“STUDY OF LEVELS OF SERUM FERRITIN IN PATIENTS WITH METABOLIC SYNDROME”

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In partial fulfilment of the requirements for the degree of

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IN

GENERAL MEDICINE

Under the guidance of

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2015

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Dr. M. VAMSHI KRISHNA

LIST OF ABBREVIATIONS

AACE	-	American Association of Clinical Endocrinology
AMP	-	Adenosine Mono Phosphate
ARBs	-	Angiotensin II type I Receptor Blockers
BMI	-	Body Mass Index
CAD	-	Coronary Artery Disease
CRP	-	C - Reactive Protein
CVD	-	Coronary Vascular Disease
DM	-	Diabetes Mellitus
ECG	-	Electrocardiogram
EGIR	-	European Group For The Study Of Insulin Resistance
ELISA	-	Enzyme Linked ImmunoSorbent Assay
FBS	-	Fasting Blood Sugar
FFAs	-	Free Fatty Acids
HDL	-	High Density Lipoprotein
HH	-	Hereditary Haemochromatosis
HMW	-	High Molecular Weight
HPA	-	Hypothalamic-pituitary-adrenal axis
IFG	-	Impaired Fasting Glucose
IGT	-	Impaired glucose tolerance
IHD	-	Ischemic Heart Disease
IL-6	-	InterLeukin-6
LDL	-	Low Density Lipoprotein
LMW	-	Low Molecular Weight
MS	-	Metabolic Syndrome

NCEP	-	National Cholesterol Education Program
NO	-	Nitric Oxide
OHA	-	Oral Hypoglycemic Agent
PPARγ	-	Peroxisome Proliferator Activated Receptor γ
PPBS	-	Post Prandial blood sugar
RE	-	Reticulo-Endothelial cells
rNCEP	-	Revised National Cholesterol Education Program
T2DM	-	Type 2 Diabetes Mellitus
TG	-	TriGlycerides
TNFα	-	Tumor Necrosis Factor α
TZD	-	Thiazolidinedione
VLDL	-	Very Low Density Lipoprotein
WHO	-	World Health Organization

ABSTRACT

Background:

The metabolic syndrome is a constellation of central obesity, Hypertriglyceridemia, low HDL cholesterol, hyperglycemia, and hypertension. Elevated serum ferritin levels independently predicted incident type 2 diabetes in prospective studies in apparently healthy men and women. In cross-sectional studies, elevated ferritin levels have been associated with hypertension, dyslipidemia, elevated fasting insulin and blood glucose and central adiposity.

The present study was done to determine the association of serum Ferritin in Metabolic Syndrome as well as to determine the relation between individual component of metabolic syndrome & number of components metabolic syndrome and plasma ferritin. It is a Correlational clinical single group study.

Objectives:

To study the relationship between serum ferritin levels and metabolic syndrome and its components.

Materials and Methods:

The study was conducted in BLDEU's Shri B. M. Patil Medical College, hospital and research center, Vijayapur. Our study included 150 patients of metabolic syndrome diagnosed as per NCEP ATP3 criteria.

Results:

In the present study, there were 88 males & 62 females with mean age distribution of 56.0±10.1. Majority of patients (57.3%) were above 45 yrs of age. There were only 6 patients below 35yrs of age. Mean BMI in our study was 29.4±12.1, with 123(82%) of patients meeting criteria for central obesity according to NCEP ATP3 guidelines. In our study 119 (79%) of patients had blood pressure

recording of more than 135/85mmhg. 100 (66.7) were known hypertensives on treatment. In our study 112 (79.9%) of patients were on treatment for diabetes mellitus, 11(7.3%) patients were not having diabetes mellitus. In our study 91(60.7%) patients had abnormal total cholesterol (>200mg/dl), 100(66.7%) patients had abnormal triglycerides (>150mg/dl) and 104 (69.3%) patients had abnormal HDL (<40mg/dl in males, <50 in females). There were 59 (39.4%) patients with 3 components of metabolic syndrome, 46 (30.7%) with 4 components and 45 (30%) with 5 components of metabolic syndrome. The present study revealed that Serum ferritin was increasing significantly with increasing number of components of metabolic syndrome with P value <0.001. It also showed that individual components of metabolic syndrome had significant correlation with increasing number of components of metabolic syndrome. Of all the components, central obesity and hypertensive were increasingly associated with metabolic syndrome with a significant p value of <0.001 while dyslipidemia (both triglycerides and HDL criteria) also showed similar correlation of statistical significance (p value of 0.002 and 0.001).

CONCLUSION:

There is a positive association between elevated iron stores, measured by serum ferritin levels, and the prevalence of the metabolic syndrome. Serum ferritin levels correlated with increasing number of components of the metabolic syndrome. There is a positive correlation between individual components of metabolic syndrome with increasing number of components of metabolic syndrome.

Key words: metabolic syndrome, ferritin

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INTRODUCTION

The metabolic syndrome (MS) is a modern disease, characterized by excess weight, high blood pressure, high blood sugar, high triglycerides and low HDL levels. It is a combination of inter-connected factors that increase the risk of coronary heart disease (CHD), other forms of cardiovascular atherosclerotic diseases (CVD), and Type 2 Diabetes Mellitus (DM). According to Martinez-Gonzalez et al. Metabolic syndrome is an interplay of lifestyle and environmental factors.

Other abnormalities such as chronic pro-inflammatory and pro-thrombotic states, micro albuminuria and sleep apnea have been added to the entity of to this syndrome. Besides the many components and clinical implications of MS, there is still no universally accepted pathogenic mechanism or clearly defined diagnostic criteria. Ever since Reaven described about it in 1988[1], many definitions have been published by organizations including the National Cholesterol Education Program (NCEP), the International Diabetes Federation, and the World Health Organization, among others. Among these, the 2001 Third Report of the NCEP's Adult Treatment Panel is the most widely used definition because of its simple approach for diagnosing the MS by using risk factors which are easily measureable. 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); reduced high-density lipoprotein (HDL) cholesterol (men <40 mg/dl; women <50 mg/dl); Systemic hypertension (>130 mm Hg systolic and >85 mm Hg diastolic); 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. The 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. The rNCEP definition also includes patients who are being treated for dyslipidemia, hyperglycemia, or systemic hypertension

The incidence of Metabolic Syndrome has been increasing over the past 2 decades. Its prevalence is increasing in both childhood and young adulthood which will impact the global health burden .The prevalence of MS varies as it depends on the criteria used in different definitions, and the composition (sex, age, race and ethnicity) of the population studied. The prevalence of MS is high and rising in all western societies, which could be a result of the obesity epidemic[2].

The close association of type 2 diabetes mellitus and atherosclerotic cardiovascular disease suggest that they share a common physiologic cause, postulated to be resistance to insulin. Insulin resistance is associated with a cluster of risk factors recognized as the metabolic syndrome. Some studies indicated that increased accumulation of iron in the body affects the synthesis and secretion of insulin by the pancreas and compromises insulin action on target tissues leading to insulin resistance.

Ferritin is the stored form of iron in the body. Within the cells, iron is stored complexed to protein as ferritin or hemosiderin. Apoferritin binds to free ferrous iron and stores it in the ferric state. As ferritin accumulates within cells of the reticuloendothelial system, protein aggregates are formed as hemosiderin. Iron in ferritin can be extracted for release by the RE cells. Under steady state conditions, the serum ferritin level correlates with total body iron stores; thus, the serum ferritin measurement is the most convenient laboratory test to estimate iron stores.

Elevated serum ferritin levels independently predicted incident type 2 diabetes mellitus in prospective studies in apparently healthy men and women. In cross-

sectional studies, elevated ferritin levels have been associated with hypertension, dyslipidemia, elevated fasting insulin and blood glucose and central adiposity. The association between elevated iron stores and the metabolic syndrome, however, has not been well explored.

Some studies indicated that serum ferritin could be added to routine evaluation of metabolic syndrome patients; this would help identify a subgroup of individuals at risk for iron-related tissue damage. While some studies have shown that elevated iron stores were positively associated with the prevalence of the metabolic syndrome other studies concluded that it may become advisable to routinely screen for mildly elevated or even high-normal serum ferritin concentrations in the context of glucose intolerance.

A number of similar studies have been done in other countries but very few studies have been done in India. In the future, actively lowering body iron stores may become a tool in preventing type 2 diabetes mellitus in selected subgroups. Therefore, the present study was undertaken to find the levels of serum ferritin in patients with MS and to correlate the levels of serum ferritin with the different components of MS, so as to examine the relationship of serum ferritin with each of the components of MS, which might provide clues to the preferential pathways operative in different cardio-metabolic risks.

AIMS AND OBJECTIVES

1. To study the relationship between levels of serum ferritin & metabolic syndrome.
2. To evaluate the relationship between serum ferritin & different components of metabolic syndrome.

REVIEW OF LITERATURE

Metabolic syndrome is a combination of medical disorders that increase the risk of developing cardiovascular disease and diabetes. It affects one in five people, and prevalence increases with age. Some studies estimate the prevalence in the USA to be up to 25% of the population[3].

Metabolic syndrome is also known as metabolic syndrome X, syndrome X, insulin resistance syndrome, Reaven's syndrome, and CHAOS[4]. A similar condition in overweight horses is referred to as equine metabolic syndrome; it is unknown if they have the same etiology

History

The term "metabolic syndrome" dates back to at least the late 1950s, but came into common usage in the late 1970s to describe various associations of risk factors with diabetes that had been noted as early as the 1920s[5].

In 1923, Kylin first described the clustering of hypertension, hyperglycemia, and gout as a syndrome. The Marseilles physician Dr. Jean Vague, in 1947, observed that upper body obesity appeared to predispose to diabetes, atherosclerosis, gout and calculi[5].

Avogaro, Crepaldi and co-workers described six moderately obese patients with diabetes, hypercholesterolemia, and marked hypertriglyceridemia all of which improved when the patients were put on a hypocaloric, low-carbohydrate diet[6].In 1977, Haller used the term "metabolic syndrome" for associations of obesity, diabetes mellitus, hyperlipoproteinemia, hyperuricemia, and Hepatic steatosis when describing the additive effects of risk factors on atherosclerosis[7]. 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[8,9].

The term "insulin resistance syndrome" had been widely used which makes insulin resistance a common denominator of the syndrome. In 1999, the WHO proposed a unifying definition for the syndrome and called it Metabolic syndrome as it was not established that insulin resistance was the cause of all the components of the syndrome.[10]

Definitions of MS

The use of different criteria by various studies in defining MS has created confusion in determining the prevalence of MS. The WHO[10], the EGIR[11], the NCEP[12], the AACE[13] and the IDF[14] have proposed different definitions for this syndrome.

The new IDF definition emphasizes the importance of central obesity defined by ethnic specific values. WHO[10], EGIR[11], NCEP[12], AACE[13] and IDF[14] definitions of MS are as follows.

A. WHO definition[10]

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 (>1.7mmol/l or > 150 mg/dL) and/or
- Low HDL-cholesterol (<0.9mmol/l in men, < 1.0mmol/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/m2.

- 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).

B. EGIR definition for non-diabetic individuals[11]

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

- Hyperglycemia (fasting plasma glucose >6.1mmol/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 HDLcholesterol

  < 1.0 mmol/l [<39 mg/dL] or treated for dyslipidemia).

C. NCEP definition[12]

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).

D. AACE definition for non-diabetic individuals[13]

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).

E. IDF definition[14]

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 (>1.7mmol/l or > 150 mg/dL), or specific treatment for this lipid abnormality.
- Reduced HDL-cholesterol (< 1.03mmol/l or <40mg/dl in men, <1.29 mmol/l or <50mg/dl in women), or specific treatment for dyslipidaemia.
- 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 (>5.6mmol/l or 100mg/dl), or previously diagnosed type 2 diabetes.

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

EPIDEMIOLOGY

World Scenario:

According to the modified NCEP ATP III criteria the prevalence of MS having >3 components was 19.52%. The prevalence of MS in males was almost double (25.16%) which was highly significant (P=0.008). The prevalence of MS was almost same in the age groups of 20-40yrs and 41-60yrs (20.16% and 20.76%), and there was marginal decrease in the age group of >60yrs(16.66%). 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[10] 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).[15]

In 1998, the study done by the Singapore National Health Survey including 4,723 subjects of Chinese, Malay, and Asian-Indian ethnicity, demonstrated that the age-adjusted prevalence of MS as defined by the NCEP criteria[12] were 9.4, 18.7, and 20.4% for Chinese, Malays, and Asian-Indians, respectively. The prevalence rates increased to 14.8, 24.2, and 28.8% for the three ethnic groups, respectively when MS was defined according to APC criteria.[18]

In another study which included 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[10] definition was slightly higher in men (15.7%) than in women (14.2%). The prevalence of MS as defined by WHO criteria[10] in the European non diabetic adults was 15%.[16] In Omani adults aged 20 years and over, the prevalence of MS as defined by the NCEP criteria was 21.0% (men: 19.5%, women: 23.0%).[17] In a study which in included 40,698 Korean metropolitan subjects (26,528

men, 14,170 women) aged 20-82 years, the age-adjusted prevalence of MS as defined by the NCEP criteria[12] was 6.8% in total (5.2% male, 9.0% female).[19]

Indian Scenario

Different studies around the world, which included population samples, indicated that the prevalence varies from 8% (India) to 24% (United States) in men and from 7% (France) to 46% (India) in women.[20]

Among the 2 studies conducted in India, the first study[21] used the obesity criteria which was suitable for Indians, while the second study[22] used the standard ATP III definition of obesity. The studies reported prevalence of 13% in Jaipur and 41% in Chennai.[21] In the two study groups the prevalence of obesity was almost similar (31% versus 33%), even though different definitions used. Larger differences were observed for the prevalence of elevated triglycerides (46% vs. 30%), hypertension (55% vs. 39%) and elevated fasting plasma glucose (27% vs. 5%); which indicate that these risk factors would have a greater impact than obesity alone.

Many studies[23-25] have shown 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.[26]

Components of MS

The components of MS are IFG, IGT, insulin resistance, overweight/obesity, hypertension, and dyslipidemia, and incident diabetes. The most important and consistent risk factors among these are impaired glucose regulation (IGR), obesity, and insulin resistance.

1. Impaired glucose regulation

IGT was found to be a strong predictor of development of diabetes.[27] The Hoorn Study has shown 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.[28]

2. Obesity

Overweight, obesity, or weight gain has been shown as 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.[29] In this study 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 ($p<0.001$). The Bruneck Study which included a age and sex stratified random sample of 1,000 individuals aged 40- 79 years, confirmed that BMI was a predictor of incident diabetes, independently of other components of MS such as IFG, IGT, insulin resistance, hypertension, and dyslipidemia.[30]

3. Insulin resistance

In a prospective study of Pima Indians adjusted only for gender, the 90th percentile of fasting insulin level was associated with a 15.8-fold increased risk of incident diabetes compared with the 10th percentile.[31] The San Antonio Heart Study[32] (SAHS) which included 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 associated with a significant 2.3-fold increased risk of development of diabetes over an 8-year follow-up.

4. Dyslipidemia

The Norwegian population-based Finnmark study concluded that HDL cholesterol was inversely related to incident diabetes in women, but not in men, after adjustment for other risk factors such as BMI, diastolic blood pressure (DBP), glucose and ethnicity. After adjusting for age, triglycerides were positively related to the incidence of diabetes in men and women.[33] The MONICA (Monitoring of Trends and Determinants in Cardiovascular Disease) Augsburg Cohort Study[34] also displayed an inverse association between HDL-cholesterol and incident diabetes in both the genders.

5. Hypertension

The study done in Netherlands including 5,700 men and women, aged 20 to 65yrs showed that after adjusting for age and BMI, SBP and DBP were still associated with the incidence of diabetes in men [35]. The MONICA Augsburg Cohort Study[34] 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[34]. A study[36] reported that the Swedish women whose SBP was at least 145 mm Hg had 2.2 times the risk of developing diabetes than 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[37]. Micro albuminuria is also associated with increased risk of CVD in both diabetic and non-diabetic individuals[38]. The 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[40].

PATHOPHYSIOLOGY

The adipocytes (fat cells) of the visceral fat increase plasma levels of TNFα and alter the levels of a number of other substances (e.g., adiponectin, resistin, PAI-1). TNFα has been shown to cause the production of inflammatory cytokines and possibly to trigger cell signaling by interaction with a TNFα receptor that may lead to insulin resistance. An experiment with rats that were fed a diet one-third of which was sucrose has been proposed as a model for the development of the metabolic syndrome. The sucrose first elevated blood levels of triglycerides, which induced visceral fat and ultimately resulted in insulin resistance[41]. This progression from visceral fat to increased TNFα to insulin resistance may have some similarity in the development of metabolic syndrome in humans.

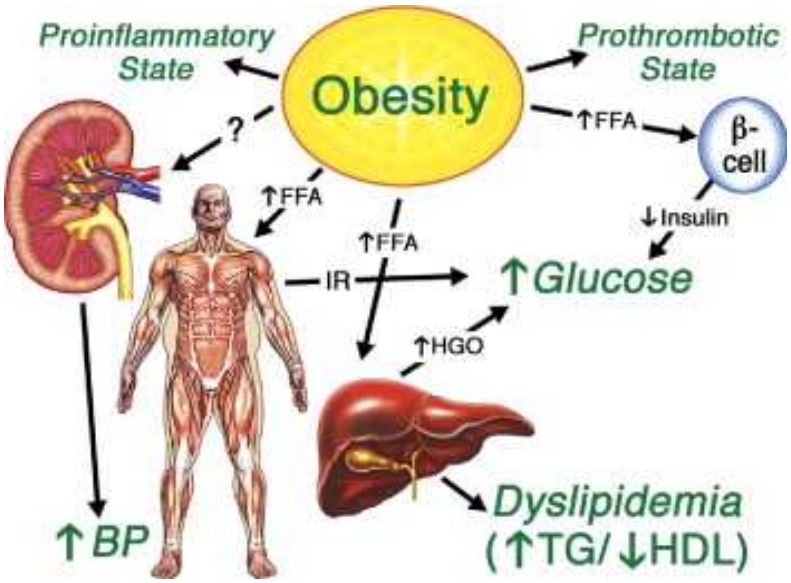

Figure 1: Pathophysiology of the metabolic syndrome

Although the underlying mechanism of the syndrome is not completely understood, environmental factors such as obesity and sedentary lifestyle together with unknown genetic triggers, increase susceptibility to the syndrome[42]. The environmental factors in the mechanism of MS include birth weight, childhood obesity, smoking, alcohol, social status and age.

A. Birth weight

Low birth weight and inadequate nutrition after birth are correlated with abnormal glucose tolerance, dyslipidemia and hyperinsulinemia in later adulthood. A study showed that MS was found in 22% of 64-year-old men whose birth weights were 2.95 kg or less. Their risk of developing MS was more than 10 times greater than that of men whose birth weights were more than 4.31 kg[43].

B. Childhood obesity

The development adulthood risk of CVD and type2 diabetes could be related to the somatic growth as a child and not necessarily to intrauterine growth. In the westernized countries, the proportion of children born with underweight is decreasing whereas the prevalence of MS is on the rise. This proves that low birth weight may not be the etiology of type 2 diabetes and CVD[44]. Conversely, obesity is increasing in the industrialized countries among all age groups, and thus making obesity an important risk factor for MS. In a study conducted among obese adults, the risk of MS was lower among obese adults, who had not been obese as children, compared to obese adults who had also been obese as children[45].

C. Smoking

The results of 54 published studies showed that, 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 apo-lipoprotein AI when compared to non-smokers[46]. It was shown that when the degree of insulin-mediated glucose uptake (insulin sensitivity) was compared in smoking and non-smoking men, the measures of insulin sensitivity were significantly lower in smokers [47].

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[48]. A Korean study reported that smoking of 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 respectively. According to this study, 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[49].

