ASSESSMENT OF END ORGAN DAMAGE IN YOUNG HYPERTENSIVE FEMALE PATIENTS WITH AND WITHOUT METABOLIC SYNDROME A COMPARATIVE CROSS SECTIONAL STUDY AT A TERTIARY CARE HOSPITAL IN CHENNAI

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CHENNAI 600010

THE TAMILNADU DR. M.G.R MEDICAL UNIVERSITY

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DR. P.PARANTHAMAN, M.D.,
Professor and HOD,
Department of General Medicine,
Govt. Kilpauk Medical College
Chennai- 600010

Professor & HOD
Department of Medicine
Govt. Kilpauk Medical College
Chennai-10.

DR. R. SHANTHIMALAR, M.D., D.A.,
DME (FAC) / DEAN,
Govt. Kilpauk Medical College and
Hospital, Chennai - 600010

DECLARATION

I solemnly declare that this dissertation entitled "**COMPARISON OF ALBUMINURIA, RETINOPATHY AND LEFT VENTRICULAR HYPERTROPHY AMONG YOUNG HYPERTENSIVE FEMALE PATIENTS WITH AND WITHOUT METABOLIC SYNDROME "- A Comparative Cross sectional Study**" is a bonafide and genuine research work carried out by me at Government kilpauk medical College-chennai during the academic year 2020-2023 under the guidance and supervision of DR.P.PARANTHMAN, Professor AND HOD, Department of Medicine, GOVERNMENT KILPAUK MEDICAL COLLEGE, CHENNAI. This dissertation is submitted to The Tamil Nadu Dr.M.G.R Medical University, towards the partial fulfillment of requirement for the award of M.D. Degree in General Medicine (Branch -I).

Aswathy

Place: CHENNAI
Date: 15/12/2022

Dr. ASWATHY T MENON

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Guide & Supervisor sign with Seal.

Professor & HOD
Department of Medicine
Govt. Kilpauk Medical College
Chennai-10.

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Submitter email	aswathymnn732@gmail.com
Similarity	13%
Analysis address	aswathymnn732.tnmg@analysis.urkund.com

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ABSTRACT

Abstract

Objective:

To compare target organ damage-albuminuria, retinopathy and left ventricular hypertrophy in young hypertensive female patients with and without metabolic syndrome.

Methods:

Young hypertensive females with hypertension duration of 5-
10 yearsare chosen from hypertension clinic and are screened for metabolic syndrome. They are divided into two groups.

A) Young hypertensive females with metabolic syndrome

B) Young hypertensive females without metabolic syndrome

Routine blood investigations are done for both the groups.

Both the groups are then screened for end organ damage-

* Fundus examination is done to look for retinopathy changes

*2D Echo is done to look for left ventricular hypertrophy

*Urine routine is done to look for albuminuria

Results:

Total 400 cases , out of which 170 cases have been diagnosed as metabolic syndrome , among the subset population 60.6% had LVH, 39.4% had no LVH, significant albuminuria was seen in 61.8% , and retinopathy was seen 68.2% of the subset. Among the albuminuria cases , trace was seen in 10%, 1+ was seen 37.6%, 2+ was seen 13.5%.in retinopathy cluster 33.5% had grade 1, grade 2 was seen 22.3%, grade 3 was seen 9.4%

Conclusion

Prevalence of metabolic syndrome is very high in our society which goes unnoticed.Metabolic syndrome seems to amplify hypertension- related cardiac and renal changes, over and above the potential contribution of each single component of this syndrome. From the study,it is evident that prevalence of left ventricular hypertrophy,albuminuria and retinopathy is more in hypertensives

with metabolic syndrome(as defined by NCEP 3 criteria) than those without metabolic syndrome.

ABBREVIATIONS

- MS-METABOLIC SYNDROME
- RDW – Red Cell Distribution Width
- MetS – Metabolic Syndrome
- CIMT -Carotid Intimal Media Thickness
- BUN – Blood Urea Nitrogen
- IDF - The International Diabetes Federation
- IFG – Impaired Fasting Glucose
- LDL C -Low Density Lipoprotein Cholesterol
- FPG -Fasting Plasma Glucose
- WHR – Waist Hip Ratio
- BMI - Body Mass Index
- HB - HEMOGLOBIN
- SBP – Systolic Blood Pressure
- RBC – Red blood cells
- DBP – Diastolic Blood Pressure
- HDL C – High Density Lipoprotein Cholesterol

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INTRODUCTION

INTRODUCTION

Arterial hypertension is often associated with various metabolic abnormalities including abdominal obesity, dyslipidaemia, elevated plasma glucose and insulin resistance, which are the main features of the metabolic syndrome (MS), previously known as either the insulin resistance syndrome, or X syndrome or deadly quartet or dysmetabolic syndrome . Recently, the World Health Organ ization (WHO) the American Association of Clinical Endocrinologists and the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATPIII) proposed working definitions for this syndrome.

Amongst these definitions the one suggested by NCEP-ATPIII is the simplest and the most practical and according to which MS may be diagnosed when three or more abnormalities (impaired glucose metabolism, elevated blood pressure, hypertriglyceridaemia, low HDL cholesterol and central obesity) cluster in the same person] The adverse prognostic impact of the MS, as defined by NCEP-ATPIII, has recently been documented in men and in women with no history of cardiovascular disease, in hypercholesterolaemic men and in hypertensive patients It is conceivable that the increased cardiovascular risk conferred by MS in hypertensive subjects may in part be mediated through preclinical end-organ damage.

Our study was undertaken to evaluate the influence of MS, defined according to the NCEP-ATPIII criteria, on some cardiac, renal and retinal markers of target organ damage, in a large group of non diabetic young and middle-aged essential hypertensives without clinical or laboratory evidence of cardiovascular and renal diseases.

The independent relationships between LV mass and MS, and between AER and MS, were confirmed in multivariate regression models including MS together with its individual components.MS may amplify hypertension-related cardiac and renal changes, over and above the potential contribution of each single component of this syndrome. As these markers of target organ damage are well-known predictors of cardiovascular events, our results may partly explain the enhanced cardiovascular risk associated with MS

AIM

AND

OBJECTIVES

AIM

To compare target organ damage- albuminuria, retinopathy and left ventricular hypertrophy in young hypertensive female patients with and without metabolic syndrome.

OBJECTIVES

The aim of our study was to analyze, in a wide group of young essential hypertensive female patients, the influence of metabolic syndrome (MS) (defined according to the criteria laid down in the Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults) on markers of preclinical cardiac, renal and retinal damage.

REVIEW

OF

LITERATURE

REVIEW OF LITERATURE

METABOLIC SYNDROME

Obesity, particularly abdominal obesity, is associated with resistance to the effects of insulin on peripheral glucose and fatty acid utilization, often leading to type 2 diabetes mellitus. Insulin resistance, the associated hyperinsulinemia and hyperglycemia, and adipocyte cytokines (adipokines) may also lead to vascular endothelial dysfunction, an abnormal lipid profile, hypertension, and vascular inflammation, all of which promote the development of atherosclerotic cardiovascular disease (CVD) A similar profile can be seen in individuals with abdominal obesity who do not have an excess of total body weight

The co-occurrence of metabolic risk factors for both type 2 diabetes and CVD (abdominal obesity, hyperglycemia, dyslipidemia, and hypertension) suggested the existence of a "metabolic syndrome". Other names applied to this constellation of findings have included syndrome X, the insulin resistance syndrome, the deadly quartet, or the obesity dyslipidemia syndrome. Genetic predisposition, lack of exercise, and body fat distribution all affect the likelihood that an individual with obesity will develop diabetes or CVD.

It should be noted that questions have been raised as to whether metabolic syndrome captures any unique pathophysiology implied by calling it a "syndrome" and whether metabolic syndrome confers risk beyond its individual

components. These questions raise uncertainty about the value of diagnosing metabolic syndrome in individual patients. These arguments will be reviewed at the end of this discussion Regardless of whether metabolic syndrome is considered a unique entity, individual components need to be identified and managed to decrease the associated morbidity and mortality

The definition, prevalence, clinical implications, and therapy of metabolic syndrome will be reviewed here, including the limited data in children and adolescents. The pathogenesis of the relationship between obesity and type 2 diabetes and other causes of insulin resistance are discussed separately.

Metabolic syndrome should not be confused with another disorder called syndrome X in which angina pectoris occurs in patients with normal coronary arteries.

DEFINITION

There are several definitions for metabolic syndrome, leading to some difficulty in comparing data from studies using different criteria.

The National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) is the most widely used. Abdominal obesity is not a prerequisite for diagnosis; the presence of any three of the five criteria listed constitutes a diagnosis of metabolic syndrome.

Because metabolic syndrome traits co-occur, patients identified with one or just a few traits are likely to have other traits as well as insulin resistance [25]. Whether it is valuable to assess insulin resistance in addition to more readily measured traits of the syndrome is uncertain. In addition, although no formal definitions of metabolic syndrome include glycated hemoglobin (A1C), abnormal A1C (5.7 to 6.4 percent) is increasingly accepted and used to define impaired glycemia in patients with metabolic syndrome.

National Cholesterol Education Program ATP III — Guidelines developed by the 2001 NCEP ATP III focused explicitly on the risk of cardiovascular disease (CVD) and did not require evidence of insulin or glucose abnormalities, although abnormal glycemia is one of the criteria . ATP III metabolic syndrome criteria were updated in 2005 in a statement from the American Heart Association (AHA)/National Heart, Lung, and Blood Institute (NHLBI) . Updates include the following:

●Lowering the threshold for abnormal fasting glucose to 100 mg/dL, corresponding to the American Diabetes Association (ADA) criteria for impaired fasting glucose (IFG)

●Explicitly including diabetes in the hyperglycemia trait definition

●Explicitly including use of drugs for lipid control or blood pressure control in the dyslipidemia and hypertension trait definitions, respectively

ATP III criteria define metabolic syndrome as the presence of any three of the following five traits:

●Abdominal obesity, defined as a waist circumference ≥102 cm (40 in) in men and ≥88 cm (35 in) in females

●Serum triglycerides ≥150 mg/dL (1.7 mmol/L) or drug treatment for elevated triglycerides

●Serum high-density lipoprotein (HDL) cholesterol <40 mg/dL (1 mmol/L) in males and <50 mg/dL (1.3 mmol/L) in females or drug treatment for low HDL cholesterol

●Blood pressure ≥130/85 mmHg or drug treatment for elevated blood pressure

●Fasting plasma glucose (FPG) ≥100 mg/dL (5.6 mmol/L) or drug treatment for elevated blood glucose

International Diabetes Federation — The International Diabetes Federation (IDF) updated their metabolic syndrome criteria in 2006; central obesity was an essential element in this definition, with different waist circumference thresholds set for different race/ethnicity group . In 2009, in an attempt to harmonize the criteria used to define metabolic syndrome, the IDF along with several organizations (including the AHA, the NHLBI, the World Heart Federation, and The International Association for the Study of Obesity, and the International Atherosclerosis Society) eliminated an increased waist

circumference as a diagnostic requirement. They now recommend using the following five criteria, with the presence of any of three qualifying for the diagnosis of metabolic syndrome

●Increased waist circumference, with ethnic-specific waist circumference cut-points

●Triglycerides ≥150 mg/dL (1.7 mmol/L) or treatment for elevated triglycerides

●HDL cholesterol <40 mg/dL (1.03 mmol/L) in men or <50 mg/dL (1.29 mmol/L) in females, or treatment for low HDL

●Systolic blood pressure ≥130, diastolic blood pressure ≥85, or treatment for hypertension

●FPG ≥100 mg/dL (5.6 mmol/L) or previously diagnosed type 2 diabetes; an oral glucose tolerance test is recommended for patients with an elevated FPG, but it is not required

Comparing criteria in defining populations — Using data from the National Health and Nutrition Examination Survey (NHANES) 1999 to 2002 database, 39 percent of United States adult participants met IDF criteria for metabolic syndrome, compared with 34.5 percent using the ATP III criteria . The two definitions overlapped for 93 percent of subjects in determining presence or absence of metabolic syndrome. When applied to an urban population in the

United States, the IDF criteria categorized 15 to 20 percent more adults with metabolic syndrome than the ATP III criteria [2]

The relative value of different metabolic syndrome definitions in terms of prognosis and management appears to be similar As examples:

●In a prospective cohort study of a random sample of British females (n = 3589) aged 60 to 79 years, who were free of coronary heart disease (CHD) at baseline, all three definitions of metabolic syndrome were modestly and similarly associated with CHD risk [29]. The age-adjusted hazard ratios (HRs) for the IDF, World Health Organization (WHO), and NCEP syndromes were 1.32 (95% CI 1.03-1.70), 1.45 (95% CI 1.00-2.10), and 1.38 (95% CI 1.00-1.93), respectively.

●Similarly, when data from the Framingham population are examined using ATP III, IDF, and European Group for the Study of Insulin Resistance (EGIR) definitions of metabolic syndrome, roughly equivalent associations for incident type 2 diabetes (HR 3.5, 95% CI 2.2-5.6; HR 4.6, 95% CI 2.7-7.7; HR 3.3, 95% CI 2.1-5.1, respectively) and for CVD (HR 1.8, 95% CI 1.4-2.3; HR 1.7, 95% CI 1.3-2.3; HR 2.1, 95% CI 1.6-2.7, respectively) are observed . Thus, risk-factor clustering defines increased risk for type 2 diabetes and CVD.

The WHO, ATP III, and IDF definitions include type 2 diabetes as syndrome traits. Experts do not all agree that type 2 diabetes should be part of the definition, as the importance of the syndrome is that it identifies patients at

increased risk for the development of diabetes. Most patients with type 2 diabetes have features of metabolic syndrome, in which it identifies those at greater risk of macrovascular but not microvascular complications. Management of patients with type 2 diabetes should follow clinical guidelines, whether or not they also meet criteria for metabolic syndrome.

Other potential markers — Metabolic syndrome has been recognized as a pro inflammatory, pro thrombotic state, associated with elevated levels of C-reactive protein (CRP), interleukin (IL)-6, and plasminogen activator inhibitor (PAI)-1]. Inflammatory and pro thrombotic markers are associated with an increased risk for subsequent CVD and type 2 diabetes [35-38], although adipokines and inflammatory markers explained only a small part of the association between metabolic syndrome and CHD mortality in one study . Additionally, a causal association between elevated CRP and metabolic syndrome was not demonstrated in a study of phenotype patterns associated with metabolic syndrome and CRP levels.

The value of measurement or treatment of inflammatory or vascular function markers in the setting of metabolic syndrome is unknown. Use of these markers should be considered for clinical purposes only in the setting of CVD risk assessment and reduction (see "C-reactive protein in cardiovascular disease"). AHA/US Centers for Disease Control and Prevention (CDC) guidelines emphasize that CRP testing still belongs in the category of optional, based on

clinical judgment rather than recommended routinely, because the magnitude of its independent predictive power remains uncertain [3]

EPIDEMIOLOGY AND RISK FACTORS

Epidemiology — The prevalence of metabolic syndrome, as defined by the 2001 Adult Treatment Panel III (ATP III) criteria, was evaluated in 8800 United States adults participating in the third National Health and Nutrition Examination Survey (NHANES III, 1988 to 1994) The overall prevalence was 22 percent, with an age-dependent increase (6.7, 43.5, and 42.0 percent for ages 20 to 29, 60 to 69, and >70 years, respectively) . Among this cohort, Mexican Americans had the highest age-adjusted prevalence (31.9 percent). Among Black Americans and Mexican Americans, the prevalence was higher in females than in males (57 and 26 percent higher, respectively)

Metabolic syndrome has become increasingly prevalent. Using data from the NHANES 2011 to 2016 database, 34.7 percent of participants met ATP III criteria for metabolic syndrome compared with 22 percent in NHANES III (1988 to 1994) [43,44]. In the 2011 to 2016 cohort, the prevalence was lowest among those identifying as non-Hispanic Asian and highest among those identifying as Hispanic and "other"; among all groups, the prevalence increased with advancing age

In addition, metabolic syndrome, defined by the 2005 revised ATP III criteria, was assessed in 3300 adult Framingham Heart Study participants without diabetes or cardiovascular disease (CVD) At baseline, the prevalence of metabolic syndrome was 26.8 percent in males and 16.6 percent in females. After eight years of follow-up, there was an age-adjusted 56 percent increase in prevalence among males and a 47 percent increase among females.

Weight as a risk factor — increased body weight is a major risk factor for metabolic syndrome. In NHANES III, metabolic syndrome was present in 5 percent of those at normal weight, 22 percent of those with overweight, and 60 percent of those with obesity. In the Framingham Heart Study cohort, an increase in weight of 2.25 kg or more over 16 years was associated with a 21 to 45 percent increase in the risk for developing the syndrome. A large waist circumference alone identifies up to 46 percent of individuals who will develop metabolic syndrome within five years

The rapidly increasing prevalence of obesity among adults in the United States is likely to lead to even higher rates of metabolic syndrome in the near future highlighting the importance of obesity prevention and improving physical activity levels.

Some normal-weight individuals are at increased risk of hypertension, CVD, and diabetes]. It is unknown if these individuals represent a distinct sub phenotype of metabolic syndrome (ie, "normal weight, metabolically obese"). In

a genome-wide association study evaluating 19 common genetic variants associated with insulin resistance (defined by elevated fasting insulin concentrations), a metabolic profile consistent with a genetically common, subtle form of lipodystrophy in the general population was identified. These 11 genetic variants were associated with increased levels of metabolic risk traits, liver markers, type 2 diabetes, and coronary artery disease but lower body mass index (BMI) and increased visceral-to-subcutaneous adipose tissue ratio. These data suggest reduced subcutaneous adiposity as a mechanism linking the components of metabolic syndrome.

Other risk factors — In addition to age, race, and weight, other factors associated with an increased risk of metabolic syndrome in NHANES included postmenopausal status, smoking, low household income, high carbohydrate diet, no alcohol consumption, and physical inactivity .In the Framingham Heart Study, soft drink and sugar-sweetened beverage consumption was also associated with an increased risk of developing adverse metabolic traits and metabolic syndrome Use of atypical antipsychotic medications, especially clozapine, significantly increases risk for metabolic syndrome In addition, poor cardiorespiratory fitness is an independent and strong predictor of metabolic syndrome

A parental history of metabolic syndrome increases risk, and genetic factors may account for as much as 50 percent of the variation in levels of metabolic syndrome traits in the offspring

CLINICAL IMPLICATIONS

Metabolic syndrome is an important risk factor for subsequent development of type 2 diabetes and/or cardiovascular disease (CVD). Thus, the key clinical implication of a diagnosis of metabolic syndrome is identification of a patient who needs aggressive lifestyle modification focused on weight reduction and increased physical activity

Identification of patients at high metabolic risk — Health care providers should assess individuals for metabolic risk at routine clinic visits. The Endocrine Society clinical guidelines suggest evaluation at three-year intervals in individuals with one or more risk factors. The assessment should include measurement of blood pressure, waist circumference, fasting lipid profile, and fasting glucose.

In patients identified as having metabolic syndrome aggressive lifestyle intervention (weight reduction, physical activity) is warranted to reduce the risks of type 2 diabetes and CVD. Assessment of 10-year risk for CVD, using a risk assessment algorithm, such as the Framingham Risk Score or Systematic Coronary Risk Evaluation (SCORE), is useful in targeting individuals for medical intervention to lower blood pressure and cholesterol.

Risk of type 2 diabetes — Prospective observational studies demonstrate a strong association between metabolic syndrome and the risk for subsequent development of type 2 diabetes [In a meta-analysis of 16 multiethnic cohort studies, the relative risk (RR) of developing diabetes ranged from 3.53 to 5.17, depending upon the definition of metabolic syndrome and the population studied [70]. As an example, in an analysis of 890 nondiabetic Pima Indians, 144 developed diabetes over four years of follow-up. Metabolic syndrome increased the RR for incident diabetes by 2.1-fold with the Adult Treatment Panel III (ATP III) definition and 3.6-fold using the World Health Organization (WHO) definition. This difference highlights the importance of insulin resistance (a required characteristic of the WHO definition) in the pathogenesis of type 2 diabetes.

In several cohorts, the risk of diabetes increased with increasing number of components of metabolic syndrome. While metabolic syndrome predicts increased risk for diabetes, it is not clear whether this adds additional important information [4,]. In a prospective cohort study of 5842 Australian adults, metabolic syndrome (defined by WHO, ATP III, the European Group for the Study of Insulin Resistance [EGIR], or the International Diabetes Federation [IDF]) was not superior to fasting plasma glucose or a published diabetes prediction model (including age, sex, ethnicity, fasting plasma glucose, systolic

blood pressure, high-density lipoprotein [HDL] cholesterol, body mass index [BMI], and family history) in identifying individuals who developed diabetes

Risk of cardiovascular disease — Three meta-analyses, which included many of the same studies, found that metabolic syndrome increases the risk for incident CVD (RRs ranging from 1.53 to 2.18) and all-cause mortality (RRs 1.27 to 1.60) .

The increased risk appears to be related to the risk-factor clustering or insulin resistance associated with metabolic syndrome rather than simply to obesity. This was illustrated by the following studies:

●In a study of the Framingham population, people with obesity but without metabolic syndrome did not have a significantly increased risk of diabetes or CVD However, individuals with obesity and metabolic syndrome had a 10-fold increased risk for diabetes and a twofold increased risk for CVD relative to normal-weight people without metabolic syndrome. Normal-weight people meeting revised 2005 ATP III criteria for metabolic syndrome had a fourfold increased risk for diabetes and a threefold increased risk for CVD.

●In a study of 211 people with moderate obesity (BMI 30 to 35), insulin sensitivity varied six fold, and those with the greatest degree of insulin resistance had the highest blood pressure, triglyceride concentrations, and fasting and two-hour post oral glucose blood sugar levels, and the lowest HDL concentrations, despite equal levels of obesity [5]

Thus, not all individuals with moderate obesity have the same risk for developing CVD or diabetes; risks differ as a function of insulin sensitivity, with insulin-resistant, individuals at highest risk.

The risk also may be related to underlying subclinical CVD (as measured by electrocardiography [ECG], echocardiography, carotid ultrasound, and ankle-brachial blood pressure) in individuals with metabolic syndrome . In the Framingham Offspring study, 51 percent of 581 participants with metabolic syndrome had subclinical CVD, and the risk of overt CVD in these individuals was greater than in individuals with metabolic syndrome without subclinical CVD (hazard ratio [HR] 2.67 versus 1.59). Subclinical CVD was also predictive of overt CVD in subjects without metabolic syndrome (HR 1.93, 95% CI 1.15-3.24).

