normal total cholesterol levels. Among them, 60.98% had raised serum GGT levels, and 39.02% had normal serum GGT levels. This difference was statistically not significant (p=0.072)

Table 24. Association of Hs-CRP with serum GGT levels

Hs-CRP	Serum GGT levels				Total	
	Normal		Raised			
	No	%	No	%	No	%
Normal	1	25.00	3	75.00	4	100.00
Abnormal	34	35.42	62	64.58	96	100.00
Total	**35**	**35.00**	**65**	**65.00**	**100**	**100.00**

p = 0.669

In this study, of the 96% of the patients with abnormal hs-CRP levels, 64.58% had raised serum GGT, and 35.42% of the patients had normal serum GGT levels. However, this difference was statistically not significant (p=0.669).

Table 25. Association of HOMA-IR with serum GGT levels

HOMA-IR	Serum GGT levels				Total	
	Normal		Raised			
	No	%	No	%	No	%
Normal	11	55.00	9	45.00	20	100.00
Abnormal	24	30.00	56	70.00	80	100.00
Total	**35**	**35.00**	**65**	**65.00**	**100**	**100.00**

p = 0.036

In this study, 80% of the patients were found with abnormal HOMA IR levels. Among these, 70% had raised serum GGT levels, and 30% had normal serum GGT levels, and this difference was statistically significant (p=0.036).

Table 26. Comparison of study variables in patients with normal and raised serum GGT levels

Variables	Serum GGT levels				p value
	Normal		Raised		
	Mean	SD	Mean	SD	
Age (Years)	50.89	12.70	50.35	8.70	0.826
Duration of DM (years)	6.29	6.94	4.12	2.83	0.275
Body mass index (Kg/m2)	27.31	1.27	27.48	1.52	0.565
Waist circumference (Cms)	93.26	1.46	93.85	3.03	0.194
SBP (mm Hg)	145.71	15.77	147.54	16.49	0.589
DBP (mm Hg)	86.06	13.04	89.05	9.62	0.238
FBS (mg/dL)	135.03	32.63	141.06	32.79	0.382
HbA1c (%)	8.13	2.01	8.36	2.06	0.592
HOMA IR	4.97	2.51	5.95	2.11	0.055
Triglycerides	177.46	33.18	188.80	38.16	0.126
HDL	38.71	2.81	37.58	2.74	0.058
Cholesterol	162.89	32.73	172.06	34.41	0.193
Hs-CRP	7.27	2.03	7.49	5.89	0.788

Table 26 shows comparison of study characteristics in patients with raised and normal serum GGT levels. No statistically significant difference was observed in patients with normal and raised GGT levels.

Table 27. Correlate serum gamma glutamyl transferase levels with the different components of metabolic syndrome

Components of Mets	Distribution (n=100)	
	r	**R^2**
Waist circumference	0.093	0.008
Systolic blood pressure	0.090	0.008
Diastolic blood pressure	0.124	0.015
Fasting blood sugar	-0.002	<0.001
HDL	-0.081	0.001
Triglycerides	0.031	0.001

In the present study the value of Pearson's correlation coefficient was nearer to the value zero. Although it was a positive correlation, the relationship between MeTs components and serum GGT levels was weak ($r \approx 0.000$)

Chapter 6

Discussion

DISCUSSION

Elevations in serum γ-glutamyl transferase (GGT) activity have been known to be associated with alcohol intake and liver disease. It has been also been found useful to predict morbidity and mortality independently, in these situations.[119]

Modest increases of GGT may be an early marker of cellular oxidative stress and may explain the strong association of serum GGT with many cardiovascular risk factors and disease. Oxidative stress, assessed by circulating prostaglandin F2α levels, is recognized to be related to obesity.[119]

Increases in GGT activity have been found to predict hypertension, as well as incident cases of type 2 diabetes.[9-11] GGT activity also predicted all-cause and coronary heart disease (CHD) mortality, independent of alcohol intake or liver disease.[119] An epidemiological study also suggest that higher serum GGT levels is associated with development of CVD risk factors, including diabetes, hypertension, and the MS.

Hence, importance of early detection of Metabolic syndrome (MS) cannot be over-emphasized for implementing primary preventive measures in susceptible subjects. Such measures have been shown to be effective in reducing the community burden of diabetes and coronary heart disease. Thus, the search for simple diagnostic & prognostic markers for MS has been a subject of research of worldwide interest, especially in countries like India, with high prevalence of MS. Serum GGT levels measurement fulfills requirement of such a marker and indeed, has shown promising results in the research conducted so far.

In three recent, large-scale, prospective studies, Japanese men[28], Framingham Study[29] and cross-sectionally among Turkish adults[30] MS was found to be associated with increased GGT activity. However, in Indian situation, the clinical picture remains unclear, due to lack of such large scale studies. It is notable that the Indian situation is considered to be unique due to highest in the world incidences of diabetes, coronary heart disease and MS. This has been variously attributed to lifestyle, dietary differences and genetic predisposition.

Hence, the need was felt to undertake present study in Indian subjects, to evaluate association of serum GGT levels in subjects with MS, and to correlate serum GGT levels with the different components of MS. Thus, the study results would be helpful to appraise the usefulness of Serum GGT, as a diagnostic marker in MS, along with its limitations, if any, in the Indian context.

This one year study was conducted from January 2012 to December 2012 in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on a total of 100 patients with metabolic syndrome based on IDF criteria.

In the present study, 65% of the MS patients presented with raised serum GGT levels, while 35% of the MS patients had normal serum GGT levels. Although, this difference was statistically significant, it was apparent that a sizeable chunk (35%) would have evaded detection of MS, if GGT elevation is taken as a sole diagnostic parameter for MS. This has impacted the conceptual predictive value, sensitivity, and specificity of the serum GGT in detecting MS. However, aggregating other known parameters of the MS with GGT can enhance

the diagnostic utility of the GGT for screening MS. Presently, the metabolic disturbances in MS are not yet fully clarified, and GGT being a metabolic derivative, the reason for the presence of normal GGT in known MS patients, still eludes us.

In this study, the commonest age group was 41 to 50 years, which comprised of 42% of the patients, followed by 27% with 51 to 60 years, and 17% between 31 to 40 years. Serum GGT levels were raised in 69.05% of the patients aged 41 to 50 compared to 30.95% of the patients who had normal serum GGT levels. Also, the mean age in patients with normal GGT levels was 50.88 ± 12.69 years, compared to 50.35 ± 8.70 years among the patients with raised GGT levels. These findings suggest that, association between serum GGT levels and MS was independent of age (p=0.700). Similar age profile was reported in a study from Turkey[119] in patients with MS with mean age being 51.3 ± 3.2 years. Another study from Turkey[120] showed that, mean age of the patients with normal (51.7 ± 11.7 years) and raised (52.4 ± 9.8) serum GGT was comparable (p=0.170). This study also found that, GGT activity was associated with age inversely.

In this study, 59% patients were males and 41% were females. This is a fair reflection of gender distribution in the society. Among the males 64.41% of patients and in females 65.85% of patients had raised serum GGT levels (p=0.881). Further, mean serum GGT levels among males were 83.74 ± 18.30, while in females they were found to be 83.90 ± 21.02 (p=0.969). These findings suggest that, serum GGT levels in both sexes were comparable and gender has no particular influence on GGT levels. A study from Turkey[119] reported similar

observations, where the authors showed that, serum GGT levels were comparable in male and females (p=0.280). In contrast, another study from Turkey[120] performed to assess the role of GGT in predicting MS, 61.9% of the patients were females, and the mean GGT levels in female were 18.2 U/L, and in males the same were 25.7 U/L and there was statistically significant difference between genders in mean GGT levels.

In this study, 77.78% patients with all the five components of MS, had raised serum GGT levels (p<0.001). Also, the mean serum GGT levels were significantly higher (87.62 ± 17.57) in patients with all the five component abnormality, compared to four component (77.85 ± 22.93) and three component (75.90 ± 14.22) abnormalities (p<0.034). These findings show the positive association between MS and raised serum GGT levels. Presence of higher number of components of MS correlated well with raised serum GGT levels. Similar findings were reported in a study on 3451 Framingham Study participants, which showed that, the risk of MS increased with higher GGT (multivariable-adjusted hazard ratio [HR] per SD increment log-GGT, 1.26 [95%CI; 1.18 to 1.35]). The study concluded that, an increase in serum GGT predicts onset of MS, and suggested that, GGT is a marker of metabolic and cardiovascular risk.[29] A recent study from Korea also reported that, MS components were considerably under the influence of GGT.[118] A study from Turkey on 754 men and 802 women reported doubling in GGT activity, and found to be associated with a rise of 74% in MS likelihood, independent of other confounders (p<0.001).[119] A cross-sectional study from Japan showed that, higher serum GGT was significantly associated with MS and its components in

the general population.[117] Rantala *et al* investigated the relationship between GGT and MS and revealed a highly significant relationship between GGT and the components of the MS, even after adjustment for age, body mass index and alcohol consumption.[125] In another study of Sakugawa *et al*,[126] the rise in serum GGT level correlated with components of MS.

In this study, 86% of the patients had BMI between 25.00 to 29.99 Kg/m^2. Among these 67.44% had raised serum GGT levels, compared to 32.56% of the patients with normal serum GGT levels, suggesting positive association between serum GGT levels, body mass index and MS (p=0.034). It was observed that, the mean serum GGT levels in patients with BMI > 30 Kg/m^2 were high (90.00 ± 6.67) compared to those with BMI between 25 to 29.99 Kg/m^2 (82.96 ± 20.18) but the difference was statistically not significant (p=0.461). In patients with normal (27.31 ± 1.27 Kg/m^2) and raised (27.48 ± 1.52 Kg/m^2) serum GGT levels the body mass index was comparable (p=0.565). In contrast, a recent study from Turkey[119] showed that, body mass index in patients with raised serum GGT levels was high (30.3 ± 5.00 Kg/m^2) compared to individuals with normal serum GGT levels (28.1 ± 5.1 Kg/m^2) ($p<0.001$). BMI was also observed to be a determinant of GGT levels in Tromso study.[127]

In this study, 99% of the patients had abnormal waist circumference, and of these, 65.66% had raised serum GGT levels, while 34.34% of the patients had normal serum GGT levels. However, this difference was statistically not significant (p=0.171).

In the present study, 55% of the patients presented with history of hypertension. Most of the patients had <5 years of duration (69.09%). On clinical examination, 32% of the patients were detected as hypertensive, while 13% had normal blood pressure. Among hypertensive, 71.26% of the patients had raised serum GGT levels, compared to 28.74% with normal serum GGT levels, suggesting strong association between raised serum GGT levels and hypertension as a component of MS ($p<0.001$). This is in agreement with other studies[29,119] in whom GGT levels were also shown to predict onset of hypertension.

In the present study, history of diabetes was present in 65% of the patients with majority of them had duration of < 5 years (76.92%). Raised serum GGT levels were noted among 64.95% of the patients with diabetes, while 35.05% had normal serum GGT levels but, this difference was statistically not significant ($p=0.951$) showing weak or no association of raised serum GGT levels, with diabetes mellitus, as component of MS.

But, in patients with poor diabetic control i.e., HbA1c > 8, significantly higher number of patients (72%) had raised serum GGT levels ($p=0.039$) and also, significantly higher proportion of patients (70%) with insulin resistance, had raised serum GGT levels ($p=0.036$), indicating strong association of raised serum GGT levels with poor diabetic control and insulin resistance.

In the present study, of the 86% of the patients with abnormal HDL, 70.93% had raised serum GGT levels and 29.07% had normal serum GGT levels. This difference was statistically significant ($p=0.002$). Majority (84%) of the

patients had raised triglycerides. Among them, raised serum GGT levels were noted in 67.86% compared 32.14% with normal serum GGT levels, but this difference was statistically not significant (p=0.170).

No statistically significant association was observed between raised serum GGT levels with total cholesterol (p=0.072) and hs-CRP (p=0.669).