D. Alcohol

Studies have shown that there was reduced risk of MS and developing type2 diabetes by consumption of light to moderate alcohol. The biological mechanisms reported to explain this observation include an improvement of the lipid profile, especially HDL cholesterol and increasing insulin sensitivity[49].

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. 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[50].

E. Diet

The food habits of man have changed dramatically in the recent times. Major dietary change include a large increase in the consumption of fat and added sugar in the diet, an increase in animal food products and a fall in total cereal and fiber intake[51]. 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, a demographic shift toward an overall positive energy balance that has increased over the past few decades has been observed [52].

Intake of high total fat and saturated fat and low carbohydrates and fiber, correlated with higher fasting insulin concentrations[53]. Intake of high total fat has 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%)[54]. High fat intake has been shown to predict development of IGT in a group of healthy subjects and progression from IGT to type2 diabetes in a group of subjects with IGT[55]. 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[56].

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[57]. Compared to a refined-grain diet, whole-grain diet resulted in higher concentrations of insulin sensitivity and lower concentrations of fasting insulin[58].

F. Physical inactivity

The modern day advances in technology and transportation have reduced the need for physical activity in daily life leading to low levels of physical activity, which are associated with most components of MS, especially with an increased risk of obesity. The appeal of television, electronic games, and computers has increased the time spent in sedentary pursuits among children and adults.[59] A cohort study (1989 to 1997) in China which included 2,485 adults aged 20 to 45 years 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.[60,61]

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.[62] Exercise also has pronounced effects upon the metabolism of glucose because exercising muscle may increase glucose uptake 7- to 20- fold.[63] The Finnish Diabetes Prevention Study (DPS)[64] and the Diabetes Prevention Program (DPP)[65] in the United States revealed a 58% reduction in the risk of diabetes in high-risk subjects who enhanced physical activity. The DPS[64] 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 study in China[66], 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 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[67].

G. Obesity

The adoption of a more sedentary lifestyle and an increased intake of energy-rich diets, obesity is becoming increasingly common worldwide. It is now 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[68]. According the 4th CNHS[69] 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 in the clustering of the individual traits of MS.

A study in Hong Kong showed that, increasing BMI and WHR were closely associated with increased concentrations of TG and apo B, increased ratios between LDL and HDL (LDL/HDL) cholesterol, increased ratios between apo B and LDL (apo B/LDL), increased fasting and 2-h plasma glucose and insulin, and as well as decreased concentrations of HDL after adjustment for age, smoking, and insulin resistance[70].

The relationship between obesity and insulin sensitivity is well established. Visceral abdominal tissue (VAT) and subcutaneous abdominal tissue (SAT), were

measured from computed tomography scans, which were performed at the L4/L5 vertebral region. 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.[71] The NHANES II (National Health and Nutrition Examination Survey II) study[72] found obese women to be four times more likely to develop diastolic hypertension than non-obese women. In the Framingham population study[73], weight gain had a stronger relationship with blood pressure in males than in females. Thus obesity is an important risk factor of type 2 diabetes.[74]

PRESENTATION OF MS

The symptoms of MS may be related to any of the component disorders, such as the polyphagia (increased hunger), polydipsia (thirst), or polyuria (urination) that may accompany hyperglycemia. Symptoms may be related to any of the cardiovascular and other complications, such as chest pain or shortness of breath, and 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. Associated diseases and signs are: hyperuricemia, fatty liver (especially in concurrent obesity) progressing to non-alcoholic fatty liver disease, polycystic ovarian syndrome (in women), and acanthosis nigricans.

The history of tobacco use is important for identifying additional risks which may exacerbate the increased cardiovascular complications associated with MS. A family history of hypertension, diabetes mellitus and hypertriglyceridemia should be obtained as genetics may play an important role in MS. At present, studies indicate that no gene or group of genes has been implicated for MS, suggesting that the environment exerts substantial influence.[75]

The physical examination may reveal such as elevated blood pressure and abdominal obesity which are 2 of the 5 diagnostic criteria of MS. Measurement and documentation of waist circumference are important routines when screening for MS. 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 indicates 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-B1, 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.[76]

The revised NCEP and IDF definitions of metabolic syndrome are almost similar and it can be expected that may identify many of the same individuals as having metabolic syndrome. The differences are that IDF state that if BMI>30 kg/m2 central obesity can be assumed and waist circumference does not need to be measured which potentially excludes any subject without increased waist circumference if

BMI<30. The IDF uses geography-specific cut points for waist circumference, while NCEP uses only one set of cut points for waist circumference regardless of geography.[12,14]

PREVENTION

Various strategies have been proposed to prevent the development of metabolic syndrome. These include increased physical activity (such as walking 30 minutes every day)[77], and a healthy, reduced calorie diet[78]. There are many studies that support the value of a healthy lifestyle as above. However, one study stated that these measures are effective in only a minority of people, primarily due to a lack of compliance with lifestyle and diet changes[16]. The International Obesity Taskforce states that interventions on a sociopolitical level are required to reduce development of the metabolic syndrome in populations[79].

A 2007 study of 2,375 male subjects over 20 years suggested that daily intake of a pint of milk or equivalent dairy products more than halved the risk of metabolic syndrome[80]. Other studies both support and dispute the authors' findings[81].

MANAGEMENT OF MS

The first line treatment is change of lifestyle (i.e., caloric restriction and physical activity). However, drug treatment is frequently required. Generally, the individual disorders that comprise the metabolic syndrome are treated separately. Diuretics and ACE inhibitors may be used to treat hypertension. Cholesterol drugs may be used to lower LDL cholesterol and triglyceride levels, if they are elevated, and to raise HDL levels if they are low. Use of drugs that decrease insulin resistance, e.g., metformin and thiazolidinediones, is controversial; this treatment is not approved by the U.S. Food and Drug Administration.

A 2003 study indicated that cardiovascular exercise was therapeutic in approximately 31% of cases. The most probable benefit was to triglyceride levels, with 43% showing improvement; but fasting plasma glucose and insulin resistance of 91% of test subjects did not improve[16]. Many other studies have supported the value of increased physical activity and restricted caloric intake (exercise and diet) to treat metabolic syndrome.

IDF recommended treatment of the individual components of the metabolic syndrome

Atherogenic dyslipidaemia

Aims for therapy:

Lower TG (as well as lowering ApoB and non-HDL cholesterol) Raise HDL-c levels

Reduce LDL-c levels (elevated levels represent a high risk in the metabolic syndrome)

Options:

Fibrates (PPAR alpha agonists) improve all components of atherogenic dyslipidaemia and appear to reduce the risk for CVD in people with metabolic syndrome. The Veterans

Affairs High-Density Lipoprotein Intervention Trial (VA-HIT) showed that raising HDL-c concentrations using a fibrate in patients with well-established CHD and both a low HDL-c and a low LDL-c level will significantly reduce the incidence of major coronary events[82].Statins to reduce all ApoB-containing lipoproteins and to achieve ATP III goals for LDL-c as well as for non-HDL-c (ATP III, 2001). Several clinical studies have confirmed the benefits of statin therapy[83,84]. Fibrates in combination with statins but may be complicated by side effects.

Elevated blood pressure

Categorical hypertension (BP ≥ 140/≥ 90 mm Hg) should be treated according Seventh Report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure (JNC 7) recommendations[85].

In patients with established diabetes, antihypertensive therapy should be introduced at BP ≥ 130/≥ 80 mm Hg.

Options:

Angiotensin converting enzyme inhibitors and angiotensin receptor blockers are useful antihypertensive drugs, with some clinical trials (but not all) suggesting they carry advantages over other drugs in people with diabetes. At this time, however, the majority of clinical trials suggest that the risk reduction associated with antihypertensive drugs is the result of blood pressure lowering per se and not due to a particular type of drug.

No particular agents have been identified as being preferable for hypertensive patients who also have the metabolic syndrome.

Insulin resistance and hyperglycaemia

There is growing interest in the possibility that drugs that reduce insulin resistance will delay the onset of type 2 diabetes and will reduce CVD risk when metabolic syndrome is present. The Diabetes Prevention Program (DPP) showed that metformin therapy in people with prediabetes will prevent or delay the development of diabetes and recent thiazolidinedione studies have also demonstrated efficacy in delaying or preventing type 2 diabetes in people with impaired glucose tolerance (IGT) and insulin resistance[82-84]. Similarly, other studies have shown that both acarbose and orlistat can be used to delay the development of type 2 diabetes in people with IGT[85,86].

Currently there is no data suggesting that thiazolidinediones reduce the risk of CVD in those with the metabolic syndrome, IGT or diabetes.

FERRITIN

Ferritin is a globular protein complex consisting of 24 protein subunits and is the main intracellular iron storage protein in both prokaryotes and eukaryotes, keeping iron in a soluble and non-toxic form. Ferritin which is not combined with iron is called apoferritin.

Description

Ferritin is a protein, which is present in every cell type. Its molecular weight is 450 kDa and consists of 24 subunits In vertebrates, these subunits are both the light (L) and the heavy (H) type with an apparent molecular weight of 19 kDA or 21 kDA respectively. In plants and bacteria the complex only consists of the H-chain type. Inside the ferritin shell, iron ions form crystallites together with phosphate and hydroxide ions. The resulting particle is similar to the mineral ferrihydrite. Each ferritin complex can store about 4500 iron (Fe3+) ions.

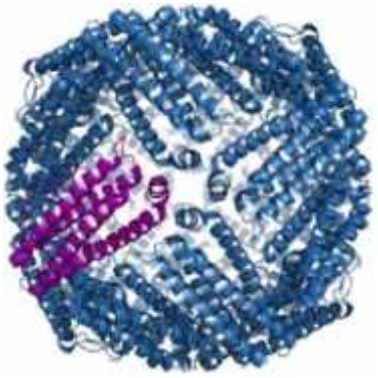

Figure 2: Structure of the ferritin complex

Mitochondrial ferritin is a protein precursor. It is classified as a metal-binding protein which is located within the mitochondria. After the protein is taken up by the mitochondria it is processed into a mature protein and is then assembled as a

functional ferritin shell. Its structure was determined at 1.70 angstroms by using the X-ray diffraction technique. It contains 182 residues.

Functions

Free iron is toxic to cells as it acts as a catalyst in the formation of free radicals from reactive oxygen species via the Fenton Reaction. Hence protective mechanisms have been evolved in our bodies to bind iron in various tissue compartments. Iron is stored complexed to protein as ferritin or hemosiderin in the cells. Apoferritin binds to free ferrous iron and stores it in the ferric state. As ferritin accumulates within cells of the reticuloendothelial system, protein aggregates are formed as hemosiderin. Iron in ferritin or hemosiderin can be extracted for release by the RE cells. Under steady state conditions, the serum ferritin level correlates with total body iron stores; thus, the serum ferritin FR5Rl is the most convenient laboratory test to estimate iron stores.

The molecular function of mitochondrial ferritin includes ferroxidase activity, iron ion binding, oxidoreductase activity, ferric iron binding, metal ion binding as well as transition metal binding. It also participates in iron ion transport across membranes, oxidation-reduction reactions and cellular iron ion homeostasis.

Diagnostic uses

Serum ferritin levels are measured in patients as part of the iron studies workup for anemia and for restless legs syndrome. The ferritin levels measured have a direct correlation with the total amount of iron stored in the body. Normal blood levels are 30-300 ng/mL for males and 15-200 ng/mL for females

Lowered

Low serum ferritin levels indicate decreased iron in the body, which is a risk factor that could lead to anemia. Low ferritin levels (<50 ng/mL) have been

associated with symptoms of restless legs syndrome even in the absence of anemia. In the setting of anemia, serum ferritin is the most sensitive lab test for iron deficiency anemia.

Elevated

High serum ferritin levels indicate excess iron in the body, which would normally be excreted in the stool. Ferritin is used as a marker for iron overload disorders, such as hemochromatosis and porphyria in which the ferritin level may be abnormally raised.[87]

As ferritin is also an acute-phase reactant, it is often elevated in the course of disease. A normal leucocyte count and erythrocyte sedimentation rate can be used to exclude elevated ferritin caused by acute phase reactions. Ferritin can also be elevated during periods of acute malnourishment.[88]

The Role of Iron in Diabetes and Its Complications

A common complication of iron overload diseases such as haemochromatosis is non-insulin dependent diabetes mellitus. About 53-80% of patients with haemochromatosis develop diabetes. The development of diabetes in haemochromatosis is related to the magnitude of the excess iron[89]. In a cross sectional, population based study of over 1000 middle aged men in eastern Finland the fasting concentrations of serum insulin and blood glucose were raised in men with high serum concentrations of ferritin which an indicator of raised stores of iron[90]. It has been suggested that free radicals and lipid peroxidation play a part in the etiology of diabetes and iron is a catalyst of free radical stress. Formation of hydroxyl radicals catalysed by iron may play an important part in the development of diabetes since the cells that produce insulin are extraordinarily sensitive to damage from oxidation[91]. In another cohort study low plasma concentrations of vitamin E were associated with an

increased incidence of diabetes, which supports this theory[92]. There are, however, no other studies of the association between iron stores and the incidence of diabetes in a healthy population.

The main property of iron which is involved in the pathophysiology of the disease is the ease with which it is reversibly oxidized and reduced. This property, while essential for its metabolic functions, makes iron potentially hazardous because of its ability to participate in the generation of powerful oxidant species such as hydroxyl radical[93]. Oxygen normally accepts four electrons and is converted directly to water. However, partial reduction of oxygen can and does occur in biological systems. Thus, the sequential reduction of oxygen along the univalent pathway leads to the generation of superoxide anion, hydrogen peroxide, hydroxyl radical, and water[93,94]. Superoxide and hydrogen peroxide appear to be the primary generated species. These species may then play a role in the generation of additional and more reactive oxidants, including the highly reactive hydroxyl radical (or a related highly oxidizing species) in which iron salts play a catalytic role in a reaction. This reaction is commonly referred to as the metal catalyzed Haber-Weiss reaction[93]. Because iron participates in the formation of reactive oxygen species, organisms take great care in the handling of iron. Indeed, iron sequestration in transport and storage proteins may contribute to antioxidant defenses. It is now well established that oxidants can cause the release of catalytic iron[93]. Thus, a vicious cycle is initiated that leads to the formation of more reactive oxygen species.

Iron overload is not a prerequisite for iron to mediate either diabetes or its complications. Important in its pathophysiology is the availability of so-called catalytic iron or iron that is available to participate in free radical reactions.

The role of iron in the induction of diabetes

Systemic iron overload could contribute to abnormal glucose metabolism was first demonstrated by the observation that the frequency of diabetes is increased in classic hereditary hemochromatosis (HH). However, with the discovery of novel genetic disorders of iron metabolism, it is obvious that iron overload, irrespective of the cause or the gene involved, results in an increased incidence of type 2 diabetes. The role of iron in the pathogenesis of diabetes is suggested by 1) an increased incidence of type 2 diabetes in diverse causes of iron overload and 2) reversal or improvement in diabetes (glycemic control) with a reduction in iron load achieved using either phlebotomy or iron chelation

therapy. Recently, a link has been established between increased dietary iron intake, particularly eating red meat and increased body iron stores, and the development of diabetes. A causative link with iron overload is suggested by of the improvement in insulin sensitivity and insulin secretion with frequent blood donation and decreased iron stores[95,96].

Although the exact mechanism of iron-induced diabetes is uncertain, it is likely to be mediated by three key mechanisms:

1. Insulin deficiency
2. Insulin resistance and
3. Hepatic dysfunction

An understanding of the pathogenic pathways of iron-induced diabetes is derived mainly from studies on animal models of hemochromatosis.

A mouse model of hemochromatosis showed that iron excess and oxidative stress mediate apoptosis of pancreatic islets which result in decreased insulin secretory capacity[97]. The high susceptibility of pancreatic islets to oxidative damage

can be related to the nearly exclusive reliance on mitochondrial metabolism of glucose for glucose-induced insulin secretion and the low expression of antioxidant defense system[98]. A high expression of divalent metal transporter additionally predisposes them for more accumulation of iron than other cells[99] and potentiates the danger from iron-catalyzed oxidative stress.

In studies on thalassemic patients, insulin resistance is significantly increased[100,101]. In recent human studies a high prevalence of abnormal glucose homeostasis was demonstrated in individuals with hemochromatosis[102]. Using glucose tolerance tests, they demonstrated not only that insulin secretion is impaired but also that there is insulin resistance. The mechanisms for insulin resistance include the possibility of iron overload causing resistance directly or through hepatic dysfunction[103]. In a study of patients with unexplained hepatic iron overload, most were found to be insulin resistant, which suggests a common etiologic link among hepatic iron, hepatic dysfunction, and insulin resistance[104].

The role of iron in endothelial and vascular disease

The possibility that iron status has a role in CVD was postulated in 1981[105]. The man-woman ratio for median serum ferritin levels for ages 18–45 years is 3.8, which is similar to the increased risk for heart disease, with the reduced risk against heart disease in women ending with the onset of menopause. Epidemiologic studies in overt iron overload states such as transfusional iron overload and hemochromatosis have shown that the incidence of cardiac disease is increased[106] and that treatment with iron chelation improves cardiovascular outcome[107,108]. Similarly, several studies have demonstrated a direct association between increased iron intake, body iron stores, and cardiovascular risk in the general population. Increased intake of heme iron is associated with increased cardiovascular events[109-112], and increased body iron

stores are associated with myocardial infarction in a prospective epidemiological study[113]. Additionally, varieties of cardiovascular risk factors are associated with iron overload and commonly cluster in MS.

A close relationship between iron stores and cardiovascular risk factors in women of reproductive age in the U.S has been demonstrated[112]. The association was seen with total cholesterol, triglycerides, diastolic blood pressure, and glucose, factors that often cluster in individual patients. Additional evidence of the role of iron can also be derived from studies on surrogate markers such as carotid atherosclerosis finding a positive association with iron stores[114]. However, several other studies argue against an association between increased iron intake and body iron stores and cardiovascular risk[115-120]. One possible reason for these conflicting data is the lack of precision of markers that were used to indicate iron load. In most of these studies, serum ferritin has been used as an indicator of iron load; however, serum ferritin also increases with a variety of inflammatory and stressful conditions. Similarly, other markers indicative of iron status in the body such as transferrin saturation are not reflective of total body iron stores or the presence of reactive forms of iron in blood. In fact, NTBI may be present in the serum even when transferrin is not fully saturated [121].

Pathologic mechanisms for iron in promoting vascular disease can be derived from cell culture studies, animal models, and human functional studies (vascular reactivity). In cell culture models, the addition of NTBI to human endothelial cell cultures increases surface expression of adhesion molecules[122,123] and also increases monocyte adherence to the endothelium. These abnormalities can be corrected by the addition of iron chelators such as desferoxamine and dipirydyl. Such an addition decreases expression of adhesion molecules and monocyte adherence[122-124].

In human studies of end-stage renal disease patients, intravenous iron therapy has been shown to increase vascular and systemic oxidative stress[125-127], promote atherosclerosis[127], and increase the risk of arterial thrombosis[126]. Further, intravenous iron has been shown to cause impaired flow-mediated dilatation in the brachial artery, a surrogate for endothelial dysfunction[128]. Conversely, improvement in vascular reactivity after phlebotomy in patients with high-ferritin type 2 diabetes further supports these observations[129]. Additionally, several recent studies on cardiovascular evaluation and outcome in high-frequency blood donors demonstrate improvement in surrogate markers of vascular health such as decreased oxidative stress and enhanced vascular reactivity when compared with low-frequency donors[128]. However, conflicting data exists regarding the relationship between decreased iron stores from frequent blood donation and hard end points such as a decrease in cardiovascular events and mortality[130].

Elevated serum ferritin levels independently predicted incident type 2 diabetes in prospective studies in apparently healthy men and women[131]. Study by Claudia Bozzini et al[132] conclude that serum ferritin could be added to routine evaluation of metabolic syndrome patients; this would help identify a subgroup of individuals at risk for iron-related tissue damage. In cross-sectional studies, elevated ferritin levels have been associated with hypertension, dyslipidemia, elevated fasting insulin and blood glucose and central adiposity[133]. The association between elevated iron stores and the metabolic syndrome, however, has been less well explored.