While metabolic syndrome predicts increased risk for CVD, it is not clear whether this adds additional important information. As examples:

●Elevated triglyceride and low HDL cholesterol levels were as strong of a predictor of vascular events as the presence of metabolic syndrome (by ATP III criteria) in a prospective study of a population of patients with angiographically determined coronary artery disease.

●The Framingham Risk Score was a better predictor of coronary heart disease (CHD) and stroke than metabolic syndrome (ATP III criteria with obesity defined by an elevated BMI rather than waist circumference) in a prospective study of 5128 British males aged 40 to 59 years followed for 20 years

●Low HDL cholesterol and high blood pressure were better predictors of CHD than metabolic syndrome in a prospective study of 2737 males from the same cohort

Other associations — metabolic syndrome has also been associated with several obesity-related disorders including:

●Fatty liver disease with steatosis,fibrosis and cirrhosis.

●Hepatocellular carcinoma and intrahepatic cholangiocarcinoma.

●Chronic kidney disease (CKD; defined as a glomerular filtration rate less than 60 mL/min per 1.73 m2) and microalbuminuria. In a report from National Health and Nutrition Examination Survey (NHANES III), metabolic syndrome in multivariate analysis significantly increased the risk of both CKD and microalbuminuria (adjusted odds ratio [OR] 2.6 and 1.9, respectively)]. The risk of both complications increased with the number of components of metabolic syndrome. In a prospective cohort study, 10 percent of individuals with metabolic syndrome at baseline subsequently developed CKD compared with 6 percent among those without metabolic syndrome.

●Polycystic ovary syndrome.

●Sleep-disordered breathing,

- including obstructive sleep apnea.

●Hyperuricemia and gout .

Several components of metabolic syndrome, including hyperlipidemia, hypertension, and diabetes, have been associated with an increased risk of cognitive decline and dementia. Metabolic syndrome (when associated with a high level of inflammation) may also be associated with cognitive decline in older adults.

THERAPY

In 2001, the Adult Treatment Panel III (ATP III) recommended two major therapeutic goals in patients with metabolic syndrome]. These goals were reinforced by a report from the American Heart Association (AHA) and the National Institutes of Health (NIH) and by clinical guidelines from the Endocrine Society :

●Treat underlying causes (overweight/obesity and physical inactivity) by intensifying weight management and increasing physical activity

●Treat cardiovascular risk factors if they persist despite lifestyle modification

There is no direct evidence that attempting to prevent type 2 diabetes and cardiovascular disease (CVD) by treating metabolic syndrome is as effective as attaining the above goals. It is possible to treat insulin resistance with drugs that enhance insulin action (eg, thiazolidinediones and metformin). However, the ability of such an approach to improve outcomes compared with weight reduction and exercise alone is not yet well supported by clinical trials

Lifestyle modification — Aggressive lifestyle modification focused on weight reduction and increased physical activity is the primary therapy for the management of metabolic syndrome . The importance of weight management in preventing progression of metabolic syndrome components is illustrated by the Coronary Artery Risk Development in Young Adults (CARDIA) study [6]. In this observational study of 5115 young adults (ages 18 to 30 years), increasing body mass index (BMI) over 15 years was associated with adverse progression of metabolic syndrome components compared with young adults who maintained stable BMI over the study period, regardless of baseline BMI.

Weight reduction is optimally achieved with a multimodality approach including diet, exercise, and possible pharmacologic therapy, as with orlistat

Diet — Several dietary approaches have been advocated for treatment of metabolic syndrome. Most patients with metabolic syndrome are overweight,

and weight reduction, which improves insulin sensitivity, is an important outcome goal of any diet

The following specific diet approaches have been recommended:

●The Mediterranean diet may be beneficial []. In a study comparing the Mediterranean diet (high in fruits, vegetables, nuts, whole grains, and olive oil) with a low-fat, prudent diet, subjects in the Mediterranean diet group had greater weight loss, lower blood pressure, improved lipid profiles, improved insulin resistance, and lower levels of markers of inflammation and endothelial dysfunction .

●The Dietary Approaches to Stop Hypertension (DASH) diet (daily sodium intake limited to 2400 mg, and higher in dairy intake than the Mediterranean diet), compared with a weight reducing diet emphasizing healthy food choices, resulted in greater improvements in triglycerides, diastolic blood pressure, and fasting glucose, even after controlling for weight loss .

●Foods with low glycemic index may improve glycemia and dyslipidemia . A diet that is low in glycemic index/glycemic load, replacing refined grains with whole grains, fruits, and vegetables, and eliminating high-glycemic beverages, may be particularly beneficial for patients with metabolic syndrome. The impact of the glycemic index itself versus the increase in high-fiber foods that accompanies a lower glycemic index diet is uncertain .

●A high-fiber diet (≥30 g/day) resulted in similar weight loss as compared with a more complex diet recommended by the AHA (fruits, vegetables, whole grain, high fiber, lean animal and vegetable proteins, reduction in sugar-sweetened beverages, moderate to no alcohol intake) ? In this trial, 240 patients with metabolic syndrome (mean BMI 35 kg/m2) were randomly assigned to one of the diets. After 12 months, weight loss occurred in both treatment groups (-2.1 versus -2.7 kg, respectively), and there were similar improvements in diastolic and systolic blood pressure.

Exercise — Exercise may be beneficial beyond its effect on weight loss by more selectively removing abdominal fat, at least in females [108]. Physical activity guidelines recommend practical, regular, and moderate regimens for exercise. The standard exercise recommendation is a daily minimum of 30 minutes of moderate-intensity (such as brisk walking) physical activity. Increasing the level of physical activity appears to further enhance the beneficial effect .

for coronary heart disease (CHD), suggesting that the negative energy balance induced by diet and exercise are necessary for achieving the metabolic benefits of weight loss .

Prevention of type 2 diabetes — Although not strictly addressing metabolic syndrome, clinical trials have shown that lifestyle modifications can substantially reduce the risk of development of type 2 diabetes and the levels of

risk factors for CVD in patients at increased risk. Prevention of type 2 diabetes is discussed in detail elsewhere.

In the Diabetes Prevention Program (DPP), 3234 subjects with obesity and impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) were randomly assigned to one of the following groups :

●Intensive lifestyle changes with the aim of reducing weight by 7 percent through a low-fat diet and exercise for 150 minutes per week

●Treatment with metformin (850 mg twice daily) plus information on diet and exercise

●Placebo plus information on diet and exercise

At an average follow-up of three years, fewer patients in the intensive lifestyle group developed diabetes (14 versus 22 and 29 percent in the metformin and placebo groups, respectively). Metabolic syndrome (using ATP III criteria) was present in 53 percent of DPP participants at baseline. In the remaining subjects (n = 1523), both intensive lifestyle intervention and metformin therapy reduced the risk of developing metabolic syndrome (three-year cumulative incidences of 51, 45, and 34 percent in the placebo, metformin, and lifestyle groups, respectively).

Oral hypoglycemic agents — Among the oral hypoglycemic agents used to treat type 2 diabetes, metformin and the thiazolidinedione (rosiglitazone and

pioglitazone) improve glucose tolerance in part by enhancing insulin sensitivity. The role of these agents in patients with metabolic syndrome, to prevent diabetes, has not been definitively established and, furthermore, rosiglitazone has been removed from the market).

●Metformin may prevent or delay the development of diabetes in subjects with impaired glucose tolerance. In the DPP trial described above, metformin therapy plus instructions on diet and exercise was associated with a 31 percent reduction in the risk of developing diabetes compared with placebo (at three years, diabetes developed in 22 versus 29 percent); however, metformin was less effective than intensive lifestyle modification (diabetes developed in 22 versus 14 percent) [93]. Both intensive lifestyle intervention and metformin therapy were effective for prevention of metabolic syndrome in patients who did not have the syndrome at baseline.

●Metformin may reduce the incidence of diabetes-related end points. In a subgroup analysis from the United Kingdom Prospective Diabetes Study (UKPDS), metformin was associated with significant reductions in any diabetes-related end point (sudden death, hypo- or hyperglycemia causing death, myocardial infarction (MI), angina, heart failure, stroke, renal failure, amputation, retinopathy, monocular blindness or cataract extraction) and all-cause mortality compared with conventional therapy with diet.

There are no data on glycemic control goals in patients with metabolic syndrome who are not diabetic. Recommendations are to treat IFG and IGT with weight loss of approximately 5 to 10 percent of the baseline weight; at least 30 minutes per day of moderately intense physical activity; and dietary therapy with a low intake of saturated fats, trans fats, cholesterol, and simple sugars, and increased intake of fruits, vegetables, and whole grains.

Routine pharmacoprevention for diabetes with any agent is not recommended. However, metformin could be considered in certain individuals with both IFG and IGT). In addition, when patients cross the diabetic diagnostic threshold, immediate therapy with metformin is recommended

Cardiovascular risk reduction — Reversal of the metabolic syndrome may be associated with a reduction in the risk of cardiovascular disease. As an example, in a retrospective cohort study including over nine million Korean adults followed for 3.5 years, reversal of metabolic syndrome was associated with a reduction in the risk of developing a major cardiovascular event (rate ratio [RR] 0.85, 95% CI 0.83-0.87) [114]. Among the individual metabolic syndrome criteria, recovery from hypertension was most strongly associated with a reduction in cardiovascular risk.

Guidelines recommend reduction of component CVD risk factors that comprise metabolic syndrome including treatment of hypertension, improved glycemic control in patients with diabetes, and lowering of serum cholesterol.

Lipid lowering — ATP III recommended a goal serum low-density lipoprotein (LDL) cholesterol of less than 100 mg/dL (2.6 mmol/L) for secondary prevention in patients with type 2 diabetes [], and subsequent studies have suggested a more aggressive goal of less than 80 mg/dL (2.1 mmol/L) with a regimen that includes administration of a statin.

Evidence does not support metabolic syndrome as a coronary risk equivalent in terms of goals for lipid management []. However, among patients with elevated serum LDL cholesterol and established coronary disease in the Scandinavian Simvastatin Survival Study (4S) trial, those with characteristics of metabolic syndrome (lowest quartile for high-density lipoprotein [HDL] cholesterol and highest quartile for triglycerides) had both the highest risk of major coronary events and the greatest benefit (48 percent risk reduction) from statin therapy .Treatment of patients with known coronary disease and metabolic syndrome with atorvastatin 80 mg, compared with atorvastatin 10 mg, decreased the rate of major cardiovascular events at five years (9.5 versus 13 percent, hazard ratio [HR] 0.71, 95% CI 0.61-0.84)

Antihypertensive therapy — There are conflicting data on whether angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) used to treat hypertension in type 2 diabetes may also help to reduce insulin resistance.

Hypertension control is important in patients with diabetes mellitus. The goal blood pressure may be somewhat lower than that in the general population and varies with the presence or absence of diabetic nephropathy with proteinuria. It is not clear if the lower goal applies to patients with metabolic syndrome, but it may be reasonable to aim for such a goal.

The value of ACE inhibitors and ARBs in hypertensive patients with metabolic syndrome who do not have CVD or diabetes is not known.

CHILDREN AND ADOLESCENTS

Definition — metabolic syndrome also occurs in children and adolescents but there is no consensus on the definition . As in adults, this lack of consensus makes it difficult to compare studies that use different diagnostic criteria and leaves the clinician without any clear parameters for assessing the long-term clinical implications of metabolic syndrome in children or for tracking the effectiveness of lifestyle interventions.

The International Diabetes Federation (IDF) definition of metabolic syndrome in children 10 to 16 years old is similar to that used by the IDF for adults, except that the definition for adolescents uses ethnic-specific waist circumference percentiles and one cutoff level for high-density lipoprotein (HDL) rather than a sex-specific cutoff . For children 16 years and older, the adult criteria can be used. For children younger than 10 years of age, metabolic

syndrome cannot be diagnosed, but vigilance is recommended if the waist circumference is ≥90th percentile.

Prevalence and risk factors — When clinically applied, these pediatric definitions result in varying prevalence rates [127-130]. The United States prevalence of metabolic syndrome (defined by the modified Adult Treatment Panel III [ATP III] criteria) is estimated to be approximately 9 percent based upon a National Health and Nutrition Examination Survey (NHANES III) survey of 1960 children >12 years of age []. However, pubertal growth and development is characterized by changes in metabolic traits that characterize the syndrome, resulting in significant individual variability in the categorical diagnosis . In one study of 1098 adolescents, as many as half of the adolescents initially classified as having metabolic syndrome lost the diagnosis during the three-year observation period, while others acquired the diagnosis .

The racial and ethnic distribution of metabolic syndrome is similar to that seen in adults, with the highest prevalence in Mexican Americans, followed by non-Hispanic White Americans and non-Hispanic Black Americans (12.9, 10.9, and 2.9 percent, respectively). The Native American population may be the group at greatest risk for metabolic syndrome as illustrated by a population-based study of Canadian Native (Oji-Cree) children and adolescents (10 to 19 years) that reported a 19 percent prevalence rate (defined by ATP III criteria) [7]

Among children with obesity, the prevalence of metabolic syndrome is high and increases with worsening obesity []. This was illustrated in a study of children and adolescents who underwent a comprehensive metabolic assessment including 439 with obesity, 31 with overweight, and 20 with a normal BMI. Metabolic syndrome was present in 39 and 50 percent of subjects with moderate and severe obesity, respectively. By contrast, no overweight or normal-weight children met the criteria for metabolic syndrome.

Risk factors in childhood that could predict emergence of metabolic syndrome were identified in a longitudinal study of a cohort from the National Heart, Lung, and Blood Institute (NHLBI) Growth and Health Study (NGHS) . Girls aged 9 and 10 years (n = 1192) were followed for 10 years. Metabolic syndrome (defined by ATP III criteria) was present in 0.2 percent at baseline and in 3.5 percent of Black and 2.4 percent of White girls at ages 18 and 19. Waist circumference and serum triglycerides at baseline were predictive of subsequent metabolic syndrome. For every increase of 1 cm in waist circumference at year 2, the risk of developing metabolic syndrome increased by 7.4 percent; for every increase of 1 mg/dL in triglyceride level at baseline, the risk of metabolic syndrome increased 1.3 percent. Race was not a significant independent factor in this study.

In summary, the prevalence of metabolic syndrome is high among children and adolescents with obesity and increases with the severity of the obesity, and with central adiposity in particular. However, there is instability in the diagnosis of metabolic syndrome during pubertal development, making prevalence estimates less reliable []. Consistency in the clinical diagnosis is required to better define the natural history of the syndrome in children and adolescents and to assess the long-term clinical implications.

Clinical implications — There are few longitudinal studies in children and adolescents with metabolic syndrome. In contrast to the data from adults, therefore, long-term cardiovascular and diabetes risks are not well defined. In one cohort study of 771 adults (mean age 38) who had participated in the Lipid Research Clinics study as children and adolescents 22 to 31 years previously, the incidence of self-reported cardiovascular disease (CVD) was more common in adults who exhibited metabolic syndrome traits as children than in those who did not (19.4 versus 1.5 percent, odds ratio [OR] 14.6, 95% CI 4.8-45.3) . Of 31 children who had metabolic syndrome traits in the initial study, 21 (68 percent) had adult metabolic syndrome. Increasing body mass index (BMI) was strongly associated with risk of adult metabolic syndrome.

Thus, the definition of metabolic syndrome may be clinically useful for risk stratification and therapeutic intervention in pediatrics.

Lifestyle modification that emphasizes reduction of established risk factors, such as promotion of a healthy diet, exercise, weight loss, and smoking cessation, is the main therapeutic goal in children and adolescents with obesity, regardless of a metabolic syndrome diagnosis. This topic is reviewed in detail separately.

A CRITICAL LOOK AT THE METABOLIC SYNDROME

The American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) published a joint statement raising questions about whether the components of metabolic syndrome, as defined above, warrant classification as a true "syndrome" . The arguments raised include:

●Lack of clarity of definition, with criteria differing between the Adult Treatment Panel III (ATP III), World Health Organization (WHO), and other definitions; many published studies use further modifications to classify subjects with metabolic syndrome.

●Multiple different phenotypes included within metabolic syndrome, with indications for differing treatment strategies. As an example, a patient with a large waist circumference, high triglycerides, and high fasting glucose would need to be managed differently than a patient with high blood pressure, low high-density lipoprotein (HDL), and high triglycerides.

●Lack of a consistent evidence base for setting the thresholds for the various components in the definitions.

●Inclusion of patients with clinical cardiovascular disease (CVD) or diabetes as part of the syndrome that is intended to define risk for these diseases.

●Unclear pathogenesis uniting the components of the syndrome; insulin resistance may not underlie all factors and is not a consistent finding in some definitions.

●Other risk factors for CVD that are not components of metabolic syndrome, such as inflammatory markers, may have equal or greater bearing on risk.

●The CVD risk associated with metabolic syndrome has not been shown to be greater than the sum of its individual components

The critical weakness of metabolic syndrome construct is that treatment of the syndrome is no different than treatment for each of its components. Virtually all agree clustering of risk factors for diabetes and CVD is a real phenomenon. All agree that the presence of one component of metabolic syndrome should lead to evaluation for other risk factors. Whether patient benefit is gained from diagnosing patients with a syndrome of such uncertain characteristics or predictive value remains an open question. The advice remains to treat individual risk factors when present and to prescribe therapeutic lifestyle changes and weight management for patients with obesity and multiple risk factors

ALBUMINURIA

Definition:

Albuminuria was defined using the most recent guidelines of the American Diabetes Association's Standards of Medical Care . Albumin and creatinine concentrations were measured in first morning spot urine samples by chemiluminescence immunoassay (Siemens Immulite 2000, USA) and by the automatic analyzer using Jaffe's kinetic method (Biobase-Crystal, Jinan, China), respectively. The urinary ACR was then calculated and expressed in units of mg/g. Albuminuria was defined by a urinary ACR of 30 mg/g or greater. In participants without albuminuria, low-grade albuminuria was defined according to the highest quartile of the baseline urinary ACR (≥11.13 mg/g).

Microalbuminuria clusters with the metabolic syndrome, and both conditions predict cardiovascular disease mortality. The reported relationships of microalbuminuria with the individual components of the metabolic syndrome (*ie*, hyperglycemia, insulin resistance, hypertension, dyslipidemia, abdominal obesity) are variable. Each of these components, as well as intrauterine effects and diet and other lifestyle factors, may contribute to elevated risk of microalbuminuria in certain population groups. Recent evidence indicates a role for oxidation and inflammation in cardiovascular disease, and endothelial

dysfunction (exacerbated by factors such as dyslipidemia) may be the mediator of this relationship. Because endothelial dysfunction can also be manifested as microalbuminuria, this provides a potential explanation of the observed association of the metabolic syndrome, chronic inflammation, and microalbuminuria

The urine dipstick is a relatively insensitive marker for albuminuria, not becoming positive until albumin excretion exceeds 300 to 500 mg/day. Using a specific assay for albumin is a more sensitive technique. The normal rate of albumin excretion is less than 30 mg/day (20 mcg/min); persistent albumin excretion between 30 and 300 mg/day (20 to 200 mcg/min) is called moderately increased albuminuria (formerly called "microalbuminuria") [1,2]. Albumin excretion above 300 mg/day (200 mcg/min) is considered to represent overt or dipstick positive proteinuria (also called severely increased albuminuria [formerly called "macroalbuminuria").

Initial studies demonstrated that moderately increased albuminuria may be the earliest clinical manifestation of diabetic nephropathy in patients with type 1 diabetes, and first begins to appear five years after diagnosis. This is no longer thought to be the case, as albuminuria levels are quite variable early in the course of disease. In addition, many individuals with diabetes progress to end-stage kidney disease without ever having significantly elevated albuminuria

Moderately increased albuminuria is often present at diagnosis in patients with type 2 diabetes and may reflect underlying cardiovascular disease rather than diabetic kidney disease

Yearly testing for albuminuria is recommended in patients with both type 1 diabetes (starting five years after disease onset) and type 2 diabetes (starting at disease onset). Assessment of albuminuria and estimated glomerular filtration rate are needed for kidney disease staging.

In addition to being associated with diabetic nephropathy, moderately increased albuminuria is associated with cardiovascular disease in both patients with and without diabetes. These studies will be reviewed here

DETECTION

Establishing the diagnosis of moderately increased albuminuria (formerly called "microalbuminuria") requires the demonstration of a persistent elevation in albumin excretion above 30 mg/day. Transient elevations in the excretion of albumin can be seen in the following settings [3]

●Fever

●Infection

●Exercise

●Heart failure

●Nonspecific joint inflammation

●Poor glycemic control (hemoglobin A1C greater than 8 percent)

●Elevation in blood pressure (greater than 160/100 mmHg)

●Hyperlipidemia (LDL cholesterol greater than 120 mg/dL)

Urine albumin concentration — Although 24-hour urine collection is the gold standard for the detection of moderately increased albuminuria [9,], it has been suggested that screening can be more simply achieved by a timed urine collection or an early morning specimen to minimize changes in urine volume that occur during the day [9]. moderately increased albuminuria is unlikely if the albumin excretion rate is below 20 mcg/min in a timed collection or the urine albumin concentration is less than 20 to 30 mg/L in a random specimen. Higher values (particularly those just above this range) may represent false positive results and should be confirmed by repeated measurements [9]

There are also a variety of semi quantitative dipsticks, such as Clinitek Microalbumin Dipsticks and Micral-Test II test strips, which can be used to test for moderately increased albuminuria if urine albumin excretion cannot be directly measured.