A study sought to evaluate serum GGT activity in patients with MS reported higher prevalence of hypertension and dyslipidemia in patients with MS. Compared with controls, patients with MS had significantly higher serum GGT [(median 21, interquartile range (16-33) vs. 19 (14-26) U/l; p=0.008] and C-reactive protein levels [6.2 (3.6-9.4) vs. 5.0 (3.1-7.0) U/l; p=0.044]. A high GGT activity (>40 U/l) was determined in 14.5% of the patients with MS and in 4.4% of the control subjects (p=0.012). Serum GGT level showed significant correlations with MS (r=0.24, p=0.001), CRP (r=0.20, p=0.003), triglyceride (r=0.18, p=0.006), HDL cholesterol (r=-0.19, p=0.004), aspartate aminotransferase (r=0.15, p=0.02), alanine aminotransferase (r=0.32, p=0.001), and alkaline phosphatase (r=0.16, p=0.01). This significant association continued only for MS (β=-0.25, p=0.03), HDL cholesterol (β=-0.18, p=0.03), and alkaline phosphatase (β=0.17, p=0.01) in multivariate regression analysis. The study findings suggested that, patients with MS have higher serum GGT and CRP levels compared with controls.[120]

In a cohort of 1667 adults, in a general population, evaluated prospectively at 4 year's follow-up in Turkey, reported that elevated serum GGT confers risk, additively to BMI, hypertension, MS, and type 2 diabetes.[119]

A cross-sectional, single-center study, to know if the liver function tests (LFT), especially GGT, have a predictive value in diagnosis of Metabolic syndrome (MS) on 908 subjects, reported that when the sample is divided into quartiles of the GGT levels, increase in GGT is positively correlated with increased MS prevalence. In ROC analysis, GGT was strongly associated with the IDF diagnostic components, as is each individual IDF component, except elevated systolic blood pressure.[24]

Some epidemiological studies also suggest that higher serum GGT levels is associated with development of CVD risk factors, including diabetes, hypertension, and the metabolic syndrome.[128]

Overall, the findings of this study have successfully shown that, in Indian situation, serum GGT levels are significantly elevated in patients with MS, and it can play an important role in early diagnosis of MS, with a high degree of certainty. Also, high GGT levels may indicate presence of higher number of components of MS. These findings are also mostly corroborated by findings of various overseas studies.

The results obtained from the study may be better interpreted in the light of knowledge of structural short-comings of the study. Firstly, the sample size of the study was small and was obtained not from cross-sectional general population, but from patients/their relatives visiting hospital. This may have introduced an element of bias in the study. The cross-sectional numbers of subjects required (at least 10,000 of general population) for a strong predictive value, were beyond the scope of this limited study. Secondly, determination of

prognostic importance of GGT was not possible due to short period of the study. Thirdly, high number of the patients presented with all the five components, and that many patients had long standing diabetes, may be a reflective confirmation of the Indian scenario of high incidence of diabetes mellitus and MS. Fourthly, statistical calculations of exact positive predictive value, specificity and sensitivity of GGT were precluded due to small, non-cross-sectional sample size. Fifthly, several patients were on variety of medications, especially Beta-blockers, Statins, and others, which are known to have pleomorphic effects including anti-oxidant, endothelial function improving properties. Thereby reducing oxidative stress, correspondingly reflecting reduced serum GGT levels. This may have resulted in poorer correlation with a given component/parameter in the study.

Thus, in view of promising results obtained in this small study, it may be inferred that there is urgent & strong need for a large-scale, epidemiologic, long-term, multi-center, controlled, single blind study, in the Indian setting, for clarifying the role of GGT, so that definitive clinical guidelines could be finalized. In the meantime, without hesitation, it is whole-heartedly recommended that serum GGT may be relied upon along with other markers to screen/detect MS cases, so that vigorous primary preventive measures may be instituted in eligible subjects.

Chapter 7

Conclusion

CONCLUSION

Based on the results of this study, it may be concluded that, MS is associated with raised serum GGT levels, as almost two-third subjects of the study population (65%) presented with raised serum GGT levels. Also, raised serum GGT levels may indicate presence of higher numbers of metabolic syndrome components.

Further, raised serum GGT levels correlated well with hypertension, and HDL, whereas, no correlation was found between waist circumference and diabetes mellitus. Despite the negative correlation between diabetes mellitus with raised serum GGT levels, glycaemic control (HbA1c), insulin resistance and body mass index showed positive association with raised serum GGT levels. Also, serum GGT levels were comparable in both sexes and in all the age groups.

Thus, the findings in this study indicate that serum GGT levels can be a useful diagnostic marker for early detection of MS. This finding is in confirmation with the results of various independent studies all over the world.

However, comparatively lesser numbers of subjects studied, and being an observational study, may seem to limit recommendation of wider application of extrapolated results. But, the study observations certainly justify conduction of a large, single blind, randomised, multi-center study to further confirm and clarify the usefulness of serum GGT as a diagnostic marker in metabolic syndrome.

Chapter 8

Summary

SUMMARY

Serum GGT level is a promising diagnostic marker for early detection of MS. It has also been shown to be an independent risk factor for the mortality and morbidity of cardiovascular diseases. MS is a cluster of inter-connected factors that directly increase the risk of cardiovascular atherosclerotic diseases and type 2 diabetes mellitus. Hence, its early detection with a widely available and simple diagnostic marker is important.

The present study was conducted to evaluate the association of serum GGT levels in subjects with MS, and to correlate serum GGT levels with the different components of metabolic syndrome. This would appraise the role of serum GGT as a diagnostic marker in early detection of metabolic syndrome.

This one year study was conducted from January 2012 to December 2012 in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum, on a total of 100 patients with MS, based on IDF criteria.

In this study, 59% patients were males and 41% were females. The commonest age group was 41 to 50 years comprised of 42% of patients. There were no significant gender differences in GGT levels. History of diabetes was present in 65% of the patients and 55% had hypertension. Diabetic complications e.g. retinopathy was noted in 46% of the patients, and 44% of the patients had nephropathy. In this study, of the 63% patients presented with all the five metabolic syndrome components.

Raised serum GGT levels were noted in 65% of the patients, while 35% of the patients had normal serum GGT levels. Among patients with all the five component abnormality, the mean serum GGT levels were significantly high (87.62 ± 17.57) ($p<0.034$). Serum GGT levels were comparable in both the sexes and in all the age groups. Raised serum GGT levels correlated well with hypertension and HDL, whereas no correlation was found between waist circumference and diabetes mellitus. Raised serum GGT levels also correlated well with glycaemic control (HbA1c), insulin resistance, and body mass index.

Based on the results of this study, it can be confirmed that the serum GGT levels can serve as a useful marker for diagnosis, and early detection of metabolic syndrome.

However, in strictest terms, since present study has a comparatively smaller sample size and being observational in design, could limit wider application of results. Still, the need for a large scale, properly designed scientific investigation is emphasized for further firmer clinical guidelines on usefulness of serum GGT marker in MS.

Chapter 9

Bibliography

BIBLIOGRAPHY

1. Pervanidou EKP, Kaltsas G, Chrousos G. Metabolic syndrome: definitions and controversies. BMC Med 2011;9:48.

2. Reaven GM. Banting lecture 1988. Role of insulin resistance in human disease. Diabetes. 37 1988:1595-607.

3. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA. 285 2001:2486-97.

4. International Diabetes Federation. The IDF Consensus Worldwide Definition of the Metabolic Syndrome. Belgium: International Diabetes Federation Brussels; 2006

5. World Health Organization. Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications. Report of a WHO Consultation. Part 1:Diagnosis and Classification of Diabetes and Mellitus (publ. no.WHO/NCD/NCS/99.2). Geneva: World Health Organization;1999.

6. Moebus S, Hanisch J, Neuhäuser M, Aidelsburger P, Wasem J, Jöckel K. Assessing the prevalence of the Metabolic Syndrome according to NCEP ATP III in Germany: feasibility and quality aspects of a two step approach in 1550 randomly selected primary health care practices. Ger Med Sci 2006;4:Doc07

7. Grundy SM, Brewer HB, Cleeman JI, Smith SC, Lenfant C. Definition of metabolic syndrome: report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. Circulation 2004:109:433-38.

8. Cornier MA, Dabelea D, Hernandez TL, Lindstrom RC, Steig AJ, Stob NR, et al. The metabolic syndrome. Endocr Rev 2008;29:777-822.

9. Hollman G, Kristenson M. The prevalence of the metabolic syndrome and its risk factors in a middle-aged Swedish population--mainly a function of overweight? Eur J Cardiovasc Nurs 2008;7:21-6.

10. Hillier TA, Fagot-Campagna A, Eschwege E, Vol S, Cailleau M, Balkau B. Weight change and changes in the metabolic syndrome as the French population moves towards overweight: the D.E.S.I.R. cohort. Int J Epidemiol 2006;35:190-6.

11. do Carmo I, Dos Santos O, Camolas J, Vieira J, Carreira M, Medina L, et al. Overweight and obesity in Portugal: national prevalence in 2003-2005. Obes Rev 2008;9:11-9.

12. Ervin RB. Prevalence of metabolic syndrome among adults 20 years of age and over, by sex, age, race and ethnicity, and body mass index: United States, 2003-2006. Natl Health Stat Report 2009;13:1-7.

13. Athyros VG, Ganotakis ES, Tziomalos K, Papageorgiou AA, Anagnostis P, Griva T, et al. Comparison of four definitions of the metabolic

syndrome in a Greek (Mediterranean) population. Curr Med Res Opin 2010;26:713-9.

14. Harzallah F, Alberti H, Ben KF. The metabolic syndrome in an Arab population: a first look at the new International Diabetes Federation criteria. Diabet Med 2006;23:441-4.

15. Sharifi F, Mousavinasab SN, Saeini M, Dinmohammadi M. Prevalence of metabolic syndrome in an adult urban population of the west of Iran. Exp Diabetes Res 2009;2009:136501.

16. Timoteo A, Santos R, Lima S, Mamede A, Fernandes R, Ferreira R. Does the new International Diabetes Federation definition of metabolic syndrome improve prediction of coronary artery disease and carotid intima-media thickening? Rev Port Cardiol 2009;28:173-81.

17. Ma WY, Li HY, Hung CS, Lin MS, Chiu FC, Lin CH, et al. Metabolic syndrome defined by IDF and AHA/NHLBI correlates better to carotid intima-media thickness than that defined by NCEP ATP III and WHO. Diabetes Res Clin Pract 2009;85:335-41.

18. Zabetian A, Hadaegh F, Azizi F. Prevalence of metabolic syndrome in Iranian adult population, concordance between the IDF with the ATPIII and the WHO definitions. Diabetes Res Clin Pract 2007;77:251-7.

19. Pandit K, Goswami S, Ghosh S, Mukhopadhyay P, Chowdhury S. Metabolic syndrome in South Asians. Indian J Endocr Metab 2012;16;44-55.

20. Kamble P, Deshmukh PR, Garg N. Metabolic syndrome in adult population of rural Wardha, central India. Indian J Med Res 2010;132:701-5.

21. Pemminati S, Prabha Adhikari MR, Pathak R, Pai MR. Prevalence of metabolic syndrome (METS) using IDF 2005 guidelines in a semi urban south Indian (Boloor Diabetes Study) population of Mangalore. J Assoc Physicians India 2010;58:674-7.

22. Misra A, Khurana L. Obesity and the metabolic syndrome in developing countries. J Clin Endocrinol Metab 2008;93:S9-30.

23. Ordovas JM: Genetic links between diabetes mellitus and coronary atherosclerosis. Curr Atheroscler Rep 2007;9:204-10.

24. Kasapoglu B, Turkay C, Bayram Y, Koca C. Role of GGT in diagnosis of metabolic syndrome: a clinic-based cross-sectional survey. Indian J Med Res 2010;132:56-61.

25. Wannamethee G, Ebrahim S, Shaper AG. Gamma-glutamyltransferase: determinants and association with mortality from ischemic heart disease and all causes. Am J Epidemiol 1995;142:699–708.

26. Bots ML, Salonen JT, Elwood PC, Nikitin Y, Freire de Concalves A, Inzitari D, et al. Gamma-glutamyltransferase and risk of stroke: the EUROSTROKE project. J Epidemiol Community Health 2002;56 (Suppl. 1):I25–9.

27. Nilssen O, Førde OH, Brenn T. The Tromsø Study: distribution and population determinants of gamma-glutamyltransferase. Am J Epidemiol 1990;132:318–26.

28. Nakanishi N, Suzuki K, Tatara K. Serum gamma-glutamyltransferase and risk of metabolic syndrome and type 2 diabetes in middle-aged Japanese men. Diabetes Care 2004;27(6):1427-32.

29. Lee DS, Evans JC, Robins SJ, Wilson PW, Albano I, Fox CS, et al. Gamma glutamyl transferase and metabolic syndrome, cardiovascular disease, and mortality risk: the Framingham Heart Study. Arterioscler Thromb Vasc Biol 2007;27:127–33.

30. Onat A, Hergenç G, Karabulut A, Türkmen S, Doğan Y, Uyarel H, et al. Serum gamma glutamyltransferase as a marker of metabolic syndrome and coronary disease likelihood in nondiabetic middle-aged and elderly adults. Prev Med 2006;43:136–9.