Study by Megan jehn, MHS, Jeanne M Clarke *et al*[131] conclude that elevated iron stores were positively associated with the prevalence of the metabolic syndrome. Study conducted by Earl S Ford, MD, Mary E Cogswell, DRPH[134] conclude that elevated serum ferritin concentration was associated with an increased risk of

diabetes.

Study by Istvan s vari, BSC, Beverley balkau, PhD,Adrian kettaneh[133] was the first prospective study associating ferritin & transferrin with the metabolic syndrome & its components. When the iron stores are elevated, the incidence of the metabolic syndrome is increased in men & both pre and post menopausal women.

Study by Michael Haap, MD; Andreas Fritsche, MD et al[135] conclude that it may become advisable to routinely screen for mildly elevated or even high-normal serum ferritin concentrations in the context of glucose intolerance. In the future, actively lowering body iron stores may become a tool in preventing type 2 diabetes in selected subgroups.

Study by JM Fernandez-Real, W Ricart-Engel et al[136] conclude that the correlations among serum ferritin and diastolic blood pressure, HDL quotient, glucose area under the curve suggest that serum ferritin could be a marker of the insulin resistance syndrome. Serum ferritin may also be an independent determinant of poor metabolic control in the diabetic patient.

MATERIALS AND METHODS

SOURCE OF DATA:

The information for this study was collected from outpatients and inpatients of BLDEU Shri B.M.Patil Medical College hospital and research centre, Vijayapur who are diagnosed with Metabolic Syndrome between November 2013 to April 2015.

METHOD OF COLLECTION OF DATA

Information was collected through prepared proforma from each patient. All the patients were interviewed as per the prepared proforma and then a complete clinical examination was performed which was followed by laboratory investigations.

INCLUSION CRITERIA:

- Patients diagnosed with Metabolic Syndrome with any 3 of the 5 criteria set by

  ATP – III. Adult Treatment Panel – III Criteria

1. Elevated Blood Pressure (systolic > 130mm of hg and diastolic > 85mm of hg or treatment for previously diagnosed hypertension)
2. Low HDL Cholesterol (< 40 mg/dl in males and < 50 mg/dl in females or on specific treatment for this lipid abnormality)
3. Elevated serum triglycerides (> 150 mg/dl)
4. Waist circumference > 102cm in males and 88 cm in females
5. Raised fasting blood glucose > 100 mg/dl or previously diagnosed diabetes.

- Age more than 18years.

EXCLUSION CRITERIA:

- Age less than 18 years
- Patients with history suggestive of hemochromatosis (serum ferritin > 300 for men ;

> 200 for women)

- Pregnant women
- Patients with abdominal mass or ascites
- Patients with severe heart, liver or kidney failure
- Patients who received treatment for anemia in the last 3 months.
- Patients who donated blood in the last 4 months

HBsAg/HCV antibody positive patients.

LIST OF INVESTIGATIONS

1. Serum ferritin
2. Serum total cholesterol
3. Serum triglycerides
4. Serum HDL
5. Serum LDL
6. Serum VLDL
7. Fasting blood sugar
8. Postprandial blood sugar
9. Complete Blood Count
10. ESR
11. Urine routine
12. Peripheral Smear Study
13. HBsAg/HCV when required

PROCEDURES PERFORMED

Waist circumference: Waist circumference will be measured at the midpoint between the lower edge of the ribcage and the top of the iliac crest.

Blood pressure: The average of two recordings with 30 minute interval by using the appropriate sphygmomanometer cuff will be considered as the blood pressure of that patient.

After selecting the patient for the study detailed history taking, physical examination and relevant investigations were done.

SAMPLE SIZE:

- The prevalence of Metabolic Syndrome as taken from the API text book of internal medicine 9th edition is 11 %[13] (p)
- At confidence interval of 95% (Z_α) allowing $\pm$ 5 (d) margin of error

$$n = \frac{(Z_\alpha)^2 (p) (q)}{d^2}$$

p = Prevalence

q = 100 – p

d = Margin of error

Z_α = Standardized normal deviate.

- The calculated sample size is 150 using the above statistical formula.

STATISTICAL ANALYSIS:

Data were analysed using

- Mean ± SD
- Diagrams
- Chi-square test
- ANOVA

Chi-Square Test

$$\chi^2 = \frac{\sum(Oi - Ei)^2}{Ei}$$

, Where Oi is Observed frequency and Ei is Expected frequency

Analysis of Variance:

F test for K Population means

Objective: To test the hypothesis that K samples from K Populations with the same mean.

Limitations: It is assumed that populations are normally distributed and have equal variance. It is also assumed that samples are independent of each other.

Method: Let the jth sample contain nj elements(j=1,2,…K). Then the total number of elements is

$$N = \sum nj \qquad x.j = \sum \frac{xij}{nj}$$

$$S_1^2 = \frac{\sum_{i=1}^{n1} \sum (x1 - \overline{x.}_j)^2}{N - K} \qquad S_2^2 = \frac{\sum nj(\overline{x.}_j - \overline{x.}.)^2}{K - 1}$$

F=S22/S12 Which follows F distribution (K-1, N-K)

OBSERVATION AND RESULTS

Study Design:

A Correlational clinical single group study with 150 patients study was undertaken in Shri. B.M. Patil medical college and research center, Vijaypur to study the relationship of serum ferritin with metabolic syndrome.

Table1: Mean & SD value of Parameters under study

	N= 150	
Parameters	**Mean**	**±SD**
Age(yrs)	56.0	10.1
BMI (kg/m2)	29.4	2.1
WC (cm)	101.8	7.9
SBP (mm)	144.2	15.4
DBP(mm)	91.1	8.0
Hypertensive (yrs)	3.7	3.6
Type 2 DM (yrs)	5.0	4.4
HB%	14.4	0.8
TC (cell/cmm)	10010.0	13258.7
MCV	94.8	4.1
MCHC	32.0	3.8
ESR	11.5	6.5
FBS(mg/dl)	155.9	31.0
PPBS(mg/dl)	207.0	37.8
TOTAL CHOLESTEROL(mg/dl)	202.8	43.1
HDL(mg/dl)	40.9	8.5
LDL(mg/dl)	115.7	32.5
VLDL(mg/dl)	46.2	20.1
TRIGLYCERIDES(mg/dl)	159.5	25.0
FERRITIN(ng/l)	110.3	64.2

Table 2: Age distribution of patients studied

Age (Yrs)	N	Percent
<=35	6	4
36-45	13	8.7
46-55	41	27.3
56-65	58	38.7
>=66	32	21.3
Total	150	100

Mean ± SD: 56.0 ± 810.1

Figure 1: Age distribution of patients studied

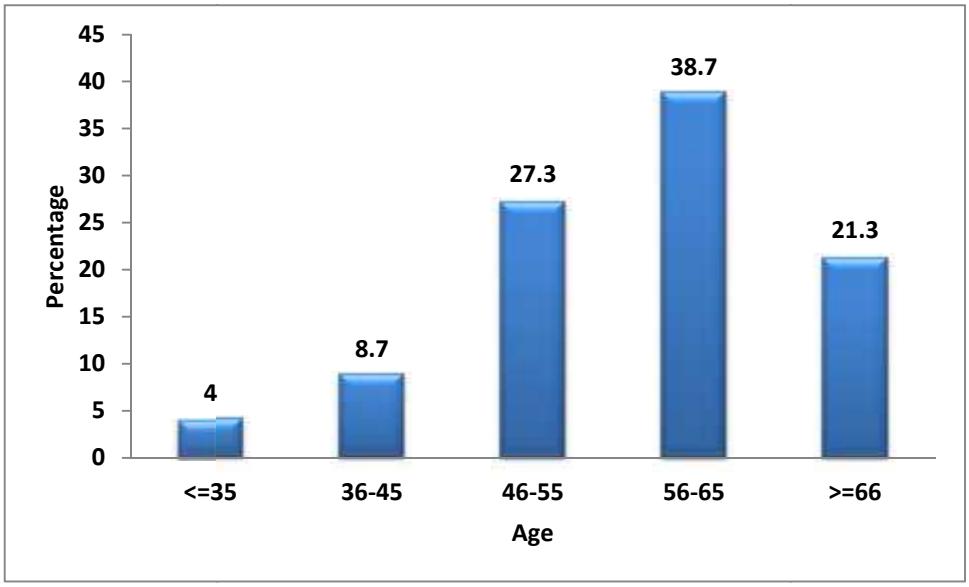

Figure 3: Age distribution of patients studied

There were 150 patients in this study. Majority of patients (57.3%) were above 45 yrs of age. There were only 6 patients below 35 yrs of age.

Table 3: Gender distribution of patients studied

Sex	N	Percent
Male	88	58.7
Female	62	41.3
Total	150	100

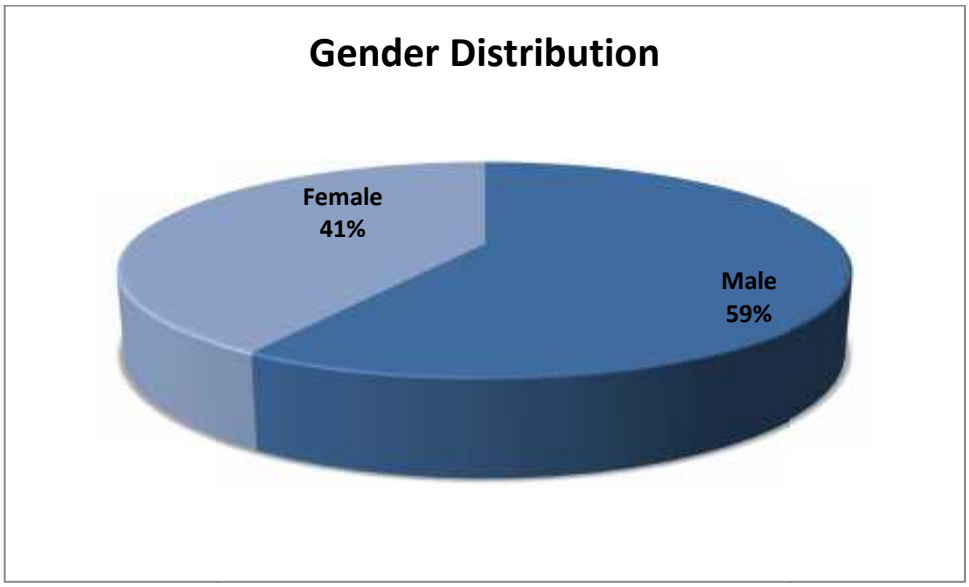

Figure 4: Gender distribution of patients studied

In the present study, there were 88 males & 62 females. 58.6% were males and 41.4% were females.

Table 4: BMI (kg/m2) distribution of patients studied

BMI	N	Percent
25-30	90	60
30-35	60	40
Total	150	100

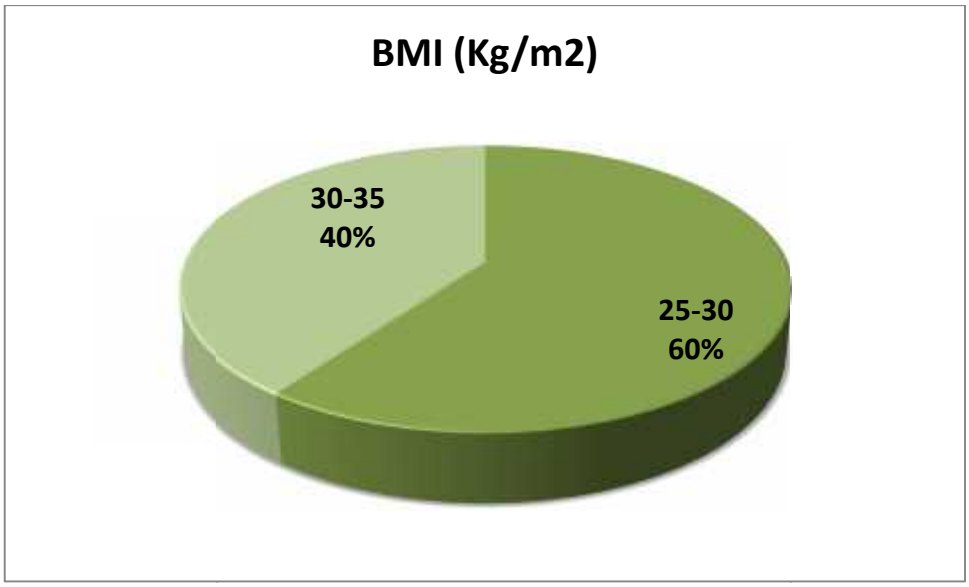

Figure 5: Distribution of BMI in patients studied

Mean BMI in our study was 29.4 ± 2.1. All the patients included in this study had BMI of >25kg/m^2

Table 5: Waist Circumference (cm) distribution of patients studied

Central Obesity	N	Percent
Male <102; Female <88	27	18
Male ≥102; Female ≥88	123	82
Total	150	100

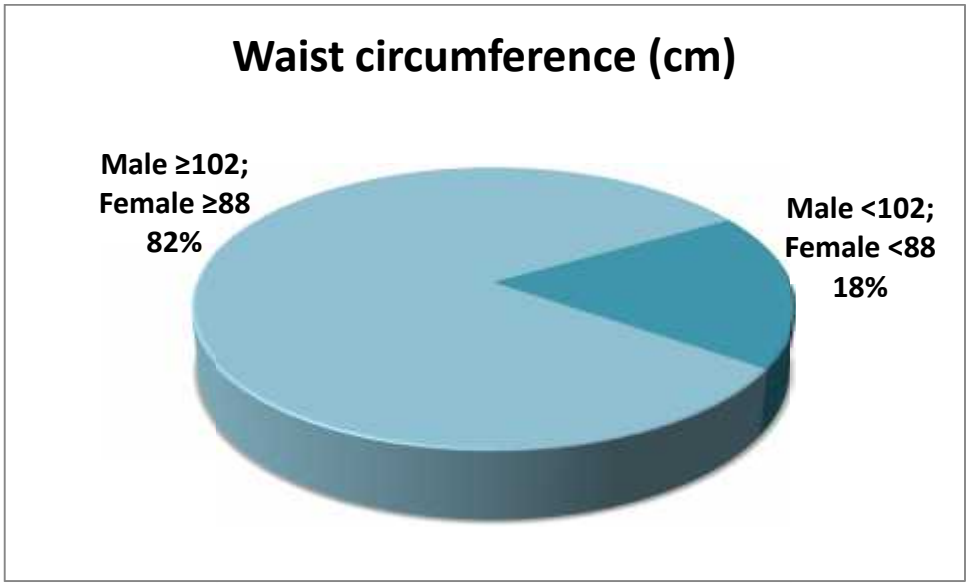

Figure 6: Distribution of waist circumference in patients studied

123(82%) patients had central obesity with a mean waist circumference of 101.8 ± 7.9

Table 6: Distribution of patients with history of hypertension

Hypertension	No.	Percent
No	50	33.3
Yes	100	66.7
Total	150	100

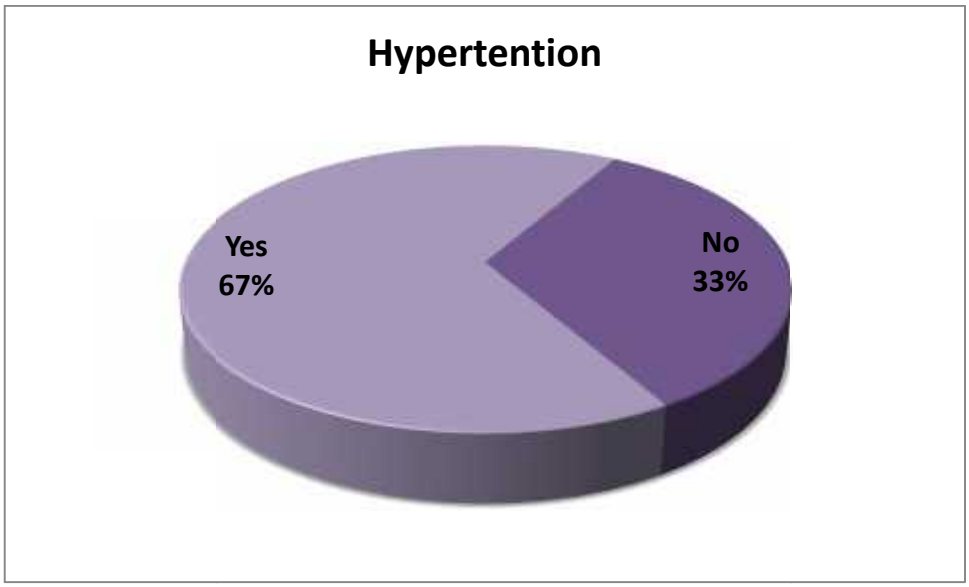

Figure 7: Distribution of patients with history of hypertension

Table 7: Distribution of BP (mm) of patients studied

BP	N	Percent
<130/85	31	20.7
≥130/85	119	79.3
Total	150	100

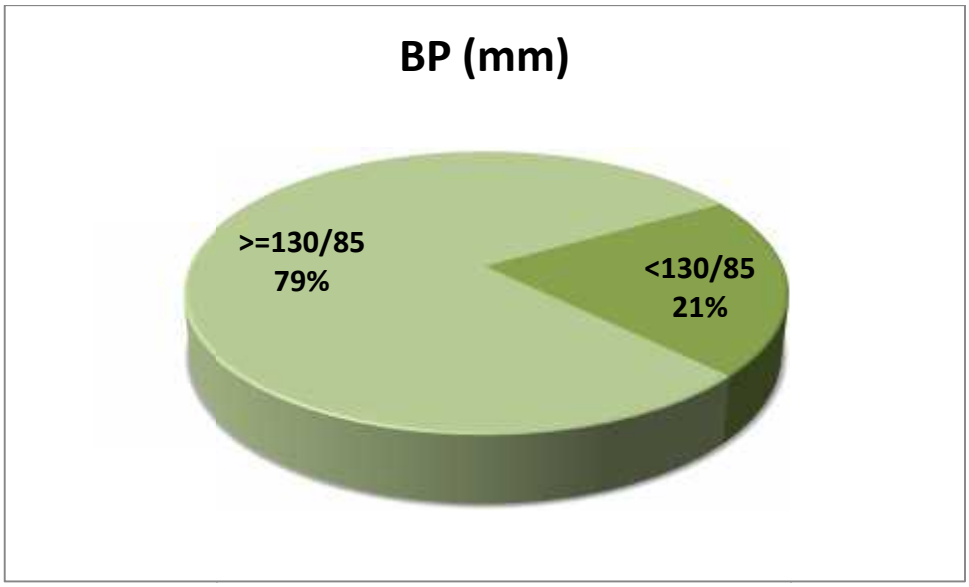

Figure 8: Distribution of blood pressure in patients studied

In our study 119 (79%) of patients had blood pressure readings of more than 135/85mmhg. 66.7% patients were known hypertensives on treatment.