The reported sensitivity and specificity of these tests range from 80 to 97 percent and 33 to 80 percent, respectively

. However, none of these approaches are recommended over formal quantitation

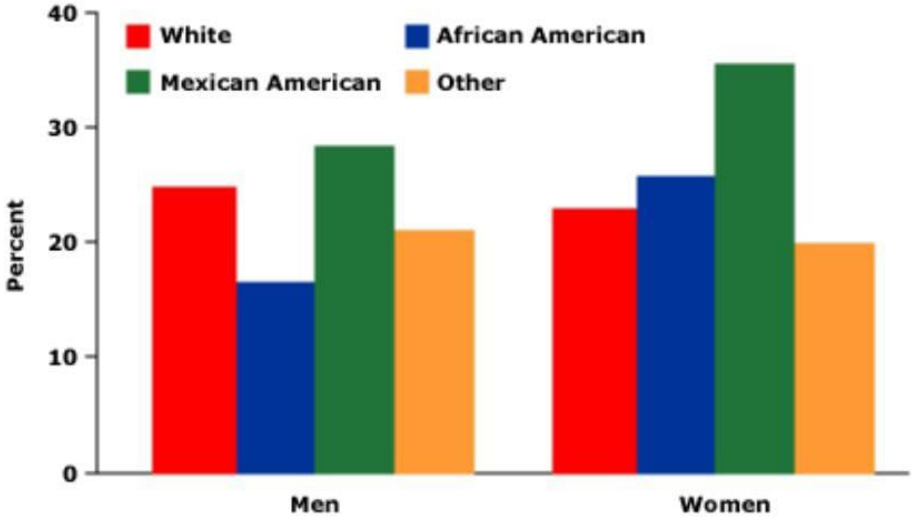
The dipstick assessment, however, is the least sensitive and specific for determination of albuminuria . One problem with measuring the urine albumin concentration or estimating it with a sensitive dipstick is that false negative and false positive results can occur since the urine albumin concentration is

determined by the urine volume as well as the amount of albuminuria [Thus, at a particular rate of albumin excretion, a substantial increase or decrease in urine volume will respectively lower and raise the urine albumin concentration. The confounding effect of the urine volume can be minimized by repeated measurements on early morning specimens

Albumin-to-creatinine ratio — The confounding effect of variations in urine volume on the urine albumin concentration can be avoided by calculation of the urine albumin-to-creatinine ratio in an untimed urine specimen. A value 30 to 300 mg/g of creatinine (or, using standard [SI] units, 3.4 to 34 mg/mmol of creatinine) suggests that albumin excretion is between 30 and 300 mg/day and therefore that moderately increased albuminuria is probably present Values above 300 mg/g (or 34 mg/mmol) are indicative of severely increased albuminuria (formerly called "macroalbuminuria"). This classification system requires that at least two of three specimens fall within the high or very high albuminuric range

In one report, 24-hour urine collections and random, single-void urine specimens for albumin and creatinine were obtained in 14 normal subjects, 13 with type 1 diabetes, and 12 with type 2 diabetes A close correlation was noted between the two measurements and the within-patient variability was small. A random albumin-to-creatinine ratio above 30 mg/g had a sensitivity of 100 percent for the detection of moderately increased albuminuria. Similar findings have been noted by others .

Prevalence of NCEP ATP III metabolic syndrome among subjects in the NHANES III survey by race/ethnicity and sex

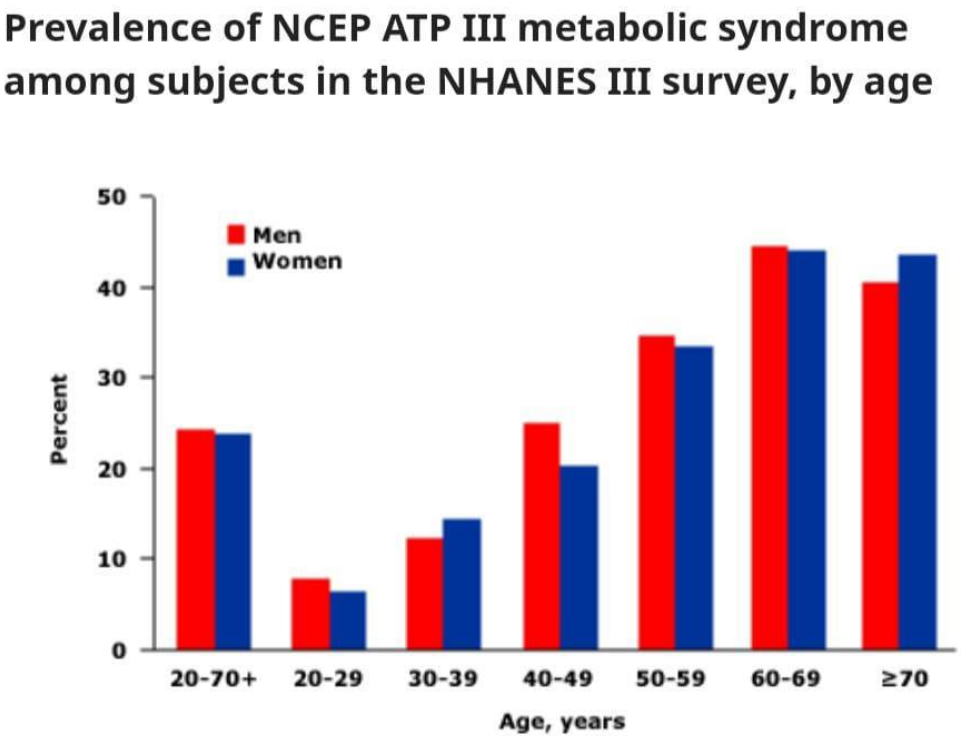


Adapted from: Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. JAMA 2002; 287:356.

Dipstick Protein reading	Protein excretion gm/24 hours	Protein excretion mg/dL
Negative	<0.1	<10
Trace	0.1-0.2	15
1+	0.2-0.5	30
2+	0.5-1.5	100
3+	2.0-5.0	300
4+	>5.0	>1000

RETINOPATHY IN SUBJECTS WITH METABOLIC SYNDROME BUT NO HISTORY OF DIABETES

In the absence of a clinical diagnosis of diabetes, associations have already been found between the metabolic syndrome and macro- or microvascular pathologies such as atherosclerosis, arteriosclerosis, and endothelial dysfunction. Several studies examined the associations between the independent components of the metabolic syndrome with the development of retinal vascular injury, by measuring the mean retinal artery and venous caliber. In this study, components of the metabolic syndrome including large waist circumference, lower HDL cholesterol levels, and higher BP were independently associated with reduced mean retinal arterial caliber in non-diabetic persons. Individuals with hypertriglyceridemia were significantly more likely to have arteriovenous nicking and later develop retinopathy. These finding clearly show an association between the MS and retinal vascular dysfunction.



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

Following the earlier notion that dyslipidemia plays a critical role in DR, several studies examined the individual components observed in the metabolic syndrome in relation to DR. Similar to the impact of dyslipidemia, there is conflicting data as to the association of the metabolic syndrome with the development of retinopathy lesions in non-diabetic subjects. One study of obese individuals older than the age of 40, found no significant correlation between the metabolic syndrome and retinopathy once diabetes and hypertension were controlled for. Another population study found no significant association in the incidence of retinopathy and the metabolic syndrome in the non-diabetic population, but there was a significant association between hypertension and retinopathy

In contrast, studies focusing on specific patient populations found differing results. A recent study in a Chinese population identified a positive correlation between the metabolic syndrome and retinopathy in the examined non-diabetic subjects. In a study of Japanese adults, the metabolic syndrome was found to be associated with retinopathy; a larger waist circumference was associated with wider venular diameter and retinopathy lesions; a higher blood pressure level was associated with focal arteriolar narrowing, arteriovenous nicking, enhanced arteriolar wall reflex and narrower arteriolar diameter; and a higher triglyceride level was associated with enhanced arteriolar wall reflex. In the Hoorn study, in the Netherlands, there was significant correlation of retinopathy with the

combination of high waste-to-hip ratio (WHR), HbA1c level, and hypertension in non-diabetics and in glucose-impaired subjects, supporting a role for insulin resistance in the pathogenesis of retinopathy.

Interestingly, there was no significant correlation between incidence of retinopathy with serum levels of triglycerides, and total cholesterol or body mass index (BMI). Despite generalized obesity indicated by high BMI not being associated with retinopathy, a high-body-fat percentage indicated by WHR has been shown to be significantly associated with development of retinopathy in patients with type-2 diabetes. Similar to the Hoorn study, the WHR was also an independent risk factor in the diabetic patients in the EURODIAB study. These discrepancies speak to a number of possible factors including the inability of the BMI calculation to accurately estimate body composition while the WHR is an indicator for central obesity and is associated with insulin resistance. In addition, differences in measurement methods and quantification for incidence and/or rate of progression of retinopathy. The other factor is that dysfunction of adipose tissue has been shown to increase oxidative stress and subsequent cytokine, contributing to the pathogenesis of retinopathy. Given that hyperglycemia and hypertension are the strongest risk factors for the development of retinopathy lesions, and that these two conditions are contributors to the diagnosis of the metabolic syndrome, it may be beneficial to modify the clinical approach to individuals with the metabolic syndrome,

namely those with hypertension and hyperglycemia coupled with obesity, calculated by WHR, in order to prevent or slow the development of hyperglycemia, hypertension, and hypertriglyceridemia, which in turn could possibly delay the onset of retinopathy lesions and visual impairment in subjects with these comorbidities.

DEVELOPMENT OF RETINOPATHY IN SUBJECTS WITHOUT A HISTORY OF DIABETES

Retinopathy has been defined in different studies to include microaneurysms, retinal hemorrhages, hard exudates, cotton wool spots, retinal venular abnormalities (venous beading and tortuosity), intraretinal microvascular abnormalities, and new blood vessels[8]. Although, hyperglycemia and hypertension are strongly associated with incident retinopathy, there are other etiologies including ocular and systemic causes. Ocular etiologies include central or branch retinal vein occlusion, retinal telangiectasia (“spider veins”), and retinal macroaneurysms[8]. Systemic causes range from the hypertension, carotid atherosclerotic disease, previous head radiotherapy, severe forms of all anemias, and other blood abnormalities such as sickle cell. Systemic diseases such as lupus, toxoplasmosis, and acquired immune deficiency syndrome have also been associated with the development of retinopathy lesions in patients with no history of diabetes [8]. There are several studies that examined the association of the components of metabolic syndrome with the development of

retinopathy lesions in non-diabetic subjects. With this in mind, the focus of this review will primarily be the impact of metabolic syndrome on the development of retinopathy lesions in patients with established history of primary-DM or without history of diabetes. This review will also discuss some of the mechanisms through which metabolic syndrome can contribute to the development of retinopathy.

RETINOPATHY IN PATIENTS WITH METABOLIC SYNDROME AND HISTORY OF DIABETES

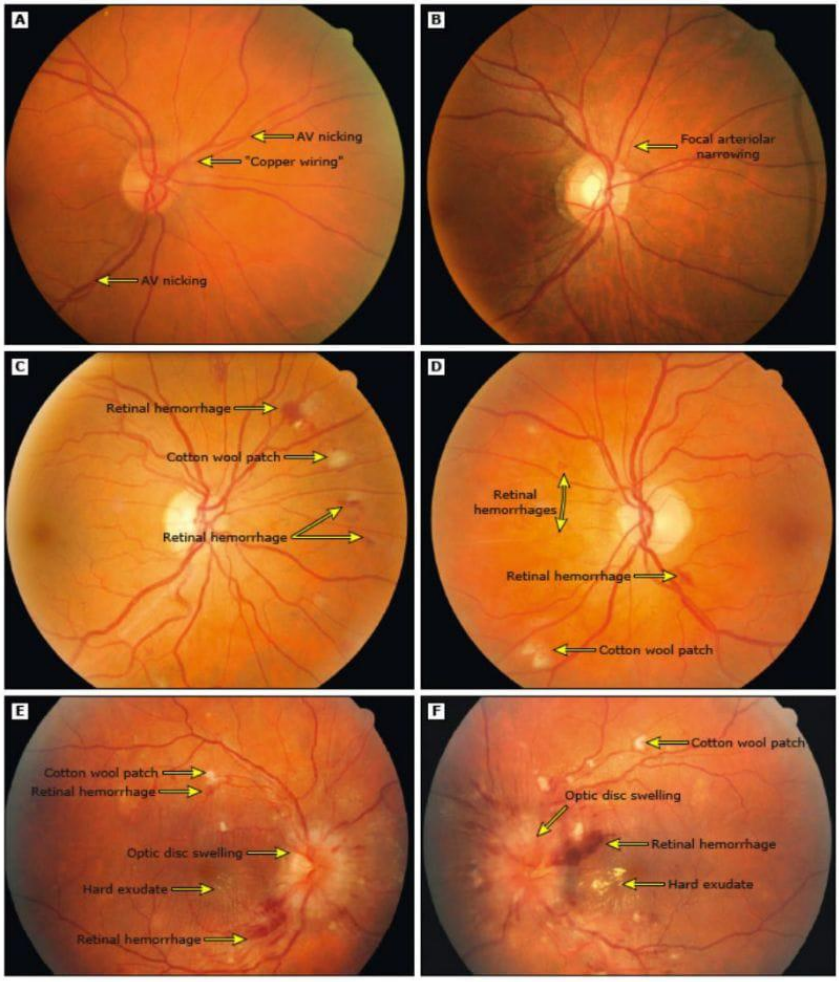
Traditionally, the development of DR in patients with type 1 or type 2 diabetics has been linked to the associated hyperglycemia. Whether the existence of metabolic syndrome in these patients can accelerate or aggravate the incidence of DR is not clear. For example, the findings of the landmark studies, Land mark clinical trials including United Kingdom Prospective Diabetes Study (UKPDS) in patients with type-2 diabetes, the Diabetic Control and Complications Trial (DCCT), in patients with type-1 diabetes and its follow-up, the Epidemiology of Diabetes and Interventions and Complications (EDIC)

were traditionally interpreted that tight glycemic control significantly delayed development of DR. However, the level of reduction was significantly lower in patients with type 2 diabetes (25%) and 76% in patients with type 1 diabetes, suggesting that factors outside of hyperglycemia associated with type 2 diabetes

may play a role in the pathology of the microvascular complications such as retinopathy.

DIABETIC RETINOPATHY

Retinal fundus photographs of hypertensive retinopathy



Representative digital retinal fundus photographs of mild (A,B), moderate (C,D), and severe (E,F) hypertensive retinopathy, as graded with the simplified classification:

(A) Mild hypertensive retinopathy is indicated by the presence of generalized arteriolar narrowing, arteriovenous (AV) nicking, and opacification of the arteriolar wall ("copper wiring").

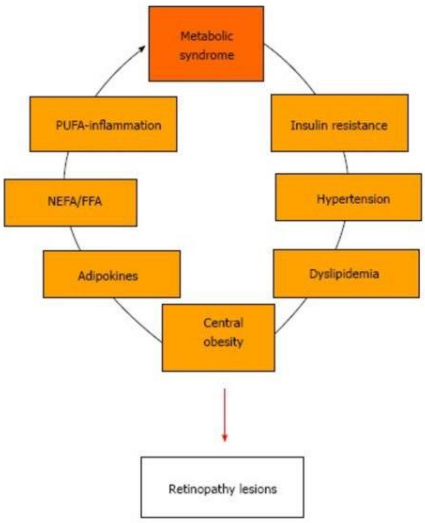
(B) Mild hypertensive retinopathy with focal arteriolar narrowing.

(C,D) Moderate hypertensive retinopathy with multiple retinal hemorrhages and cotton wool patches.

(E,F) Severe hypertensive retinopathy with swelling of the optic disk, retinal hemorrhages, hard exudates, and cotton wool patches.

Among the microvascular complications of diabetes, diabetic retinopathy (DR) is among the most feared one. Retinopathy has traditionally been viewed as a product of ischemic insult; however, this topic is well documented in other reviews. DR is broadly classified into two stages: Non proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR). Classification is determined by the presence of neovascularization in the retina. NPDR typically precedes PDR and is divided into the following stages: Mild, moderate, severe, and very severe. These stages are based on the likelihood that the retinopathy will progress to PDR. Clinically, a patient with NPDR presents with microvascular abnormalities such as micro aneurysms and hemorrhage, affecting the macula and posterior retina. Vascular abnormalities, such as an increased permeability of the retinal vasculature and serum leakage, contribute to capillary loss and subsequent ischemia. PDR is defined by the presence of neovascularization and is divided into the following stages: Early, high risk, and severe neovascularization. In response to retinal hypoperfusion, an increase in local production of vasoproliferative factors such as vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF) occurs as a maladaptive protection mechanism. Increased levels of VEGF are traditionally correlated with stabilization of the transcription factor hypoxia-inducible factor-1 (HIF-1) levels under hypoxic conditions Both VEGF and PDGF are strongly associated with neovascularization via induction of new vascular development typically from optic disc or retinal vessels This neovascularization further

compounds the damage by contributing to the development of preretinal and vitreous hemorrhage, fibrosis, potential retinal detachment, and blindness

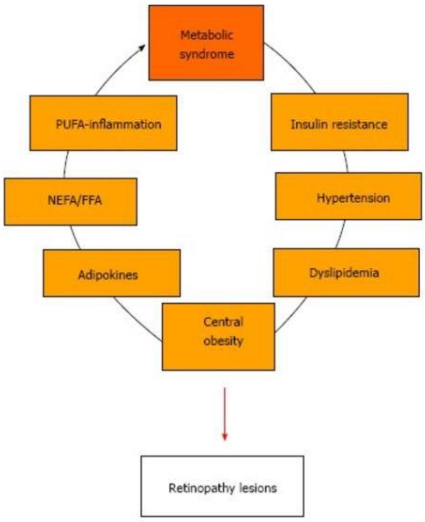


Schematic presentation of the multiple pathways involved in metabolic syndrome including hypertension, central obesity, dyslipidemia, adipose tissue and adipokine's dysfunction, altered free fatty acids levels and polyunsaturated fatty acid metabolism leading to local and systemic inflammation. FFA: Free fatty acids; PUFA: Polyunsaturated fatty acid.

CURRENT THERAPEUTICS FOR DIABETIC RETINOPATHY

The mainstay standard of care for DR is the laser treatment, a highly effective procedure to slowdown visual loss in patients with PDR. The laser-mediated photocoagulation seals leaking blood vessels directly or by eliminating abnormal newly formed blood vessels in the periphery of the retina that is thought to be involved in VEGF production[6]. With VEGF being a common product strongly associated with the progression of DR, current pharmacologic treatment strategies have been based on its local inhibition within the retina[]. Anti-angiogenic therapy was developed in attempt to improve vision in patients with diabetic macular edema (DME) as well as PDR. Indeed, monthly injections

of ranibizumab, an anti-VEGF improved vision, reduced the risk of further vision loss. These results were observed after 2-years and were sustained for 3-years[38]. Anti-VEGF treatment improved macular edema in diabetic patients as well as when it was used in combination with panretinal photocoagulation in patients with PDR. The reported side effects of ranibizumab in "as - needed" treatment regimen over a 5-year.



Schematic presentation of the multiple pathways involved in metabolic syndrome including hypertension, central obesity, dyslipidemia, adipose tissue and adipokine's dysfunction, altered free fatty acids levels and polyunsaturated fatty acid metabolism leading to local and systemic inflammation. FFA: Free fatty acids; PUFA: Polyunsaturated fatty acid.

INSULIN RESISTANCE AND THE METABOLIC SYNDROME

Researchers have proposed several mechanisms for the development of insulin resistance and the metabolic syndrome. These include: Genetic defects in proteins involved in the insulin action cascade, increased levels of visceral adiposity, free fatty acid levels (FFA), and chronic inflammation. Insulin resistance in adipose tissue, regardless its molecular or environmental basis,

causes decrease in FFA uptake by fat cells and/ or increase in FFA release from fat cells. Under the insulin resistant state, there is impaired glucose handling by skeletal muscle and adipose tissue. This impaired glucose intake is a significant contributor to the hyperglycemia and associated vascular endothelial damage observed in insulin resistant individuals. Additionally, insulin is important in the signaling for nitric oxide release from vascular endothelial cells, resulting in vasodilation and reduced vascular resistance, which reduces blood pressure. Thus, there is a strong association between the presence and extent of insulin resistance with hypertension due to increased vascular resistance and impaired glucose regulation

Hypertension, affecting 29.8% of United States adults[7] represents the best known systemic condition associated with non-diabetic retinopathy. Hypertension is an established risk factor for the development of several cardiovascular complications including retinopathy, atherosclerosis, and aneurysms. Poorly controlled systemic hypertension causes worsening of microvascular disease of the eye like DR

. Hypertensive retinopathy shared the pathophysiology of damaged retinal vascular endothelium similar to DR. In contrast to the metabolic damage in DR, this vascular endothelial damage is mechanically induced by increased blood flow. Despite the relationship between retinopathy and hypertension in patients without history of diabetes, one study, “the Hoorn”, identified retinopathy 8 of

the 17 individuals without history of diabetes who developed retinopathy did not have hypertension. In addition, HbA1c level and waste to hip ratio (WHR) were risk factors in the nondiabetic individuals. These finding suggest that retinal pathologies begin to develop prior to a clinical diagnosis of hypertension that eventually result in retinopathy.

RETINOPATHY IN SUBJECTS WITH METABOLIC SYNDROME BUT NO HISTORY OF DIABETES

In the absence of a clinical diagnosis of diabetes, associations have already been found between the metabolic syndrome and macro- or microvascular pathologies such as atherosclerosis, arteriosclerosis, and endothelial dysfunction. Several studies examined the associations between the independent components of the metabolic syndrome with the development of retinal vascular injury, by measuring the mean retinal artery and venous caliber. In this study, components of the metabolic syndrome including large waist circumference, lower HDL cholesterol levels, and higher BP were independently associated with reduced mean retinal arterial caliber in non-diabetic persons. Individuals with hypertriglyceridemia were significantly more likely to have arteriovenous nicking and later develop retinopathy .These finding clearly show an association between the MS and retinal vascular dysfunction.

Following the earlier notion that dyslipidemia plays a critical role in DR, several studies examined the individual components observed in the metabolic syndrome in relation to DR. Similar to the impact of dyslipidemia, there is conflicting data as to the association of the metabolic syndrome with the development of retinopathy lesions in non-diabetic subjects. One study of obese individuals older than the age of 40, found no significant correlation between the metabolic syndrome and retinopathy once diabetes and hypertension were controlled .Another population study found no significant association in the incidence of retinopathy and the metabolic syndrome in the non-diabetic population, but there was a significant association between hypertension and retinopathy.

In contrast, studies focusing on specific patient populations found differing results. A recent study in a Chinese population identified a positive correlation between the metabolic syndrome and retinopathy in the examined non-diabetic subjects. In a study of Japanese adults, the metabolic syndrome was found to be associated with retinopathy; a larger waist circumference was associated with wider venular diameter and retinopathy lesions; a higher blood pressure level was associated with focal arteriolar narrowing, arteriovenous nicking, enhanced arteriolar wall reflex and narrower arteriolar diameter; and a higher triglyceride level was associated with enhanced arteriolar wall reflex. In the Hoorn study, in the Netherlands, there was significant correlation of retinopathy with the

combination of high waste-to-hip ratio (WHR), HbA1c level, and hypertension in non-diabetics and in glucose-impaired subjects, supporting a role for insulin resistance in the pathogenesis of retinopathy.