31. Kylin. Genetic dissection of the syndrome X in the rat. Biochem Biophys Res Commun. 1923;269:660-5.

32. Lindahl B, Asplund K, Eliasson M, Evrin PE. Insulin resistance syndrome and fibrinolytic activity:the northern Sweden MONICA study. Int J Epidemiol. 1996;25:291-9.

33. Tiengo A, Del Prato S. Plurimetabolic syndrome:association of diabetes, dyslipidemia, and arterial hypertension. Cardiologia. 1995;40:237-43.

34. World Health Organization. Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications. Report of a WHO Consultation. Part 1:Diagnosis and Classification of Diabetes and Mellitus (publ. no.WHO/NCD/NCS/99.2). Geneva: World Health Organization;1999.

35. Balkau B, Charles MA. Comment on the provisional report from the WHO consultation. European Group for the Study of Insulin Resistance (EGIR). Diabet Med 1999;16:442-3.

36. Bloomgarden ZT. American Association of Clinical Endocrinologists (AACE) consensus conference on the insulin resistance syndrome:25-26 August 2002, Washington, DC. Diabetes Care 2003;26:933-9.

37. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults:findings from the third National Health and Nutrition Examination Survey. JAMA. 2002;287:356-9.

38. Balkau B, Charles MA, Drivsholm T, Borch-Johnsen K, Wareham N, Yudkin JS, et al. Frequency of the WHO metabolic syndrome in European cohorts, and an alternative definition of an insulin resistance syndrome. Diabetes Metab. 2002;28:364-376.

39. Hu G, Qiao Q, Tuomilehto J, Balkau B, Borch-Johnsen K, Pyorala K. Prevalence of the metabolic syndrome and its relation to all-cause and cardiovascular mortality in nondiabetic European men and women. Arch Intern Med. 2004;164:1066-76.

40. Al-Lawati JA, Mohammed AJ, Al-Hinai HQ, Jousilahti P. Prevalence of the metabolic syndrome among Omani adults. Diabetes Care. 2003;26:1781-5.

41. Lee WY, Park JS, Noh SY, Rhee EJ, Kim SW, Zimmet PZ. Prevalence of the metabolic syndrome among 40,698 Korean metropolitan subjects. Diabetes Res Clin Pract. 2004;65:143-9.

42. Tan CE, Ma S, Wai D, Chew SK, Tai ES. Can we apply the National Cholesterol Education Program Adult Treatment Panel definition of the metabolic syndrome to Asians? Diabetes Care. 2004;27:1182-6.

43. Gogia A. Agarwal PK. Metabolic syndrome. Indian J Med Sci 2006;60 (2):72-81.

44. Ramachandran A, Snehalatha C, Satyavani K, Sivasankari S, Vijay V. Metabolic syndrome in urban Asian Indian adults-a population study using modified ATP III criteria. Diabetes Res Clin Pract 2003;60:199-204.

45. Gupta A, Gupta R, Sarna M, Rastogi S, Gupta VP, Kothari K. Prevalence of diabetes, impaired fasting glucose and insulin resistance syndrome in an urban Indian population. Diab Res Clin Pract 2003;61:69-76.

46. Pekkanen J, Tuomilehto J, Uutela A, Vartiainen E, Nissinen A. Social class, health behaviours and mortality among men and women in eastern Finland. BMJ 1995;311:589-93.

47. Davey SG, Neaton JD, Wentworth D, Stamler J. Mortality differences between black and white men in USA: Contribution of income and other risk factors among men screened for the MRFIT. Lancet 1998;351:934-9.

48. Kaplan GA, Keil JE. Socioeconomic factors and cardiovascular disease: A review of the literature. Circulation 1993;88:1973-98.

49. Ford ES, Giles WH, Mokdad AH. Increasing prevalence of the metabolic syndrome among U.S. Adults. Diabetes Care. 2004;27(10):2444-9.

50. Edelstein SL, Knowler WC, Bain RP, Andres R, Barrett-Connor EL, Dowse GK, et al. Predictors of progression from impaired glucose tolerance to NIDDM: An analysis of six prospective studies. Diabetes. 1997;46:701-10.

51. de Vegt F, Dekker JM, Jager A, Hienkens E, Kostense PJ, Stehouwer CD, et al. Relation of impaired fasting and postload glucose with incident type 2 diabetes in a Dutch population:The Hoorn Study. JAMA. 2001;285:2109-13.

52. Chan JM, Rimm EB, Colditz GA, Stampfer MJ, Willett WC. Obesity, fat distribution, and weight gain as risk factors for clinical diabetes in men. Diabetes Care. 1994;17:961-9.

53. Bonora E, Kiechl S, Willeit J, Oberhollenzer F, Egger G, Meigs JB, et al. Population-based incidence rates and risk factors for type 2 diabetes in white individuals:the Bruneck study. Diabetes. 2004;53:1782-9.

54. Lillioja S, Mott DM, Spraul M, Ferraro R, Foley JE, Ravussin E, et al. Insulin resistance and insulin secretory dysfunction as precursors of non-insulin dependent diabetes mellitus. Prospective studies of Pima Indians. N Engl J Med. 1993;329:1988-92.

55. Haffner SM, Valdez RA, Hazuda HP, Mitchell BD, Morales PA, Stern MP. Prospective analysis of the insulin-resistance syndrome (syndrome X). Diabetes. 1992;41:715-22.

56. Njolstad I, Arnesen E, Lund-Larsen PG. Sex differences in risk factors for clinical diabetes mellitus in a general population:a 12-year follow-up of the Finnmark Study. Am J Epidemiol. 1998;147:49-58.

57. Meisinger C, Thorand B, Schneider A, Stieber J, Doring A, Lowel H. Sex differences in risk factors for incident type 2 diabetes mellitus:the MONICA Augsburg cohort study. Arch Intern Med. 2002;162:82-9.

58. Stolk RP, van Splunder IP, Schouten JS, Witteman JC, Hofman A, Grobbee DE. High blood pressure and the incidence of non-insulin dependent diabetes mellitus:findings in a 11.5 year follow-up study in The Netherlands. Eur J Epidemiol. 1993;9:134-9.

59. Dotevall A, Johansson S, Wilhelmsen L, Rosengren A. Increased levels of triglycerides, BMI and blood pressure and low physical activity increase the risk of diabetes in Swedish women. A prospective 18-year follow-up of the BEDA study. Diabet Med. 2004;21:615-22.

60. Mogensen CE, Christensen CK. Predicting diabetic nephropathy in insulin-dependent patients. N Engl J Med. 1984;311:89-93

61. Yudkin JS, Forrest RD, Jackson CA. Microalbuminuria as predictor of vascular disease in non-diabetic subjects. Islington Diabetes Survey. Lancet. 1988;2:530-3.

62. Jensen JS, Borch-Johnsen K, Jensen G, Feldt-Rasmussen B. Atherosclerotic risk factors are increased in clinically healthy subjects with microalbuminuria. Atherosclerosis. 1995;112:245-52.

63. Jager A, Kostense PJ, Nijpels G, Heine RJ, Bouter LM, Stehouwer CD. Microalbuminuria is strongly associated with NIDDM and hypertension, but not with the insulin resistance syndrome: the Hoorn Study. Diabetologia. 1998;41:694-700.

64. Lithell HO, McKeigue PM, Berglund L, Mohsen R, Lithell UB, Leon DA. Relation of size at birth to non-insulin dependent diabetes and insulin concentrations in men aged 50-60 years. BMJ. 1996;312:406-10.

65. Barker DJ, Hales CN, Fall CH, Osmond C, Phipps K, Clark PM. Type 2 (non-insulin dependent) diabetes mellitus, hypertension and hyperlipidaemia (syndrome X):relation to reduced fetal growth. Diabetologia. 1993;36:62-7.

66. Vanhala M. Childhood weight and metabolic syndrome in adults. Ann Med. 1999;31:236-9.

67. Vanhala M, Vanhala P, Kumpusalo E, Halonen P, Takala J. Relation between obesity from childhood to adulthood and the metabolic syndrome:population based study. BMJ. 1998;317:319.

68. Craig WY, Palomaki GE, Haddow JE. Cigarette smoking and serum lipid and lipoprotein concentrations:an analysis of published data. BMJ. 1989;298:784-8.

69. Facchini FS, Hollenbeck CB, Jeppesen J, Chen YD, Reaven GM. Insulin resistance and cigarette smoking. Lancet. 1992;339:1128-30.

70. Will JC, Galuska DA, Ford ES, Mokdad A, Calle EE. Cigarette smoking and diabetes mellitus:evidence of a positive association from a large prospective cohort study. Int J Epidemiol. 2001;30:540-6.

71. Lee WY, Jung CH, Park JS, Rhee EJ, Kim SW. Effects of smoking, alcohol, exercise, education, and family history on the metabolic syndrome as defined by the ATP III. Diabetes Res Clin Pract 2005;67:70-7.

72. Sierksma A, Patel H, Ouchi N, Kihara S, Funahashi T, Heine RJ, et al. Effect of moderate alcohol consumption on adiponectin, tumor necrosis factoralpha, and insulin sensitivity. Diabetes Care. 2004;27:184-9.

73. Freiberg MS, Cabral HJ, Heeren TC, Vasan RS, Curtis Ellison R. Alcohol Consumption and the Prevalence of the Metabolic Syndrome in the U.S.:A cross-sectional analysis of data from the Third National Health and Nutrition Examination Survey. Diabetes Care. 2004;27:2954-9.

74. Yoon YS, Oh SW, Baik HW, Park HS, Kim WY. Alcohol consumption and the metabolic syndrome in Korean adults:the 1998 Korean National Health and Nutrition Examination Survey. Am J Clin Nutr. 2004;80:217-24.

75. Du Y, Melchert HU, Knopf H, Braemer-Hauth M, Gerding B, Pabel E. Association of serum caffeine concentrations with blood lipids in caffeine-drug users and nonusers - results of German National Health Surveys from 1984 to 1999. Eur J Epidemiol. 2005;20:311-6.

76. Arnlov J, Vessby B, Riserus U. Coffee consumption and insulin sensitivity. JAMA. 2004;291:1199-201.

77. Salazar-Martinez E, Willett WC, Ascherio A, Manson JE, Leitzmann MF, Stampfer MJ, et al. Coffee consumption and risk for type 2 diabetes mellitus. Ann Intern Med. 2004;140:1-8.

78. Rosengren A, Dotevall A, Wilhelmsen L, Thelle D, Johansson S. Coffee and incidence of diabetes in Swedish women:a prospective 18-year follow-up study. J Intern Med. 2004;255:89-95.

79. Tuomilehto J, Hu G, Bidel S, Lindstrom J, Jousilahti P. Coffee consumption and risk of type 2 diabetes mellitus among middle-aged Finnish men and women. JAMA. 2004;291:1213-9.

80. Li BQ, Zhang HL, Shu QL. Studies on the extraction of polysaccharide from middle and low gradegreen tea and the effectiveness on blood-glucose depressing. J Tea Sci 1996;16:67-72

81. Waltner-Law ME, Wang XL, Law BK, Hall RK, Nawano M, Granner DK. Epigallocatechin gallate, a constituent of green tea, represses hepatic glucose production. J Biol Chem. 2002;277:34933-34940.

82. Hosoda K, Wang MF, Liao ML, Chuang CK, Iha M, Clevidence B, et al. Antihyperglycemic effect of oolong tea in type 2 diabetes. Diabetes Care. 2003;26:1714-8.

83. Bennett PH. Type 2 diabetes among the Pima Indians of Arizona:an epidemic attributable to environmental change? Nutr Rev. 1999;57:S51-4.

84. Lako JV, Nguyen VC. Dietary patterns and risk factors of diabetes mellitus among urban indigenous women in Fiji. Asia Pac J Clin Nutr. 2001;10:188-93.

85. Hetzel B, Michael T. The Lifestyle Factor: Lifestyle and Heath. Melbourne: Penguin, 1987.

86. Boyce VL, Swinburn BA. The traditional Pima Indian diet. Composition and adaptation for use in a dietary intervention study. Diabetes Care. 1993;16:369-71.

87. Popkin BM. The nutrition transition and obesity in the developing world. J Nutr. 2001;131:871S-3.

88. Putnam J. U.S. food supply providing more food and calories. Food Rev. 1999;22:2–12.

89. Marshall JA, Bessesen DH, Hamman RF. High saturated fat and low starch and fibre are associated with hyperinsulinaemia in a non-diabetic population:the San Luis Valley Diabetes Study. Diabetologia. 1997;40:430-8.

90. Swinburn BA, Boyce VL, Bergman RN, Howard BV, Bogardus C. Deterioration in carbohydrate metabolism and lipoprotein changes induced by modern, high fat diet in Pima Indians and Caucasians. J Clin Endocrinol Metab. 1991;73:156-65.