Table 8: Duration of Diabetes (yrs) of patients studied

Duration of DM	No.of years	Percent
0	38	25.3%
1-5	60	40%
6-10	41	27.3%
More than 10	11	7.3%
Total	150	100%

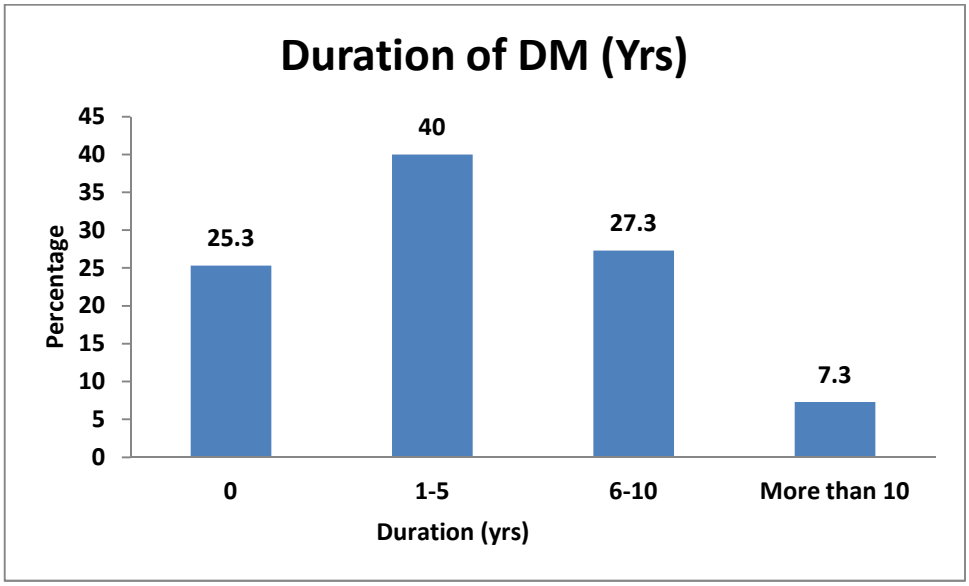

Figure 9: Distribution of duration of diabetes mellitus in patients studied

112 (79.9%) of patients were on treatment for diabetes mellitus, 11(7.3%) patients were not having diabetes mellitus.

Table 9: Distribution of FBS (mg/dl) of patients studied

FBS	N	Percent
<100 mg/dl	11	7.3
≥100 mg/dl	139	92.7
Total	150	100

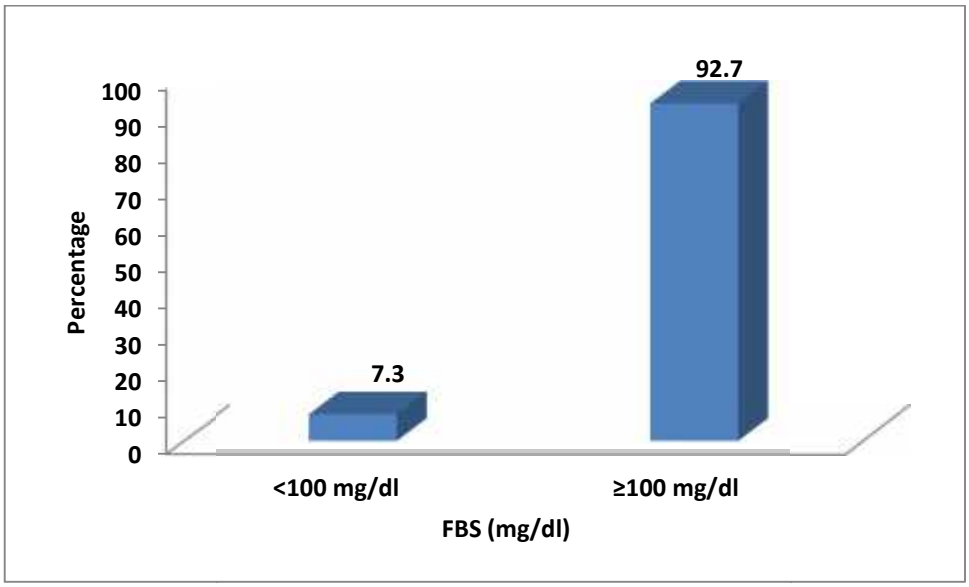

Figure 10: Distribution of fasting blood sugar in patients studied

In our study 11 (7.3%) patients had FBS less than 100mg/dl and were non diabetic. Among 139 (92.7%) patients who had FBS more than 100mg/dl, 27 (18%) patients did not hav history of diabetes.

Table 10: Distribution of HDL (mg/dl) of patients studied

HDL	N	Percent
Male >40; female >50 mg/dl	46	30.7
Male ≤40; female ≤50 mg/dl	104	69.3
Total	150	100

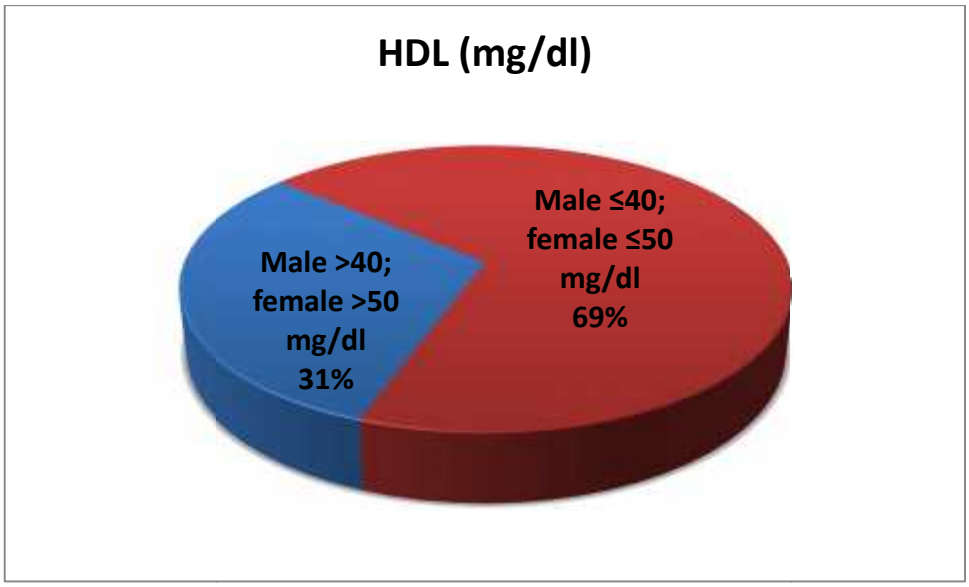

Figure 11: Distribution of HDL in patients studied

In our study 46 (30.7%) patients had HDL above 50mg/dl and 104(69.3%) patients had abnormal HDL (<40mg/dl in males, <50 in females)

Table 11: Distribution of TRIGLYCERIDES (mg/dl) of patients studied

TRIGLYCERIDES	N	Percent
<150	50	33.3
≥150	100	66.7
Total	150	100

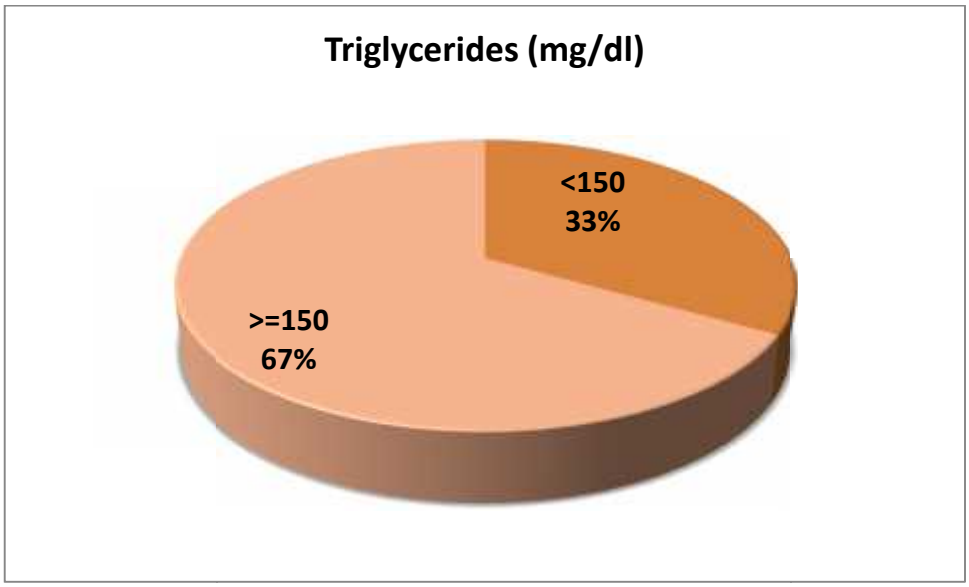

Figure 12: Distribution of triglycerides in patients studied

In our study 100 (66.7%) patients had triglycerides above 150mg/dl and 50(33.3%) patients had HDL below 150mg/dl.

Table 12: Distribution of TOTAL CHOLESTEROL (mg/dl) of patients studied

TOTAL CHOLESTEROL	N	Percent
<200	91	60.7
≥200	59	39.3
Total	150	100

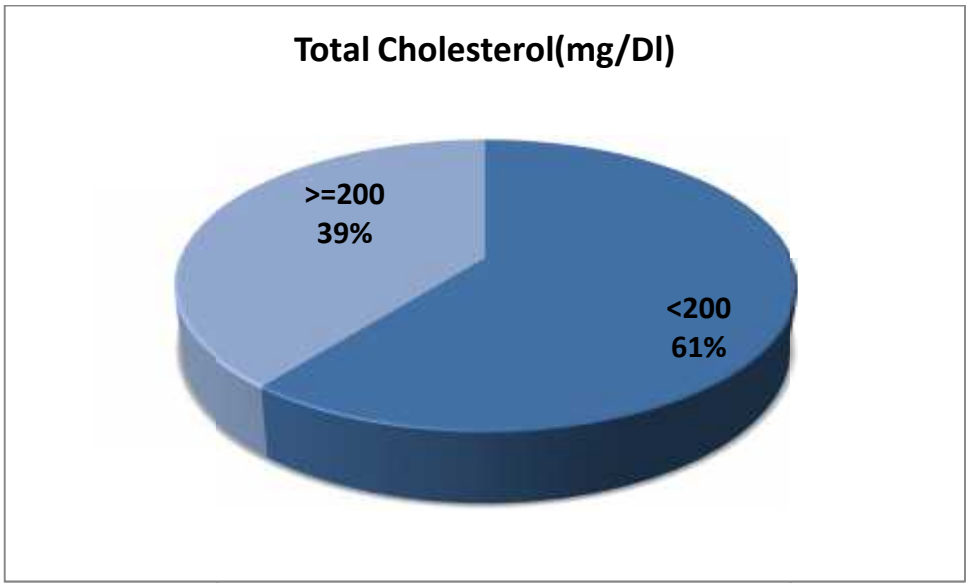

Figure 13: Distribution of total cholesterol in patients studied

In our study 91 (60.7%) patients had total cholesterol above 200mg/dl and 59(39.3%) patients had total cholesterol below 200mg/dl.

Table 13: Urine examination of patients studied

		N	Percent
Urine Albumin	**Normal**	116	77.3
	Abnormal	34	22.7
Urine Sugar	**Normal**	91	60.7
	Abnormal	59	39.3
Microscopy cell/hpf	**Normal**	108	72
	Abnormal	42	28
	Total	150	100

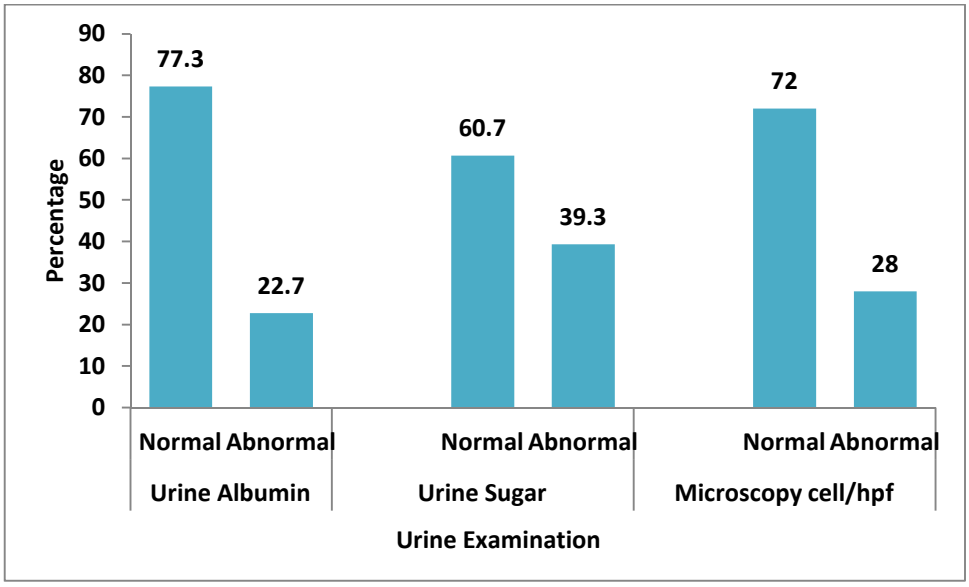

Figure 14: Results of urine examination in patients studied

In our study albuminuria was found in 22.7% of the subjects and glycosuria was found in 39.3% of the subjects.

Table 14: Distribution of FERRITIN (ng/l) of patients studied

FERRITIN	N	Percent
≤50	21	14
51-100	58	38.7
101-150	34	22.7
151-200	21	14
More than 200	16	10.7
Total	150	100

In our study mean serum ferritin was 110.3 ± 64.5 and 71 patients had serum ferritin values >100mg/dl

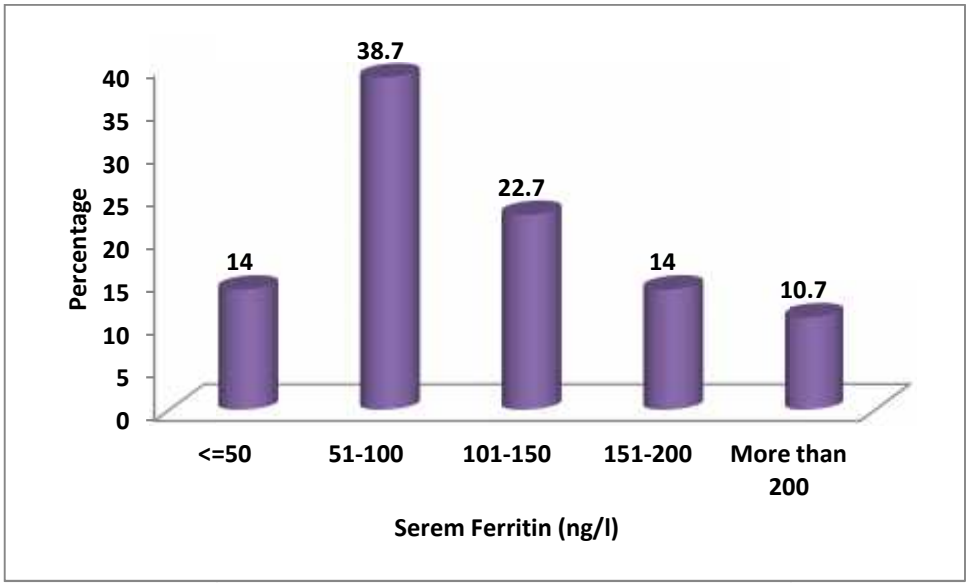

Figure 15: Distribution of serum ferritin in patients studied

In this study we categorized the patients according to their serum ferritin value into 5 groups i.e. <50 ng/dl, 51 to 100 ng/dl, 101 to 151 ng/dl, 151 to 200 ng/dl and > 200 ng/dl. Most of the patients (51.4%) had serum ferritin value in the range of 51 to 150 ng/dl

Table 15: Number of components of metabolic syndrome

MS components	N	Percent
3	59	39.4
4	46	30.7
5	45	30
Total	150	100

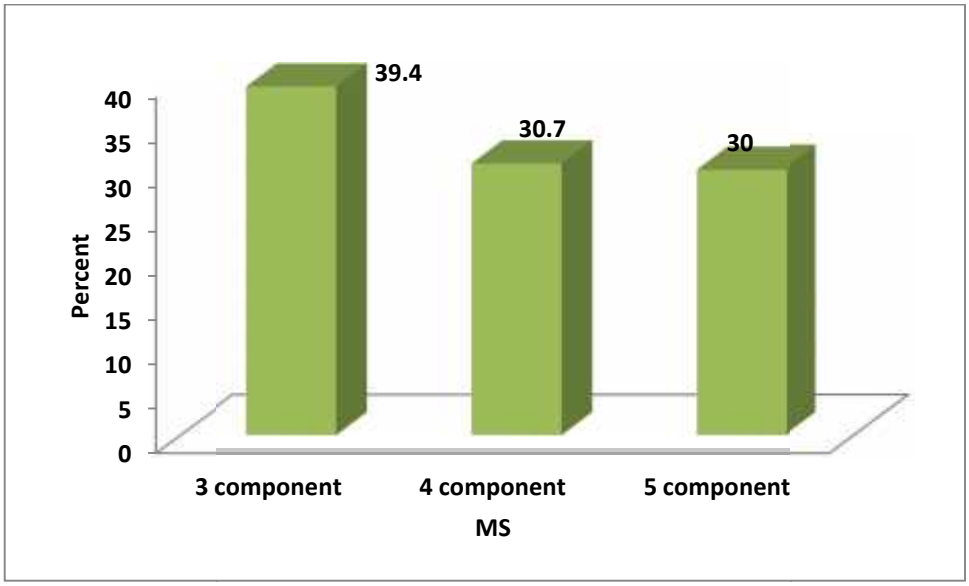

Figure 16: Distribution of number of components of MS in patients studied

In our study 45 subjects (30%) had all 5 components, 46 (30.7%) had 4 components and 59 (39.4%) had only 3 components of metabolic syndrome

Table 16: Mean Serum ferritin ng/l according to Number of components of metabolic syndrome

MS components	No.	FERRITIN level		ANOVA
		Mean	Std. Deviation	p value
3 component	59	60.6	30.4	0.000
4 component	46	114.7	54.2	
5 component	45	170.9	51.3	
Total	150	110.3	64.2	

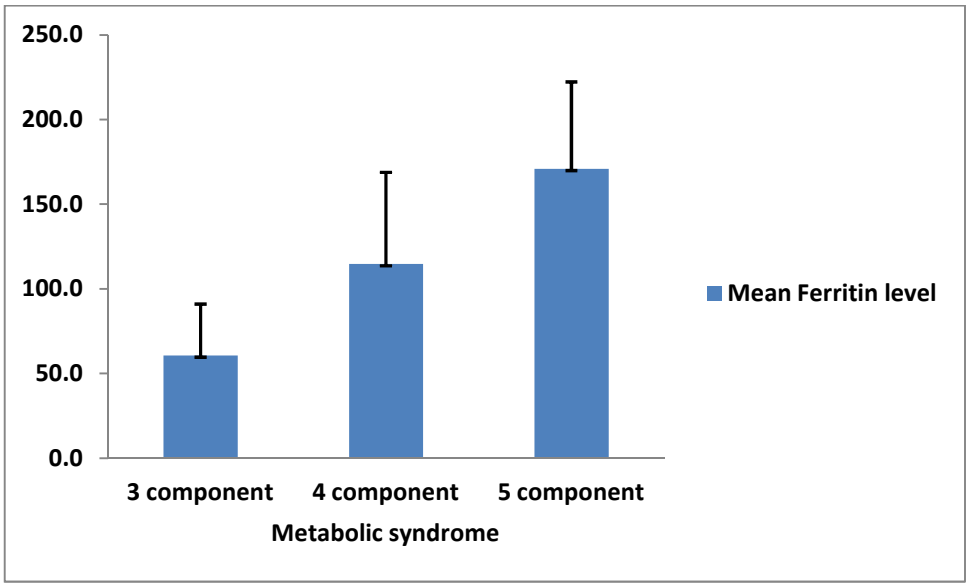

Figure 17: Correlation of mean ferritin level and number of components of MS.

In our study the mean value of serum ferritin was significantly increasing with the increasing number of components of MS with p value <0.001.