Interestingly, there was no significant correlation between incidence of retinopathy with serum levels of triglycerides, and total cholesterol or body mass index (BMI) Despite generalized obesity indicated by high BMI not being associated with retinopathy, a high-body-fat percentage indicated by WHR has been shown to be significantly associated with development of retinopathy in patients with type-2 diabetes. Similar to the Hoorn study, the WHR was also an independent risk factor in the diabetic patients in the EURODIAB study. These discrepancies speak to a number of possible factors including the inability of the BMI calculation to accurately estimate body composition while the WHR is an indicator for central obesity and is associated with insulin resistance. In addition, differences in measurement methods and quantification for incidence and/or rate of progression of retinopathy. The other factor is that dysfunction of adipose tissue has been shown to increase oxidative stress and subsequent cytokine, contributing to the pathogenesis of retinopathy [8]. Given that hyperglycemia and hypertension are the strongest risk factors for the development of retinopathy lesions, and that these two conditions are contributors to the diagnosis of the metabolic syndrome, it may be beneficial to modify the clinical approach to individuals with the metabolic syndrome,

namely those with hypertension and hyperglycemia coupled with obesity, calculated by WHR, in order to prevent or slow the development of hyperglycemia, hypertension, and hypertriglyceridemia, which in turn could possibly delay the onset of retinopathy lesions and visual impairment in subjects with these comorbidities.

RETINOPATHY IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE

Although insulin resistance is a key pathogenic factor in both non-alcoholic fatty liver disease (NAFLD) and metabolic syndrome, few studies examined the relationship between NAFLD and retinopathy in the presence or absence of diabetes. Central adiposity and visceral fat are important source of triglycerides leading to steatosis and NAFLD

The prevalence increases in subjects with impaired glucose tolerance (43%) and in subjects with newly diagnosed DM. The NHANES III was conducted by the Centers for Disease Control and Prevention using a nationwide probability sample of the United States non-institutionalized civilian population from 1988 to 1994. While a strong association between diabetes and retinopathy was observed, NAFLD was not associated with retinopathy in the non-diabetic population [75]. No significant relationship between NAFLD and incident retinopathy was observed in either diabetic or non-diabetic after adjusting for

the confounders such as age, gender, ethnicity, and metabolic components. In addition, this same study found no significant increase in DR prevalence in individuals with both DM and NAFLD. In contrast, prior studies observed a positive association between pediatric NAFLD participants and the degree of retinopathy signs. Additionally, NAFLD was associated with increased rates of chronic kidney disease and proliferative diabetic retinopathy in individuals with type 2 diabetes in Italy. Of note, NAFLD was not significantly correlated with the incidence of retinopathy in patients with NPDR after adjusting for multiple factors.

RETINOPATHY IN PATIENTS WITH METABOLIC SYNDROME AND HISTORY OF DIABETES

Traditionally, the development of DR in patients with type 1 or type 2 diabetics has been linked to the associated hyperglycemi.Whether the existence of metabolic syndrome in these patients can accelerate or aggravate the incidence of DR is not clear. For example, the findings of the landmark studies, Land mark clinical trials including United Kingdom Prospective Diabetes Study (UKPDS) in patients with type-2 diabetes, the Diabetic Control and Complications Trial (DCCT), in patients with type-1 diabetes[and its follow-up, the Epidemiology of Diabetes and Interventions and Complications (EDIC)were traditionally interpreted that tight glycemic control significantly delayed development of DR. However, the level of reduction was significantly lower in

patients with type 2 diabetes (25%) and 76% in patients with type 1 diabetes, suggesting that factors outside of hyperglycemia associated with type 2 diabetes may play a role in the pathology of the microvascular complications such as retinopathy[. Also, the tight metabolic control, individually and coupled with other interventions, has been shown to significantly decrease the incidence of retinopathy, while also increasing the quality and duration of life in these patients[With this population beginning to live longer, the rates and incidence of comorbid metabolic syndrome and type 1 diabetes has begun to increase as this population begins to be more representative of the general United States population

Another study in patients with type 1 diabetes found that tight glycemic control had threshold effectiveness at reducing the incidence of retinopathy. When looking for other associations, they found that once the duration of hyperglycemia was controlled for, increased WHR and fasting triglyceride levels were the only other factors strongly associated with the incidence of retinopathy in these patients Interestingly, a study in Belgium found that patients with type 1 diabetes who are overweight and had higher BMI had more retinopathy than normal-weight diabetic patients. Patients with retinopathy were older and had a longer diabetes duration and higher A1C than individuals without retinopathy[However, one study took a different approach to studying this relationship by estimating the prevalence of DR in individuals with the

metabolic syndrome depending on the number of MS components these individuals had parameters including HbA1C. This study found a linear relationship between the number of MS components and the prevalence of DR[These findings support the relationship between the metabolic syndrome, namely the obesity and hypertriglyceridemia, and the development and/or progression of DR. Given that these conditions are strongly associated with type 2 diabetes, and are components of the metabolic syndrome, it would be logical to look into their contribution to the incidence of retinopathy in this population Other studies found positive correlations between the comorbid metabolic syndrome and type 2 diabetes with all cardiovascular complications including DR. Furthermore, other studies found that the presence of hyperinsulinemia and dyslipidemia in type 2 diabetics was associated with the onset of microvascular complications[. A case-controlled study, with data obtained from 2551 Chinese participants found that the trend to develop DR with metabolic syndrome was significantly higher than that without metabolic syndrome. Metabolic syndrome was an independent statistical indicator of the presence of DR after adjusting for age and sex as well as HbA1c and duration of diabetes]. Additively these findings bolster the claim that in addition to hyperglycemia and hypertension, the hypertriglyceridemia seen in several individuals in this population may very well play a significant role in the pathogenesis of DR in this population

MECHANISMS ASSOCIATED WITH RETINOPATHY IN THE METABOLIC SYNDROME

DR is classically perceived as microvascular disease with initial vascular endothelial damage as a direct result of hyperglycemia. Given the known pathophysiology of the components of the metabolic syndrome, as well as its association with type 2 diabetes we will discuss the common major mechanisms of pathology in both the metabolic syndrome and diabetes.

For retinopathy in patients with an established history of diabetes, hyperglycemia has been identified as primary factor evident by the strong correlation between an individual's HbA1c and the development of DR Results from the clinical trial UKPDS in patients with type 2 diabetes[and the DCCT in patients with type 1 diabetes established that intensive glycemic control significantly reduced the incidence of retinopathy. More specifically, risk reduction of DR was found to be 76% in patients with type 1 diabetes and 25% in type 2 diabetics. Several studies examined mechanisms involved in hyperglycemic damage include non-enzymatic glycosylation of vascular basement membrane, advanced glycation end products and osmotic damage due to the conversion of circulating sugars to sorbitol by aldose reductase[. Studies have found that diabetes mellitus and the metabolic syndrome both, increase reactive oxygen species (ROS) production and decrease the antioxidant capacity. This is associated with oxidative damage of cell components such as proteins,

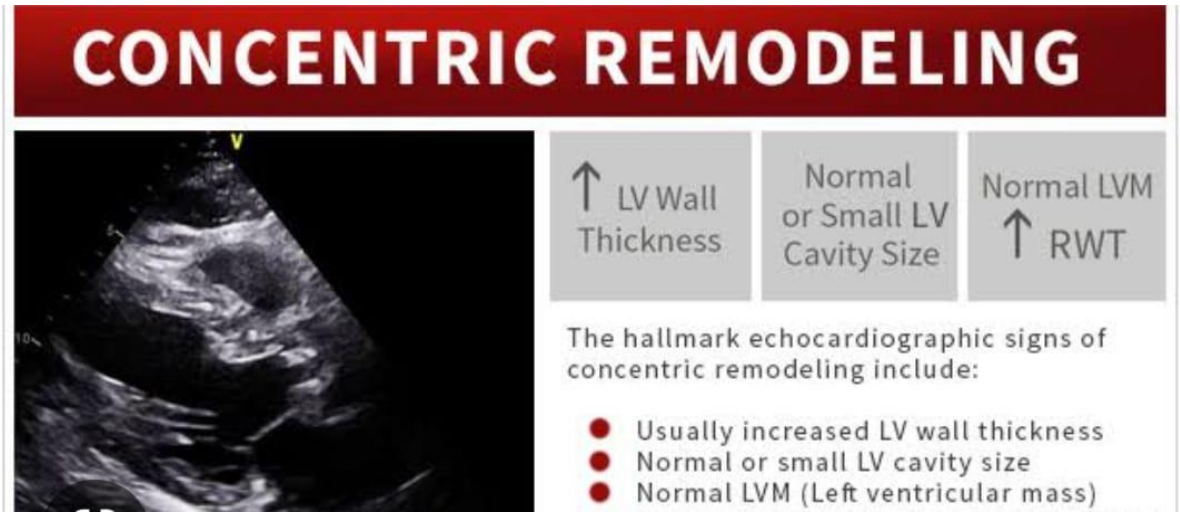
lipids, and nucleic acids can trigger a chronic inflammatory response. Impact and sources of hyperglycemia-derived oxidative stress and pro inflammatory cytokines in the diabetic retina are well-documented in the literature[108,109]. As depicted in Figure the aforementioned mechanisms result in vascular endothelial cell dysfunction and an increase in local immune cell activity resulting in a leukocyte oxidative burst and the associated increased leukostasis, vascular permeability[. Inflammation-mediated leukostasis has been linked to pericyte and endothelial cell death, retinal ischemia, and neovascularization, which contribute to vision loss in DR

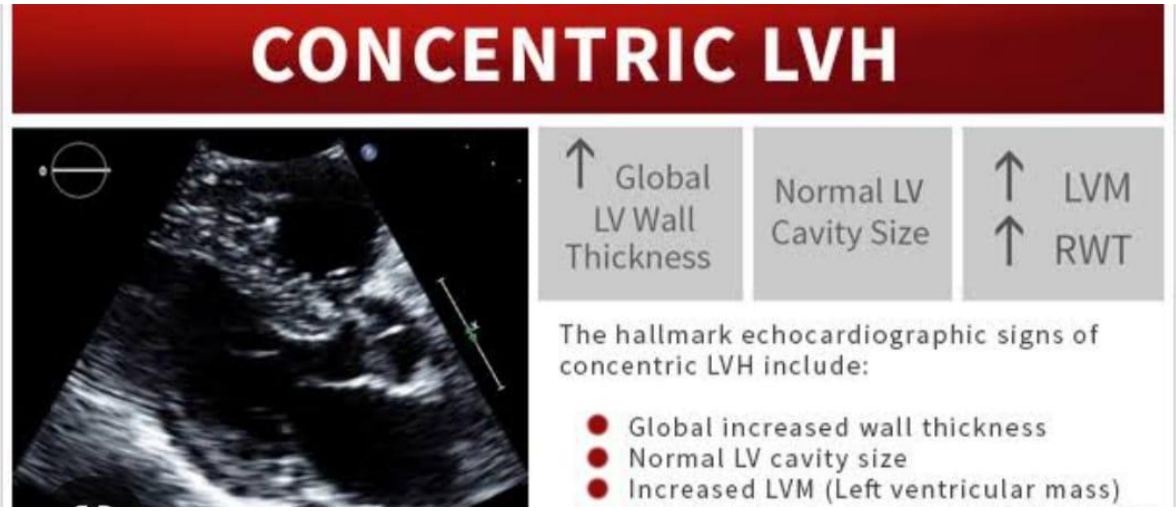
In contrast, identifying mechanisms involved in retinopathy associated with the metabolic syndrome is not a straightforward task. The metabolic syndrome is a combination of several criteria including central obesity, hypertriglyceridemia, insulin resistance, dyslipidemia Furthermore, central obesity and the excess adipose tissue observed in obese individuals partially contribute to the development of the insulin resistance syndrome and cardiovascular disease. metabolic syndrome and endocrine dysfunction of adipose tissue can be very important in the development of retinopathy lesions and progression of the DR

LEFT VENTRICULAR HYPERTROPHY

EPIDEMOLOGY

Left ventricular hypertrophy (LVH) is present in 15% to 20% of the general population. It is more often prevalent in blacks, the elderly, the obese, and in patients with hypertension.[1]. A review of echocardiographic data of 37700 individuals revealed 19%-48% prevalence of LVH in untreated hypertensives and 58%-77% in high-risk hypertensive patients. The presence of obesity also causes 2 -fold increased risk of developing LVH. The prevalence of LVH ranges from 36% (conservative criteria) to 41% (lesser conservative criteria) in the population, depending on the criteria used for defining it. LVH prevalence is not reported to be different between men and women (range 36.0% versus 37.9% (conservative criteria) and 43.5% versus 46.2% (lesser conservative criteria).The prevalence of eccentric LVH is relatively more compared to concentric hypertrophy.[11]





Pathophysiology

Left ventricular hypertrophy (LVH) and remodeling early on, are very important compensatory processes that develop over time in response to wall stress or any significant hemodynamic pressure or volumetric burden. The increased mass of muscle fibers or wall thickness serves initially as a compensatory mechanism that helps to maintain contractile forces and counteracts the increased ventricular wall stress. The benefits of increased wall thickness to compensate for elevated wall stress are offset by a significant increase in the degree of stiffness of the hypertrophied walls associated with a significant increase in diastolic ventricular pressures, which are subsequently transmitted back into the left atrium as well as the pulmonary vasculature.

As previously indicated, LVH is a compensatory but ultimately, an abnormal increase in the mass of the myocardium of the left ventricle induced by a chronically elevated workload on the heart muscle. But, pathologic LVH once

developed, puts the patient at significant risk for the development of heart failure, dysrhythmias, and sudden death. The most common etiologic cause is the heart contracting against an elevated afterload, as seen in hypertension and also seen in valvar aortic stenosis. Another cause is increased filling of the left ventricle inducing diastolic overload, which is the underlying mechanism for eccentric LVH in patients with regurgitant valvular lesions such as aortic regurgitation or mitral regurgitation and also seen in dilated cardiomyopathy. Coronary artery disease has been demonstrated to play a role in the pathogenesis of LVH, as the normal myocardium tries to compensate for tissue that has become ischemic or infarcted. One key pathophysiologic component in LVH is the concomitant development of myocardial fibrosis. Initially, fibrosis is clinically manifested by diastolic dysfunction, but systolic dysfunction will also develop with progressive disease.[12]

Based on relative wall thickness (posterior wall thickness x 2 / LV internal diameter at end-diastole), and the left ventricular mass (LVM) index (left ventricular mass normalized for body surface area or height), the left ventricular hypertrophy can be categorized into 2 types; concentric hypertrophy (increased LWM index and relative wall thickness (RWT) more than 0.42) or eccentric hypertrophy (increased LWM index and RWT less than or equal to 0.42).

Concentric left ventricular hypertrophy is an abnormal increase in left ventricular myocardial mass caused by chronically increased workload on the

heart, most commonly resulting from pressure overload-induced by arteriolar vasoconstriction as occurs in, chronic hypertension or aortic stenosis.

Eccentric left ventricular hypertrophy is induced by an increased filling pressure of the left ventricle, otherwise known as diastolic overload, which represents the underlying mechanism for volumetric or diastolic overload in patients with regurgitant valve lesions such as aortic or mitral regurgitation as well as in the case of dilated cardiomyopathy. In patients with coronary artery disease, these mechanisms can play a role in an attempt to compensate for ischemic or infarcted myocardial tissue. This type of sustained increase in wall stress along with cytokine and neuro-activation stimulates the development of myocardial hypertrophy or increasing muscle thickness with the deposition of the extracellular matrix. This increased mass of muscle fibers or wall thickness serves initially as a compensatory mechanism that helps to maintain contractile forces and counteracts the increased ventricular wall stress. The benefits of increased wall thickness to compensate for elevated wall stress are offset by a significant increase in the degree of stiffness of the hypertrophied walls associated with a significant increase in diastolic ventricular pressures, which are subsequently transmitted back into the left atrium as well as the pulmonary vasculature.

One key pathophysiologic component in LVH is the concomitant development of myocardial fibrosis. Initially, fibrosis is clinically manifested by diastolic dysfunction, but systolic dysfunction will also develop with progressive disease.

Myocardial fibrosis appears to be pathophysiologically linked to the renin-angiotensin-aldosterone system (RAAS). Evidence has been established that angiotensin II produces a profibrotic effect in the myocardial tissue of hypertensive patients. This explains why angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) are among the most potent agents in the treatment of hypertension, especially from the standpoint of morbidity and mortality. LVH has been shown to be a consistent predictor of cardiovascular morbidity as well as mortality in hypertensive patients.[3] Certain antihypertensive therapies that induce regression of LVH decrease rates of major adverse cardiovascular events and enhance survival, regardless of the degree of blood pressure reduction. The clinical importance is two-fold: 1) recognizing that LVH can be a modifiable risk factor and 2) that management choices are significantly more complex than just controlling the blood pressure.

Genomics may also play a significant role in the pathogenesis of LVH. Mutated genes that encode proteins of the sarcomere have a direct etiologic relationship in patients who present with hypertrophic cardiomyopathy. Also, there seems to

be a genetic predisposition evidenced by the fact that some mildly hypertensive patients develop LVH while others do not.

EVALUATION

Electrocardiography (ECG) is the least expensive and most readily available test for the diagnosis of LVH. While its specificity is relatively high, its low sensitivity makes the clinical utility somewhat limited. Various criteria for LVH by ECG have been suggested over the years. Most criteria utilize the voltage in one or more leads, QRS duration, secondary ST-T wave abnormalities, or left atrial abnormalities. The best recognized established ECG criteria are the Cornell voltage, the Cornell product, the Sokolow-Lyon index, as well as the Estes-Romhilt point scoring system.

ECG is relatively insensitive in diagnosing LVH because it relies on the measurement of the electrical activity of the heart by electrodes placed on the surface of the skin to predict the left ventricular mass. The intracardiac electrical signal is problematic to measure in this way because the measurements are impacted by all elements that lie between the heart muscle and the ECG electrodes, specifically fat, fluid, and air. Because of the variations in these elements, ECG underdiagnoses LVH in patients with pleural effusions, pericardial effusions, anasarca, obesity as well as chronic obstructive pulmonary disease (COPD). Also, LVH diagnosed by ECG is strongly impacted by both

age and ethnicity. While electrocardiography is not sensitive and cannot be used to definitively exclude the diagnosis of LVH, it still plays a diagnostic and management role. In the Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) study, LVH regression (diagnosed by ECG utilizing the Sokolow-Lyon index or the Cornell product criteria) in response to losartan (Cozaar) improved clinical cardiovascular outcomes independent of blood pressure response.

An echocardiogram is the test of choice in establishing the diagnosis of LVH. Its sensitivity is significantly higher than ECG, and the test can also diagnose other abnormalities such as left ventricular dysfunction (both systolic as well as diastolic) and valvular heart disease. Cardiac ultrasound utilizes transthoracic or transesophageal positioning of the transducer to measure the left ventricular end-diastolic diameter, posterior wall thickness, and interventricular septum thickness. From these measurements and the patient's height and weight, the LV mass index can be determined. According to the American Society of Echocardiography and/European Association of Cardiovascular Imaging, LVH is defined as an increased left ventricular mass index (LVMI) to greater than 95 g/m in women and increased LVMI to greater than 115 g/m in men. Despite the advantages of echocardiography and Doppler analysis, an important consideration in using this tool as a screening test in all hypertensive patients is its significant cost when compared to ECG.

In terms of specific testing for LVH, cardiac magnetic resonance imaging (MRI) is now considered the gold standard as it is even more precise and reproducible than cardiac ultrasound. It can accurately estimate LV mass and determines if other structural cardiac abnormalities are present. The widespread use of MRI is severely restricted in clinical practice due to its cost, logistics, and limited availability. While it may never be useful in screening for LVH, it has a significant role in clinical research and in the assessment of cardiovascular anatomy in certain clinical situations.

Treatment / Management

The management of LVH depends on the etiology. Treatment involves lifestyle changes, and depending upon the cause, may include medication, surgery, and an implantable device for the prevention of sudden cardiac death. LVH treatment should be aggressive because patients with LVH are at the highest risk for cardiovascular events and mortality. The goal is to regress LVH and prevent LV dysfunction and progression to heart failure. Two-third of the patients with LVH are hypertensive. Blood pressure (BP) control is essential for preventing further deterioration and complications. Angiotensin-converting enzyme inhibitors (ACE-Is), angiotensin receptor blockers (ARBs), long-acting calcium channel blockers (CCBs), or thiazide/thiazide-like diuretics are the

recommended antihypertensives for LVH. The antihypertensive therapy benefits the patient by reducing BP and may regress LVH independent of BP reduction, leading to reduced adverse cardiovascular events and mortality.[10]

The other common cause of LVH is aortic stenosis. Patients with aortic stenosis usually have a 10 to 20 years asymptomatic latent period, during which increasing LV outflow obstruction and pressure load on the myocardium, may gradually change the composition of myocardial extracellular matrix leading to LVH. Usually, aortic valve replacement (AVR) is recommended in symptomatic patients, but if the echocardiographic findings show rapidly progressing aortic stenosis with LV dysfunction, AVR would be recommended in asymptomatic patients to improve LV function and reduce mortality.

Athletic heart with physiological LVH does not require treatment. Discontinuation of training for a few months (3 to 6 months) is usually needed to regress LVH. LVH regression is monitored for a few months to distinguish it from cardiomyopathy. In hypertrophic cardiomyopathy patients, beta-blockers and CCBs are used to reduce the heart rate and decrease myocardial contractility so that diastolic filling can be prolonged. If symptoms persist despite medical therapy, surgical myomectomy, or septal ablation is indicated. In these specific cases, drugs like diuretics, ACEI, or ARBs are avoided because they decrease the preload and worsen the ventricular function.

Metabolic syndrome and LVH:

Metabolic syndrome (MetS) is associated with increased prevalence of echocardiographic LV hypertrophy (LVH), a potent predictor of cardiovascular (CV) outcome. Whether MetS increases risk of CV events independently of presence of LVH has never been investigated

Despite accumulating evidence that metabolic syndrome (is associated with

high cardiovascular (CV) risk (), there is still debate in the scientific community about whether identification of the metabolic syndrome improves ability to predict CV risk beyond use of single risk factors

Metabolic syndrome (MetS) is associated with increased prevalence of echocardiographic LV hypertrophy (LVH), a potent predictor of cardiovascular (CV) outcome. Whether MetS increases risk of CV events independently of presence of LVH has never been investigated. It is also unclear whether LVH predicts CV risk both in the presence and absence of MetS.