91. Marshall JA, Hoag S, Shetterly S, Hamman RF. Dietary fat predicts conversion from impaired glucose tolerance to NIDDM. The San Luis Valley Diabetes Study. Diabetes Care. 1994;17:50-6.

92. Vessby B, Tengblad S, Lithell H. Insulin sensitivity is related to the fatty acid composition of serum lipids and skeletal muscle phospholipids in 70-year-old men. Diabetologia. 1994;37:1044-50.

93. Trevisan M, Krogh V, Freudenheim J, Blake A, Muti P, Panico S, Farinaro E, Mancini M, Menotti A, Ricci G. Consumption of olive oil, butter, and vegetable oils and coronary heart disease risk factors. The Research Group ATS-RF2 of the Italian National Research Council. JAMA. 1990;263:688-92.

94. Gross LS, Li L, Ford ES, Liu S. Increased consumption of refined carbohydrates and the epidemic of type 2 diabetes in the United States:an ecologic assessment. Am J Clin Nutr. 2004;79:774-9.

95. Hill JO, Peters JC. Environmental contributions to the obesity epidemic. Science. 1998;280:1371-4.

96. Bell AC, Ge K, Popkin BM. The road to obesity or the path to prevention:motorized transportation and obesity in China. Obes Res. 2002;10:277-283.

97. Eriksson J, Taimela S, Koivisto VA. Exercise and the metabolic syndrome. Diabetologia. 1997;40:125-35.

98. DeFronzo RA, Sherwin RS, Kraemer N. Effect of physical training on insulin action in obesity. Diabetes. 1987;36:1379-85.

99. Wahren J, Felig P, Ahlborg G, Jorfeldt L. Glucose metabolism during leg exercise in man. J Clin Invest. 1971;50:2715-25.

100. Tuomilehto J, Lindstrom J, Eriksson JG, Valle TT, Hamalainen H, Ilanne-Parikka P, Keinanen-Kiukaanniemi S, Laakso M, Louheranta A, Rastas M, Salminen V, Uusitupa M. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 2001;344:1343-50.

101. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002;346:393-403.

102. Hu G, Pekkarinen H, Hanninen O, Tian H, Guo Z. Relation between commuting, leisure time physical activity and serum lipids in a Chinese urban population. Ann Hum Biol 2001;28:412-21.

103. Hagberg JM, Exercise, fitness and hypertension. In:Bouchard C (ed) Exercise, fitness and health: A consensus of current knowledge. Champaign, Illinois: Human Kinetic Books; 1990.

104. Shirai K. Obesity as the core of the metabolic syndrome and the management of coronary heart disease. Curr Med Res Opin 2004;20:295-304.

105. Keyou G, Fengying Z, Huaicheng Y. The dietary and nutritional status of Chinese population (1992 national Nutrition Survey). 1st ed., Beijing; People 's health publishing company: 1996.

106. Ko GT, Chan JC, Cockram CS. The association between dyslipidaemia and obesity in Chinese men after adjustment for insulin resistance. Atherosclerosis 1998;138:153-61.

107. Wagenknecht LE, Langefeld CD, Scherzinger AL, Norris JM, Haffner SM, Saad MF, Bergman RN. Insulin sensitivity, insulin secretion, and abdominal fat:the Insulin Resistance Atherosclerosis Study (IRAS) Family Study. Diabetes 2003;52:2490-6.

108. Van Itallie TB. Health implications of overweight and obesity in the United States. Ann Intern Med 1985;103:983-8.

109. Faloia E, Giacchetti G, Mantero F. Obesity and hypertension. J Endocrinol Invest 2000;23:54-62.

110. Zimmet PZ. Kelly West Lecture 1991. Challenges in diabetes epidemiology--from West to the rest. Diabetes Care 1992;15:232-52.

111. Joy T, Lahiry P, Pollex RL, Hegele RA. Genetics of metabolic syndrome. Curr Diab Rep 2008;8(2):141-8.

112. Puig JG, Martínez MA. Hyperuricemia, gout and the metabolic syndrome. Curr Opin Rheumatol 2008;20(2):187-91.

113. Lee DH, Jacobs DR Jr, Gross M, Kiefe CI, Roseman J, 11. Lewis CE, et al. Gamma-glutamyltransferase is a predictor of incident diabetes and hypertension: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. Clin Chem 2003;49:1358-66.

114. Jousilahti P, Rastenyte D, Tuomilehto J. Serum g-glutamyl 12. transferase, self-reported alcohol drinking, and the risk of stroke. Stroke 2000; 31: 1851-5.

115. Burtis CA, Ashwood ER, Bruns DE. Tietz textbook of clinical chemistry and molecular diagnostics. 4th Ed., Missouri: W. B. Saunders; 2006.

116. Burtis CA, Ashwood ER. Tietz fundamentals of clinical chemistry. 6th Ed. New Delhi: Elsevier (India) Private Ltd.; 2008

117. Kawamoto R, Kohara K, Tabara Y, Miki T, Otsuka N. Serum gamma-glutamyl transferase levels are associated with metabolic syndrome in

community-dwelling individuals. J Atheroscler Thromb. 2009 Aug;16(4):355-62.

118. Suh BS. The Association between Serum Gamma-Glutamyltransferase within Normal Levels and Metabolic Syndrome in Office Workers: A 4-Year Follow-up Study. Korean J Fam Med. 2012 Jan;33(1):51-8.

119. Onat A, Can G, Örnek E, Çiçek G, Ayhan E, Doğan Y. Serum γ-glutamyltransferase: independent predictor of risk of diabetes, hypertension, metabolic syndrome, and coronary disease. Obesity (Silver Spring). 2012 Apr;20(4):842-8.

120. Bozbaş H, Yıldırır A, Karaçağlar E, Demir O, Ulus T, Eroğlu S, et al Increased serum gamma-glutamyltransferase activity in patients with metabolic syndrome. Turk Kardiyol Dern Ars. 2011 Mar;39(2):122-8.

121. Siemens Dimension Clinical Chemistry System - Flex reagent cartridge. Newark, USA: Siemens Healthcare Diagnostics Inc.; 2012.

122. Pi-Sunyer FX. Obesity: criteria and classification. Proc Nutr Soc. 2000;59(4):505-9.

123. Bahijri SM, Alissa EM, Akbar DH, Ghabrah TM. Estimation of insulin resistance in non-diabetic normotensive Saudi adults by QUICKI, HOMA-IR and modified QUICKI: a comparative study. Ann Saudi Med. 2010; 30(4): 257-64.

124. Ascaso JF, Romero P, Real JT, Preigo A, Valdecabre SC, Carmena R. Insulin resistance quantification by fasting insulin plasma values and HOMA index in non diabetic population. Med Clin (Barc) 2001; 117; 530-3.

125. Rantala AO, Lilja M, Kauma H, Savolainen MJ, Reunanen 24. A, Kesaniemi YA. Gamma-glutamyl transpeptidase and the metabolic syndrome. J Intern Med 2000; 248 : 230-8.

126. Sakugawa H, Nakayoshi T, Kobashigawa K, Nakasone H, 25. Kawakami Y, Yamashiro T, et al. Metabolic syndrome is directly associated with gamma glutamyl transpeptidase elevation in Japanese women. World J Gastroenterol 2004; 10 : 1052-5.

127. Nilssen O, Førde OH. Seven-year longitudinal population study of change in gamma-glutamyltransferase: the Tromsø Study. Am J Epidemiol 1994;139:787–92.

128. Devers MC, Campbell S, Shaw J, Zimmet P, Simmons D. 27. Should liver function tests be included in definitions of metabolic syndrome? Evidence from the association between liver function tests, components of metabolic syndrome and prevalent cardiovascular disease. Diabet Med 2008; 25 : 523-9.

Annexures

Annexure I

ANNEXURE I – CONSENT FORM

"A ONE YEAR CROSS-SECTIONAL STUDY: TO STUDY THE ASSOCIATION OF SERUM GAMMA GLUTAMYL TRANSFERASE LEVELS WITH METABOLIC SYNDROME DR. PRABHAKAR KORE'S K.L.E.S HOSPITAL, BELGAUM"

Objective and purpose of the study:

This research is intended to study the association of Serum Gamma Glutamyl Transferase levels and metabolic syndrome. This study will be of great help to patients with metabolic syndrome and dyslipidemias and also predict their complications in the future.

Procedure: If you agree to be part of the research study, you will be asked the relevant history and will be subjected to relevant clinical examination and investigations. You will also have to give blood and urine samples for the necessary investigations.

Risk and Benefits:

The only risk and possible discomfort you might get is while taking blood from my arm for the investigations. It may cause swelling, pain, redness, bruising or infection (rarely happens) at the site from where the blood is drawn.

Alternatives:

Taking part in this study is voluntary. You may choose not to take part in this study, or if I decide to take part I can later change my mind and withdraw from the study. Your decision will not change the present or future health care or other services that you receive. The study doctor or sponsor may stop your

participation in this study at any time. If you choose not to take part in the study, you will receive the standard treatment for patients with your condition.

Privacy and Confidentiality:

All information collected about you during the course of this study will be kept confidential to the extent permitted by law. The code numbers will identify you in this research record. Information from this study may be published but your identity will be confidential in any publication.

Institution / Sponsor's policy:

Does not apply to this research.

Financial incentives for participation:

You will not be paid / offered any gifts /incentives for participating in the study.

Authorization to publish the results:

The results of the study would be forwarded to the KLE University, Belgaum as part of requirement towards the completion of MD degree, review and publishing.

If you have any questions about your rights as a participant, you may call:

1. Dr. **** *****
   Professor & Head of Unit,
   Dept of General Medicine,
   JNMC,
   Phone No.: ***** *****

2. Dr. **** *****
   Investigator,
   PG in General Medicine,
   JNMC,
   Phone No.: ***** *****

3. Dr. **** *****
   Chairman,
   J.N.M.C Ethical Committee for Human Research,
   Phone number: ***** *****
   Extn: ****

4. Dr. **** *****
   Professor & HOD,
   Department of Medicine, JNMC,
   Phone No: ***** *****
   Extn: **** *****

Consent Statement

I voluntarily agree to take part in this study by signing below. I may withdraw at any time. I am not giving up any of my legal rights by signing this form. My signature below indicates that I have read, or it has been read to me, this entire consent form, and have had all my questions answered.

Name of the Participant: _____ Signature / Thumb print _____

Name of the Witness _____ Signature/ Thumb print _____

Investigator Name: _____ Signature: _____

Date: Place:

Annexures

Annexure II

ANNEXURE II – PROFORMA

Case No:

Name: Age/Sex:

IP No.

Occupation:

History pertaining to metabolic syndrome

H/o Type 2 diabetes mellitus yes ☐ no ☐

If yes,

Duration of illness -

Details of treatment –

Past history of cerebrovascular events –

Past history of angina pain/ Myocardial infarction/ Ischemic heart disease or on any specific medication.