Table 17: Correlation of components of metabolic syndrome with Severity

Parameters		Severity of Metabolic syndrome						Chi square
		3 components		4 components		5 components		
		N	Percent	N	Percent	N	Percent	p value
Central Obesity	Male ≥102; Female ≥88	36	29.3	42	34.1	45	36.6	0.000
BP	≥130/85	37	31.1	37	31.1	45	37.8	0.000
DM	>100	51	36.7	43	30.9	45	32.4	0.031
HDL	≤40/50	27	26	32	30.8	45	43.3	0.000
TRIGLYCERIDES	≥150	25	25	30	30	45	45	0.000

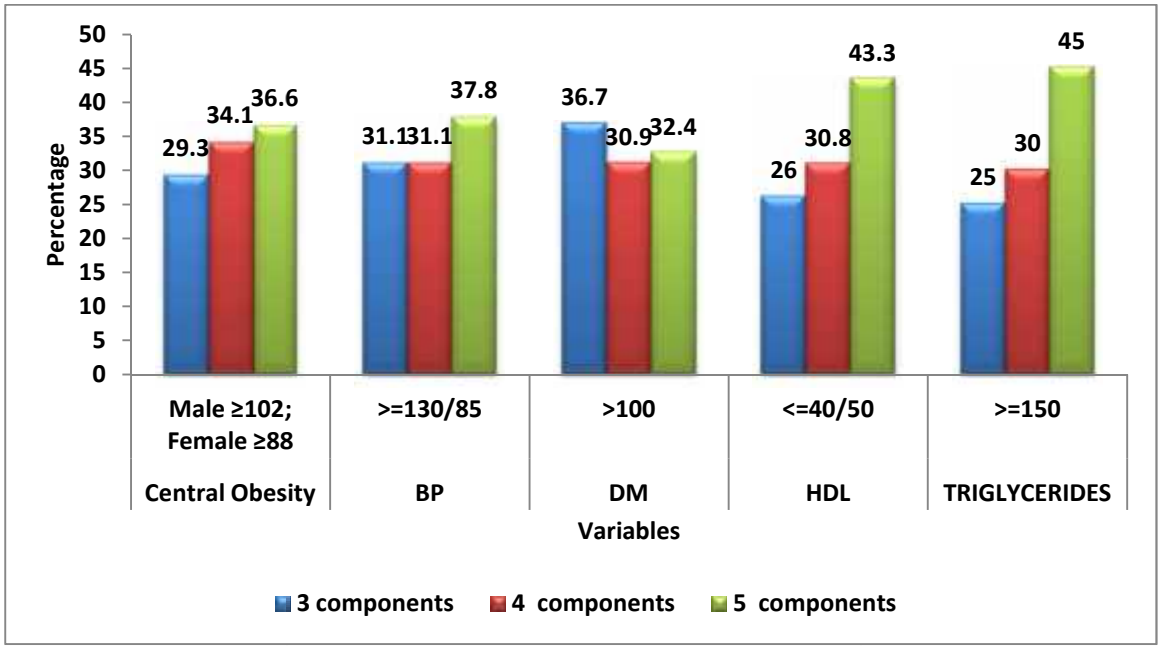

Figure 18: Correlation of severity of MS with each component of MS

Individual components of metabolic syndrome had significant correlation with increasing number of components of metabolic syndrome. Central obesity, dyslipidaemia (both triglycerides and HDL criteria) and hypertension were associated with increasing number of components of metabolic syndrome with a significant p value of <0.001. Blood sugars also showed similar correlation of statistical significance (p value of 0.03).

Table 18: Mean of clinical variables in relation to number of components of metabolic syndrome

Parameters	3 components N=59		4 components N=46		5 components N=45		p value
	Mean	SD	Mean	SD	Mean	SD	
Age (yrs)	55.9	10.1	57.3	10.6	54.8	9.5	0.501
BMI (kg/m2)	28.9	1.7	29.9	2.0	29.5	2.6	0.046
WC(cm)	99.1	7.2	101.3	8.7	105.9	6.0	0.000
SBP(mm)	139.5	16.7	144.3	13.7	150.1	13.2	0.002
DBP(mm)	88.4	8.4	92.1	8.0	93.7	6.3	0.002
Hypertensive (yrs)	2.4	2.8	4.2	3.7	5.0	3.8	0.000
Type 2 DM (yrs)	4.5	4.1	5.3	4.1	5.5	5.0	0.455
HB%	14.4	0.8	14.4	0.9	14.3	0.8	0.952
MCV	94.6	4.0	95.2	4.4	94.8	4.0	0.754
MCHC	31.1	5.6	32.6	1.9	32.5	1.7	0.058
ESR	12.3	6.4	12.6	6.9	9.3	5.8	0.026
FBS(mg/dl)	153.1	32.2	156.1	31.9	159.2	28.7	0.608
PPBS(mg/dl)	205.6	40.6	199.3	35.0	216.7	35.1	0.084
Total Cholesterol(mg/dl)	208.4	46.2	202.2	44.1	196.0	37.4	0.349
HDL(mg/dl)	43.2	9.7	41.9	8.3	37.0	5.4	0.001
LDL(mg/dl)	119.9	37.6	111.4	26.5	114.4	31.0	0.393
VLDL(mg/dl)	45.2	18.9	49.2	23.4	44.6	18.1	0.474
Triglycerides(mg/dl)	152.2	23.9	159.0	26.9	169.6	21.2	0.002
Serem Creatinine (mg/dl)	0.9	0.2	0.9	0.2	1.0	0.2	0.192

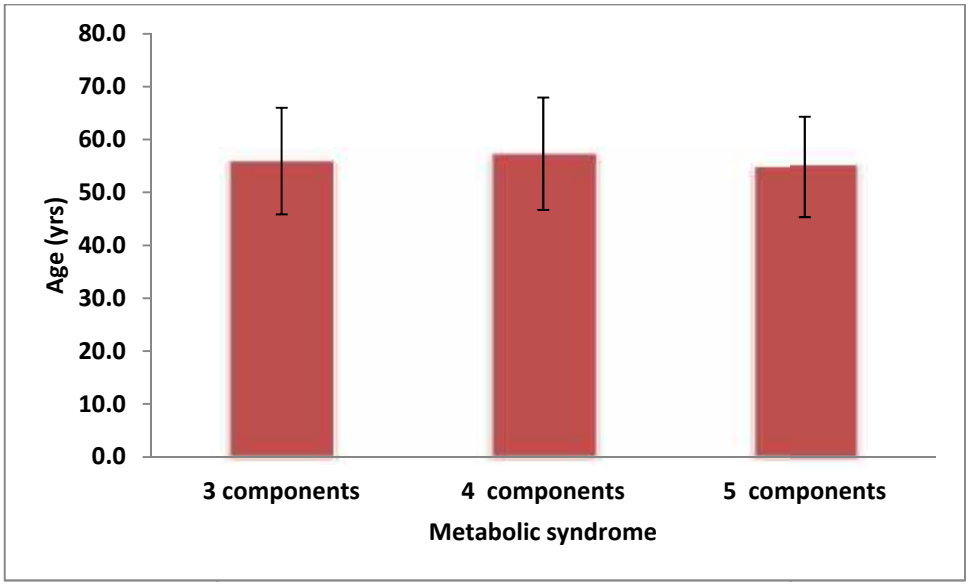

Figure 19: Correlation of age with severity of MS in patients studied

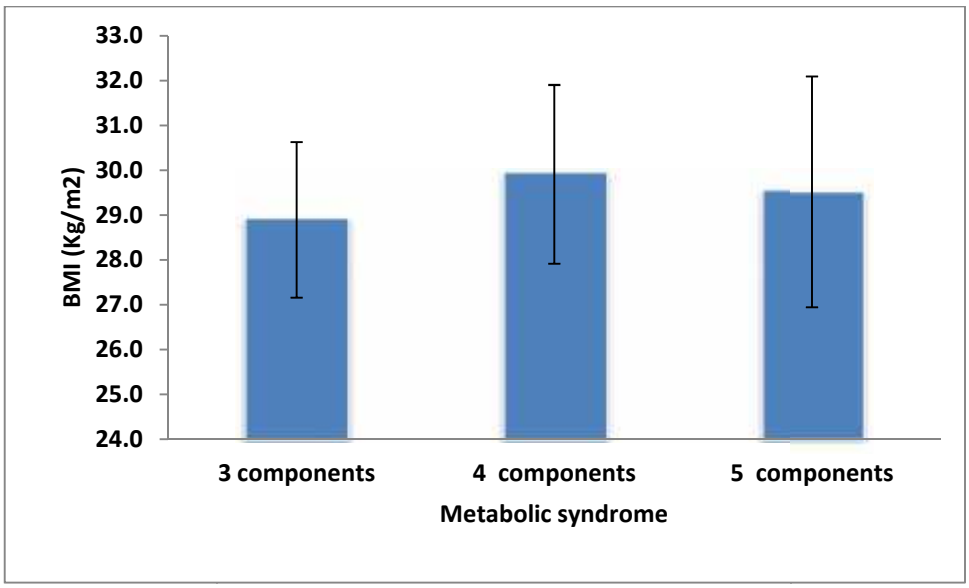

Figure 20: Correlation of BMI with severity of MS in patients studied

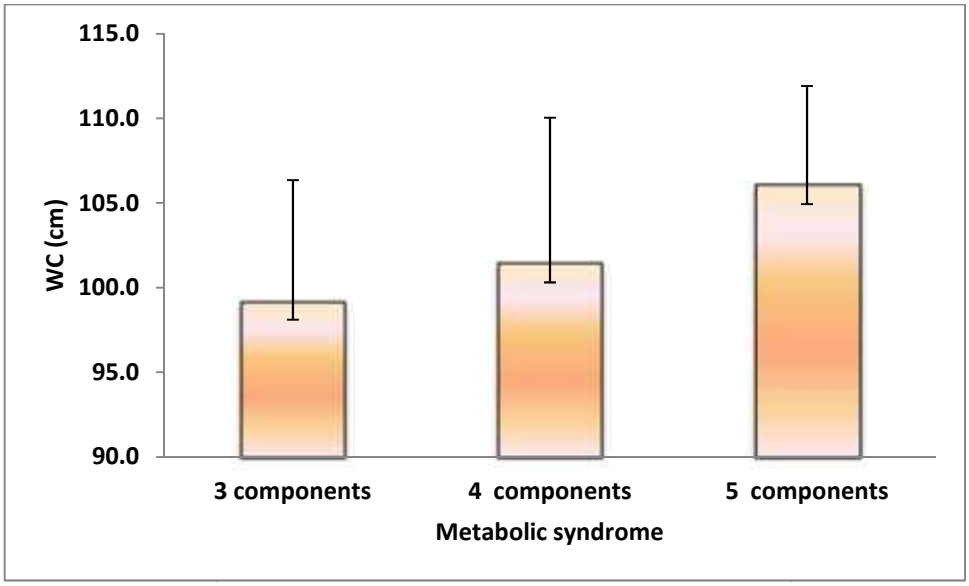

Figure 21: Correlation of waist circumference with severity of MS in patients studied

In this study WC was significantly more in patients with all 5 components of MS with p value <0.01.

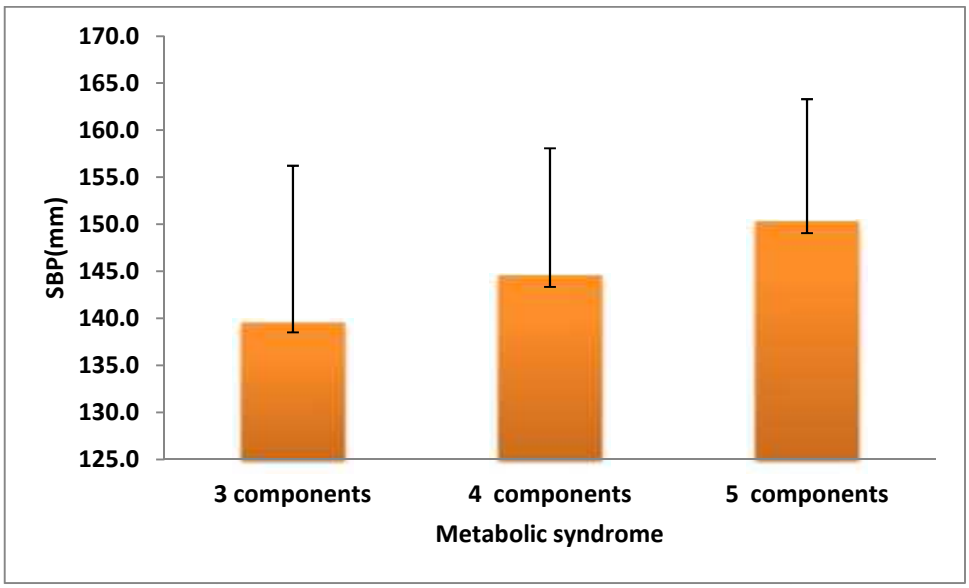

Figure 22: Correlation of SBP with severity of MS in patients studied

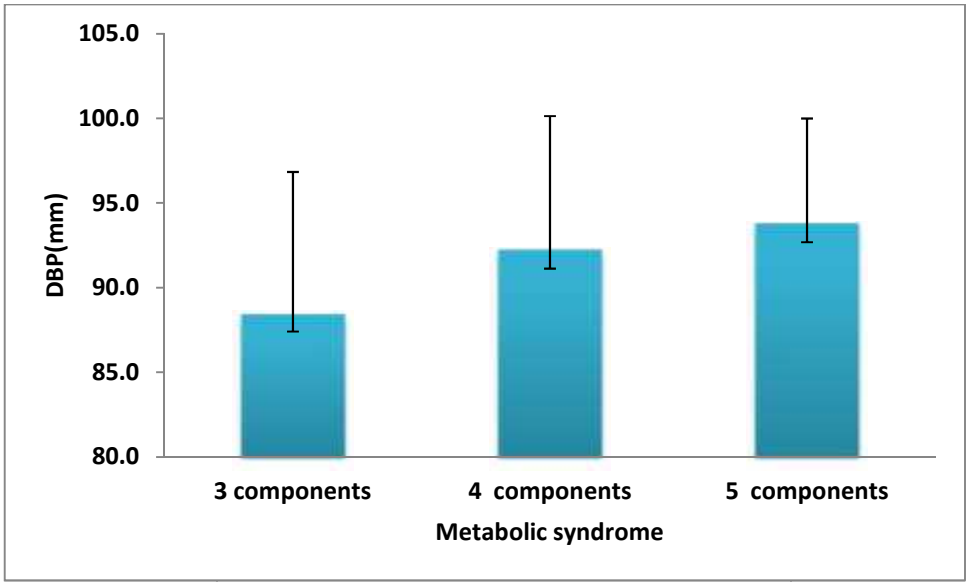

Figure 23: Correlation of DBP with severity of MS in patients studied

In our study both systolic and diastolic BP were found to be significantly higher in patients with all 5 components of MS with a p value of <0.01

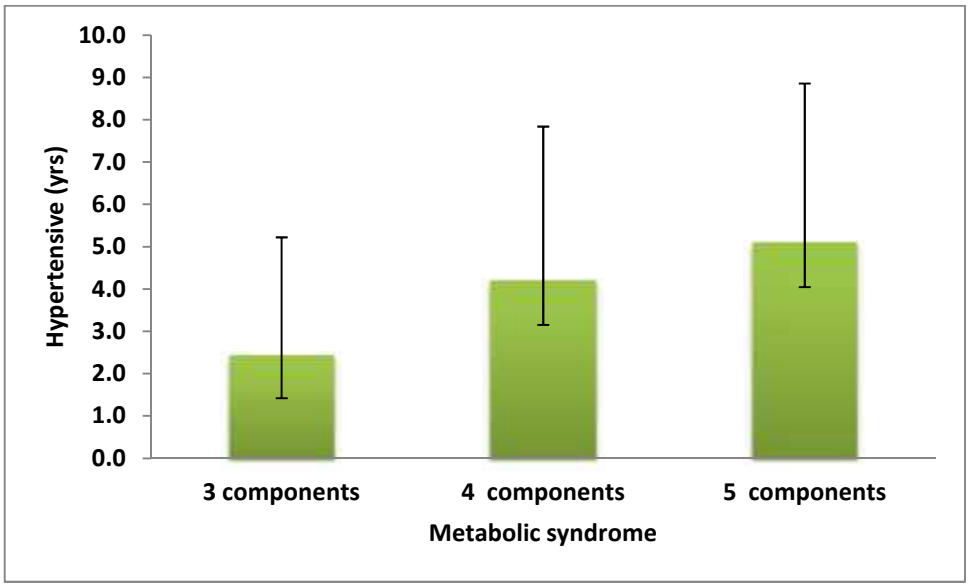

Figure 24: Correlation of hypertension with severity of MS in patients studied

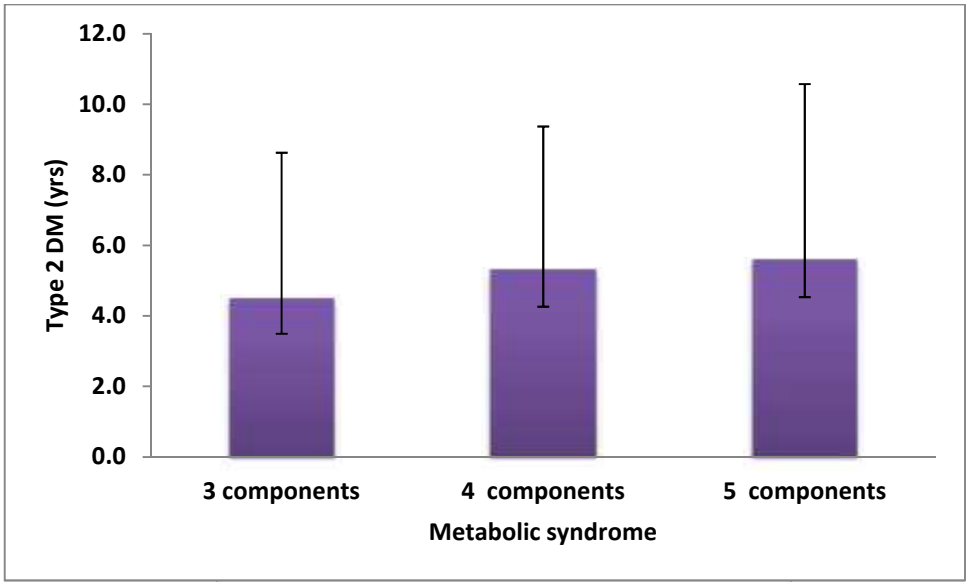

Figure 25: Correlation of diabetes mellitus with severity of MS in patients studied

In our study history of diabetes and hypertension were significantly associated with the increasing number of components of MS