Participants in the 2nd Strong Heart Study examination without prevalent coronary heart disease, congestive heart failure or renal insufficiency (plasma creatinine>2.5 mg/dL) were studied (n=2,758; 1,746 women). MetS was defined by WHO criteria. Echocardiographic LV hypertrophy was defined using population-specific cut-point value for LV mass index (>47.3 g/m2.7). After controlling for age, sex, LDL-cholesterol, smoking, plasma creatinine, diabetes,

hypertension and obesity, participants with MetS had greater probability of LVH than those without MetS (OR=1.55 [1.18-2.04], p<0.002). Adjusted hazard of composite fatal and non-fatal CV events was greater when LVH was present, in participants without (HR=2.03 [1.33-3.08]) or with MetS (HR=1.64 [1.31-2.04], both p<0.0001), with similar adjusted population attributable risk (12% and 14%). After adjustment for LVH, risk of incident CV events remained 1.47-fold greater in MetS (p<0.003), an effect, however, that was not confirmed when diabetic participants were excluded.

LVH is a strong predictor of composite 8-year fatal and non-fatal CV events either in the presence or in the absence of MetS and accounts for a substantial portion of the high CV risk associated with MetS.

Despite accumulating evidence that metabolic syndrome is associated with high cardiovascular (CV) risk , there is still debate in the scientific community about whether identification of the metabolic syndrome improves ability to predict CV risk beyond use of single risk factors (. We recently showed that metabolic syndrome significantly increases CV risk both in the general population and in hypertensive patients already at high CV risk because of LV hypertrophy, a hallmark of preclinical CV disease (13), identified by ECG (17,18), an association that persisted even when component risk factors were considered in the predictive model. However, these findings do not clarify whether at least

part of the CV risk associated with metabolic syndrome might be due to associated LV hypertrophy.

There is emerging evidence that the metabolic syndrome is in fact associated with more severe LV hypertrophy and other manifestations of preclinical CV disease (10,19-21), suggesting that part of the CV risk predicted by metabolic syndrome might be mediated by LV hypertrophy. There is no information on whether the adverse prognosis of metabolic syndrome is independent of the presence of LV hypertrophy, or on whether LV hypertrophy remains a potent predictor of CV risk both in the presence or absence of metabolic syndrome

MATERIALS

AND

METHODS

MATERIALS AND METHODS

A) STUDY DESIGN:

OBSERVATIONAL COMPARATIVE CROSS SECTIONAL STUDY

B) STUDY LOCATION:

Patients attending medicine OPD in Government Kilpauk medical college, Chennai.

C) STUDY PARTICIPANTS:

Study population was selected from young females of hypertension duration more than 5 years in outpatient department and was screened for metabolic syndrome based on the diagnostic criteria and divided into two groups-

1)Young female hypertensive patients with metabolic syndrome

2)Young female hypertensive patients without metabolic syndrome

Both the groups are then evaluated for albuminuria, left ventricular hypertrophy and retinopathy.

INCLUSION CRITERIA:

- Young females of age 18 yrs to 40 yrs

● Patients with essential hypertension as defined by American College of Cardiology/American Heart Association (ACC/AHA) for a duration of 5 to 10 years

EXCLUSION CRITERIA:

● Male patients

● Females less than 18 years of age and more than 40 years of age

● Patients with known diabetes mellitus and patients with fasting glycemia more than or equal to 126 mg/do.

● Patients with known cardiovascular diseases

● Patients with renal diseases (serum creatinine >1.5 mg/dl)

● Patients with overt proteinuria

● Patients with known cases of secondary hypertension

● Patients taking lipid lowering therapy

● Patients with cerebrovascular disease

STUDY PERIOD

6 months from the date of approval of ethical committee.

D) STUDY METHODOLOGY

HISTORY TAKING

● Detailed history has been taken from patients

- Age more than 18years and upto 40 years
- Sex- female
- Old medical records (history of diabetes/hypertension/coronary artery disease/dyslipidemia)
- Drug intake history (anti-hypertensives, anti-diabetes, drugs for ischemic heart disease, drugs for hypercholesterolemia)
- Smoking and alcohol history

CLINICAL EXAMINATION:

- level of consciousness
- orientation to time , place and person
- Body weight,height and waist circumference measured by a nurse
- Blood pressure recorded by a doctor.The latter waconsidered as the average of 3 consecutive measurements obtained by mercury sphygmomanometer,after the subject had been supine for 5 min.
- Urine analysis performed-urine spot pcr and urine albumin checked.
- Blood sample drawn to perform routine blood chemistry
- Echocardiography study done to look for left ventricular hypertrophy
- Fundus examination done to look for retinopathy changes
- BMI

LABORATORY ASSESSMENT:

- Serum fasting lipid profile including HDL and TGL
- Urine analysis performed-urine spot pcr and urine albumin checked.
- Blood sample drawn to perform routine blood chemistry
- Blood sugar levels both FBS and PPBS

NCEP ATP III criteria define metabolic syndrome as the presence of any **three** of the following five traits:

●Abdominal obesity, defined as a waist circumference ≥102 cm (40 in) in men and ≥88 cm (35 in) in females

●Serum triglycerides ≥150 mg/dL (1.7 mmol/L) or drug treatment for elevated triglycerides

●Serum high-density lipoprotein (HDL) cholesterol <40 mg/dL (1 mmol/L) in males and <50 mg/dL (1.3 mmol/L) in females or drug treatment for low HDL cholesterol

●Blood pressure ≥130/85 mmHg or drug treatment for elevated blood pressure

●Fasting plasma glucose (FPG) ≥100 mg/dL (5.6 mmol/L) or drug treatment for elevated blood glucose

Hypertension is defined by AHA /ACC as

Normal blood pressure – Systolic <120 mmHg and diastolic <80 mmHg

●Elevated blood pressure – Systolic 120 to 129 mmHg and diastolic <80 mmHg

Hypertension:

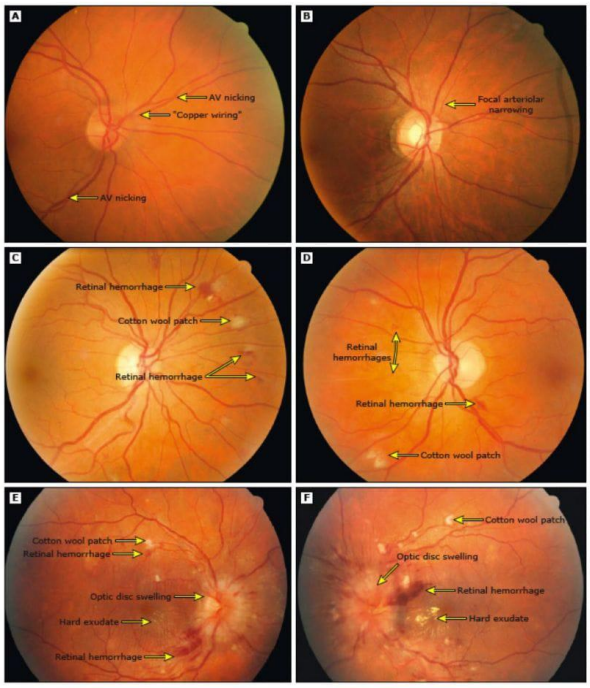
•Stage 1 – Systolic 130 to 139 mmHg or diastolic 80 to 89 mmHg

•Stage 2 – Systolic at least 140 mmHg or diastolic at least 90 mmHg

Mitchell-Wong simplification of the Keith-Wagener-Barret system is used for retinopathy

Grading is as follows:

Retinal fundus photographs of hypertensive retinopathy



Representative digital retinal fundus photographs of mild (A,B), moderate (C,D), and severe (E,F) hypertensive retinopathy, as graded with the simplified classification:

(A) Mild hypertensive retinopathy is indicated by the presence of generalized arteriolar narrowing, arteriovenous (AV) nicking, and opacification of the arteriolar wall ("copper wiring").

(B) Mild hypertensive retinopathy with focal arteriolar narrowing.

(C,D) Moderate hypertensive retinopathy with multiple retinal hemorrhages and cotton wool patches.

(E,F) Severe hypertensive retinopathy with swelling of the optic disk, retinal hemorrhages, hard exudates, and cotton wool patches.

Grade 1 (mild retinopathy) - Arteriolar narrowing (generalized and focal), AV nicking, and/or arteriolar wall opacity

Grade 2 (moderate retinopathy) - Hemorrhage, micro aneurysm, cotton wool spot, and/or hard exudate

Grade 3 (malignant retinopathy) - Moderate retinopathy plus optic disc swelling

Albuminuria Categories According to KDIGO Classification

Dipstick Protein reading	Protein excretion gm/24 hours	Protein excretion mg/dL
Negative	<0.1	<10
Trace	0.1-0.2	15
1+	0.2-0.5	30
2+	0.5-1.5	100
3+	2.0-5.0	300
4+	>5.0	>1000

Young hypertensive females with hypertension duration of 5-10 years are chosen from hypertension clinic and are screened for metabolic syndrome. They are divided into two groups.

A) Young hypertensive females with metabolic syndrome

B) Young hypertensive females without metabolic syndrome

Routine blood investigations are done for both the groups.

Both the groups are then screened for end organ damage-

* Fundus examination is done to look for retinopathy changes

*2D Echo is done to look for left ventricular hypertrophy

*Urine routine is done to look for albuminuria

As per primary study outcome, Metabolic

syndrome seems to amplifyhypertension-

related cardiac and renal changes, over and above the

potential contribution of each single component of this syndrome. Asthese mark ers of target organ damage are well-

known predictors ofcardiovascular events, our results may partly explain the en hancedcardiovascular risk associated with metabolic syndrome.

E) SAMPLE SIZE CALCULATION

Sample size

G. MULE` et al The sample size was 353

(Zα)^2 * (sigma)^2 /d2

Sigma= 1.46

d taken as 0.292

Zα=1.96

N= (1.96)^2 * 1.46*1.46/0.292*0.292

= 3.84*2.13*2.13/0.085

=300

Minimum sample size 300

So my study comprises of 400 subjects

RESULTS

Results and Observations:

The collected data were analysed with IBM SPSS Statistics for Windows, Version 23.0.(Armonk, NY: IBM Corp).To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. To find the significant difference between the bivariate samples in Independent groups the Independent sample t-test was used. To find the significance in qualitative categorical data Chi-Square test was used. In both the above statistical tools the probability value .05 is considered as significant level.

Table 1: Age distribution

Age distribution		
	Frequency	Percent
Upto 25 yrs	6	1.5
26 - 30 yrs	49	12.3
31 - 35 yrs	163	40.8
36 - 40 yrs	182	45.5
Total	400	100.0

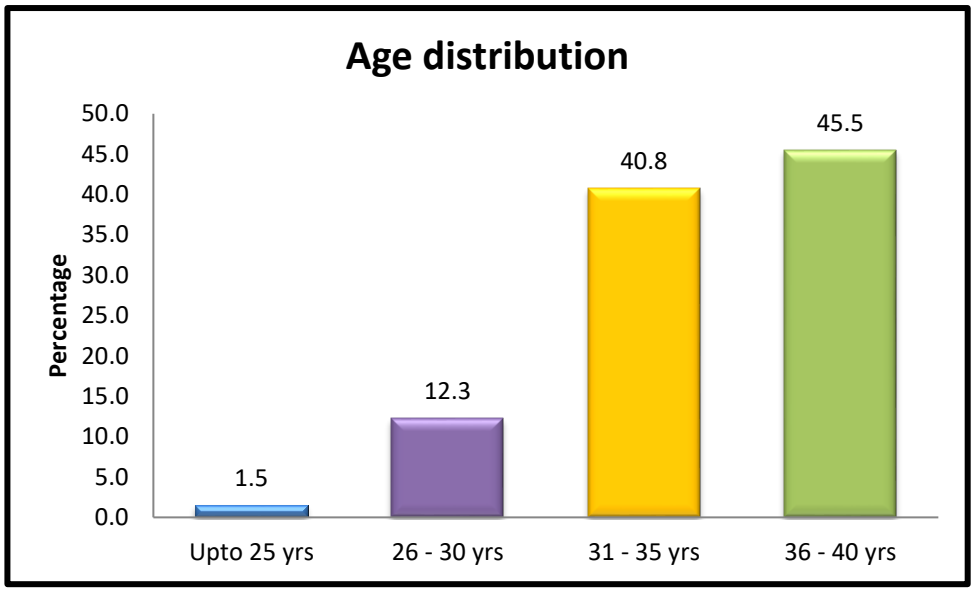


Figure 1

The above table shows Age distribution were <25 years is 1.5%, 26 – 30 years is 12.3%, 31 – 35 years is 40.8%, 36 – 40 years is 45.5%.

Table 2: Comparison of Age between Metabolic syndrome by Pearson's Chi-Square test

			Metabolic syndrome		Total	χ^2 - value	p-value
			Present	Absent			
Age	Upto 25 yrs	Count	6	0	6	17.781	0.0005 **
		%	3.5%	0.0%	1.5%		
	26 - 30 yrs	Count	29	20	49		
		%	17.1%	8.7%	12.3%		
	31 - 35 yrs	Count	71	92	163		
		%	41.8%	40.0%	40.8%		
	36 - 40 yrs	Count	64	118	182		
		%	37.6%	51.3%	45.5%		
Total		Count	170	230	400		
		%	100.0%	100.0%	100.0%		
** Highly Statistical Significance at p < 0.01 level							

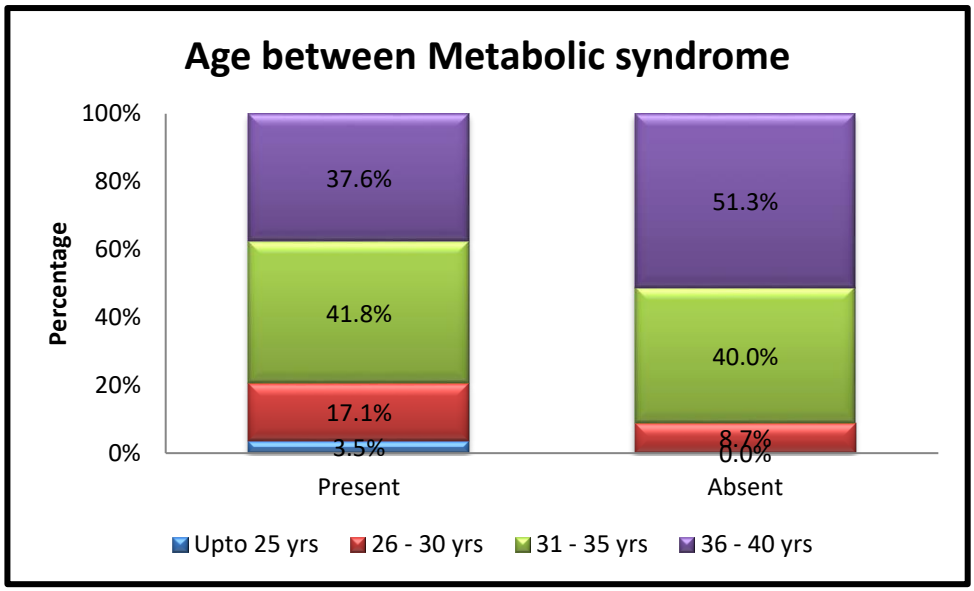


Figure 2

The above table shows comparison of Age between Metabolic syndrome by Pearson's Chi-Square test were $\chi 2=17.781$, $p=0.0005<0.01$ which shows highly statistical significance between Age and Metabolic syndrome.

Table 3: Comparison of Echo-LVH between Metabolic syndrome by Pearson's Chi-Square test

			Metabolic syndrome		Total	$\chi 2$ - value	p-value
			Present	Absent			
Echo-LVH	No	Count	67	154	221	29.996	0.0005 **
		%	39.4%	67.0%	55.3%		
	Yes	Count	103	76	179		
		%	60.6%	33.0%	44.8%		
Total		Count	170	230	400		
		%	100.0%	100.0%	100.0%		
** Highly Statistical Significance at p < 0.01 level							

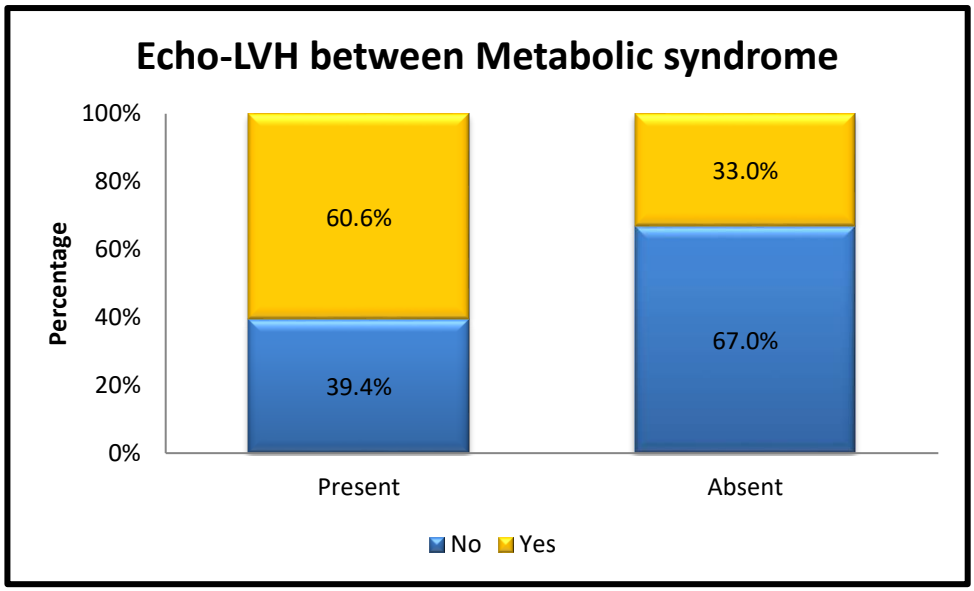


Figure 3

The above table shows comparison of Echo-LVH between Metabolic syndrome by Pearson's Chi-Square test were $\chi 2=29.996$, $p=0.0005<0.01$ which shows highly statistical significance between Echo-LVH and Metabolic syndrome.

Table 4: Comparison of U.ALB between Metabolic syndrome by Pearson's Chi-Square test

			Metabolic syndrome		Total	$\chi 2$ - value	p-value
			Present	Absent			
U.ALB	No	Count	65	158	223	36.764	0.0005 **
		%	38.2%	68.7%	55.8%		
	Yes	Count	105	72	177		
		%	61.8%	31.3%	44.3%		
Total		Count	170	230	400		
		%	100.0%	100.0%	100.0%		
** Highly Statistical Significance at p < 0.01 level							

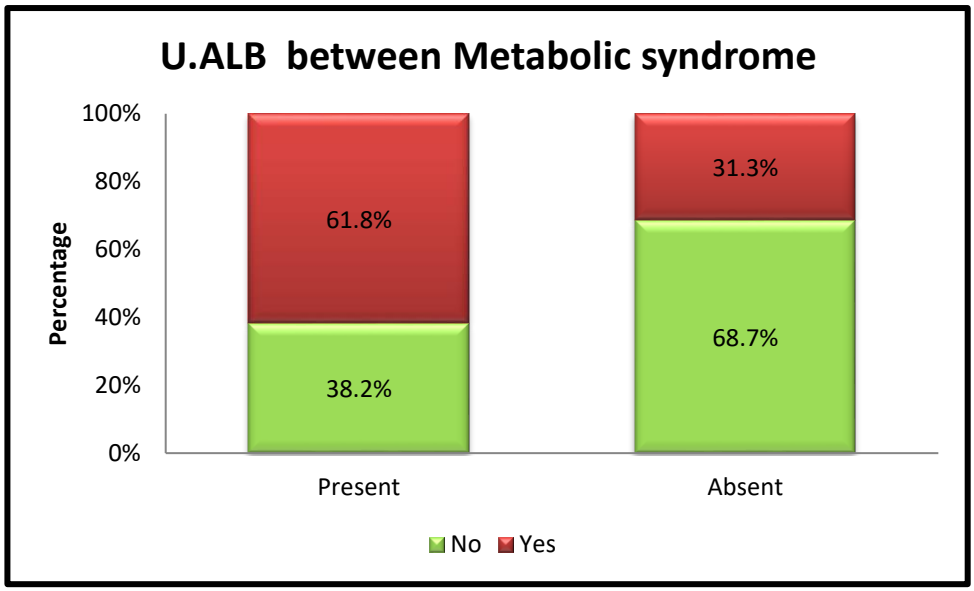


Figure 4

The above table shows comparison of U.ALB between Metabolic syndrome by Pearson's Chi-Square test were $\chi 2=36.764$, $p=0.0005<0.01$ which shows highly statistical significance between U.ALB and Metabolic syndrome.

Table 5: Comparison of Dip stick between Metabolic syndrome by Pearson's Chi-Square test

			Metabolic syndrome		Total	$\chi 2$ - value	p-value
			Present	Absent			
Dip stick	1+	Count	64	34	98	58.319	0.0005 **
		%	37.6%	14.8%	24.5%		
	2+	Count	23	4	27		
		%	13.5%	1.7%	6.8%		
	Trace	Count	17	34	51		
		%	10.0%	14.8%	12.8%		
	Nil	Count	66	158	224		
		%	38.8%	68.7%	56.0%		
Total		Count	170	230	400		
		%	100.0%	100.0%	100.0%		
** Highly Statistical Significance at p < 0.01 level							

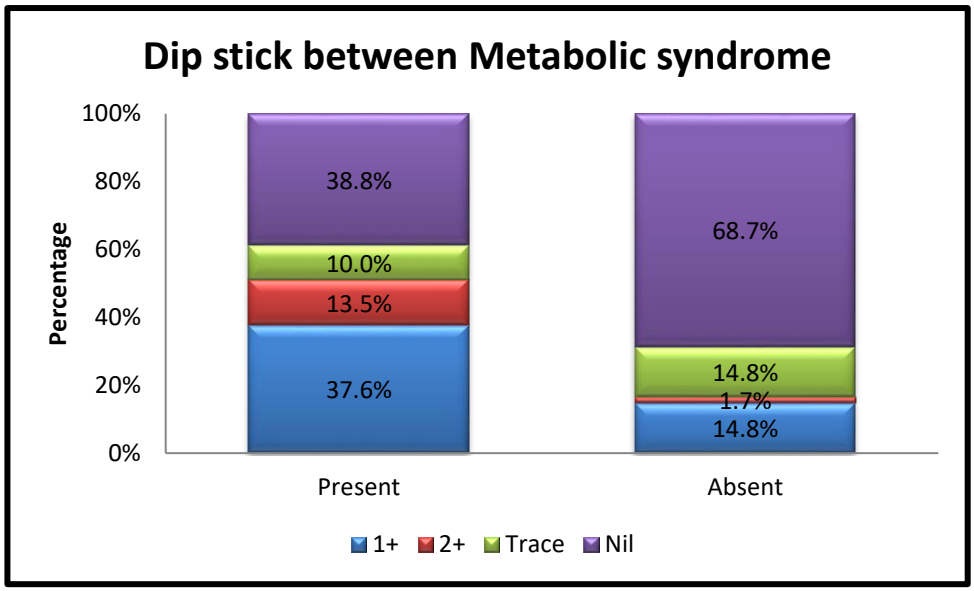


Figure 5

The above table shows comparison of Dip stick between Metabolic syndrome by Pearson's Chi-Square test were $\chi 2=58.319$, $p=0.0005<0.01$ which shows highly statistical significance between Dip stick and Metabolic syndrome.