H/o peripheral neuropathy - yes ☐ no ☐

Documented Diabetic retinopathy/surgical management of retinopathy in the past

Diabetic nephropathy yes ☐ no ☐

Diabetic foot yes ☐ no ☐

Autonomic neuropathy yes ☐ no ☐

H/o. hypertension or on specific anti- yes ☐ no ☐

hypertensive medication

H/o Peripheral vascular disease/past h/o yes ☐ no ☐

treatment for the same

K/c/o of dyslipidemia or on any specific medication yes ☐ no ☐

ON EXAMINATION:

HEIGHT:

WEIGHT:

BMI :

WAIST CIRCUMFERENCE:

BLOOD PRESSURE :

INVESTIGATIONS:

- FBS
- TOTAL TRIGLYCERIDES –
- TOTAL HDL –
- TOTAL CHOLESTEROL-
- ESTIMATED LDL -
- HbA1c -
- SERUM GAMMA GLUTAMYL TRANSFERASE LEVELS–
- FASTING INSULIN LEVELS-
- HOMA-IR – LEVELS-
- TOTAL LEUCOCYTE COUNT-
- HsCRP-

ANNEXURE III - MASTER CHART

				History														Clinical examination						Investigations							
				Type 2 DM		Cerebrovascular events									HTN							BP (mm Hg)									
Serial Number	In Patient Number	Sex	Age (Years)	History	Duration (Years)	Angina pain	Myocardial infarction	Ischaemic heart disease	Peripheral neuropathy	Diabetic retinopathy	Diabetic nephropathy	Diabetic foot	Autonomic neuropathy	History	Duration (Years)	Peripheral vascular disease	Dislipidemia	Height (Cms)	Weight (Kg)	Body mass index (Kg/m2)	Waist circumference (Cms)	Systolic	Diastolic	Fasting blood sugar (mg/dL)	HbA1c	HOMA-IR	Total Triglycerides (mg/dL)	Total HDL (mg/dL)	Total Cholesterol (mg/dL)	Hs-CRP	Sr. GGT
1	494442	M	40	-	-	-	-	-	-	-	-	-	-	+	1	-	-	150	65	28.9	97	130	86	98	6.0	7.0	170	38	210	2.0	96
2	494444	M	68	+	2	-	-	+	-	+	+	-	-	+	10	+	-	158	70	28.0	102	140	90	174	###	8.0	210	35	198	7.5	90
3	497096	F	54	+	4	-	-	-	+	+	-	-	+	+	4	-	-	160	78	30.5	110	150	85	134	9.6	8.5	198	32	170	7.8	88
4	496860	M	38	-	-	-	-	-	-	-	-	-	-	+	4	-	-	178	74	23.4	98	160	100	110	6.0	6.0	180	38	180	7.7	108
5	497115	M	40	-	-	-	-	-	-	+	-	-	-	-	-	-	-	172	72	24.3	89	150	80	117	9.8	7.5	157	39	120	8.7	81
6	497109	F	52	-	-	-	-	+	-	+	+	-	-	+	6	+	-	160	62	24.2	96	160	90	104	6.7	7.0	140	39	140	12.0	84
7	497103	M	40	-	-	-	-	-	-	-	-	-	-	-	-	-	-	170	71	24.6	94	140	100	106	6.0	4.0	149	36	150	9.0	85
8	497113	F	32	-	-	-	-	-	-	-	-	-	-	-	-	-	-	168	80	28.3	82	130	100	98	5.4	6.0	130	46	154	8.0	86
9	498136	M	47	+	1	-	-	-	-	+	-	-	+	+	5	-	+	176	78	25.2	96	140	90	142	8.6	5.5	190	34	170	4.0	90
10	499186	F	48	+	1	+	-	-	+	+	+	-	-	-	-	-	+	170	79	27.3	92	140	80	137	###	5.0	150	42	205	7.0	85
11	599591	M	64	+	4	-	+	+	-	+	+	+	+	+	4	+	+	176	82	26.5	98	150	70	128	9.7	4.0	140	34	174	3.0	103
12	500169	F	43	+	6	+	-	-	-	+	+	-	-	-	-	-	+	172	78	26.4	91	140	60	109	7.0	7.0	180	39	190	6.0	84
13	504936	M	50	-	-	-	-	+	-	-	-	-	-	+	8	-	+	180	82	25.3	94	140	90	120	6.8	8.0	210	38	210	9.0	95
14	506610	F	42	+	1	-	-	-	+	+	+	-	+	-	-	-	-	174	79	26.1	94	130	90	109	6.9	4.5	170	43	139	2.4	96
15	506805	M	53	-	-	-	-	-	-	-	-	-	-	+	6	-	-	182	88	26.6	94	150	100	117	5.6	5.0	150	40	154	4.0	70
16	507460	F	36	-	-	-	-	-	-	-	-	-	-	-	-	-	-	176	84	27.1	93	140	100	111	5.7	6.0	140	38	140	7.0	90
17	507595	M	47	+	1	-	-	-	-	-	-	+	-	-	-	-	+	174	80	26.4	94	140	85	141	8.4	6.5	157	41	150	4.0	87
18	507806	F	41	+	2	-	-	+	+	+	-	+	+	+	2	-	-	178	88	27.8	92	130	90	130	9.1	3.0	120	38	130	10.0	93
19	508263	F	35	-	-	-	-	-	-	-	-	-	-	+	1	-	-	174	79	26.1	92	140	70	112	5.4	2.0	159	44	150	7.0	80
20	510512	M	51	+	4	-	-	+	+	+	+	+	-	+	3	-	+	175	80	26.1	94	150	70	126	7.4	4.5	149	40	134	12.0	74
21	509605	M	48	-	-	-	-	-	-	-	-	-	-	-	-	-	-	182	90	27.2	96	160	90	189	9.6	7.0	160	33	168	6.0	90

ANNEXURE III - MASTER CHART

				History													Clinical examination						Investigations							
				Type 2 DM		Cerebrovascular events									HTN																
Serial Number	In Patient Number	Sex	Age (Years)	History	Duration (Years)	Angina pain	Myocardial infarction	Ischaemic heart disease	Peripheral neuropathy	Diabetic retinopathy	Diabetic nephropathy	Diabetic foot	Autonomic neuropathy	History	Duration (Years)	Peripheral vascular disease	Dislipidemia	Height (Cms)	Weight (Kg)	Body mass index (Kg/m2)	Waist circumference (Cms)	BP (mm Hg) Systolic	BP (mm Hg) Diastolic	Fasting blood sugar (mg/dL)	HbA1c	HOMA-IR	Total Triglycerides (mg/dL)	Total HDL (mg/dL)	Total Cholesterol (mg/dL)	Hs-CRP	Sr. GGT
22	511000	M	68	+	10	-	+	+	+	+	+	-	+	+	9	-	-	184	91	26.9	95	170	100	171	9.8	9.0	170	38	160	12.0	96
23	512079	F	47	+	2	-	-	-	-	-	+	+	-	+	1	+	+	180	100	30.9	93	160	80	163	8.2	4.0	210	39	200	7.0	97
24	511482	F	60	+	7	-	+	+	+	+	+	+	+	+	4	-	-	174	87	28.7	94	180	90	147	9.1	8.0	197	42	137	8.0	94
25	512742	M	62	+	5	+	+	+	+	+	+	+	+	+	5	-	+	180	101	31.2	94	130	70	162	7.8	7.5	167	38	150	5.8	98
26	513172	M	42	+	1	-	-	-	-	-	-	-	-	+	1	-	-	184	96	28.4	94	140	96	113	7.0	10.0	170	42	139	7.9	85
27	512877	F	45	+	2	-	-	+	+	+	+	+	+	-	-	-	+	175	84	27.4	94	150	70	142	8.6	5.0	180	40	167	6.0	87
28	514490	M	35	-	-	-	-	-	+	+	+	-	+	-	-	-	-	178	84	26.5	96	160	90	198	###	7.0	157	34	172	9.0	98
29	515447	F	40	-	-	-	-	-	+	+	+	-	-	-	-	-	-	180	89	27.5	94	170	90	192	###	3.0	179	35	139	9.2	97
30	514883	F	49	-	-	-	-	-	-	-	-	-	-	-	-	+	-	183	95	28.4	92	150	70	100	5.5	4.0	162	36	178	7.0	38
31	513168	M	57	+	3	-	-	+	+	+	-	-	+	-	-	-	+	186	94	27.2	93	140	100	139	8.6	8.0	159	38	172	8.4	91
32	516696	M	55	+	2	-	-	+	+	+	+	-	-	-	-	-	-	184	92	27.2	93	150	70	112	7.6	2.0	158	38	150	7.4	35
33	515493	F	47	-	-	-	-	-	-	-	-	-	-	-	-	+	-	180	100	30.9	94	140	90	111	7.0	9.0	150	40	160	8.0	97
34	516844	M	38	-	-	-	-	-	-	-	-	-	-	+	1	-	+	175	91	29.7	93	150	80	112	7.2	5.5	160	42	170	5.0	93
35	517529	F	47	+	2	-	-	+	-	+	+	+	-	+	2	-	-	171	88	30.1	93	160	80	109	7.8	6.5	167	38	209	6.0	83
36	517591	F	49	-	-	-	-	-	+	-	-	-	-	+	3	-	-	174	98	32.4	92	150	80	117	5.6	7.0	159	40	139	5.9	90
37	517783	F	42	+	1	-	-	-	+	-	-	-	-	-	-	-	-	178	89	28.1	92	140	96	112	7.6	4.0	152	38	128	3.9	104
38	516009	M	47	+	2	-	-	-	+	+	-	+	-	-	-	-	-	175	93	30.4	93	130	85	100	7.8	7.5	140	42	168	4.8	81
39	518636	F	39	-	-	-	-	-	-	-	-	-	-	-	-	-	-	176	85	27.4	92	140	90	112	6.8	8.0	150	38	170	5.4	92
40	2482598	F	68	+	10	-	-	+	-	+	+	-	+	-	-	-	-	179	86	26.8	92	110	80	108	7.9	7.0	152	42	120	6.0	42
41	1144752	M	34	-	-	-	-	-	-	-	-	-	-	-	-	-	-	176	76	24.5	93	140	80	102	5.6	9.0	140	38	140	5.0	85
42	2498470	M	42	+	1	-	-	-	-	-	-	-	-	+	1	-	-	186	90	26.0	93	150	90	129	7.8	5.5	160	39	139	6.0	87

ANNEXURE III - MASTER CHART

				History														Clinical examination						Investigations							
				Type 2 DM		Cerebrovascular events									HTN							BP (mm Hg)									
Serial Number	In Patient Number	Sex	Age (Years)	History	Duration (Years)	Angina pain	Myocardial infarction	Ischaemic heart disease	Peripheral neuropathy	Diabetic retinopathy	Diabetic nephropathy	Diabetic foot	Autonomic neuropathy	Peripheral vascular disease	History	Duration (Years)	Dislipidemia	Height (Cms)	Weight (Kg)	Body mass index (Kg/m2)	Waist circumference (Cms)	Systolic	Diastolic	Fasting blood sugar (mg/dL)	HbA1c	HOMA-IR	Total Triglycerides (mg/dL)	Total HDL (mg/dL)	Total Cholesterol (mg/dL)	Hs-CRP	Sr. GGT
43	525010	M	52	-	-	-	-	-	-	-	-	-	-	-	+	2	+	192	98	26.6	92	130	90	111	6.4	4.5	152	36	137	5.3	99
44	525554	F	48	+	3	-	-	+	-	-	+	-	-	-	+	1	-	180	87	26.9	94	140	84	112	7.8	8.5	160	38	167	4.3	95
45	2498470	M	52	-	-	-	-	-	-	-	-	-	-	-	+	4	+	188	93	26.3	93	160	80	108	6.0	6.0	158	40	170	7.2	94
46	2506676	F	46	-	-	-	-	-	-	-	-	-	-	-	+	3	-	186	96	27.7	93	170	90	109	6.0	3.0	150	38	139	6.8	106
47	2506669	F	50	+	4	-	-	-	-	+	+	-	-	-	-	-	-	178	88	27.8	94	160	90	112	8.7	6.0	178	37	208	5.4	32
48	2529966	F	46	+	2	-	-	-	-	-	+	+	-	+	2	-	-	182	91	27.5	93	150	70	118	7.9	5.0	220	38	190	8.0	108
49	2531656	M	57	+	2	-	-	-	-	+	+	-	-	+	5	-	-	178	89	28.1	93	120	80	138	7.8	8.0	159	40	169	5.8	86
50	799495	F	50	+	4	-	-	-	-	+	+	+	-	-	-	-	+	179	88	27.5	94	140	70	142	8.4	9.0	160	38	170	7.0	95
51	2548361	M	40	+	1	-	-	-	-	-	-	-	-	-	-	-	-	176	75	24.2	93	150	80	163	7.4	7.5	170	42	180	8.0	79
52	2561902	M	52	-	-	-	-	+	-	-	-	-	-	+	5	-	-	177	90	28.7	94	120	80	108	6.4	3.5	210	36	120	8.2	92
53	2553737	F	48	+	2	-	-	-	+	+	-	-	+	-	-	-	+	176	85	27.4	94	140	90	138	8.7	2.0	220	39	220	5.0	80
54	2556795	F	44	+	1	-	-	-	-	+	+	+	-	-	-	-	+	178	86	27.1	95	130	90	172	9.3	7.0	180	40	159	8.0	56
55	534895	M	54	+	1	-	-	-	-	-	-	-	+	+	2	-	-	188	94	26.6	93	160	90	222	###	2.0	240	32	170	9.2	52
56	533912	M	48	-	-	-	-	-	-	-	-	-	-	-	-	-	-	178	87	27.5	94	170	110	240	###	1.5	270	30	276	8.9	55
57	539989	F	45	-	-	-	-	-	-	-	-	-	-	-	-	-	-	176	83	26.8	95	160	96	170	9.6	8.0	250	39	202	6.8	42
58	535397	M	50	+	2	-	-	+	-	-	+	+	-	+	1	-	-	174	84	27.7	95	150	110	141	8.6	0.5	198	38	205	7.6	84
59	536758	M	55	+	6	+	+	+	+	+	+	-	+	+	6	-	-	182	88	26.6	95	160	100	157	8.2	5.0	290	37	220	8.7	93
60	537000	M	62	+	10	+	+	+	-	+	+	+	+	-	-	-	-	178	84	26.5	92	140	98	143	8.4	8.0	200	36	170	6.8	86
61	539379	M	56	+	3	-	-	-	-	-	+	+	-	-	-	-	-	179	85	26.5	93	140	90	112	8.2	9.0	210	38	200	7.2	99
62	539413	F	52	-	-	-	-	-	+	+	+	+	+	+	6	-	-	170	82	28.4	93	150	90	240	###	4.0	240	32	276	8.0	104
63	539632	M	48	+	2	+	-	-	-	-	-	-	-	+	2	-	-	170	78	27.0	94	140	80	136	8.9	5.5	220	36	229	7.9	97