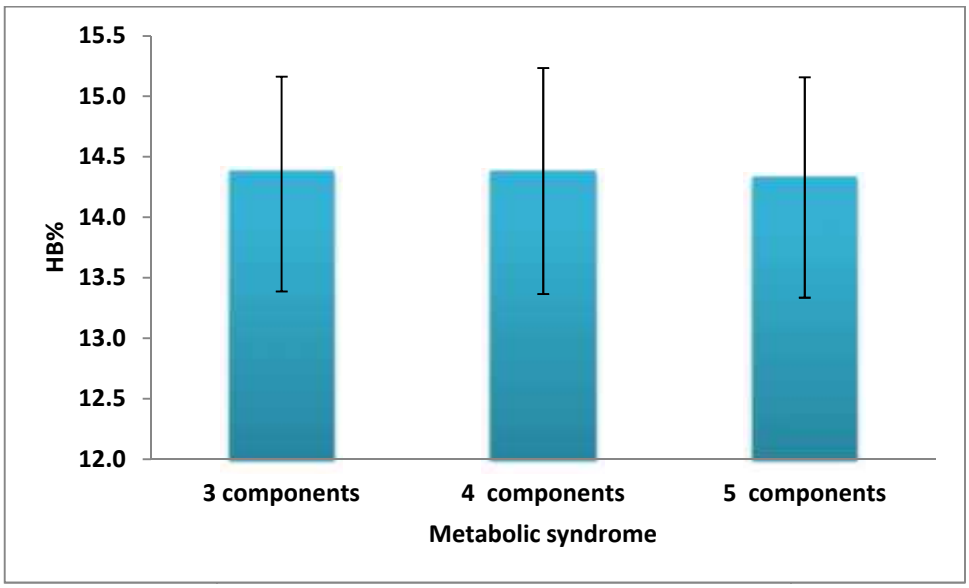

Figure 26: Correlation of hemoglobin% with severity of MS in patients studied

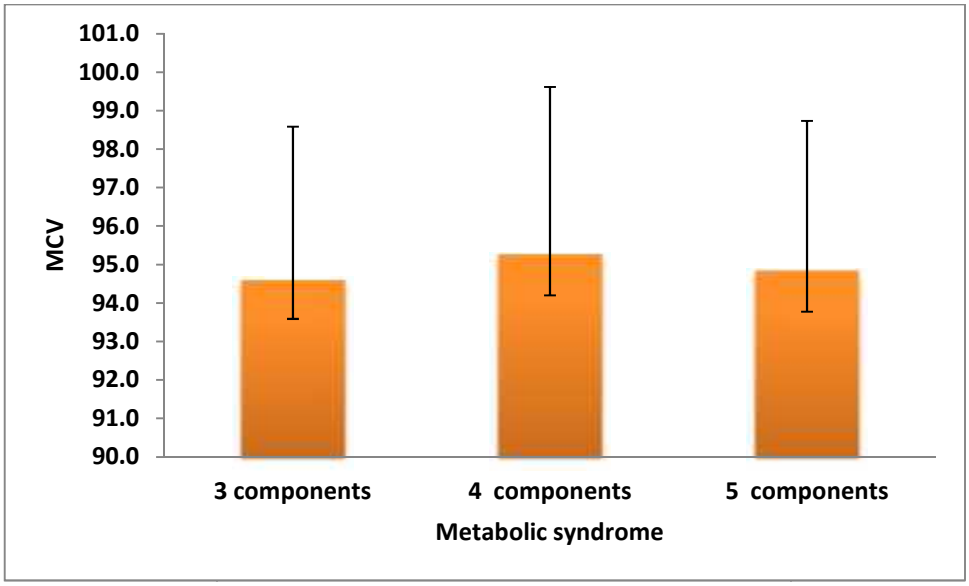

Figure 27: Correlation of MCV with severity of MS in patients studied

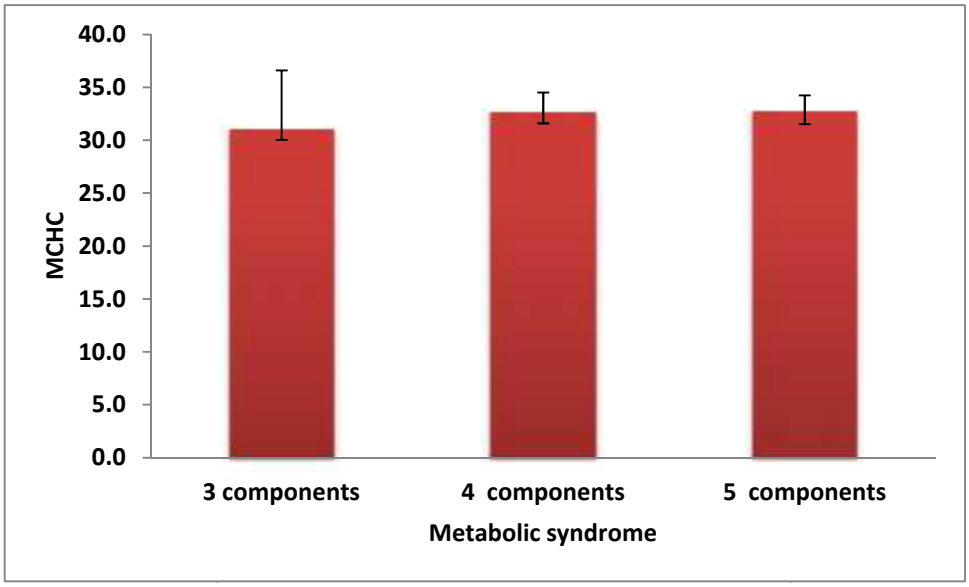

Figure 28: Correlation of MCHC with severity of MS in patients studied

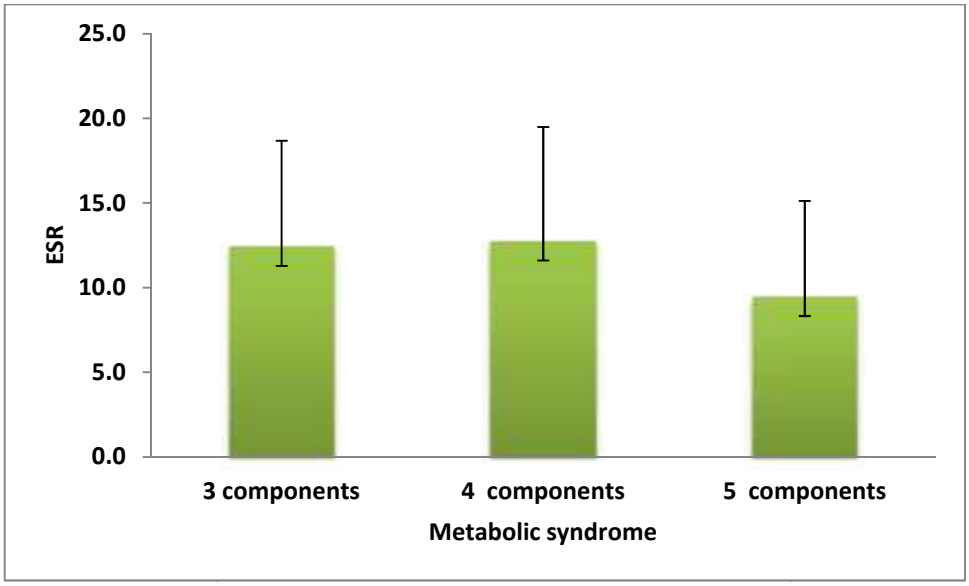

Figure 29: Correlation of ESR with severity of MS in patients studied

In our study Hb%, MCV, MCHC and ESR did show any relation with the number of components of MS

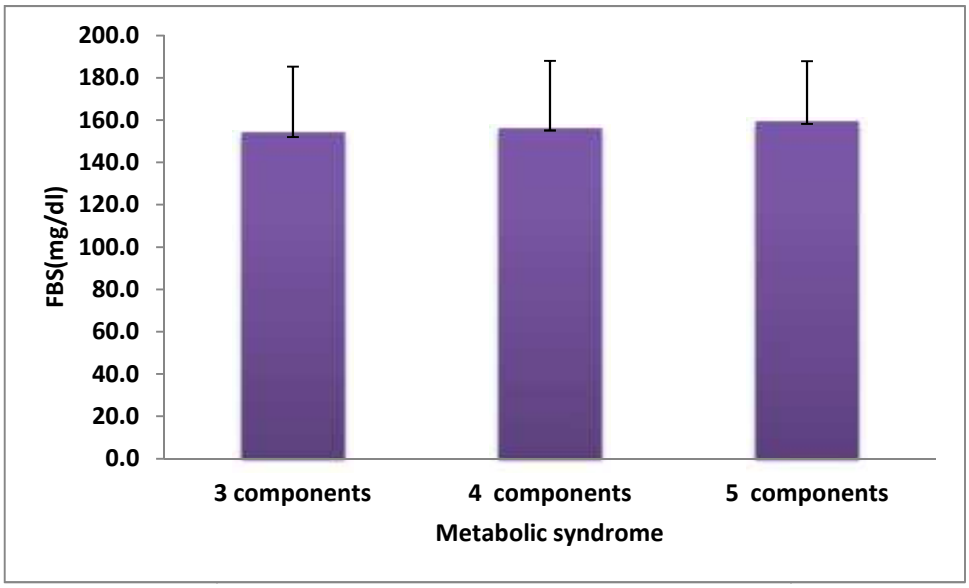

Figure 30: Correlation of FBS with severity of MS in patients studied

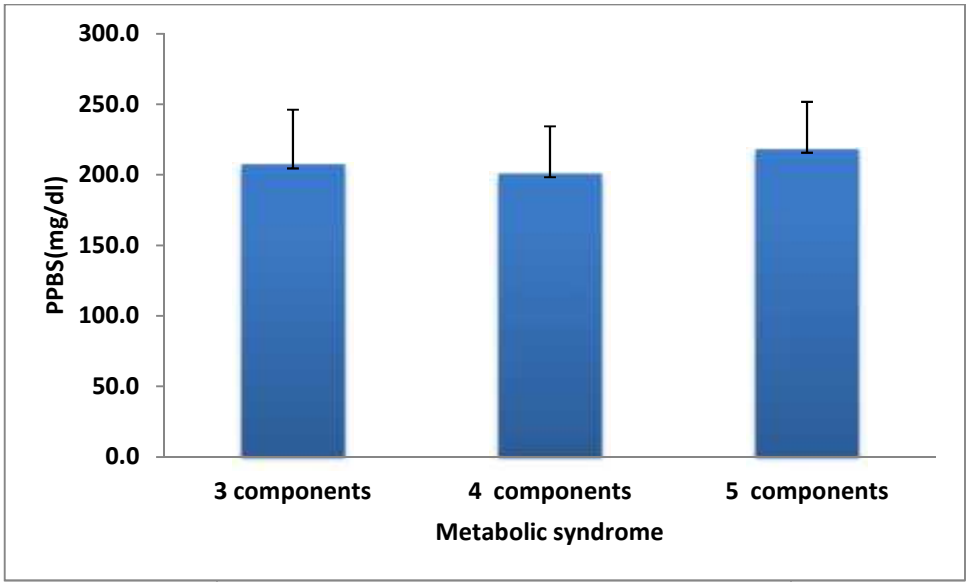

Figure 31: Correlation of PPBS with severity of MS in patients studied

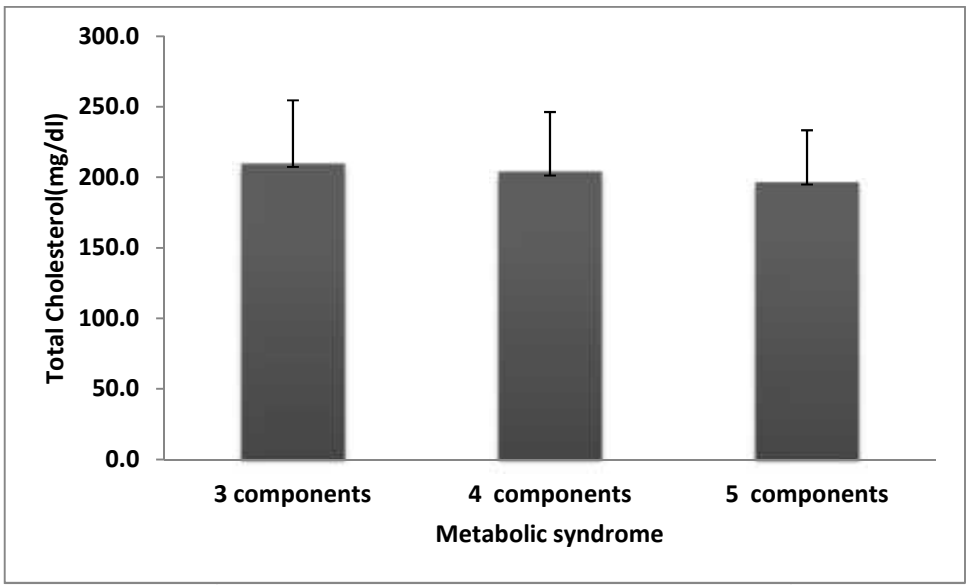

Figure 32: Correlation of total cholesterol with severity of MS in patients studied

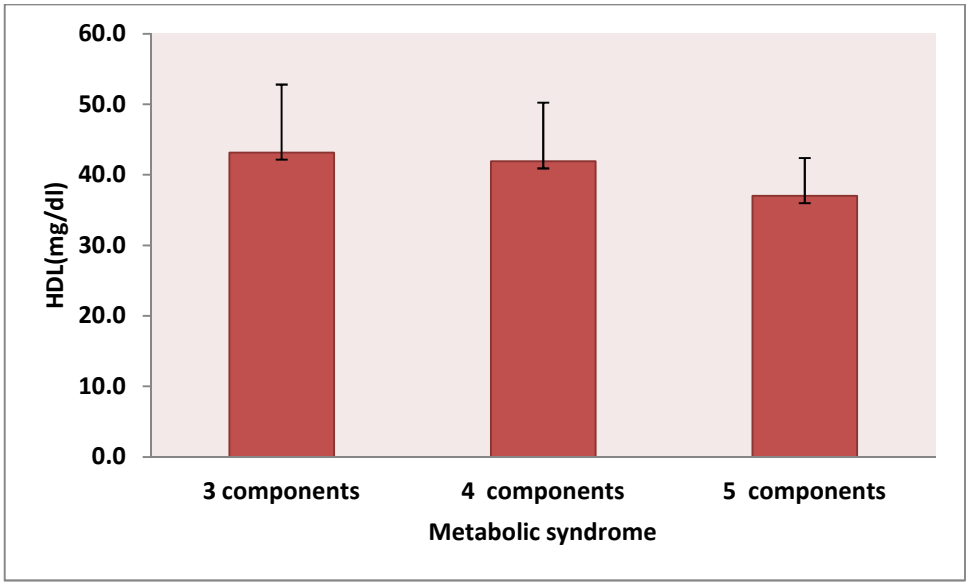

Figure 33: Correlation of HDL with severity of MS in patients studied

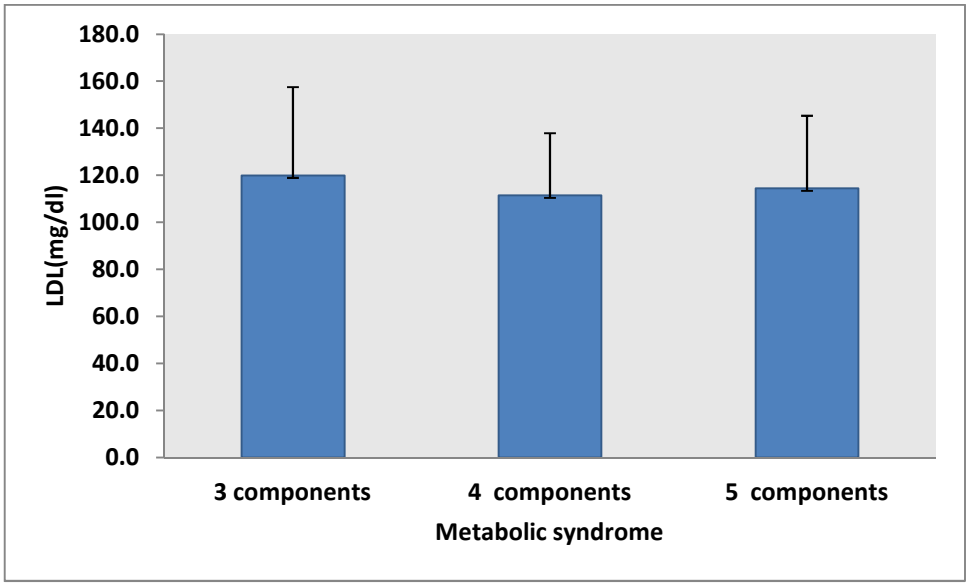

Figure 34: Correlation of LDL with severity of MS in patients studied

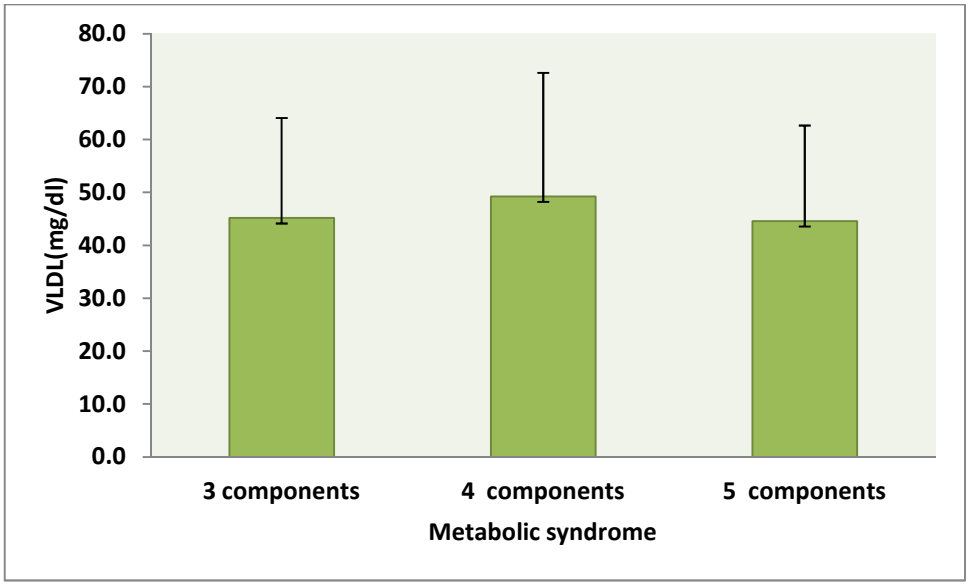

Figure 35: Correlation of VLDL with severity of MS in patients studied

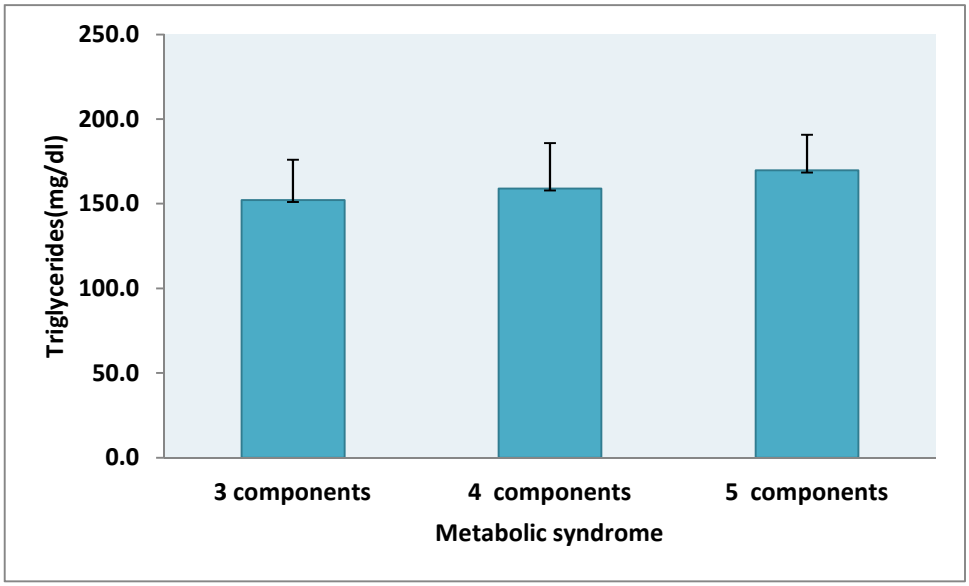

Figure 36: Correlation of triglycerides with severity of MS in patients studied

In our study triglycerides and HDL cholesterol showed significant correlation with the increasing number of components of metabolic syndrome.

DISCUSSION

There is increasing evidence that moderately elevated body iron stores, below the levels which are commonly found in hemochromatosis, may be associated with adverse health outcomes. We hypothesized that the metabolic syndrome would be more prevalent in those with moderately elevated serum ferritin levels.

The present study was done to determine the association of serum ferritin in Metabolic Syndrome as well as to determine the relation between individual component of Metabolic Syndrome & number of components metabolic syndrome and serum ferritin. It is a correlational clinical single group study with 150 patients.

Patients were evaluated with detailed history, meticulous examination and laboratory investigations which included fasting lipid profile, fasting blood sugar, postprandial blood sugar levels, complete blood picture, peripheral smear study and fasting serum ferritin levels.

As serum ferritin is an acute-phase reactant, it may be elevated in the presence of inflammation. We attempted to minimize this potential source of confounding by adjusting for ESR and by excluding those individuals with suspected inflammation, infection, and liver disease.