Table 6: Comparison of Retinopathy between Metabolic syndrome by Pearson's Chi-Square test

			Metabolic syndrome		Total	$\chi 2$ - value	p-value
			Present	Absent			
Retinopathy	No	Count	54	175	229	78.460	0.0005 **
		%	31.8%	76.1%	57.3%		
	Yes	Count	116	55	171		
		%	68.2%	23.9%	42.8%		
Total		Count	170	230	400		
		%	100.0%	100.0%	100.0%		
** Highly Statistical Significance at p < 0.01 level							

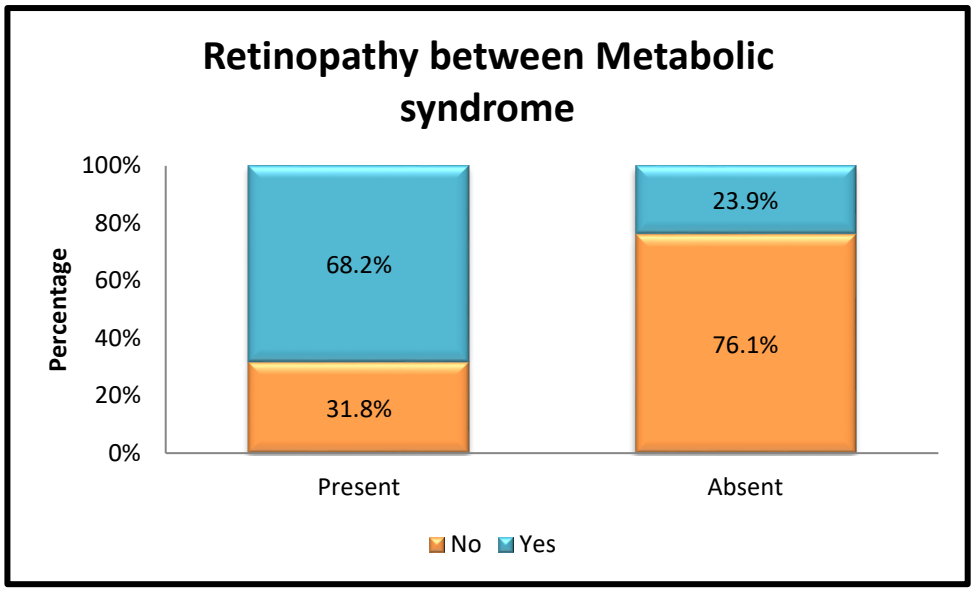


Figure 6

The above table shows comparison of Retinopathy between Metabolic syndrome by Pearson's Chi-Square test were $\chi 2=78.460$, $p=0.0005<0.01$ which shows highly statistical significance between Retinopathy and Metabolic syndrome.

Table 7: Comparison of Grade between Metabolic syndrome by Pearson's Chi-Square test

			Metabolic syndrome		Total	$\chi 2$ - value	p-value
			Present	Absent			
Grade	1	Count	57	46	103	96.512	0.0005 **
		%	33.5%	20.0%	25.8%		
	2	Count	43	9	52		
		%	25.3%	3.9%	13.0%		
	3	Count	16	0	16		
		%	9.4%	0.0%	4.0%		
	Nil	Count	54	175	229		
		%	31.8%	76.1%	57.3%		
Total		Count	170	230	400		
		%	100.0%	100.0%	100.0%		
** Highly Statistical Significance at p < 0.01 level							

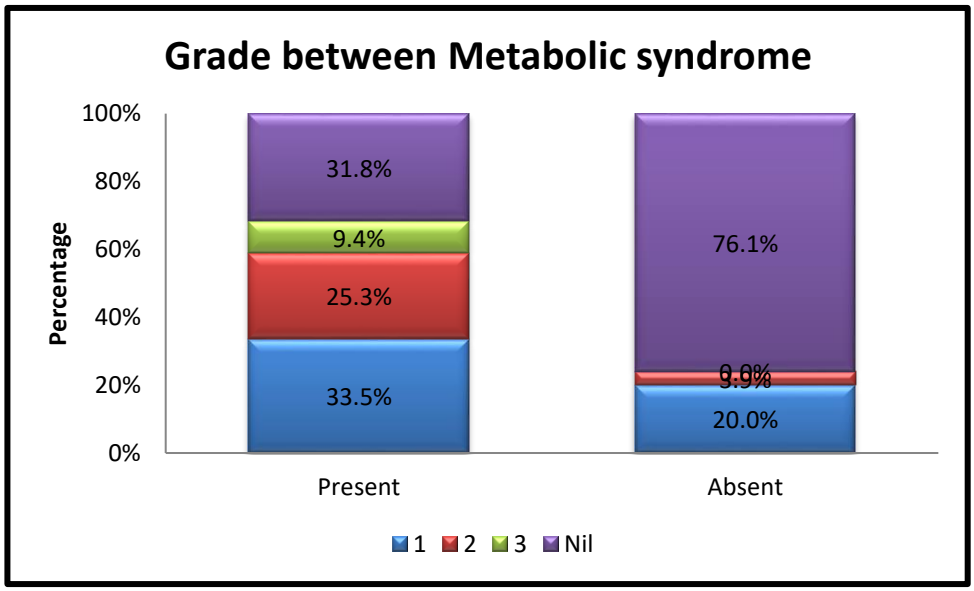


Figure 7

The above table shows comparison of Grade between Metabolic syndrome by Pearson's Chi-Square test were $\chi 2=96.512$, $p=0.0005<0.01$ which shows highly statistical significance between Grade and Metabolic syndrome.

Table 8: Comparison of Waist circumference between Metabolic syndrome by Independent sample t-test

Variable	Metabolic syndrome	N	Mean	SD	t-value	p-value
Waist circumference	Present	170	92.2	4.1	23.723	0.0005 **
	Absent	230	83.5	2.8		
** Highly Statistical Significance at p < 0.01 level						

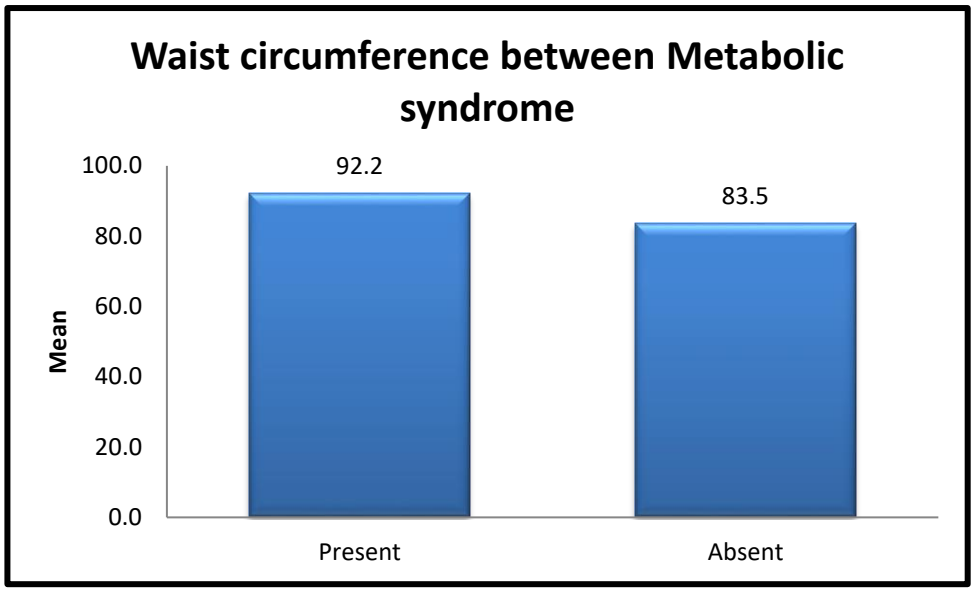


Figure 8

The above table shows comparison of Waist circumference between Metabolic syndrome by Independent sample t-test were t-value=23.723, p-value=0.0005<0.01 which shows highly statistical significance difference at p < 0.01 level.

Table 9: Comparison of S.TRIGLY between Metabolic syndrome by Independent sample t-test

Variable	Metabolic syndrome	N	Mean	SD	t-value	p-value
S.TRIGLY	Present	170	173.8	15.5	22.138	0.0005 **
	Absent	230	125.0	25.4		
** Highly Statistical Significance at p < 0.01 level						

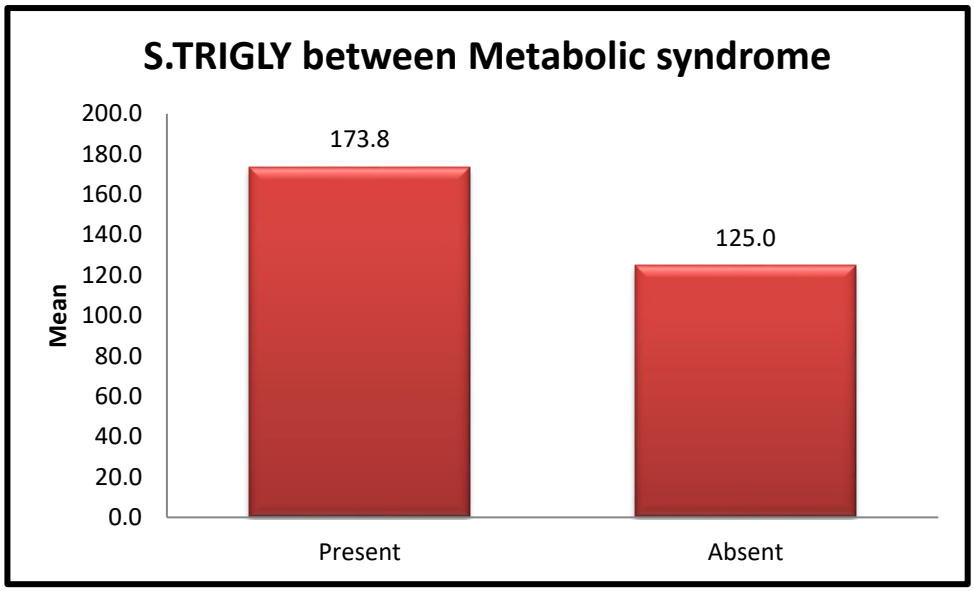


Figure 9

The above table shows comparison of S.TRIGLY between Metabolic syndrome by Independent sample t-test were t-value=22.138, p-value=0.0005<0.01 which shows highly statistical significance difference at p < 0.01 level.

Table 10: Comparison of HDL between Metabolic syndrome by Independent sample t-test

Variable	Metabolic syndrome	N	Mean	SD	t-value	p-value
HDL	Present	170	42.1	3.8	35.361	0.0005 **
	Absent	230	56.8	4.5		
** Highly Statistical Significance at p < 0.01 level						

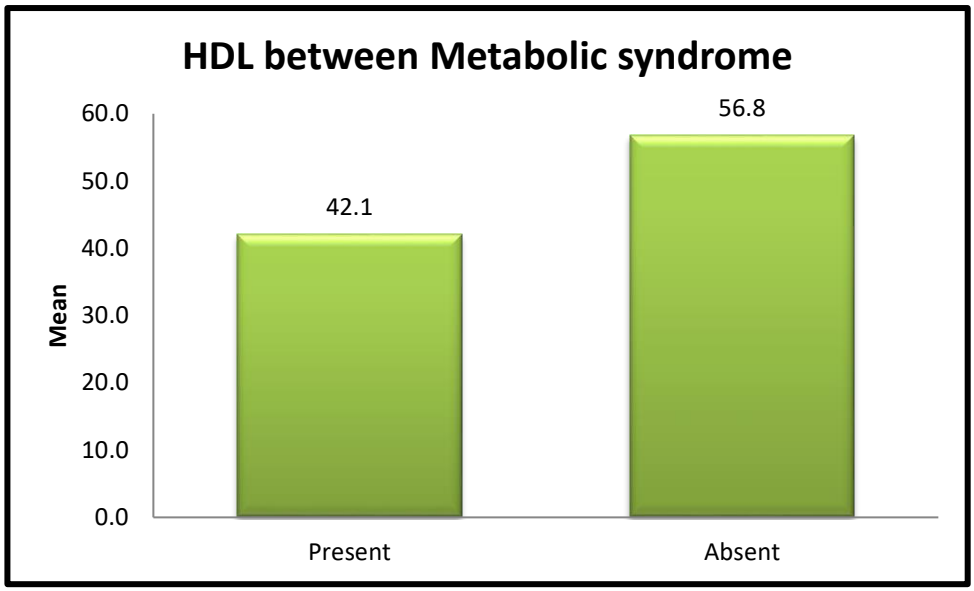


Figure 10

The above table shows comparison of HDL between Metabolic syndrome by Independent sample t-test were t-value=35.361, p-value=0.0005<0.01 which shows highly statistical significance difference at p < 0.01 level.

Table 11: Comparison of SBP between Metabolic syndrome by Independent sample t-test

Variable	Metabolic syndrome	N	Mean	SD	t-value	p-value
SBP	Present	170	146.3	9.4	7.225	0.0005 **
	Absent	230	138.6	11.4		
** Highly Statistical Significance at p < 0.01 level						

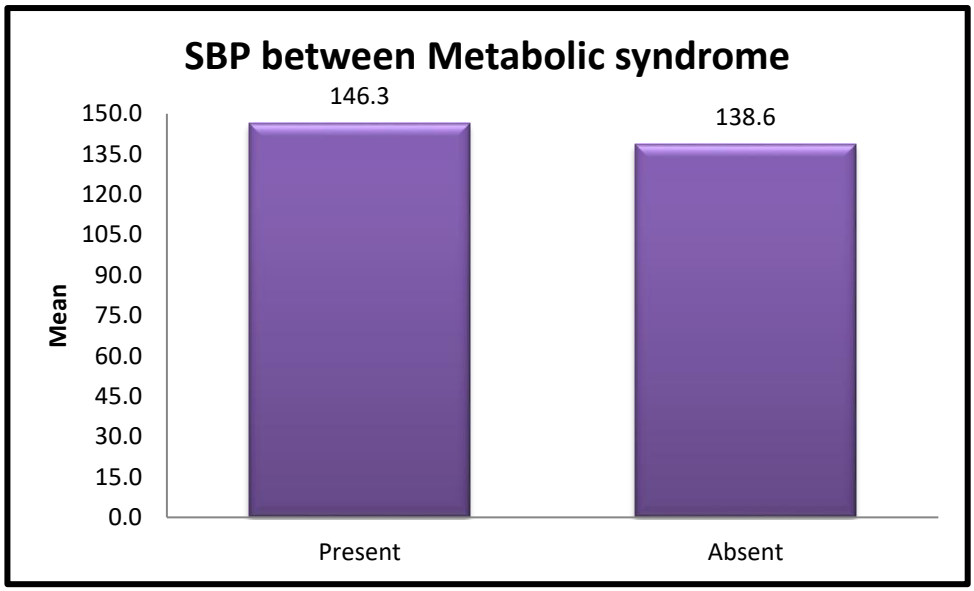


Figure 11

The above table shows comparison of SBP between Metabolic syndrome by Independent sample t-test were t-value=7.225, p-value=0.0005<0.01 which shows highly statistical significance difference at p < 0.01 level.

Table 12: Comparison of DBP between Metabolic syndrome by Independent sample t-test

Variable	Metabolic syndrome	N	Mean	SD	t-value	p-value
DBP	Present	170	87.3	6.6	2.950	0.003 **
	Absent	230	85.1	8.5		
** Highly Statistical Significance at p < 0.01 level						

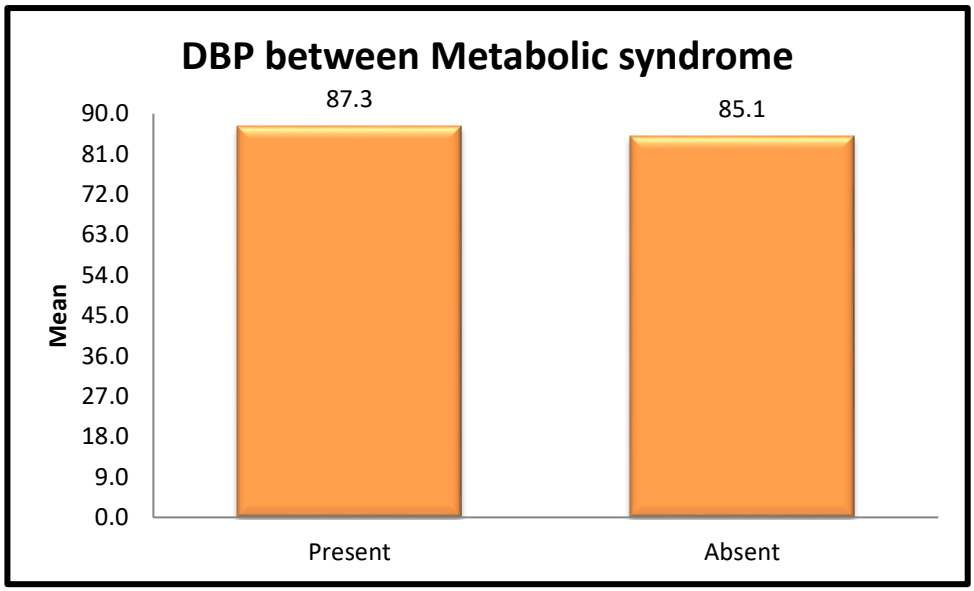


Figure 12

The above table shows comparison of DBP between Metabolic syndrome by Independent sample t-test were t-value=2.950, p-value=0.0005<0.01 which shows highly statistical significance difference at p < 0.01 level.

Table 13: Comparison of FPG between Metabolic syndrome by Independent sample t-test

Variable	Metabolic syndrome	N	Mean	SD	t-value	p-value
FPG	Present	170	146.1	24.3	31.535	0.0005 **
	Absent	230	85.2	7.7		
** Highly Statistical Significance at p < 0.01 level						

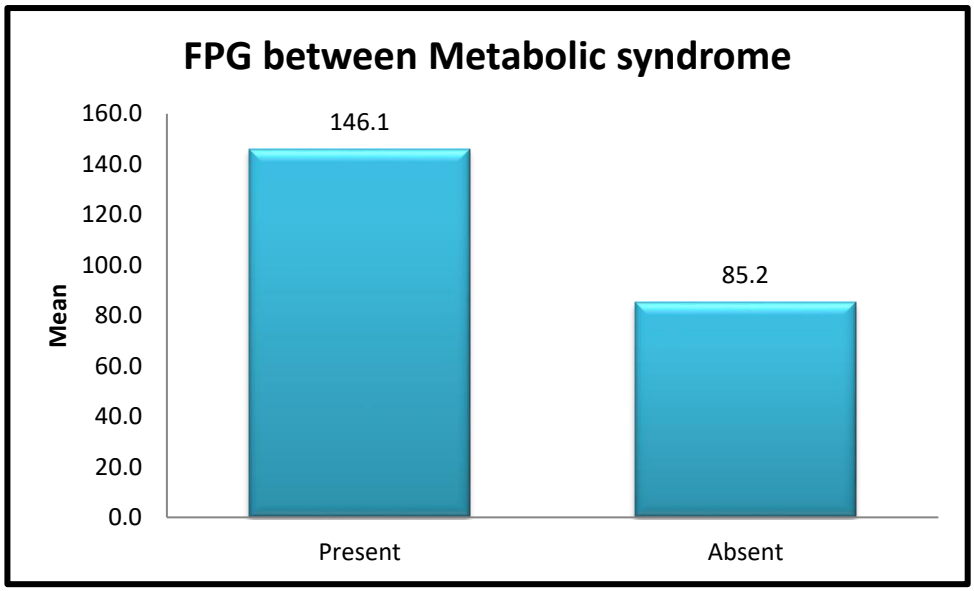


Figure 13

The above table shows comparison of FPG between Metabolic syndrome by Independent sample t-test were t-value=31.535, p-value=0.0005<0.01 which shows highly statistical significance difference at $p < 0.01$ level.

Summary

- The Age distribution were <25 years is 1.5%, 26 – 30 years is 12.3%, 31 – 35 years is 40.8%, 36 – 40 years is 45.5%.
- The Age between Metabolic syndrome by Pearson's Chi-Square test were $\chi 2=17.781$, p=0.0005<0.01 which shows highly statistical significance between Age and Metabolic syndrome.
- The Echo-LVH between Metabolic syndrome by Pearson's Chi-Square test were $\chi 2=29.996$, p=0.0005<0.01 which shows highly statistical significance between Echo-LVH and Metabolic syndrome.

- The U.ALB between Metabolic syndrome by Pearson's Chi-Square test were $\chi 2=36.764$, $p=0.0005<0.01$ which shows highly statistical significance between U.ALB and Metabolic syndrome.
- The Dip stick between Metabolic syndrome by Pearson's Chi-Square test were $\chi 2=58.319$, $p=0.0005<0.01$ which shows highly statistical significance between Dip stick and Metabolic syndrome.
- The Retinopathy between Metabolic syndrome by Pearson's Chi-Square test were $\chi 2=78.460$, $p=0.0005<0.01$ which shows highly statistical significance between Retinopathy and Metabolic syndrome.
- The Grade between Metabolic syndrome by Pearson's Chi-Square test were $\chi 2=96.512$, $p=0.0005<0.01$ which shows highly statistical significance between Grade and Metabolic syndrome.
- The Waist circumference between Metabolic syndrome by Independent sample t-test were t-value=23.723, p-value=0.0005<0.01 which shows highly statistical significance difference at $p < 0.01$ level.
- The S.TRIGLY between Metabolic syndrome by Independent sample t-test were t-value=22.138, p-value=0.0005<0.01 which shows highly statistical significance difference at $p < 0.01$ level.
- The HDL between Metabolic syndrome by Independent sample t-test were t-value=35.361, p-value=0.0005<0.01 which shows highly statistical significance difference at $p < 0.01$ level.