ANNEXURE III - MASTER CHART

				History													Clinical examination						Investigations							
				Type 2 DM		Cerebrovascular events									HTN															
Serial Number	In Patient Number	Sex	Age (Years)	History	Duration (Years)	Angina pain	Myocardial infarction	Ischaemic heart disease	Peripheral neuropathy	Diabetic retinopathy	Diabetic nephropathy	Diabetic foot	Autonomic neuropathy	Peripheral vascular disease	History	Duration (Years)	Dislipidemia	Height (Cms)	Weight (Kg)	Body mass index (Kg/m2)	Waist circumference (Cms)	BP (mm Hg) Systolic	BP (mm Hg) Diastolic	Fasting blood sugar (mg/dL)	HbA1c	HOMA-IR	Total Triglycerides (mg/dL)	Total HDL (mg/dL)	Total Cholesterol (mg/dL)	Hs-CRP	Sr. GGT
64	539634	M	48	+	4	-	-	-	-	-	-	+	-	+	1	+	+	173	79	26.4	93	110	80	144	9.6	3.0	237	39	178	6.3	89
65	541712	M	40	-	-	-	-	-	-	-	-	-	-	-	-	-	-	172	78	26.4	94	140	90	138	7.8	4.5	210	36	220	7.2	42
66	542610	F	58	+	5	-	+	+	+	+	+	-	-	-	-	-	-	170	79	27.3	94	150	85	164	8.8	0.5	200	34	166	7.8	45
67	543409	M	42	+	2	-	-	-	-	-	-	-	-	+	1	-	+	174	80	26.4	92	160	80	132	7.6	5.5	189	37	159	7.4	94
68	543410	M	47	+	1	-	-	-	-	+	-	-	-	-	-	-	-	176	88	28.4	94	110	70	128	7.9	4.0	160	40	209	6.0	80
69	542963	F	45	-	-	-	-	-	-	-	-	-	-	+	1	-	+	178	84	26.5	93	110	90	120	6.4	7.5	177	38	129	5.0	102
70	544203	F	36	+	4	-	-	-	-	-	-	-	-	-	-	-	-	179	84	26.2	92	110	60	112	5.2	3.5	160	39	110	5.6	42
71	544539	M	58	+	1	-	-	-	-	-	-	-	-	+	10	-	+	175	82	26.8	93	140	88	104	6.7	4.0	152	38	120	7.0	92
72	544663	M	52	+	2	-	-	+	+	+	-	-	-	+	2	-	-	188	99	28.0	93	150	100	141	9.8	4.5	159	40	100	8.2	38
73	452761	M	48	+	2	-	-	-	+	+	+	-	-	+	8	-	-	176	87	28.1	94	140	100	194	8.4	7.0	167	37	176	8.1	97
74	454499	M	63	-	-	-	-	-	-	-	-	-	-	+	10	-	-	173	86	28.7	93	200	100	136	7.0	9.0	220	36	199	7.2	96
75	457586	M	48	+	3	-	+	+	-	+	+	-	-	+	3	-	-	186	94	27.2	93	190	90	167	9.6	7.0	248	34	236	5.4	104
76	459674	F	59	+	10	-	-	+	+	+	+	-	-	-	-	-	+	180	89	27.5	94	140	96	185	###	4.0	256	38	200	4.8	92
77	460094	M	73	+	5	-	-	+	+	+	+	-	+	+	7	-	+	176	82	26.5	93	150	110	171	9.8	8.0	220	37	210	6.2	87
78	460236	F	62	+	6	-	-	+	-	+	+	+	+	-	-	-	-	174	80	26.4	95	140	90	129	7.6	11.0	200	40	159	7.6	98
79	460896	F	60	+	2	-	-	-	+	+	-	-	-	-	-	-	-	176	81	26.1	93	130	90	159	8.2	5.0	210	36	129	6.8	93
80	462640	M	58	+	10	-	-	-	+	+	+	+	+	+	3	-	-	184	90	26.6	94	160	110	149	9.7	3.5	214	38	204	7.2	84
81	464072	M	75	-	-	+	+	+	-	-	-	-	-	+	12	-	-	180	87	26.9	94	150	90	121	5.8	8.5	160	40	176	7.9	45
82	464390	M	58	+	8	-	-	+	-	+	+	+	+	-	-	-	-	180	89	27.5	95	130	90	163	9.2	6.5	189	38	212	7.0	40
83	464548	F	36	+	1	-	-	-	-	-	-	-	-	-	-	-	-	174	88	29.1	92	130	90	136	7.8	2.0	140	40	210	6.7	61
84	464758	F	50	+	3	-	-	-	-	-	-	-	-	+	3	-	-	176	81	26.1	93	140	70	145	8.1	4.5	130	42	119	4.8	88

ANNEXURE III - MASTER CHART

				History													Clinical examination						Investigations							
				Type 2 DM		Cerebrovascular events									HTN																
Serial Number	In Patient Number	Sex	Age (Years)	History	Duration (Years)	Angina pain	Myocardial infarction	Ischaemic heart disease	Peripheral neuropathy	Diabetic retinopathy	Diabetic nephropathy	Diabetic foot	Autonomic neuropathy	History	Duration (Years)	Peripheral vascular disease	Dislipidemia	Height (Cms)	Weight (Kg)	Body mass index (Kg/m2)	Waist circumference (Cms)	BP (mm Hg) Systolic	BP (mm Hg) Diastolic	Fasting blood sugar (mg/dL)	HbA1c	HOMA-IR	Total Triglycerides (mg/dL)	Total HDL (mg/dL)	Total Cholesterol (mg/dL)	Hs-CRP	Sr. GGT
85	461154	F	45	-	-	-	-	-	-	-	-	-	-	+	8	-	-	172	84	28.4	92	150	90	112	6.6	3.5	170	38	128	52.0	105
86	467400	M	60	+	4	-	-	-	-	-	-	-	-	+	4	-	-	183	89	26.6	92	160	90	124	7.6	5.0	180	39	131	7.0	104
87	467185	M	90	+	15	-	+	+	+	+	+	+	-	+	15	-	-	175	84	27.4	91	170	80	133	7.8	4.0	210	40	220	3.0	40
88	468103	M	52	+	2	-	-	-	-	-	-	-	-	-	-	-	+	180	85	26.2	94	150	96	138	8.3	2.0	194	38	170	6.0	89
89	470099	M	50	-	-	-	-	-	-	-	-	-	-	+	5	-	+	172	82	27.7	93	160	90	112	6.8	5.5	220	36	184	5.9	92
90	474293	F	39	-	-	-	-	-	-	-	-	-	-	-	-	-	-	173	83	27.7	92	150	80	124	6.9	7.0	180	39	210	8.1	98
91	475563	M	80	+	20	-	-	+	+	+	+	+	-	+	25	-	-	186	96	27.7	91	160	80	140	7.8	6.5	210	40	223	7.3	56
92	460236	M	54	+	1	-	-	-	-	-	-	-	+	+	2	-	-	184	90	26.6	93	160	90	222	###	0.5	240	32	170	9.2	89
93	460896	M	48	-	-	-	-	-	-	-	-	-	-	-	-	-	-	173	79	26.4	94	170	110	240	###	4.5	270	30	276	8.9	99
94	462640	F	45	-	-	-	-	-	-	-	-	-	-	-	-	-	-	180	87	26.9	95	160	96	170	9.6	8.5	250	39	168	6.8	92
95	464072	M	50	+	2	-	-	+	-	-	+	+	-	+	1	-	-	174	84	27.7	95	150	110	141	8.6	6.0	198	38	190	7.6	93
96	464390	M	55	+	6	+	+	+	+	+	+	-	+	+	6	-	-	178	85	26.8	95	160	100	157	8.2	5.5	290	37	220	8.7	94
97	464548	M	62	+	10	+	+	+	-	+	+	+	+	-	-	-	-	176	89	28.7	92	140	98	143	8.4	2.5	200	36	170	6.8	92
98	464758	M	56	+	3	-	-	-	-	-	+	+	-	-	-	-	-	171	88	30.1	93	140	90	112	8.2	4.0	210	38	200	7.2	86
99	461154	M	68	+	10	-	+	+	+	+	+	-	+	+	9	-	-	173	86	28.7	95	170	100	171	9.8	3.0	170	38	215	12.0	85
100	544539	F	47	+	2	-	-	-	-	-	+	+	-	+	1	+	+	170	80	27.7	93	160	80	163	8.2	7.0	210	39	200	7.0	99

ANNEXURE III - MASTER CHART

Serial Number	In Patient Number	Demographics			History																Clinical examination								Investigations								
					T2 DM			Cerebrovascular events								HTN																					
		Sex	Age (Years)		History	Duration (Years)		Angina pain	Myocardial infarction	Ischaemic heart disease	Peripheral neuropathy	Diabetic retinopathy	Diabetic nephropathy	Diabetic foot	Autonomic neuropathy	History	Duration (Years)		Peripheral vascular disease	Dislipidemia	Height (Cms)	Weight (Kg)	BMI (Kg/m2)		WC (Cms)		BP (mm Hg) Systolic	BP (mm Hg) Diastolic		FBS (mg/dL)		HbA1c		HOMA-IR		Total TG (mg/dL)		Total HDL (mg/dL)
1	494442	M	40	1	-	-	-	-	-	-	-	-	-	-	-	+	1	1	-	-	150	65	28.9	2	97	1	130	86	1	98	0	6.0	1	7.0	1	170	1	38
2	494444	M	68	4	+	2	1	-	-	+	-	+	+	-	-	+	10	2	+	-	158	70	28.0	2	102	1	140	90	1	174	1	###	4	8.0	1	210	1	35
3	497096	F	54	3	+	4	1	-	-	-	+	+	-	-	+	+	4	1	-	-	160	78	30.5	3	110	1	150	85	1	134	1	9.6	4	8.5	1	198	1	32
4	496860	M	38	1	-	-	-	-	-	-	-	-	-	-	-	+	4	1	-	-	178	74	23.4	1	98	1	160	100	1	110	1	6.0	1	6.0	1	180	1	38
5	497115	M	40	1	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	172	78	26.4	2	89	0	150	80	0	117	1	9.8	4	7.5	1	157	1	39
6	497109	F	52	3	-	-	-	-	-	+	-	+	+	-	-	+	6	2	+	-	160	62	24.2	1	96	1	160	90	1	104	1	6.7	2	7.0	1	140	0	39
7	497103	M	40	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	170	71	24.6	1	94	1	140	100	1	106	1	6.0	1	4.0	1	149	0	36
8	497113	F	32	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	168	80	28.3	2	82	1	130	100	1	98	0	5.4	1	6.0	1	130	0	46
9	498136	M	47	2	+	1	1	-	-	-	-	+	-	-	+	+	5	1	-	+	176	78	25.2	2	96	1	140	90	1	142	1	8.6	4	5.5	1	190	1	34
10	499186	F	48	2	+	1	1	+	-	-	+	+	+	-	-	-	-	-	-	+	170	79	27.3	2	92	1	140	80	0	137	1	###	4	5.0	1	150	0	42
11	599591	M	64	4	+	4	1	-	+	+	-	+	+	+	+	+	4	1	+	+	176	82	26.5	2	98	1	150	70	1	128	1	9.7	4	4.0	1	140	0	34
12	500169	F	43	2	+	6	2	+	-	-	-	+	+	-	-	-	-	-	-	+	172	78	26.4	2	91	1	140	60	0	109	1	7.0	3	7.0	1	180	1	39
13	504936	M	50	2	-	-	-	-	-	+	-	-	-	-	-	+	8	2	-	+	180	82	25.3	2	94	1	140	90	1	120	1	6.8	2	8.0	1	210	1	38
14	506610	F	42	2	+	1	1	-	-	-	+	+	+	-	+	-	-	-	-	-	174	79	26.1	2	94	1	130	90	1	109	1	6.9	2	4.5	1	170	1	43
15	506805	M	53	3	-	-	-	-	-	-	-	-	-	-	-	+	6	2	-	-	182	88	26.6	2	94	1	150	100	1	117	1	5.6	1	5.0	1	150	0	40
16	507460	F	36	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	176	84	27.1	2	93	1	140	100	1	111	1	5.7	1	6.0	1	140	0	38
17	507595	M	47	2	+	1	1	-	-	-	-	-	-	+	-	-	-	-	-	+	174	80	26.4	2	94	1	140	85	1	141	1	8.4	4	6.5	1	157	1	41
18	507806	F	41	2	+	2	1	-	-	+	+	+	-	+	+	+	2	1	-	-	178	88	27.8	2	92	1	130	90	1	130	1	9.1	4	3.0	0	120	0	38
19	508263	F	35	1	-	-	-	-	-	-	-	-	-	-	-	+	1	1	-	-	174	79	26.1	2	92	1	140	70	1	112	1	5.4	1	2.0	0	159	1	44
20	510512	M	51	3	+	4	1	-	-	+	+	+	+	+	-	+	3	1	-	+	175	80	26.1	2	94	1	150	70	1	126	1	7.4	3	4.5	1	149	0	40
21	509605	M	48	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	182	90	27.2	2	96	1	160	90	1	189	1	9.6	4	7.0	1	160	1	33
22	511000	M	68	4	+	10	2	-	+	+	+	+	+	-	+	+	9	2	-	-	184	91	26.9	2	95	1	170	100	1	171	1	9.8	4	9.0	1	170	1	38
23	512079	F	47	2	+	2	1	-	-	-	-	-	+	+	-	+	1	1	+	+	180	100	30.9	3	93	1	160	80	1	163	1	8.2	4	4.0	1	210	1	39
24	511482	F	60	3	+	7	2	-	+	+	+	+	+	+	+	+	4	1	-	-	174	87	28.7	2	94	1	180	90	1	147	1	9.1	4	8.0	1	197	1	42