In our study, we observed signs of dyslipidemia in 32(31.37%) patients, 20(19.6%) males and 12(11.76%) females, in the form of xanthelesma, arcus senilis, thickening of peripheral arteries. These were more commonly found in those with elevated triglyceride levels.

In the present study, there were 88 males & 62 females with mean Age distribution of 56.0±10.1. Majority of patients (41%) were in their sixth decade of life. There were only 6 patients below 35 yrs. In a study conducted by Claudia bozzini[132] et al, the mean age distribution among study population was 58.7 yrs. In a

study done by Bilgilli sebel et al[138] mean age of the patients was 51.1±11.8years.

In a study conducted by Vasilis tsimchodimos et al[140], mean BMI in study population was 29.1±3.4. In a study done by Bilgilli Sebel et al[138], all subjects of metabolic syndrome had BMI >25 Kg/m^2. Mean BMI in our study was 29.4±2.1, with 123(82%) of patients meeting criteria for central obesity according to NCEP ATP3 guidelines. All the patients had BMI > 25 Kg/m2.

In our study 119 (79.3%) patients had blood pressure recording of more than 135/85mmhg. One hundred patients (66.7%) patients were known hypertensives on treatment. In a study done by Jing Wang et al [139] diastolic blood pressures was significantly high in males when compared with females. Our study did not show such correlation.

In the present study, 122 patients (79.9%) were known diabetics on treatment,38(25.3%) patients did not have history of diabetes. In a study done by Jing Wang et al[138] fasting blood sugar was significantly high in females when compared with males. In the present study there was no statistically significant difference.

In a study done by Jing Wang et al[138] HDL cholesterol was significantly high in females when compared to males. In our study, 47(46.1%) patients had abnormal total cholesterol (>200mg/dl), 70(60.6%) patients had abnormal triglycerides (>150mg/dl), 77(75.5%) patients had abnormal HDL (<40mg/dl in males, <50 in females).

The study population was categorized in to those having 3, 4 and 5 components of metabolic syndrome. Based on the serum ferritin levels in ng/l, they were divided into 5 quartiles as >50, 51-100, 101-150, 151-200 & >200.

There were 59 (39.4%) patients with 3 components of metabolic syndrome, 46 (30.7%) with 4 components and 45 (30%) with 5 components of metabolic syndrome.

In our study, we analyzed the association of serum ferritin and other parameters of metabolic syndrome with each group containing 3, 4 and 5 components of metabolic syndrome.

The present study revealed that Serum ferritin was increasing significantly with increasing number of components of metabolic syndrome with $p < 0.001$. It also showed that individual components of metabolic syndrome had significant correlation with increasing number of components of metabolic syndrome.

Central obesity was increasingly associated with increasing number of components of metabolic syndrome with a significant p value of <0.001. Dyslipidemia (both triglycerides and HDL criteria) and blood pressure also showed similar correlation of statistical significance (p value of <0.001). Fasting blood glucose had significant correlation with the number of components of metabolic syndrome with $p = 0.03$.

In a study conducted by Claudia bozzini[132] et al, a higher concentration of ferritin was associated with the metabolic syndrome at baseline. In a similar study conducted by Megan jehn[131], it was revealed that the highest prevalence of the metabolic syndrome occurred in those with higher levels of serum ferritin. The prevalence of elevated blood pressure, elevated plasma glucose, elevated triglycerides, and abdominal adiposity all increased significantly with increasing serum ferritin. The prevalence of elevated triglycerides and abdominal adiposity also increased with increasing levels of serum ferritin. The greater the number of metabolic syndrome components present, the greater was the serum ferritin level. The results of this study were similar to our observations.

A study by Liang Sun et al[137], conclude that Elevated circulating ferritin concentrations were associated with higher risk of type 2 diabetes and metabolic

syndrome in middle-aged and elderly Chinese independent of obesity, inflammation, adipokines, and other risk factors. Supporting the crucial role of iron overload for metabolic diseases, even in a country with relatively high prevalence of iron deficiency, which is similar to our observations in present study. A study conducted by Vasilis tsimchodimos et al[140] revealed that patients with metabolic syndrome exhibited increased concentration of serum ferritin compared to control group supporting our findings.

In a study done by Bilgili Sebel et al[138] metabolic syndrome patient had significantly higher BMI, waist and hip circumference, systolic and diastolic pressure, fasting glycemia, two-hour postprandial serum glucose, total cholesterol, triglycerides, lower HDL cholesterol.

In this study, we observed a positive association between elevated iron stores, measured by serum ferritin levels, and the prevalence of the metabolic syndrome. Ferritin levels also correlated with increasing number of components of metabolic syndrome. We also observed that individual components of the metabolic syndrome correlated well with increasing number of components of metabolic syndrome.

CONCLUSION

1. There is a positive association between elevated iron stores, measured by serum ferritin levels, and the prevalence of the metabolic syndrome.
2. Serum ferritin levels correlated with increasing number of components of the metabolic syndrome.
3. There is a positive correlation between individual components of metabolic syndrome with increasing number of components of metabolic syndrome.

SUMMARY

The present study was done to determine the association of serum Ferritin in Metabolic Syndrome as well as to determine the relation between individual component of metabolic syndrome & number of components metabolic syndrome and plasma ferritin. It is a Correlational clinical single group observational study including 150 patients.

In the present study, there were 88 males & 62 females with mean Age distribution of 56.0±10.1. Majority of patients (57.3%) were above 45 yrs of age. There were only 6 patients below 35 yrs of age.

Mean BMI in our study was 29.4±12.1, with 123(82%) of patients meeting criteria for central obesity according to NCEP ATP3 guidelines.

In our study 119 (79%) of patients had blood pressure recording of more than 135/85mmhg. 100 (66.7) were known hypertensives on treatment.

In our study 112 (79.9%) of patients were on treatment for diabetes mellitus, 11(7.3%) patients were not having diabetes mellitus.

In our study 91(60.7%) patients had abnormal total cholesterol (>200mg/dl), 100(66.7%) patients had abnormal triglycerides (>150mg/dl) and 104 (69.3%) patients had abnormal HDL (<40mg/dl in males, <50 in females)

There were 59 (39.4%) patients with 3 components of metabolic syndrome, 46 (30.7%) with 4 components and 45 (30%) with 5 components of metabolic syndrome.

Present study revealed that Serum ferritin was increasing significantly with increasing number of components of metabolic syndrome with P value <0.001. It also showed that individual components of metabolic syndrome had significant correlation with increasing number of components of metabolic syndrome.

Of all the components, central obesity and hypertensive were increasingly

associated with metabolic syndrome with a significant p value of <0.001 while dyslipidaemia (both triglycerides and HDL criteria) also showed similar correlation of statistical significance (p value of 0.002 and 0.001).

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ANNEXURE-I

ETHICAL CLEARANCE CERTIFICATE

B.L.D.E. UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 13-11-2013 at 3-30 pm to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.

Title "A Study of levels of Serum ferritin in patients with Metabolic Syndrome"

—— x —— x —— x —— x ——

Name of P.G. student Dr. M. Vamshi Krishna.
Department of Medicine

Name of Guide/Co-investigator Dr Dr. M.S. Biradar.
Professor of Medicine

DR.TEJASWINI. VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

ANNEXURE-II

CONSENT FORM

TITLE OF RESEARCH: "STUDY OF LEVELS OF SERUM FERRITIN IN PATIENTS WITH METABOLIC SYNDROME."

GUIDE : DR. M.S.BIRADAR

P.G. STUDENT : DR. M. VAMSHI KRISHNA

PURPOSE OF RESEARCH:

I have been informed that the purpose of this study is to find out whether there is any association between levels of serum ferritin and metabolic syndrome.

PROCEDURE:

I understand that I will undergo detailed history and clinical examination and investigations.

RISKS AND DISCOMFORTS:

I understand that there is no risk involved and I may experience mild pain during the above mentioned procedures.

BENEFITS:

I understand that my participation in this study will help to find out whether there is any association between levels of serum ferritin and metabolic syndrome.

CONFIDENTIALITY:

I understand that the medical information produced by the study will become a part of hospital record and will be subjected to confidentiality and privacy regulations of hospital. If the data is used for publications the identity of the patient will not be revealed.

REQUEST FOR MORE INFORMATION:

I understand that I may ask for more information about the study at any time.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and I may refuse to participate or withdraw from study at any time.

INJURY STATEMENT:

I understand in the unlikely event of injury to me during the study I will get medical treatment but no further compensations.

(Signature of Guardian) (Signature of patient)

Contact no-

(If the patient is conscious, well oriented and fully aware)

ANNEXURE-III

PROFORMA

BLDEU'S SHRI B.M.PATIL MEDICAL COLLEGE

HOSPITAL AND RESEARCH CENTRE, VIJAYPUR

"STUDY OF LEVELS OF SERUM FERRITIN IN PATIENTS WITH METABOLIC SYNDROME."

Name: CASE NO:

Age: OP/IP NO:

Sex: DOA:

Religion: DOD:

Occupation:

Address:

Presenting complaints with duration:

History of presenting complaints:

Past History: Blood donation within previous 4 months yes/no

Jaundice/Hypertension/Diabetes Mellitus.

Family History: Family history of type II diabetes mellitus/ hypertension/ HCV infection/ HBsAg infection/ hemochromatosis.

Personal History:

Diet

Appetite

Sleep

Bladder and bowel habits:

Smoking/Tobacco chewing

Duration

Number of cigarettes/beedis pack year smoked

Amount of tobacco chewed

Categories:

Non smoker

Past smoker

Current smoker

Alcohol

Duration

Quantity/Frequency

Type

Categories : Non drinker

Light drinker (1-20gm of alcohol / day)

Moderate drinker (21-40gm of alcohol / day)

Heavy drinker (>41gm of alcohol / day)

Others

Treatment History: Treatment for anemia with iron suppliments within previous 3 months or on treatment for diabetes/hypertension

General Physical Examination

Pallor: present/absent

Icterus: present/absent

Cyanosis: present/absent

Clubbing: present/absent

Generalized lymphadenopathy: present/absent

Odema: present/absent

Built:

Nourishment:

Vitals

PR:

BP: in mm of mercury (mm hg)

RR:

Temp:

Weight: in Kilograms

Height: in Meters

BMI: in kg/m^2

Waist circumference: in Centimeters

SYSTEMIC EXAMINATION.

- Cardiovascular system
- Respiratory system
- Per abdomen
- Central nervous system

INVESTIGATIONS

PATHOLOGY	
1.)Complete blood count:	
Hb	gm/dl
Total count	Cells/cumm
Differential count	
Neutrophils	%
Lymphocytes	%
Eosinophils	%
Basophils	%
Monocytes	%
2.) ESR	At the end of 1st hour.
3.) Urine Routine	
Sugar	
Albumin	
Cell type	
Cell count	
4.) Peripheral Smear Study	

BIOCHEMISTRY

1)Fasting Blood sugar	
2)Postprandial Blood sugar	
3)LIPID PROFILE	
Total Cholesterol	
Triglycerides	
HDL-Cholesterol	
LDL-Cholesterol	
VLDL-Cholesterol	
4)Serum Ferritin	

MICROBIOLOGY

HBsAg antibody(when required)	
HCV antibody(when required)	

Other relevant investigations will be done when required.

CONCLUSION:

DATE: **SIGNATURE**

KEY TO MASTER CHART

A	=	Normocytic Normochromic
IP No	=	Inpatient Number
BMI	=	Body Mass Index
Hb%	=	Hemoglobin %
MCV	=	Mean Corpuscular Volume
MCHC	=	Mean Corpuscular Hemoglobin Concentration
ESR	=	Erythrocyte Sedimentation Rate
PS	=	Peripheral Smear Study
FBS	=	Fasting Blood Sugar
PPBS	=	Post Prandial Blood Sugar
HDL	=	High Density Lipoproteins
LDL	=	Low Density Lipoproteins
VLDL	=	Very Low Density Lipoproteins

MASTER CHART

												Urine						Blood									
SL. No	Name	IP No.s	Age	Sex	BMI	waist circumference(cms)	systolic BP	Diastolic BP	Hypertensive (yrs)	Type2 DM (yrs)	ALBUMIN	SUGAR	microscopy,cell/hpf	HB%	TC in cell/cmm	MCV	MCHC	PS	ESR	FBS	PPBS	TOTAL CHOLESTEROL	HDL	LDL	VLDL	TRIGLYCERIDES	CREAT	FERRITIN
1	vittal kamble	8123	64	m	28.6	98	156	96	no	4	nil	nil	nil cells	13	4400	99	31	A	5	148	199	245	49	142	54	177	0.9	53.7
2	Shivalingavva	8126	47	m	29.9	101	146	90	no	3	nil	nil	nil cells	15	7560	96	33	A	20	132	154	190	42	111	37	157	0.8	92.2
3	mantappa	8070	51	m	28.2	98	148	90	2	8	nil	nil	nil cells	14	9500	92	29.3	A	15	168	220	186	46	107	33	166	0.7	59.7
4	lakshmibai	9027	66	f	29.4	94	160	100	9	10	1+	0.01	2-3 pc	15	5650	102	37	A	5	135	168	178	52	93	33	190	0.8	87.3
5	shrisail	8947	35	m	33.5	104	140	96	no	5	nil	0.005	nil cells	14	6550	94	32.2	A	20	188	265	192	38	108	46	152	0.8	136.1
6	shivanandayya	9440	48	m	30.2	102	138	88	5	no	nil	nil	nil cells	15	9550	96	33.6	A	15	114	252	206	29	129	48	156	0.8	113.6
7	gurushanth	9422	54	m	28	88.5	150	90	3	4	nil	0.01	nil cells	14	9500	100	34.2	A	20	154	320	189	43	104	42	225	0.9	79.3
8	muragappa	7823	47	m	29.2	103	166	98	5	15	nil	nil	nil cells	15	6750	99	31	A	5	156	261	186	38	109	49	176	1.2	257.6
9	revanasiddappa	9595	59	m	30.4	114	156	100	6	7	1+	0.005	2-3 pc	14	4950	91	30	A	5	150	135	237	41	114	82	192	0.9	295
10	shakila	11487	47	f	25.9	86	156	88	4	10	nil	nil	nil cells	15	5650	97	29.9	A	5	145	159	236	56	109	71	176	1.2	56
11	muttappa	10250	60	m	31.1	103	170	100	6	8	nil	0.01	nil cells	14	10900	93	34	A	20	125	230	212	26	123	63	158	1.3	100.5
12	ningappa	10547	55	m	28.6	104	116	76	4	no	nil	nil	nil cells	16	8850	96	31	A	10	135	188	198	45	112	41	152	1.1	93
13	bijubai	11811	47	f	29.5	91	146	90	3	6	nil	nil	nil cells	14	9760	100	33	A	5	158	197	288	51	130	107	214	1.2	97.3
14	kalawati	11801	33	f	29.6	84	140	88	no	15	nil	nil	nil cells	15	5600	97	33.1	A	20	165	194	206	48	106	52	156	0.5	114
15	dyamangouda	11465	59	m	27.5	101	150	90	2	no	nil	nil	nil cells	14	7650	89	3	A	20	168	256	243	48	144	51	198	0.9	74
16	sonabai	13654	62	f	31.1	80	160	100	12	5	1+	nil	2-3pc	14	6900	101	29.3	A	10	186	220	212	36	126	50	188	0.8	103
17	revabai	13757	66	f	27.6	84	156	102	6	7	nil	0.005	nil cells	15	7850	88	34	A	20	134	216	306	57	182	67	210	1.2	59.9
18	rajashree	14463	55	f	26.5	81	172	110	no	4	nil	nil	nil cells	14	4450	91	32	A	15	212	259	233	59	134	40	172	1.1	43.3
19	baghirathi	13640	49	f	31.3	102	150	98	4	5	nil	nil	nil cells	14	9520	90	34.8	A	5	166	186	188	59	93	36	153	0.9	81.8
20	shoba	13801	42	f	28.4	84	140	90	no	4	nil	nil	nil cells	15	80500	89	29	A	20	177	223	278	58	112	108	187	0.8	23.7
21	dundappa	14413	62	m	31.7	112.5	160	96	8	no	1+	nil	2-3 pc	13	8700	100	31	A	15	134	167	131	32	76	23	90	0.8	240
22	bagirabai	13640	50	f	30.3	104	142	90	no	4	nil	nil	nil cells	15	7500	96	36.2	A	20	189	245	178	57	83	38	154	0.8	81.8
23	iranagouda	14311	49	m	31.5	102	138	88	1	4	nil	nil	nil cells	14	8750	93	32	A	5	156	196	245	36	147	62	162	0.9	128
24	mallamma	12792	53	f	29.5	88.5	126	80	no	3	nil	nil	nil cells	15	8550	97	34	A	5	144	167	213	49	112	52	174	1.2	81
25	sidannagouda	16640	52	m	29.8	103	138	88	2	8	nil	nil	nil cells	14	5670	88	31	A	5	120	186	206	49	109	48	156	0.9	60.6
26	daremma	19942	70	f	32.2	100	120	80	no	10	nil	nil	nil cells	14	8450	100	33	A	20	164	202	189	43	104	42	225	0.8	93.3
27	basavaraj	192342	64	m	33.3	104	164	102	6	5	nil	0.01	nil cells	14	5450	93	29.8	A	10	192	248	189	38	129	22	176	0.7	194
28	gangabai	18142	61	f	27.5	86	158	98	9	no	1+	nil	2-3 pc	14	6500	101	31	A	5	176	264	277	54	144	79	192	0.8	53.3
29	ashwini	19812	58	f	27.9	98	130	80	no	4	nil	nil	nil cells	16	4450	92	32.9	A	20	156	186	300	56	169	75	176	0.8	57.9
30	kondanna	225120	48	m	28.1	104	124	82	no	15	nil	nil	nil cells	14	7600	96	33.33	A	20	190	212	212	38	123	51	158	0.9	99.2
31	jayashree	216953	46	f	27.3	86	160	104	no	7	nil	nil	nil cells	14	8560	94	32	A	10	176	196	198	45	112	41	152	0.9	138.8
32	bhagamma	19316	60	f	30.2	98	150	100	10	10	2+	nil	2-3 pc	15	10300	100	31.1	A	15	166	199	288	44	137	107	214	1.2	171.4
33	prabhavathi	18223	56	f	26.2	87	144	92	5	8	nil	nil	nil cells	13	9500	98	32.6	A	20	184	213	207	38	127	42	194	1.3	140