- The SBP between Metabolic syndrome by Independent sample t-test were t-value=7.225, p-value=0.0005<0.01 which shows highly statistical significance difference at $p < 0.01$ level.
- The DBP between Metabolic syndrome by Independent sample t-test were t-value=2.950, p-value=0.0005<0.01 which shows highly statistical significance difference at $p < 0.01$ level.
- The FPG between Metabolic syndrome by Independent sample t-test were t-value=31.535, p-value=0.0005<0.01 which shows highly statistical significance difference at $p < 0.01$ level.

DISCUSSION

DISCUSSION

The main finding of the present study was the identification of a close association between MS, defined in accordance with NCEP-ATPIII criteria, and some indices of preclinical cardiac, renal and retinal damage. With regard to echocardiographic parameters, hypertensive patients with MS exhibited increased prevalence of left ventricular hypertrophy.

In the Strong Heart Study, a longitudinal investigation conducted in American Indian com- munities, a subset of the study population, including 1436 non-diabetic participants without prevalent cardiovascular disease (61.2% of which had high BP), was examined to analyse the impact of the MS on cardiac structure and function. Subjects with MS showed greater LV dimension, mass and relative wall thickness, and left atrial diameter, and a higher prevalence of LV hypertrophy, with lower mid-wall shortening than those who did not have MS .Cuspidi et al. , in 447 untreated middle-aged hypertensives, found that patients with MS had a more pronounced cardiac and extra-cardiac involvement than those without it.

Our paper, being a clinical study with a cross- sectional design, only permits us to make hypotheses

about the association of MS with cardiac hyper- trophy. For example, the latter might be explained by insulin resistance and the accompanying compensatory hyperinsulinemia, which are regarded as the pathophysiological key features underlying the MS [1]. Trophic effects of insulin on myocardial tissue have

been demonstrated in cell cultures and animal models and could be mediated, at least in part, by the insulin-like growth factor-1 receptors. However, the in vivo studies that have sought an association between insulin and LV mass have yielded conflicting results.

Moreover, insulin may affect LV mass indirectly by increasing sodium retention or endo- thelin-1 levels or by inducing sympathetic activation . Other potential biological mediators of LV hypertrophy in subjects with MS may be certain peptide hormones, secreted from white adipose tissue, such as angiotensin II, a potent growth factor in myocardial tissue [35], and leptin, whose mitogenic effect in cardiomyocytes has been recently evaluated with discrepant conclusions .

There are other important findings from our study that deserve a special mention: higher prevalence of albuminuria, observed in hypertensive subjects with MS in comparison with those without it. These results are in keeping with a recent cross-sectional evaluation of the Third National Health and Nutrition Examination Survey data in 5360 US civilian non-institutionalized sub- jects, in which a close association was found between microalbuminuria and MS (defined according to NCEP-ATPIII criteria) . In the same study, as well as in ours, the main predictors of microalbuminuria were blood pressure and glucose levels.

The relationship between AER and MS is so close that WHO recommendations include microalbuminuria amongst the criteria for diagnosing MS . Indeed, the inclusion of microalbuminuria as part of the MS has been controversial because its association with insulin resistance has been described in several , but not all, reports . Glomerular hyper filtration, expressed by an increased creatinine clearance rate, is a functional renal change that precedes glomerulosclerosis ; it is associated with obesity and with insulin resistance

Several studies showed that the MS confers an increased risk of cardiovascular morbidity and mortality . Recently it has been demonstrated that the adverse prognostic impact of MS may also be extended to hypertensive patients . Indeed, in the Progetto Ipertensione Umbria Moni- toraggio Ambulatoriale study, a prospective observational investigation of Italian adult subjects with essential hypertension, those patients with this syndrome (34% of the whole population), defined in accordance with NCEP-ATPIII criteria, ran an increased risk of developing cardiac and cerebrovascular events. The risk was attenuated but still significant amongst participants without diabetes mellitus.

It is likely that the enhanced cardiovascular risk associated with MS may be partly mediated through an increased prevalence of preclinical cardiovascular and renal changes in patients with essential hyper- tension and MS. Indeed, preclinical cardiac and renal abnormalities, such as LV hypertrophy and microalbuminuria, are recognized as significant independent predictors of adverse cardiovascular outcomes.

Another finding from our study merits a comment, this being the increased prevalence of grade I and grade II hypertensive retinopathy observed in subjects with MS when compared with persons without MS. This result is consistent with a recent cross-sectional investigation involving 11 265 participants in the Atherosclerosis Risk in Communities Study, in which associations were noted between MS and arteriovenous nicking, focal arteriolar narrowing and generalized arteriolar narrowing, even in people without diabetes or hypertension . However the prognostic significance of this finding is unclear, because the studies exploring the association between the first two degrees of hypertensive retinopathy and cardiovascular outcomes have shown inconsistent results Some other aspects of our paper need to be discussed.

In conclusion, MS seems to amplify hypertension- related cardiac and renal changes, over and above the potential contribution of each single component of this syndrome.

CONCLUSION

CONCLUSION

Prevalence of metabolic syndrome is very high in our society which goes unnoticed. Metabolic syndrome seems to amplify hypertension- related cardiac and renal changes, over and above the potential contribution of each single component of this syndrome. From the study, it is evident that prevalence of left ventricular hypertrophy, albuminuria and retinopathy is more in hypertensives with metabolic syndrome (as defined by NCEPAT 3 criteria) than those without metabolic syndrome. So rigorous follow up is needed for the cases presenting in metabolic syndrome and timely intervention is needed to halt the progression of extensive damage to vital systems .

LIMITATIONS

LIMITATIONS

- Longer follow up of the end organ damage
- Larger study size is needed for better correlation.
- Many lost to follow up
- Tedious record workup

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PROFORMA

Name

Age

Sex

I P NO:

PRESENTING COMPLAINTS

DURATION

Chest pain :

Breathlessness :

Palpitations :

Syncope :

Cough :

Haemoptysis :

Swelling of legs :

Oliguria :

Fever :

Other symptoms :

PAST HISTORY

Similar illness in the past

Diabetes mellitus

Hypertension

Coronary artery heart disease

Bronchial asthma

Jaundice

Rheumatic fever

Pulmonary tuberculosis

Transient ischaemic attacks

PERSONAL HISTORY

Smoking

Alcoholism

FAMILY HISTORY Hypertension

Diabetes mellitus

Coronary artery heart disease

CLINICAL EXAMINATION

Consciousness

Orientation

Temperature

Anaemia

Jaundice

Cyanosis

Clubbing

Pedal edema

Lymph node enlargement Jugular venous pressure

Signs of infective endocarditis Signs of liver failure

VITAL PARAMETERS

Pulse

Blood pressure

Respiratory rate

CARDIOVASCULAR SYSTEM

Heart sounds and murmurs Parasternal heave

Abnormal pulsations

RESPIRATORY SYSTEM

Respiratory rate

Breath sounds

Added sounds

ABDOMEN

Appearance

Ascites

Hepatomegaly

Spleenomegaly

CENTRAL NERVOUS SYSTEM

Higher functions

Cranial nerves Spinomotor system Sensory system Cerebellar system Spine and cranium

DIAGNOSIS :

Onset of illness Acute Chronic

Acute on chronic

INVESTIGA TIONS

Blood hemogram

Urine routine

Blood sugar

Blood urea and serum creatinine

Total Cholesterol

Serum electrolytes Electrocardiography

Chest x ray

Echocardiogram

LIVER FUNCTION TESTS

S.Bilirubin- Total

Direct

Indirect

SGOT

SGPT

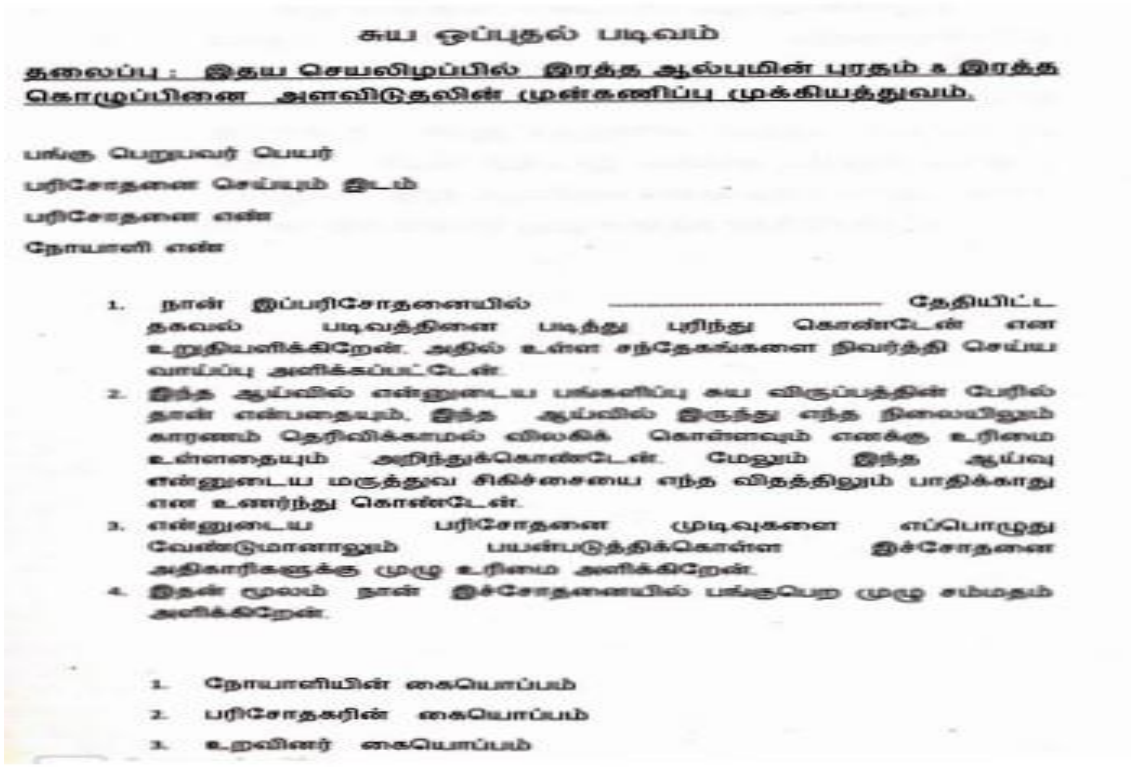
Alkaline Phosphatase

Total Proteins

Albumin

2d-echo

Fundus



சுய ஒப்புதல் படிவம்

தலைப்பு : இதய செயலிழப்பில் இரத்த ஆல்புமின் புரதம் & இரத்த கொழுப்பினை அளவிடுதலின் முன்கணிப்பு முக்கியத்துவம்.

பங்கு பெறுபவர் பெயர்
பரிசோதனை செய்யும் இடம்
பரிசோதனை எண்
நோயாளி எண்

1. நான் இப்பரிசோதனையில் _____ தேதியிட்ட தகவல் படிவத்தினை படித்து புரிந்து கொண்டேன் என உறுதியளிக்கிறேன். அதில் உள்ள சந்தேகங்களை நிவர்த்தி செய்ய வாய்ப்பு அளிக்கப்பட்டேன்.
2. இந்த ஆய்வில் என்னுடைய பங்களிப்பு சுய விருப்பத்தின் பேரில் தான் என்பதையும், இந்த ஆய்வில் இருந்து எந்த நிலையிலும் காரணம் தெரிவிக்காமல் விலகிக் கொள்ளவும் எனக்கு உரிமை உள்ளதையும் அறிந்துக்கொண்டேன். மேலும் இந்த ஆய்வு என்னுடைய மருத்துவ சிகிச்சையை எந்த விதத்திலும் பாதிக்காது என உணர்ந்து கொண்டேன்.
3. என்னுடைய பரிசோதனை முடிவுகளை எப்பொழுது வேண்டுமானாலும் பயன்படுத்திக்கொள்ள இச்சோதனை அதிகாரிகளுக்கு முழு உரிமை அளிக்கிறேன்.
4. இதன் மூலம் நான் இச்சோதனையில் பங்குபெற முழு சம்மதம் அளிக்கிறேன்.

1. நோயாளியின் கையொப்பம்
2. பரிசோதகரின் கையொப்பம்
3. உறவினர் கையொப்பம்

திருச்சி கி.ஆ.பெ விசுவநாதம் மருத்துவக்கல்லூரி மற்றும் மகாத்மா காந்தி நினைவு மருத்துவமனையில் சிகிச்சைக்காக அனுமதிக்கப்பட்டுள்ளேன். மருத்துவ சிகிச்சை உயர்நிலை பயிற்சி படிப்பில் பயிலும் மருத்துவர் அவர்களின் ஆய்வினால் எனது உடலுக்கோ மருத்துவ முறையிலோ எந்தவித பாதிப்பும் ஏற்படாது என்பதை எடுத்துக் கூறினார். மருத்துவர் இந்த ஆய்வினை செய்து பதிவு செய்து கொள்ள என் சுய நினைவோடு முழு சம்மதம் தெரிவிக்கிறேன்.

GOVERNMENT KILPAUK MEDICAL COLLEGE,

INSTITUTIONAL ETHICS COMMITTEE

Reg.No. ECR/1385/Inst/TN/2020

CERTIFICATE OF APPROVAL

IEC PROTOCOL NO	: 720/2022
TITLE OF THE STUDY	: ASSESSMENT OF END ORGAN DAMAGE IN YOUNG HYPERTENSIVE FEMALE PATIENTS WITH AND WITHOUT METABOLIC SYNDROME A COMAPARATIVE CROSS SECTIONAL STUDY AT A TERTIARY CARE HOSPITAL IN CHENNAI
PRINCIPAL INVESTIGATOR	: DR. ASWATHY T MENON
DESIGNATION	: 2ND YEAR POST GRADUATE
DEPARTMENT:	: DEPT OF GENERAL MEDICINE GOVT. KILPAUK MEDICAL COLLEGE, CHENNAI-10.

The request for an approval from the Institutional Ethics Committee (IEC) was considered on the IEC meeting held on 08/04/2022 at Government Kilpauk Medical College, Chennai-10.

The members of the Committee, the secretary and the Chairman are pleased to inform that the proposed work mentioned above, submitted by the principal Investigator is **APPROVED.**

The Principal Investigator and their team are directed to adhere to the guidelines given below:

1) You should inform the IEC in case of changes in study procedure, site, Investigator, Investigation, Guide or any other changes.
2) You should not deviate from the area of the work for which you applied for Ethical Clearance.
3) You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4) You should abide to the rules and regulations of the Institution(s)
5) You should complete the work within the specific period and if any extension of time is required, you should apply for permission again and do the work.
6) You should submit the summary of the work to the Ethical Committee on completion of the work.

MEMBER SECRETARY

Institutional Ethics Committee,
Kilpauk Medical College, Chennai.

Member Secretary
Institutional Ethics Committee,
Govt. Kilpauk Medical College,
Chennai - 6[illegible]0

DME(OSD)/DEAN

Kilpauk Medical College,
Chennai.

NAME		AGE	SEX	WAIST	S.TRIGLY	HDL	BP	FPG	MET.SYN	ECHO-LVHU.ALB		dipstick	RETINOPATHY		grade
SATHYA		26	F	96	115	40	140/90	160	YES	yes	yes	1+	yes		1
RAGINI		34	F	97	156	46	144/92	123	YES	yes	no	nil	yes		1
MAHESWARI		25	F	88	186	45	140/88	145	YES	yes	no	nil	no		nil
AAHA		40	F	89	196	36	140/90	156	YES	yes	yes	2+	yes		2
RUKMANI		39	F	99	145	42	150/90	123	YES	yes	yes	1+	yes		1
RAMYA		21	F	97	156	41	150/90	102	YES	yes	yes	1+	yes		1
SULOCHANA		30	F	102	158	39	152/80	200	YES	yes	no	nil	no		nil
NITHYA		35	F	89	163	46	160/86	211	YES	yes	yes	1+	yes		3
LAKSMI		31	F	90	169	41	160/90	165	YES	no	no	nil	yes		2
ROHINI		29	F	96	186	40	162/88	103	YES	yes	no	nil	yes		1
MARY		30	F	92	194	45	150/80	114	YES	yes	yes	2+	no		nil
VIJAYA		34	F	91	165	49	190/90	165	YES	yes	yes	trace	yes		3
MUTHULAKSHMI		39	F	98	168	48	180/90	129	YES	yes	yes	2+	yes		1

VEENA		36	F	97	167	38	160/90	185	YES	yes	no	nil	yes		1
RAMYA L		22	F	89	182	46	150/86	175	YES	yes	yes	1+	no		nil
KOKILA		32	F	88	186	45	162/84	158	YES	yes	no	nil	yes		1
MEENA		26	F	88	197	39	138/90	102	YES	yes	no	nil	yes		1
MEENAMMAL		35	F	100	163	42	140/90	123	YES	yes	yes	trace	yes		2
MARY		39	F	102	186	40	140/90	120	YES	no	yes	1+	no		nil
VASANTHA		31	F	106	196	44	140/92	130	YES	yes	yes	1+	yes		1
MARIYA		29	F	95	134	41	150/90	145	YES	yes	no	nil	yes		2
JAYASEELAM		34	F	94	196	35	138/90	162	YES	yes	yes	2+	yes		2
CHELLAMMAL		30	F	91	178	39	140/88	102	YES	yes	no	nil	no		nil
PONNI		30	F	92	164	42	150/86	120	YES	yes	no	nil	yes		1
RENUKA		36	F	93	185	46	146/90	140	YES	yes	yes	1+	yes		1
NAGAMMA		34	F	99	175	35	150/90	162	YES	yes	no	nil	yes		1
AADHIKA		29	F	98	164	40	140/90	132	YES	no	no	nil	no		nil
ARDRA		25	F	100	195	41	140/90	152	YES	yes	yes	1+	yes		2
AHAANA		34	F	88	154	46	138/90	120	YES	no	yes	1+	yes		1
GANGA		3	F	89	157	4	14	1	YES	yes	y	2	yes		1

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MALINI		23	F	88	196	41	140/92	112	YES	no	no	nil	no		nil
KALYANI		27	F	88	152	40	150/90	114	YES	yes	yes	1+	yes		2
USHA		39	F	96	153	37	142/92	132	YES	no	no	nil	yes		1
ANANDHI		32	F	97	198	39	150/92	162	YES	yes	no	nil	yes		2
KAMALA		26	F	92	178	46	150/90	130	YES	yes	yes	trace	no		nil
ANANTHA PRIYA		35	F	97	162	41	150/90	142	YES	no	yes	1+	yes		1
REKHA		34	F	91	154	45	140/92	120	YES	yes	yes	1+	yes		1
PRIYA		31	F	90	158	48	150/88	130	YES	no	no	nil	yes		1
SUHASINI		39	F	92	134	40	140/90	152	YES	yes	yes	2+	no		nil
REKKAMMA		40	F	93	164	41	150/88	162	YES	no	no	nil	yes		2
SUBHASHINI		26	F	96	168	46	162/62	102	YES	yes	no	nil	yes		2
MRITHULA		39	F	95	179	42	160/90	130	YES	no	yes	1+	yes		1
NAMITHA		32	F	88	198	46	150/90	150	YES	yes	yes	trace	no		nil
AMALA		32	F	95	182	48	140/90	126	YES	yes	yes	trace	yes		1
ARATHIBENNY		34	F	89	165	42	150/88	142	YES	no	no	nil	yes		1
AKHILA		35	F	97	168	39	152/8	10	YES	yes	ye	1+	yes		2

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ANU		35	F	90	169	38	150/80	152	YES	no	no	nil	no		nil
REMYA		39	F	91	182	37	139/90	103	YES	yes	no	nil	yes		3
RADHA		20	F	93	179	43	138/90	124	YES	no	yes	1+	yes		2
AKASHINI		40	F	90	175	46	140/90	102	YES	yes	no	nil	yes		1
ANURADHA		29	F	88	176	40	140/88	112	YES	no	no	nil	no		nil
TAMIL		36	F	92	184	44	140/90	132	YES	yes	yes	trace	yes		1
KOKILA		31	F	88	189	42	150/92	140	YES	yes	yes	1+	yes		2
YAZHINI		39	F	89	168	45	150/86	160	YES	no	yes	2+	yes		1
SWETHA		36	F	92	169	41	152/80	130	YES	yes	no	nil	no		nil
ROHINI		34	F	93	178	40	150/80	152	YES	no	yes	1+	yes		1
ASWATHY		34	F	94	195	43	150/92	155	YES	yes	no	nil	yes		1
AAMBAL		33	F	92	198	41	142/90	122	YES	no	no	nil	yes		2
BHAVIKA		31	F	95	149	43	150/92	140	YES	yes	yes	1+	no		nil
GITHA		39	F	92	165	40	160/86	114	YES	no	yes	2+	yes		3
BHANUPRIYA		39	F	86	185	45	162/62	120	YES	yes	yes	trace	yes		2
RITHYA		30	F	83	164	46	150/90	130	YES	yes	no	nil	yes		1

LALITHA		37	F	92	185	42	140/90	145	YES	no	yes	1+	no		nil
KOLAM		39	F	91	175	42	150/92	125	YES	yes	no	nil	yes		2
LAYA		34	F	96	192	41	144/92	175	YES	no	yes	1+	yes		1
JAYASEELAM		30	F	98	183	49	150/92	163	YES	yes	yes	1+	yes		1
JYOTI		35	F	93	175	46	160/86	149	YES	no	no	nil	no		nil
VARALAKSHMI		34	F	92	165	38	150/92	125	YES	yes	yes	2+	yes		2
INIYA		39	F	91	186	37	162/84	106	YES	no	yes	1+	yes		1
AAHNA		34	F	90	194	42	142/90	124	YES	yes	no	nil	yes		2
BHAIRAVI		29	F	96	164	36	154/88	112	YES	yes	yes	1+	no		nil
AAMAL		39	F	89	197	43	152/88	140	YES	no	yes	2+	yes		1
CHITRA		36	F	88	164	40	150/90	160	YES	yes	no	nil	yes		2
KAVERI		31	F	89	195	36	150/80	152	YES	no	yes	1+	yes		1
HARITA		26	F	92	178	32	150/88	175	YES	yes	yes	1+	no		nil
SAYURI		30	F	89	154	30	140/90	200	YES	no	no	nil	yes		1
ELA		39	F	92	165	46	142/92	245	YES	yes	yes	1+	yes		2
DRITI		35	F	92	185	48	152/80	130	YES	no	yes	2+	yes		3
EZHIL		3	F	93	175	4	16	1	YES	yes	n	ni	no		nil