ANNEXURE III - MASTER CHART

Serial Number	In Patient Number	Demograp			History																	Clinical examination									Investigations								
					T2 DM			Cerebrovascular events								HTN												BP (mm Hg)												
		Sex	Age (Years)		History	Duration (Years)		Angina pain	Myocardial infarction	Ischaemic heart disease	Peripheral neuropathy	Diabetic retinopathy	Diabetic nephropathy	Diabetic foot	Autonomic neuropathy	History	Duration (Years)		Peripheral vascular disease	Dislipidemia	Height (Cms)	Weight (Kg)	BMI (Kg/m2)		WC (Cms)		Systolic	Diastolic		FBS (mg/dL)		HbA1c		HOMA-IR		Total TG (mg/dL)		Total HDL (mg/dL)
25	512742	M	62	4	+	5	1	+	+	+	+	+	+	+	+	+	5	1	-	+	180	101	31.2	3	94	1	130	70	1	162	1	7.8	3	7.5	1	167	1	38
26	513172	M	42	2	+	1	1	-	-	-	-	-	-	-	-	+	1	1	-	-	184	96	28.4	2	94	1	140	96	1	113	1	7.0	3	###	1	170	1	42
27	512877	F	45	2	+	2	1	-	-	+	+	+	+	+	+	-	-	-	-	+	175	84	27.4	2	94	1	150	70	0	142	1	8.6	4	5.0	1	180	1	40
28	514490	M	35	1	-	-	-	-	-	-	+	+	+	-	+	-	-	-	-	-	178	84	26.5	2	96	1	160	90	1	198	1	###	4	7.0	1	157	1	34
29	515447	F	40	1	-	-	-	-	-	-	+	+	+	-	-	-	-	-	-	-	180	89	27.5	2	94	1	170	90	1	192	1	###	4	3.0	0	179	1	35
30	514883	F	49	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	183	95	28.4	2	92	1	150	70	0	100	0	5.5	1	4.0	1	162	1	36
31	513168	M	57	3	+	3	1	-	-	+	+	+	-	-	+	-	-	-	-	+	186	94	27.2	2	93	1	140	100	1	139	1	8.6	4	8.0	1	159	1	38
32	516696	M	55	3	+	2	1	-	-	+	+	+	+	-	-	-	-	-	-	-	184	92	27.2	2	93	1	150	70	0	112	1	7.6	3	2.0	0	158	1	38
33	515493	F	47	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	180	100	30.9	3	94	1	140	90	1	111	1	7.0	3	9.0	1	150	0	40
34	516844	M	38	1	-	-	-	-	-	-	-	-	-	-	-	+	1	1	-	+	175	91	29.7	2	93	1	150	80	1	112	1	7.2	3	5.5	1	160	1	42
35	517529	F	47	2	+	2	1	-	-	+	-	+	+	+	-	+	2	1	-	-	171	88	30.1	3	93	1	160	80	1	109	1	7.8	3	6.5	1	167	1	38
36	517591	F	49	2	-	-	-	-	-	-	+	-	-	-	-	+	3	1	-	-	174	98	32.4	3	92	1	150	80	1	117	1	5.6	1	7.0	1	159	1	40
37	517783	F	42	2	+	1	1	-	-	-	+	-	-	-	-	-	-	-	-	-	178	89	28.1	2	92	1	140	96	1	112	1	7.6	3	4.0	1	152	1	38
38	516009	M	47	2	+	2	1	-	-	-	+	+	-	+	-	-	-	-	-	-	175	93	30.4	3	93	1	130	85	1	100	1	7.8	3	7.5	1	140	0	42
39	518636	F	39	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	176	85	27.4	2	92	1	140	90	1	112	1	6.8	2	8.0	1	150	0	38
40	2482598	F	68	4	+	10	2	-	-	+	-	+	+	-	+	-	-	-	-	-	179	86	26.8	2	92	1	110	80	0	108	1	7.9	3	7.0	1	152	1	42
41	1144752	M	34	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	176	84	27.1	2	93	1	140	80	0	102	1	5.6	1	9.0	1	140	0	38
42	2498470	M	42	2	+	1	1	-	-	-	-	-	-	-	-	+	1	1	-	-	186	90	26.0	2	93	1	150	90	1	129	1	7.8	3	5.5	1	160	1	39
43	525010	M	52	3	-	-	-	-	-	-	-	-	-	-	-	+	2	1	-	+	192	98	26.6	2	92	1	130	90	1	111	1	6.4	1	4.5	1	152	1	36
44	525554	F	48	2	+	3	1	-	-	+	-	-	+	-	-	+	1	1	-	-	180	87	26.9	2	94	1	140	84	1	112	1	7.8	3	8.5	1	160	1	38
45	2498470	M	52	3	-	-	-	-	-	-	-	-	-	-	-	+	4	1	-	+	188	93	26.3	2	93	1	160	80	1	108	1	6.0	1	6.0	1	158	1	40
46	2506676	F	46	2	-	-	-	-	-	-	-	-	-	-	-	+	3	1	-	-	186	96	27.7	2	93	1	170	90	1	109	1	6.0	1	3.0	0	150	0	38
47	2506669	F	50	2	+	4	1	-	-	-	-	+	+	-	-	-	-	-	-	-	178	88	27.8	2	94	1	160	90	1	112	1	8.7	4	6.0	1	178	1	37
48	2529966	F	46	2	+	2	1	-	-	-	-	-	+	+	-	+	2	1	-	-	182	91	27.5	2	93	1	150	70	1	118	1	7.9	3	5.0	1	220	1	38

ANNEXURE III - MASTER CHART

Serial Number	In Patient Number	Demograp			History																	Clinical examination									Investigations								
					T2 DM			Cerebrovascular events								HTN												BP (mm Hg)												
		Sex	Age (Years)		History	Duration (Years)		Angina pain	Myocardial infarction	Ischaemic heart disease	Peripheral neuropathy	Diabetic retinopathy	Diabetic nephropathy	Diabetic foot	Autonomic neuropathy	History	Duration (Years)		Peripheral vascular disease	Dislipidemia	Height (Cms)	Weight (Kg)	BMI (Kg/m2)		WC (Cms)		Systolic	Diastolic		FBS (mg/dL)		HbA1c		HOMA-IR		Total TG (mg/dL)		Total HDL (mg/dL)
49	2531656	M	57	3	+	2	1	-	-	-	-	+	+	-	-	+	5	1	-	-	178	89	28.1	2	93	1	120	80	1	138	1	7.8	3	8.0	1	159	1	40
50	799495	F	50	2	+	4	1	-	-	-	-	+	+	+	-	-	-	-	-	+	179	88	27.5	2	94	1	140	70	0	142	1	8.4	4	9.0	1	160	1	38
51	2548361	M	40	1	+	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	176	89	28.7	2	93	1	150	80	0	163	1	7.4	3	7.5	1	170	1	42
52	2561902	M	52	3	-	-	-	-	-	+	-	-	-	-	-	+	5	1	-	-	177	90	28.7	2	94	1	120	80	1	108	1	6.4	1	3.5	0	210	1	36
53	2553737	F	48	2	+	2	1	-	-	-	+	+	-	-	+	-	-	-	-	+	176	85	27.4	2	94	1	140	90	1	138	1	8.7	4	2.0	0	220	1	39
54	2556795	F	44	2	+	1	1	-	-	-	-	+	+	+	-	-	-	-	-	+	178	86	27.1	2	95	1	130	90	1	172	1	9.3	4	7.0	1	180	1	40
55	534895	M	54	3	+	1	1	-	-	-	-	-	-	-	+	+	2	1	-	-	188	94	26.6	2	93	1	160	90	1	222	1	###	4	2.0	0	240	1	32
56	533912	M	48	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	178	87	27.5	2	94	1	170	110	1	240	1	###	4	1.5	0	270	1	30
57	539989	F	45	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	176	83	26.8	2	95	1	160	96	1	170	1	9.6	4	8.0	1	250	1	39
58	535397	M	50	2	+	2	1	-	-	+	-	-	+	+	-	+	1	1	-	-	174	84	27.7	2	95	1	150	110	1	141	1	8.6	4	0.5	0	198	1	38
59	536758	M	55	3	+	6	2	+	+	+	+	+	+	-	+	+	6	2	-	-	182	88	26.6	2	95	1	160	100	1	157	1	8.2	4	5.0	1	290	1	37
60	537000	M	62	4	+	10	2	+	+	+	-	+	+	+	+	-	-	-	-	-	178	84	26.5	2	92	1	140	98	1	143	1	8.4	4	8.0	1	200	1	36
61	539379	M	56	3	+	3	1	-	-	-	-	-	+	+	-	-	-	-	-	-	179	85	26.5	2	93	1	140	90	1	112	1	8.2	4	9.0	1	210	1	38
62	539413	F	52	3	-	-	-	-	-	-	+	+	+	+	+	+	6	2	-	-	170	82	28.4	2	93	1	150	90	1	240	1	###	4	4.0	1	240	1	32
63	539632	M	48	2	+	2	1	+	-	-	-	-	-	-	-	+	2	1	-	-	170	78	27.0	2	94	1	140	80	1	136	1	8.9	4	5.5	1	220	1	36
64	539634	M	48	2	+	4	1	-	-	-	-	-	-	+	-	+	1	1	+	+	173	79	26.4	2	93	1	110	80	1	144	1	9.6	4	3.0	0	237	1	39
65	541712	M	40	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	172	78	26.4	2	94	1	140	90	1	138	1	7.8	3	4.5	1	210	1	36
66	542610	F	58	3	+	5	1	-	+	+	+	+	+	-	-	-	-	-	-	-	170	79	27.3	2	94	1	150	85	1	164	1	8.8	4	0.5	0	200	1	34
67	543409	M	42	2	+	2	1	-	-	-	-	-	-	-	-	+	1	1	-	+	174	80	26.4	2	92	1	160	80	1	132	1	7.6	3	5.5	1	189	1	37
68	543410	M	47	2	+	1	1	-	-	-	-	+	-	-	-	-	-	-	-	-	176	88	28.4	2	94	1	110	70	0	128	1	7.9	3	4.0	1	160	1	40
69	542963	F	45	2	-	-	-	-	-	-	-	-	-	-	-	+	1	1	-	+	178	84	26.5	2	93	1	110	90	1	120	1	6.4	1	7.5	1	177	1	38
70	544203	F	36	1	+	4	1	-	-	-	-	-	-	-	-	-	-	-	-	-	179	84	26.2	2	92	1	110	60	0	112	1	5.2	1	4.0	1	160	1	39
71	544539	M	58	3	+	1	1	-	-	-	-	-	-	-	-	+	10	2	-	+	175	82	26.8	2	93	1	140	88	1	104	1	6.7	2	4.0	1	152	1	38
72	544663	M	52	3	+	2	1	-	-	+	+	+	-	-	-	+	2	1	-	-	188	99	28.0	2	93	1	150	100	1	141	1	9.8	4	4.5	1	159	1	40