34	nanagouda	18096	58	m	25.9	104	138	88	6	no	nil	nil	nil cells	15	4300	96	33.4	A	5	220	252	246	39	165	42	165	1.1	118.2
35	palakshi	18111	51	f	30.6	96	140	90	5	6	nil	0.01	nil cells	14	9760	90	31.9	A	5	202	286	236	31	146	59	136	1.2	112
36	siddappa	18089	62	m	25.9	106	120	84	no	15	1+	nil	2-3 pc	16	5560	89	34	A	5	122	166	229	48	116	65	159	0.5	62.1
37	madiwalappa	19001	70	m	33.2	110	148	92	10	no	nil	0.02	nil cells	14	9850	92	35.3	A	20	142	251	184	36	117	31	112	0.9	138
38	shivaji	18901	48	m	27.5	109.5	154	86	6	6	nil	nil	2-3 pc	13	6750	97	33	A	10	176	246	192	38	115	39	157	0.8	182
39	k. pandayya	18607	68	m	27.9	109	148	98	2	7	nil	nil	nil cells	15	8590	88	32.4	A	5	187	213	276	39	128	109	142	1.2	140
40	mahadevi	18883	47	f	28.1	102	128	88	6	4	nil	0.01	nil cells	14	6500	99	31.8	A	20	155	186	146	46	69	31	173	1.1	155
41	mallanna	18894	62	m	29.5	106	148	98	2	5	nil	nil	nil cells	15	7560	93	29.8	A	20	184	275	189	35	106	48	184	0.9	191
42	basappa	19118	56	m	30.2	112	156	96	10	4	1+	nil	nil cells	14	9500	101	31	A	10	167	183	176	36	113	27	191	0.8	262
43	shrimanthgouda	18341	68	m	30.9	104	128	84	6	5	nil	nil	6-8 pc	15	5650	92	32.9	A	5	166	210	267	37	163	67	165	0.7	229
44	gurubai	225106	58	f	27.1	102	140	90	5	4	nil	0.01	nil cells	14	4400	99	31	A	10	135	182	233	43	147	43	189	0.9	158
45	sundarabai	225108	65	f	26.8	88.5	148	90	1	4	1+	nil	nil cells	15	7560	96	33	A	10	148	176	168	48	86	34	152	1.2	171
46	amitha	225109	28	f	27.4	103	128	84	no	5	nil	0.015	2-3 pc	14	9500	92	29.3	A	20	132	199	259	53	98	108	197	1.3	27
47	siddram	225111	66	m	29.7	109	160	100	9	2	1+	0.01	1-2RBCs	15	5650	102	37	A	5	168	210	255	33	187	35	178	1.1	207
48	siddappa	225112	48	m	30.3	111	148	96	5	no	nil	nil	nil cells	14	6550	94	32.2	A	20	135	189	187	37	113	37	186	1.2	211
49	ramannagouda	225107	56	m	29.5	110	138	88	10	3	nil	nil	1-3pc	16	9550	96	33.6	A	5	188	210	185	36	89	60	177	0.5	232
50	morawade	43198	58	m	26.9	102.5	120	80	no	4	1+	nil	nil cells	14	9500	100	34.2	A	10	140	236	235	41	148	46	185	0.9	52.8
51	jagadish	43199	51	m	33.5	103	126	80	no	10	nil	0.01	nil cells	15	6750	99	31	A	15	154	176	183	43	94	46	151	0.8	62.2
52	pooja	43200	29	f	28.6	102	140	90	no	no	nil	nil	2-3 RBCs	14	4950	91	30	A	5	122	198	196	44	102	50	162	1.2	153.3
53	jeevita	43201	39	f	30.4	104	126	76	no	10	nil	0.015	nil cells	14	5650	97	29.9	A	10	108	164	168	54	93	21	154	1.1	63.4
54	suresh	43202	57	m	32.1	102.5	120	70	no	5	nil	0.01	nil cells	15	10900	93	34	A	10	145	156	156	48	76	32	156	0.9	26.32
55	saraswati	43203	39	f	29.8	92	110	80	no	no	nil	0.005	3-4 pc	14	8850	96	31	A	10	125	244	226	54	110	62	168	0.8	30.5
56	kiran	43204	46	m	32.4	108.5	146	90	4	4	nil	0.01	2-3 pc	14	9760	100	33	A	5	135	264	168	32	89	47	152	1.2	195.5
57	ambali	43205	45	m	31.1	112	156	96	3	15	1+	nil	nil cells	15	5600	97	33.1	A	20	158	210	188	34	110	44	148	0.5	103.4
58	sagar	43206	54	m	27	106	128	84	no	7	1+	0.01	nil cells	13	7650	89	3	A	20	165	194	176	48	96	32	158	0.9	43.1
59	vanitha	43207	64	f	28.2	89	120	80	no	5	nil	nil	2-3 pc	15	6900	101	29.3	A	10	168	183	148	51	72	25	153	0.8	64.1
60	siddamma	3999	56	f	27.6	102	138	94	5	no	nil	0.02	nil cells	14	7850	88	34	A	15	102	156	156	58	77	21	154	1.2	58.1
61	ravikumar	225116	57	m	30.8	104	148	90	no	no	2+	0.015	nil cells	15	4450	91	32	A	20	96	161	168	44	93	31	189	1.1	45.3
62	bhagyashree	48340	65	f	28.6	100	160	100	4	9	nil	0.02	2-3 pc	14	9520	90	34.8	A	5	212	265	156	48	76	32	156	0.8	164.7
63	neelamma	48341	46	f	31.1	102	140	96	15	5	1+	nil	nil cells	14	80500	89	29	A	5	192	245	226	44	122	60	128	1.3	104
64	mahendra	48342	63	m	26.4	105	138	88	7	no	nil	nil	nil cells	14	8700	100	31	A	5	100	156	168	42	89	37	152	1.1	69.33
65	vijayalakshmi	48344	62	f	28.2	94	150	90	10	no	nil	nil	nil cells	14	7500	96	36.2	A	20	103	149	188	54	98	46	168	1.2	68.51
66	kavitha	11941	70	f	29.8	101	166	98	8	no	nil	0.015	nil cells	16	8750	93	32	A	10	94	166	176	58	86	32	158	0.5	42.2
67	bhagirathi	48349	46	f	30.1	96	140	90	no	5	1+	nil	3-4RBCs	14	9540	94	32.2	A	5	176	222	148	51	72	25	130	0.5	59.9
68	rajeshwari	48338	62	f	27.4	98	156	88	6	8	nil	nil	2-3 pc	14	4650	96	33.6	A	20	166	200	156	52	76	25	144	0.9	58.1
69	basanna	3479	73	m	18.2	113	170	100	15	no	nil	nil	3-4RBCs	15	6750	100	34.2	A	5	184	207	140	38	56	46	166	0.8	208.4
70	kasturibai	3977	46	f	28.6	98	148	98	no	4	1+	0.01	nil cells	13	10500	99	31	A	20	189	156	168	52	90	26	142	1.2	34.3
71	padmavathi	4350	58	f	30.9	102	138	88	5	4	1+	nil	nil cells	15	5600	91	30	A	5	192	267	288	58	187	43	132	1.1	59.4
72	roopa	5217	44	f	31.7	106	148	98	7	3	nil	nil	2-3 pc	14	6800	97	29.9	A	10	176	216	229	53	141	35	149	0.8	62
73	jayashree	4085	51	f	28.2	96	130	80	no	8	nil	nil	4-6pc	16	8750	93	34	A	15	156	201	178	36	103	39	151	0.7	79
74	indrabai	5405	56	f	29.8	100	156	90	5	10	nil	nil	nil cells	14	4550	96	31	A	5	156	199	196	55	107	34	118	1.3	62.9
75	banagar . B . C	5445	66	m	30.1	110	140	90	4	no	nil	0.02	nil cells	13	8960	100	33	A	10	94	156	212	34	146	32	143	1.1	60.2

76	shivanand	5273	56	m	27.4	106	138	94	5	no	nil	0.02	nil cells	15	9540	96	31	A	10	99	160	158	39	82	37	138	1.2	32.9
77	nagayyaswami	6200	57	f	26.2	98	148	90	4	4	nil	0.015	nil cells	14	8500	94	32	A	10	164	199	188	32	123	33	136	0.5	110
78	sharanawwa	9730	76	f	30.6	106	160	100	4	no	1+	0.01	3-4 pc	15	9650	100	31.1	A	5	107	157	168	44	93	31	144	0.9	56.8
79	ramappa	11431	54	m	27.9	109	140	96	5	7	nil	nil	nil cells	13	9000	98	32.6	A	20	186	229	156	38	76	42	156	0.8	211.3
80	roop singh	11673	54	m	32.4	112.5	138	88	2	10	nil	0.005	nil cells	14	6300	96	33.4	A	20	122	196	226	34	160	32	168	1.2	162.5
81	girimallappa	11654	39	m	31.7	108	130	80	no	8	nil	0.01	nil cells	13	7050	90	31.9	A	10	142	184	168	32	89	44	152	1.3	76.7
82	hanamawwa	11211	62	f	29.3	102	166	98	3	no	1+	0.01	nil cells	14	8500	89	34	A	5	176	197	188	44	110	34	168	1.1	185.6
83	devakemma	10391	56	f	31.5	88.5	140	90	4	6	nil	nil	nil cells	15	4900	92	35.3	A	5	167	210	176	48	96	32	158	1.2	144
84	girijabai	11857	68	f	30.1	91	156	88	10	no	nil	0.01	nil cells	14	11000	97	33	A	5	99	164	148	39	72	37	130	0.5	48.1
85	ningappa	11482	58	m	30.1	109	170	100	8	no	nil	nil	nil cells	13	5630	88	32.4	A	20	104	153	156	31	89	36	144	0.5	66.7
86	shamshad	12530	56	m	32.2	115.5	116	76	5	5	2+	nil	nil cells	14	6000	99	31.8	A	10	167	234	140	28	66	51	198	0.9	270
87	shreedevi	12135	45	f	33.3	103	146	90	1	7	nil	nil	nil cells	16	8540	94	34	A	5	166	189	168	42	95	31	152	0.8	132
88	mallappa	14197	66	m	27.5	104	140	88	3	no	nil	nil	2-3 pc	14	9600	94	32.2	A	20	100	152	288	28	207	47	139	1.2	64.7
89	sunil	15441	48	m	27.9	109	150	90	9	5	nil	nil	nil cells	14	6900	96	33.6	A	5	176	245	229	39	151	39	151	1.1	193
90	shoba	15109	36	f	28.1	88.5	160	100	5	4	1+	nil	nil cells	16	7850	100	34.2	A	20	166	191	178	36	103	39	131	0.8	120
91	yasmeen	15107	58	f	27.3	106	156	102	10	5	nil	nil	nil cells	13	4450	99	31	A	5	184	199	188	47	110	31	151	0.7	266
92	umesh	225123	51	m	30.2	114	172	110	no	no	nil	0.01	nil cells	15	9520	91	30	A	20	98	161	215	24	140	51	134	0.9	31.5
93	ashwini	15216	29	f	30.9	106	150	98	6	no	nil	nil	nil cells	14	80500	97	29.9	A	15	102	155	168	28	101	39	129	1.2	34.9
94	sharanawwa	13246	70	f	27.1	98	120	80	no	5	nil	0.02	nil cells	15	8700	93	34	A	20	122	194	182	48	97	37	111	1.3	60.8
95	mahesh	225117	56	m	26.8	110.5	160	96	8	2	nil	nil	2-3pc	14	7500	96	31	A	5	142	182	236	31	163	42	156	1.1	242
96	afriz	225121	56	m	27.4	98	122	76	no	no	1+	nil	nil cells	15	4400	100	33	A	5	176	156	234	32	162	40	198	1.2	76.2
97	suchitra	225125	37	f	29.7	94	128	80	no	3	nil	0.01	nil cells	14	7560	97	33.1	A	5	166	217	188	42	114	32	143	0.5	62.7
98	sunil	225126	51	m	30.3	109.5	126	80	no	4	nil	nil	nil cells	15	9500	88	34	A	20	184	223	196	34	123	39	156	0.9	96
99	akshay	225127	62	m	29.5	110	138	88	3	10	1+	nil	nil cells	14	5650	91	32	A	10	187	266	146	28	70	48	169	0.8	285
100	ajay	225128	42	m	26.9	109.5	180	110	8	20	nil	nil	2-3 pc	15	6550	90	34.8	A	5	162	194	162	36	88	38	198	1.2	136
101	chandu	225129	68	m	27.3	109	164	102	10	22	1+	0.01	nil cells	14	9550	89	29	A	5	122	159	168	38	96	34	168	1.1	141
102	rekha	225130	52	f	33.2	100	158	98	5	12	nil	nil	nil cells	16	9500	100	31	A	5	134	168	234	44	156	34	148	0.9	106
103	paraveshamma	17207	70	f	30.4	104	140	90	no	5	nil	0.015	nil cells	14	6750	96	36.2	A	20	176	200	184	48	107	29	144	0.8	113
104	shivagond	17144	62	m	32.1	105	124	82	4	1	nil	0.01	nil cells	15	9500	93	32	A	10	184	276	156	28	82	46	129	0.9	126.5
105	durgappa	16873	56	m	29.7	103	110	80	no	3	nil	nil	nil cells	14	5650	94	32.2	A	20	155	186	156	36	82	38	138	0.8	41.7
106	rajeshwar	17205	68	m	30.3	103	116	80	no	9	nil	nil	nil cells	14	6550	96	33.6	A	10	184	229	288	32	200	56	132	1.2	40
107	shreedevi	16956	39	f	29.5	102	126	80	no	5	nil	nil	2-3 pc	15	9550	100	34.2	A	5	167	268	222	32	150	40	138	1.1	37
108	shilpa	17005	62	f	26.9	104	138	88	8	10	nil	0.01	nil cells	14	9500	99	31	A	15	166	249	268	30	167	71	119	0.8	123
109	amrutha	16887	44	f	27.3	102	120	80	no	no	1+	nil	nil cells	14	6750	91	30	A	20	190	231	298	38	177	83	136	0.7	33
110	ashrith	225118	68	m	33.2	106.5	120	80	no	6	nil	0.015	nil cells	15	4950	97	29.9	A	5	176	222	168	36	95	37	159	0.9	89
111	geetha	16886	58	f	30.4	90	128	80	no	5	nil	0.01	2-3 pc	13	5650	93	34	A	5	166	196	188	44	111	33	154	1.1	70
112	basavappa	16959	65	m	32.1	104	120	80	no	8	nil	0.005	nil cells	15	10900	96	31	A	5	184	241	198	31	129	38	140	1.2	36
113	nagamma	16885	54	f	26.7	98	110	80	no	no	1+	0.01	nil cells	14	8850	100	33	A	20	217	248	306	37	201	68	148	0.5	33
114	pramila	16854	66	f	28.8	89	136	90	7	4	nil	nil	nil cells	15	9760	94	31	A	10	202	254	184	38	114	32	146	0.9	110
115	sarah	16872	48	f	29.6	102	122	80	no	4	nil	0.01	2-3 pc	14	5600	94	32	A	20	122	187	198	38	121	39	134	0.8	133
116	thoufiq	21011	56	m	28.9	99.5	156	90	5	3	nil	nil	nil cells	14	7650	100	31.1	A	10	142	169	184	38	109	37	135	0.9	67
117	ramu	20727	58	m	27.1	103	158	108	4	8	2+	0.02	2-3 pc	14	6900	98	32.6	A	5	166	194	264	48	168	48	186	1.2	130

118	shanthanna	20271	51	m	29.8	100.5	144	100	5	10	nil	0.015	nil cells	14	7850	96	33.4	A	20	166	191	286	34	212	40	148	1.3	57
119	siddaraya	20552	62	m	32.4	103.5	138	86	4	no	nil	0.02	nil cells	16	4450	90	31.9	A	5	101	166	268	36	134	98	188	1.1	78
120	vittal	20872	70	m	29.4	100	146	92	4	no	nil	nil	nil cells	14	9520	89	34	A	20	176	261	220	22	120	78	140	1.2	53.8
121	shivashankareppa	20416	68	m	27	110	128	84	5	4	1+	nil	nil cells	14	80500	92	35.3	A	5	166	209	188	43	113	32	152	0.5	100
122	shareppa	20829	56	m	28.2	109	188	96	no	15	nil	nil	6-8 pc	15	8700	97	33	A	5	184	237	260	39	121	100	182	0.9	173.8
123	darala	20432	58	m	27.6	104	154	92	no	7	nil	0.015	nil cells	13	7500	88	32.4	A	20	210	244	256	43	121	92	151	0.8	114
124	vijay kumar	20500	51	m	28.6	98	148	98	2	10	nil	nil	nil cells	15	8750	93	34	A	10	167	192	178	31	104	33	129	1.2	68.5
125	bhimaraya	20360	62	m	31.1	113	144	96	9	8	nil	nil	2-3 pc	14	8550	96	31	A	5	166	179	210	32	122	56	164	1.1	160
126	kalappa	17278	70	m	28.6	104	156	102	no	no	nil	nil	1-2RBCs	16	5670	100	33	A	5	98	153	168	34	93	41	154	1.2	90.8
127	sharanappa	17407	68	m	29.5	103.5	142	94	5	no	nil	0.01	nil cells	14	8450	97	33.1	A	5	98	157	156	38	76	42	156	0.5	69.5
128	lakshmi	17929	68	f	29.6	84	140	90	3	15	nil	nil	1-3pc	13	5450	88	34	A	20	166	186	226	44	140	42	146	0.5	58
129	sanjeev	16737	51	m	30.3	106	156	96	no	no	1+	nil	nil cells	15	6500	91	32	A	10	104	164	168	32	89	47	152	0.9	132
130	siddaraya	15759	62	m	29.8	101.5	150	90	6	5	nil	0.02	nil cells	14	4450	90	34.8	A	20	201	269	188	34	110	44	148	0.8	62
131	iranna	17804	70	m	29.4	112	158	110	4	7	nil	0.015	2-3 RBCs	13	7600	89	29	A	20	158	185	176	48	96	32	158	1.2	120
132	sharanappa	17401	68	m	30.2	108.5	164	100	6	4	nil	0.02	nil cells	15	8560	100	31	A	15	122	186	148	50	72	26	130	1.1	138
133	akbar ali	17308	68	m	31.3	102	134	88	4	5	1+	nil	nil cells	14	10300	93	34	A	20	142	194	156	38	89	29	144	0.8	199
134	vittal	17563	70	m	29.5	98	154	96	3	4	nil	nil	3-4 pc	15	9500	96	31	A	5	202	256	140	48	66	26	130	0.7	203
135	shivanand	17144	62	m	31.1	114	166	104	no	5	nil	nil	2-3 pc	14	4300	100	33	A	5	134	187	168	38	91	31	152	1.3	221
136	sahebgouda	16738	56	m	29.5	109	138	88	2	4	nil	0.015	nil cells	15	9760	97	33.1	A	5	142	194	288	28	207	53	262	1.1	191
137	basappa	18328	68	m	30.6	112.5	144	92	12	4	2+	nil	nil cells	14	5560	88	34	A	20	186	268	184	38	114	32	156	1.2	153
138	sunil	210495	39	m	29.8	108.5	156	96	6	5	nil	nil	2-3 pc	15	9850	91	32	A	10	166	256	198	38	121	39	184	0.5	193
139	preeth	210494	35	f	31.4	84	138	84	no	2	nil	nil	nil cells	14	6750	90	34.8	A	5	184	276	184	48	109	27	135	0.9	53
140	beemareppa	210491	56	m	28.6	100	140	90	4	no	nil	0.01	nil cells	15	8590	89	29	A	5	149	194	264	38	188	48	126	0.8	39.7
141	prasannappa	210490	68	m	31.1	114	138	94	5	5	1+	nil	2-3 pc	14	9760	100	31	A	5	186	232	186	34	121	31	198	1.2	176
142	annakka	18360	66	f	33.5	103	148	90	8	no	nil	nil	nil cells	16	5600	93	34	A	5	95	162	268	36	128	104	188	1.3	92
143	sharan basavaraj	207602	62	m	28.2	100	160	100	no	10	nil	nil	nil cells	14	7650	96	31	A	5	142	184	220	24	120	76	140	1.1	59
144	shivappa	204676	56	m	29.8	108.5	140	96	1	no	nil	nil	nil cells	15	6900	100	33	A	5	104	176	188	33	123	32	152	1.2	73.3
145	bhemanna	205774	68	m	30.1	109	138	88	3	no	nil	0.02	nil cells	14	7850	97	33.1	A	20	187	248	288	49	132	107	214	0.5	105.5
146	sangappa	205424	58	m	27.4	99	150	90	2	6	nil	0.02	3-4RBCs	14	4450	88	34	A	10	155	193	188	34	110	44	138	0.5	34.7
147	annappa	14321	48	m	34.5	115	170	100	no	7	nil	0.005	nil cells	15	7500	100	31	A	20	190	251	140	48	66	26	159	1.1	108.7
148	bhimsingh	18051	65	m	26.2	101.5	166	98	4	15	nil	0.015	2-3 pc	15	9520	91	32	A	5	184	218	176	38	96	42	146	0.9	53.3
149	narayan	18199	54	m	30.6	109	140	90	6	no	nil	0.01	3-4RBCs	14	80500	90	34.8	A	20	167	259	148	30	82	36	183	0.8	144
150	zubedha	205473	46	f	30.6	95.8	156	88	9	5	1+	nil	nil cells	14	8700	89	29	A	5	166	274	156	38	89	27	154	1.2	188