ANNEXURE III - MASTER CHART

Serial Number	In Patient Number	Demograp			History																	Clinical examination										Investigations								
					T2 DM			Cerebrovascular events									HTN																									
		Sex	Age (Years)		History	Duration (Years)		Angina pain	Myocardial infarction	Ischaemic heart disease	Peripheral neuropathy	Diabetic retinopathy	Diabetic nephropathy	Diabetic foot	Autonomic neuropathy	History	Duration (Years)		Peripheral vascular disease	Dislipidemia	Height (Cms)	Weight (Kg)	BMI (Kg/m2)		WC (Cms)		BP (mm Hg)			FBS (mg/dL)		HbA1c		HOMA-IR		Total TG (mg/dL)		Total HDL (mg/dL)	
73	452761	M	48	2	+	2	1	-	-	-	+	+	+	-	-	+	8	2	-	-	176	87	28.1	2	94	1	140	100	1	194	1	8.4	4	7.0	1	167	1	37
74	454499	M	63	4	-	-	-	-	-	-	-	-	-	-	-	+	10	2	-	-	173	86	28.7	2	93	1	200	100	1	136	1	7.0	3	9.0	1	220	1	36
75	457586	M	48	2	+	3	1	-	+	+	-	+	+	-	-	+	3	1	-	-	186	94	27.2	2	93	1	190	90	1	167	1	9.6	4	7.0	1	248	1	34
76	459674	F	59	3	+	10	2	-	-	+	+	+	+	-	-	-	-	-	-	+	180	89	27.5	2	94	1	140	96	1	185	1	###	4	4.0	1	256	1	38
77	460094	M	73	4	+	5	1	-	-	+	+	+	+	-	+	+	7	2	-	+	176	82	26.5	2	93	1	150	110	1	171	1	9.8	4	8.0	1	220	1	37
78	460236	F	62	4	+	6	2	-	-	+	-	+	+	+	+	-	-	-	-	-	174	80	26.4	2	95	1	140	90	1	129	1	7.6	3	###	1	200	1	40
79	460896	F	60	3	+	2	1	-	-	-	+	+	-	-	-	-	-	-	-	-	176	81	26.1	2	93	1	130	90	1	159	1	8.2	4	5.0	1	210	1	36
80	462640	M	58	3	+	10	2	-	-	-	+	+	+	+	+	+	3	1	-	-	184	90	26.6	2	94	1	160	110	1	149	1	9.7	4	3.5	0	214	1	38
81	464072	M	75	4	-	-	-	+	+	+	-	-	-	-	-	+	12	3	-	-	180	87	26.9	2	94	1	150	90	1	121	1	5.8	1	8.5	1	160	1	40
82	464390	M	58	3	+	8	2	-	-	+	-	+	+	+	+	-	-	-	-	-	180	89	27.5	2	95	1	130	90	1	163	1	9.2	4	6.5	1	189	1	38
83	464548	F	36	1	+	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	174	88	29.1	2	92	1	130	90	1	136	1	7.8	3	2.0	0	140	0	40
84	464758	F	50	2	+	3	1	-	-	-	-	-	-	-	-	+	3	1	-	-	176	81	26.1	2	93	1	140	70	1	145	1	8.1	4	4.5	1	130	0	42
85	461154	F	45	2	-	-	-	-	-	-	-	-	-	-	-	+	8	2	-	-	172	84	28.4	2	92	1	150	90	1	112	1	6.6	2	3.5	0	170	1	38
86	467400	M	60	3	+	4	1	-	-	-	-	-	-	-	-	+	4	1	-	-	183	89	26.6	2	92	1	160	90	1	124	1	7.6	3	5.0	1	180	1	39
87	467185	M	90	4	+	15	3	-	+	+	+	+	+	+	-	+	15	3	-	-	175	84	27.4	2	91	1	170	80	1	133	1	7.8	3	4.0	1	210	1	40
88	468103	M	52	3	+	2	1	-	-	-	-	-	-	-	-	-	-	-	-	+	180	85	26.2	2	94	1	150	96	1	138	1	8.3	4	2.0	0	194	1	38
89	470099	M	50	2	-	-	-	-	-	-	-	-	-	-	-	+	5	1	-	+	172	82	27.7	2	93	1	160	90	1	112	1	6.8	2	5.5	1	220	1	36
90	474293	F	39	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	173	83	27.7	2	92	1	150	80	0	124	1	6.9	2	7.0	1	180	1	39
91	475563	M	80	4	+	20	3	-	-	+	+	+	+	+	-	+	25	3	-	-	186	96	27.7	2	91	1	160	80	1	140	1	7.8	3	6.5	1	210	1	40
92	460236	M	54	3	+	1	1	-	-	-	-	-	-	-	+	+	2	1	-	-	184	90	26.6	2	93	1	160	90	1	222	1	###	4	0.5	0	240	1	32
93	460896	M	48	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	173	79	26.4	2	94	1	170	110	1	240	1	###	4	4.5	1	270	1	30
94	462640	F	45	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	180	87	26.9	2	95	1	160	96	1	170	1	9.6	4	8.5	1	250	1	39
95	464072	M	50	2	+	2	1	-	-	+	-	-	+	+	-	+	1	1	-	-	174	84	27.7	2	95	1	150	110	1	141	1	8.6	4	6.0	1	198	1	38
96	464390	M	55	3	+	6	2	+	+	+	+	+	+	-	+	+	6	2	-	-	178	85	26.8	2	95	1	160	100	1	157	1	8.2	4	5.5	1	290	1	37

ANNEXURE III - MASTER CHART

Serial Number	In Patient Number	Demographics			History																Clinical examination								Investigations								
					T2 DM			Cerebrovascular events								HTN																						
		Sex	Age (Years)		History	Duration (Years)		Angina pain	Myocardial infarction	Ischaemic heart disease	Peripheral neuropathy	Diabetic retinopathy	Diabetic nephropathy	Diabetic foot	Autonomic neuropathy	History	Duration (Years)		Peripheral vascular disease	Dislipidemia	Height (Cms)	Weight (Kg)	BMI (Kg/m2)		WC (Cms)		Systolic	Diastolic		FBS (mg/dL)		HbA1c		HOMA-IR		Total TG (mg/dL)		Total HDL (mg/dL)
97	464548	M	62	4	+	10	2	+	+	+	-	+	+	+	+	-	-	-	-	-	176	89	28.7	2	92	1	140	98	1	143	1	8.4	4	2.5	0	200	1	36
98	464758	M	56	3	+	3	1	-	-	-	-	-	+	+	-	-	-	-	-	-	171	88	30.1	3	93	1	140	90	1	112	1	8.2	4	4.0	1	210	1	38
99	461154	M	68	4	+	10	2	-	+	+	+	+	+	-	+	+	9	2	-	-	173	86	28.7	2	95	1	170	100	1	171	1	9.8	4	3.0	0	170	1	38
100	544539	F	47	2	+	2	1	-	-	-	-	-	+	+	-	+	1	1	+	+	170	80	27.7	2	93	1	160	80	1	163	1	8.2	4	7.0	1	210	1	39

0 Normal
1 Abnormal

ANNEXURE III - MASTER CHART

	Total CHL (mg/dL)		Hs-CRP		Serum GGT		Components
1	210	1	2.0	0	57	0	4
1	198	0	7.5	1	73	0	5
1	170	0	7.8	1	58	1	5
1	180	0	7.7	1	60	0	5
1	120	0	8.7	1	75	0	3
1	140	0	12.0	1	77	1	4
1	150	0	9.0	1	70	0	4
1	154	0	8.0	1	81	1	3
1	170	0	4.0	1	55	0	5
1	180	0	7.0	1	57	1	3
1	174	0	3.0	0	60	0	4
1	190	0	6.0	1	63	1	4
1	210	1	9.0	1	56	0	5
1	139	0	2.4	0	66	1	5
0	154	0	4.0	1	70	0	3
1	140	0	7.0	1	65	1	4
0	150	0	4.0	1	62	0	4
1	130	0	10.0	1	59	1	4
1	150	0	7.0	1	80	1	5
0	134	0	12.0	1	74	0	3
1	168	0	6.0	1	40	0	5
1	160	0	12.0	1	66	0	5
1	200	1	7.0	1	31	0	5
1	137	0	8.0	1	34	0	5

ANNEXURE III - MASTER CHART

	Total CHL (mg/dL)		Hs-CRP		Serum GGT		Components
1	150	0	5.8	1	54	0	5
0	139	0	7.9	1	45	0	4
1	167	0	6.0	1	38	0	4
1	172	0	9.0	1	47	0	5
1	139	0	9.2	1	49	0	5
1	178	0	7.0	1	38	0	3
1	172	0	8.4	1	32	0	5
1	150	0	7.4	1	35	0	4
1	160	0	8.0	1	45	0	4
0	170	0	5.0	1	40	0	4
1	169	0	6.0	1	32	0	5
1	139	0	5.9	1	34	0	5
1	128	0	3.9	1	38	0	5
0	168	0	4.8	1	36	0	3
1	170	0	5.4	1	38	0	4
1	120	0	6.0	1	42	0	4
1	140	0	5.0	1	36	0	3
1	139	0	6.0	1	58	0	5
1	137	0	5.3	1	38	0	5
1	167	0	4.3	1	29	0	5
0	170	0	7.2	1	53	0	4
1	139	0	6.8	1	50	0	4
1	168	0	5.4	1	32	0	5
1	190	0	8.0	1	18	0	5

ANNEXURE III - MASTER CHART

	Total CHL (mg/dL)		Hs-CRP		Serum GGT		Components
0	169	0	5.8	1	46	0	4
1	170	0	7.0	1	45	0	4
0	180	0	8.0	1	49	0	3
1	120	0	8.2	1	52	0	5
1	160	0	5.0	1	30	0	5
1	159	0	8.0	1	56	1	5
1	170	0	9.2	1	52	0	5
1	276	1	8.9	1	55	0	5
1	168	0	6.8	1	42	0	5
1	190	0	7.6	1	45	0	5
1	220	1	8.7	1	49	0	5
1	170	0	6.8	1	48	0	5
1	200	1	7.2	1	46	0	5
1	276	1	8.0	1	45	0	5
1	229	1	7.9	1	37	0	5
1	178	0	6.3	1	42	0	5
1	220	1	7.2	1	42	0	5
1	166	0	7.8	1	45	0	5
1	159	0	7.4	1	68	0	5
0	179	0	6.0	1	47	0	3
1	129	0	5.0	1	70	1	5
1	110	0	5.6	1	42	0	4
1	120	0	7.0	1	52	0	5
0	100	0	8.2	1	38	0	4

ANNEXURE III - MASTER CHART

	Total CHL (mg/dL)		Hs-CRP		Serum GGT		Components
1	176	0	8.1	1	35	0	5
1	199	0	7.2	1	77	0	5
1	236	1	5.4	1	78	0	5
1	200	1	4.8	1	32	0	5
1	210	1	6.2	1	67	0	5
1	159	0	7.6	1	38	0	5
1	129	0	6.8	1	30	0	5
1	174	0	7.2	1	60	0	5
0	176	0	7.9	1	45	0	4
1	170	0	7.0	1	40	0	5
1	210	1	6.7	1	61	1	4
1	119	0	4.8	1	40	0	4
1	128	0	52.0	1	38	0	5
1	131	0	7.0	1	58	0	5
0	160	0	3.0	0	40	0	4
1	170	0	6.0	1	38	0	5
1	184	0	5.9	1	52	0	5
1	210	1	8.1	1	48	0	4
0	123	0	7.3	1	20	0	4
1	170	0	9.2	1	52	0	5
1	276	1	8.9	1	55	0	5
1	168	0	6.8	1	42	0	5
1	190	0	7.6	1	45	0	5
1	220	1	8.7	1	49	0	5

ANNEXURE III - MASTER CHART

	Total CHL (mg/dL)		Hs-CRP		Serum GGT		Components
1	170	0	6.8	1	48	0	5
1	200	1	7.2	1	46	0	5
1	160	0	12.0	1	50	0	5
1	200	1	7.0	1	40	0	5

Annexures

Annexure III

ANNEXURE III – MASTER CHART

-	-	Absent
+	-	Present
BP	-	Blood pressure
bpm	-	Beats per minute
DM	-	Diabetes mellitus
E	-	Expired
HbA1c	-	Glycated haemoglobin
HOMA	-	Homoeostatic model assessment
Hs-CRP	-	Highly sensitive C reactive protein
I	-	Improved
IR	-	Insulin resistance
mg/dL	-	Milligram per deciliter
mm Hg	-	Millimeter of mercury
N	-	Normal
NIHS	-	National Institutes of Health Stroke
S	-	Unchanged
Sr. GGT	-	Serum gamma glutamyl transpeptidase
W	-	Worsened