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ELAKIYA		31	F	95	196	46	152/88	100	YES	yes	yes	1+	yes		1
DEEPTHI		35	F	94	157	40	142/90	123	YES	no	yes	1+	yes		2
KRITHIKA		32	F	96	156	42	152/88	152	YES	yes	no	nil	yes		1
SARO		34	F	85	164	41	142/92	145	YES	no	yes	2+	no		nil
ALAKA		27	F	96	194	47	136/80	175	YES	yes	yes	2+	yes		2
PADMINI		31	F	82	185	49	136/80	162	YES	no	no	nil	yes		1
CHELLAMMAL		39	F	93	196	35	130/90	130	YES	yes	yes	1+	yes		1
HIMAJA		34	F	86	197	39	139/90	155	YES	no	yes	1+	no		nil
GITANJALI		35	F	92	165	37	150/86	140	YES	yes	no	nil	yes		1
GAYATHRI		39	F	91	168	42	140/90	130	YES	yes	yes	trace	no		nil
DIANA		29	F	90	175	42	146/90	145	YES	no	yes	trace	yes		2
ARATHIBENNY		40	F	89	179	46	140/88	162	YES	yes	no	nil	yes		2
VINEETHA		35	F	88	165	43	150/88	130	YES	no	yes	1+	yes		2
ARATHIBENNY		32	F	96	194	41	152/88	145	YES	yes	yes	1+	no		nil
HIMAJA		31	F	92	162	39	160/86	162	YES	no	no	nil	yes		1
SHILPA		30	F	91	157	35	152/8	18	YES	yes	ye	1+	no		nil

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RAHEEMA		37	F	97	169	34	142/92	150	YES	no	yes	2+	yes		2
ELAKYA		32	F	94	185	45	148/92	165	YES	yes	no	nil	no		nil
MADHI		29	F	97	194	42	148/94	145	YES	yes	yes	1+	yes		1
JYOTIBALA		31	F	92	164	40	138/96	162	YES	no	yes	1+	yes		3
IYALISAI		39	F	96	158	41	130/92	175	YES	yes	no	nil	yes		2
ISHVA		34	F	93	175	43	138/90	165	YES	no	yes	trace	no		nil
DRITI		39	F	92	172	46	140/92	198	YES	yes	yes	1+	yes		1
ARSHIA		36	F	91	176	39	152/80	132	YES	no	no	nil	no		nil
AADHYA		39	F	90	193	37	154/88	147	YES	yes	yes	1+	yes		2
EZHILARASI		32	F	97	188	36	140/88	156	YES	no	yes	1+	no		nil
AVISHAKA		34	F	89	164	46	150/88	152	YES	yes	no	nil	yes		1
ANSHULA		39	F	92	196	42	160/86	142	YES	yes	yes	2+	yes		3
BHAIRAVI		36	F	91	178	40	150/90	136	YES	no	yes	1+	yes		2
AKSHARA		39	F	91	168	43	142/92	125	YES	yes	no	nil	no		nil
BHAVIKA		33	F	90	175	41	146/90	145	YES	no	yes	1+	yes		1
AKSHAYA		32	F	92	195	46	146/90	135	YES	yes	yes	2+	no		nil

SANJU		34	F	96	176	42	150/88	125	YES	no	no	nil	yes		1
ESWARI		39	F	89	183	49	154/88	196	YES	yes	yes	1+	no		nil
DWANI		37	F	91	175	46	140/88	154	YES	no	yes	1+	yes		1
SAADHIKA		37	F	90	196	43	144/92	128	YES	yes	no	nil	yes		2
UDITI		32	F	98	185	40	148/64	135	YES	yes	yes	trace	yes		3
YAMINI		30	F	89	172	41	152/94	135	YES	no	yes	1+	no		nil
VAIBHAVI		39	F	88	195	43	150/90	162	YES	yes	no	nil	yes		2
REMYA		39	F	92	176	46	134/62	120	YES	no	yes	1+	no		nil
AMBUJAM		36	F	86	156	45	142/92	152	YES	yes	yes	1+	yes		1
ALAKA		35	F	86	168	40	136/88	230	YES	no	no	nil	no		nil
GEETHA		37	F	89	198	43	152/88	166	YES	yes	yes	1+	yes		3
ANJALI		32	F	85	169	42	142/90	175	YES	no	yes	trace	yes		2
HITA		30	F	97	165	41	162/88	130	YES	yes	no	nil	yes		1
GIRIJA		39	F	88	152	40	148/64	145	YES	yes	yes	1+	no		nil
HIBHA		37	F	89	167	49	160/86	122	YES	no	yes	2+	yes		3
GEETIKA		34	F	86	196	42	130/90	160	YES	yes	no	nil	no		nil
DEESHA		3	F	89	154	4	15	2	YES	no	y	tr	yes		2

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DWANI		39	F	99	153	46	150/90	204	YES	yes	yes	1+	no		nil
BHANUPRIYA		30	F	96	154	42	130/80	152	YES	no	no	nil	yes		1
ANANYA		36	F	91	168	41	136/86	162	YES	yes	yes	1+	yes		2
DHWANI		35	F	92	162	40	138/84	132	YES	no	yes	1+	yes		1
ANASUYA		37	F	95	164	43	130/80	145	YES	yes	no	nil	no		nil
SANGEETHA		32	F	93	193	46	140/90	165	YES	yes	yes	trace	yes		2
VEENA		37	F	98	172	45	165/90	175	YES	no	yes	2+	no		nil
VENILLA		34	F	98	171	49	140/90	125	YES	yes	no	nil	yes		2
SUPRIYA		35	F	96	168	42	150/92	135	YES	no	yes	1+	no		nil
NILA		39	F	89	164	40	136/80	135	YES	yes	yes	1+	yes		1
URMILA		32	F	90	161	41	142/92	148	YES	no	no	nil	yes		2
YAAZHINI		34	F	92	153	46	140/88	149	YES	yes	yes	1+	yes		1
EZHILARASI		34	F	91	167	39	146/90	150	YES	no	yes	trace	no		nil
AMMULU		37	F	94	162	35	136/86	148	YES	yes	no	nil	yes		2
DORA		39	F	92	154	38	138/84	149	YES	yes	yes	2+	no		nil
KUTTI		30	F	97	153	42	134/6	15	YES	no	ye	2+	yes		1

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DEVAKI		36	F	93	164	46	142/90	148	YES	yes	no	nil	no		nil
RADHA		35	F	89	196	40	136/86	149	YES	no	yes	1+	yes		1
THANGAM		34	F	90	185	41	144/92	150	YES	yes	yes	1+	yes		2
CHAITHANYA		30	F	88	164	46	152/80	148	YES	no	no	nil	yes		3
LAKSHMI		39	F	88	164	41	146/90	149	YES	yes	yes	2+	no		nil
ALPHONSO		35	F	89	162	40	162/88	150	YES	no	yes	trace	yes		1
DURGA		32	F	90	182	48	152/94	148	YES	yes	no	nil	no		nil
AADAB		32	F	92	169	42	144/92	149	YES	yes	yes	1+	yes		2
GLORY		37	F	97	176	46	140/90	150	YES	no	yes	1+	no		nil
SULU		39	F	98	192	49	146/90	148	YES	yes	no	nil	yes		3
RATHNAM		30	F	88	182	35	130/90	149	YES	no	yes	1+	yes		3
SANVIKA		36	F	85	194	39	140/90	150	YES	yes	yes	2+	yes		2
SHAILAJA		35	F	90	173	46	142/90	151	YES	no	no	nil	no		nil
AGNES		32	F	88	182	42	152/80	152	YES	yes	yes	1+	yes		3
SANGAVI		39	F	89	164	41	162/62	153	YES	no	yes	1+	no		nil
VISHAKA		36	F	89	198	40	162/88	154	YES	yes	yes	1+	yes		1

MERLIN		32	F	92	178	43	140/92	155	YES	yes	no	nil	no		nil
VEENA		34	F	91	193	48	140/92	156	YES	no	yes	nil	yes		1
ASHITHA		36	F	95	159	38	130/92	157	YES	yes	yes	2+	yes		3
RIYA		39	F	102	182	35	152/88	158	YES	no	yes	trace	yes		2
MARIYA		30	F	88	173	46	136/88	159	YES	yes	no	nil	no		nil
MUTHULAKSHMI		36	F	96	162	41	138/90	160	YES	no	yes	1+	yes		3
PATTU		34	F	97	175	40	130/90	161	YES	yes	no	nil	no		nil
KUTTI		36	F	86	167	43	130/90	162	YES	no	no	nil	yes		2
CHITTU		36	F	90	196	49	130/90	163	YES	yes	yes	1+	no		nil
KANNU		39	F	87	145	48	140/88	164	NO	no	no	nil	no		nil
AMMULU		30	F	86	117	40	130/80	84	NO	no	no	nil	no		nil
URMIKA		36	F	85	142	42	134/62	79	NO	yes	no	nil	no		nil
VANI		35	F	88	135	56	110/70	90	NO	no	no	nil	yes		1
SHANTHI		32	F	84	138	52	150/86	86	NO	no	yes	2+	no		nil
VENBA		33	F	86	128	54	142/90	89	NO	yes	no	nil	no		nil
ROJA		33	F	84	136	53	160/86	91	NO	no	no	nil	no		nil
SAYURI		3	F	85	149	5	15	9	NO	no	n	ni	no		nil

		5				6	0/86	2			o	l		
RAGHAVI		39	F	87	125	62	160/92	94	NO	yes	no	nil	yes	1
REKHA		33	F	82	129	51	142/56	96	NO	no	yes	1+	no	nil
NILA		32	F	83	148	63	160/90	98	NO	no	no	nil	no	nil
USHA		35	F	79	124	52	142/80	99	NO	yes	no	nil	no	nil
RAJA		34	F	79	124	50	140/86	75	NO	no	no	nil	no	nil
KALYANI		33	F	85	142	54	140/90	76	NO	no	no	nil	yes	1
PRIYAVEMBU		31	F	82	136	52	136/90	77	NO	yes	yes	trace	no	nil
RIYA		29	F	83	128	56	142/90	78	NO	no	no	nil	no	nil
DURGA		29	F	84	114	58	140/84	79	NO	no	no	nil	no	nil
BABY		39	F	86	100	59	130/80	80	NO	yes	no	nil	no	nil
DARSHANA		37	F	87	129	54	140/92	81	NO	no	no	nil	yes	1
HARINI		30	F	82	103	55	150/90	82	NO	no	yes	1+	no	nil
NIMMY		34	F	79	105	62	136/86	83	NO	yes	no	nil	no	nil
JOSE		31	F	85	108	61	130/80	75	NO	no	no	nil	no	nil
KIRAN		36	F	86	136	53	140/90	76	NO	no	no	nil	no	nil
MAYURI		37	F	87	142	58	140/9	77	NO	yes	no	nil	yes	1

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SEETHA		39	F	79	102	50	126/80	78	NO	no	yes	1+	no		nil
NIKITA		35	F	87	120	54	142/80	79	NO	no	no	nil	no		nil
THANGAM		32	F	85	140	53	140/92	75	NO	yes	no	nil	no		nil
SANJEEVI		31	F	84	160	51	142/56	75	NO	no	no	nil	no		nil
RISHITHA		37	F	81	145	52	110/80	75	NO	no	no	nil	yes		1
GOWSHIKA		35	F	83	129	58	136/80	76	NO	yes	yes	1+	no		nil
MITHILA		37	F	86	123	56	134/62	77	NO	no	no	nil	no		nil
NARMADHA		30	F	85	135	59	150/90	78	NO	no	no	nil	no		nil
PRISCLY		31	F	84	136	52	152/88	79	NO	yes	no	nil	no		nil
SASIKALA		36	F	85	148	56	136/80	80	NO	no	no	nil	yes		2
PRIYA		32	F	86	126	59	110/80	81	NO	no	yes	trace	no		nil
SANJITHA		34	F	82	114	69	136/86	76	NO	yes	no	nil	no		nil
POORNI		36	F	79	128	64	152/94	77	NO	no	no	nil	no		nil
SULEKHA		39	F	89	106	62	110/80	78	NO	no	no	nil	no		nil
JAYA		34	F	84	106	61	160/92	75	NO	yes	no	nil	yes		1
SWATITHRA		31	F	86	102	63	162/88	76	NO	no	yes	trace	no		nil

EZHIL		32	F	82	112	60	152/88	77	NO	no	no	nil	no		nil
SUMAN		33	F	84	114	52	160/90	78	NO	yes	no	nil	no		nil
VIVEKA		33	F	85	135	53	160/90	79	NO	no	no	nil	no		nil
THANGAM		35	F	86	129	58	140/90	80	NO	no	no	nil	yes		1
SHRUTHI		29	F	82	127	59	152/94	81	NO	yes	yes	trace	no		nil
SHREKHA		26	F	83	105	56	134/62	82	NO	no	no	nil	no		nil
NIVEDHA SUBHASREE		39	F	86	116	52	130/90	83	NO	no	no	nil	no		nil
SREE		32	F	84	119	54	134/62	84	NO	yes	no	nil	yes		2
LAKSHMI		39	F	87	108	53	136/80	85	NO	no	no	nil	no		nil
RITHIKA		35	F	82	135	58	140/88	86	NO	no	yes	1+	no		nil
MARY		33	F	86	134	50	152/80	85	NO	yes	no	nil	no		nil
JANSI		36	F	84	128	52	136/86	85	NO	no	no	nil	yes		1
RANI		34	F	82	106	59	140/88	84	NO	no	no	nil	no		nil
ALIYA		31	F	81	107	56	152/94	83	NO	yes	no	nil	no		nil
AFNA		32	F	83	124	51	160/86	83	NO	no	yes	trace	no		nil
AISHU		36	F	82	136	62	140/90	82	NO	no	no	nil	yes		1
RANI		3	F	86	145	6	14	8	NO	yes	n	ni	no		nil

		2				3	2/56	1			o	l			
RATHNAM		33	F	85	149	60	134/62	81	NO	no	yes	1+	no		nil
AISWARYA		39	F	84	103	54	152/94	80	NO	no	no	nil	no		nil
ALIYA		36	F	82	107	57	150/88	79	NO	yes	no	nil	yes		1
AISHA		34	F	83	126	58	130/92	79	NO	no	yes	trace	no		nil
CHANDRA		40	F	86	99	56	142/80	78	NO	no	no	nil	no		nil
SAI		40	F	85	120	58	142/90	77	NO	yes	no	nil	no		nil
SUPRIYA		34	F	83	135	54	136/86	77	NO	no	yes	1+	yes		1
NIRANJANA		39	F	81	139	58	140/92	76	NO	no	no	nil	no		nil
KANNI		32	F	87	140	59	152/80	75	NO	yes	no	nil	no		nil
SHYAMALA		34	F	86	110	62	142/56	74	NO	no	yes	1+	no		nil
RITHIKA		39	F	82	119	61	134/62	74	NO	no	no	nil	yes		1
NATANA		40	F	86	114	63	152/80	73	NO	yes	no	nil	no		nil
THARA		35	F	87	108	58	134/62	72	NO	no	yes	trace	no		nil
KANJANA		33	F	85	132	59	140/90	72	NO	no	no	nil	no		nil
JYOTHI		32	F	86	98	61	130/92	71	NO	yes	no	nil	yes		2
RAMYA		34	F	87	135	57	140/9	70	NO	no	ye	1+	no		nil

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RAHEEMA		31	F	82	136	63	150/92	70	NO	no	no	nil	no		nil
JAYA		35	F	81	142	59	140/90	69	NO	yes	no	nil	no		nil
HARINI		36	F	86	147	52	140/90	68	NO	no	yes	1+	yes		1
LEKSHMI		35	F	82	129	54	150/88	68	NO	no	no	nil	no		nil
REVATHI		39	F	83	102	59	162/62	67	NO	yes	no	nil	no		nil
SULEKHA		37	F	87	124	58	130/92	66	NO	no	yes	trace	no		nil
SHRUTHY		37	F	85	124	58	152/88	66	NO	no	no	nil	yes		1
NAYIKA		37	F	86	102	59	140/92	65	NO	yes	no	nil	no		nil
SUNDHARI		39	F	82	109	63	162/62	85	NO	no	yes	1+	no		nil
GANILA		35	F	83	143	61	130/92	85	NO	no	no	nil	no		nil
VENILLA		32	F	86	144	64	130/80	85	NO	yes	no	nil	yes		2
SUBHASHINI		34		84	120	58	140/88	85	NO	no	yes	2+	no		nil
REKHA		36	F	87	138	59	160/86	85	NO	no	no	nil	no		nil
PRIYA		39	F	81	134	57	126/80	85	NO	yes	no	nil	no		nil
HEMA		36	F	80	129	50	140/90	85	NO	no	yes	trace	yes		1
SUJITHA		39	F	85	127	58	130/90	85	NO	no	no	nil	no		nil

NAMITHA		36	F	82	142	59	170/94	85	NO	yes	no	nil	no		nil
SAI		34	F	85	135	53	136/80	85	NO	no	yes	1+	no		nil
RANI		35	F	82	139	62	142/56	85	NO	no	no	nil	yes		2
CHITHRA		39	F	84	126	55	140/90	85	NO	yes	no	nil	no		nil
KAVYA		37	F	87	103	63	120/80	86	NO	no	yes	trace	no		nil
RUKMANI		39	F	85	100	62	140/90	87	NO	no	no	nil	no		nil
KAMALA		37	F	79	106	54	150/92	88	NO	yes	no	nil	yes		1
NITHYA		30	F	78	124	53	136/88	89	NO	no	yes	trace	no		nil
ARUHI		35	F	85	135	50	130/90	90	NO	no	no	nil	no		nil
BHAIRAVI		39	F	82	146	59	130/90	91	NO	yes	no	nil	no		nil
RANJITHAM		34	F	83	125	58	140/90	92	NO	no	yes	trace	yes		1
PONNI		39	F	86	149	56	130/92	93	NO	no	yes	1+	no		nil
KARNIKA		39	F	87	123	62	120/80	85	NO	yes	no	nil	no		nil
CHETANA		36	F	80	132	64	136/88	86	NO	no	no	nil	no		nil
KARTHIKA		37	F	84	120	63	152/80	87	NO	no	no	nil	yes		1
RAGAVI		39	F	85	106	64	136/88	88	NO	yes	yes	trace	no		nil
RAMALA		3	F	81	99	6	12	8	NO	no	y	tr	no		nil

KSHMI		9				3	0/80	9			es	ace			
SUKUMARI		35	F	87	104	67	136/88	90	NO	no	no	nil	no		nil
RATHNAM		37	F	86	107	68	140/88	91	NO	yes	no	nil	yes		1
KUMARI		34	F	82	110	62	140/90	92	NO	no	no	nil	no		nil
RAGAVI		32	F	83	123	53	140/92	93	NO	no	yes	1+	no		nil
AMALA		34	F	85	124	54	136/88	94	NO	yes	yes	1+	no		nil
BHEEMA		39	F	81	145	59	126/80	95	NO	no	no	nil	yes		1
KALKI		30	F	82	105	57	150/92	96	NO	no	no	nil	no		nil
PRIYA		37	F	87	116	50	150/88	85	NO	yes	no	nil	no		nil
AMALU		39	F	79	108	53	160/92	86	NO	no	yes	trace	no		nil
CHELLAMMAL		39	F	78	134	58	130/92	87	NO	no	yes	trace	yes		1
PONNI		33	F	76	139	56	130/90	88	NO	yes	no	nil	no		nil
ABINAYA		40		85	109	57	130/90	89	NO	no	no	nil	no		nil
AAMBAL		40	F	84	110	59	140/90	90	NO	no	no	nil	no		nil
MEENAKSHI		39	F	87	100	56	140/92	91	NO	yes	yes	1+	yes		2
RAMALAKSHMI		37	F	84	132	51	136/90	92	NO	no	yes	1+	no		nil
AKHILA		36	F	82	106	53	126/8	93	NO	no	no	nil	no		nil

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POONKULALI		39	F	83	123	58	140/86	94	NO	yes	no	nil	no		nil
VENMA		39	F	81	142	68	160/92	95	NO	no	no	nil	yes		1
KANALI		36	F	87	106	64	152/88	96	NO	no	yes	trace	no		nil
PRIYA		39	F	87	108	52	142/56	97	NO	yes	yes	trace	no		nil
JASMINE		39	F	87	109	58	130/90	98	NO	no	no	nil	no		nil
KALINI		39	F	86	124	53	130/90	98	NO	no	no	nil	yes		1
IZHAIYINI		36	F	85	142	50	130/92	98	NO	yes	no	nil	no		nil
ATHIRA		40	F	81	136	54	152/88	97	NO	no	yes	1+	no		nil
MARY		39	F	80	102	52	136/88	97	NO	no	yes	1+	no		nil
RUPA		36	F	85	135	53	162/88	85	NO	yes	no	nil	yes		1
KRISHNA		35	F	86	136	54	162/84	85	NO	no	no	nil	no		nil
SATHYA		34	F	82	142	53	150/90	85	NO	no	no	nil	no		nil
AKHILA		35	F	84	146	58	160/92	85	NO	yes	yes	trace	no		nil
MADHUBALA		39	F	83	102	56	140/92	86	NO	no	yes	trace	yes		1
VENILLA		34	F	85	125	57	152/88	87	NO	no	no	nil	no		nil
ANURADHA		32	F	87	139	56	140/90	88	NO	yes	no	nil	no		nil

VANNAMUHIL		35	F	76	142	52	140/88	89	NO	no	no	nil	no		nil
THENMOZHI		33	F	72	143	62	130/90	90	NO	no	yes	trace	yes		1
KAVI		30	F	85	139	64	130/92	91	NO	yes	yes	trace	no		nil
MANI		39	F	79	105	60	140/88	77	NO	no	no	nil	no		nil
ROMA		36	F	82	111	68	142/80	78	NO	no	no	nil	no		nil
KANMANI		35	F	86	122	64	138/84	79	NO	yes	no	nil	yes		1
MAIVIZHI CHELVI		37	F	84	129	56	110/80	80	NO	no	yes	trace	no		nil
ANGAYAR		35	F	79	136	59	150/90	81	NO	no	yes	trace	no		nil
AANDAL		40	F	78	142	52	152/80	82	NO	yes	no	nil	no		nil
MATHI		39	F	82	140	54	140/90	83	NO	no	no	nil	yes		1
EZHILARASI		30	F	80	144	54	136/88	84	NO	no	no	nil	no		nil
KANTHI		35	F	82	102	53	140/84	85	NO	yes	yes	1+	no		nil
KAYAL VILI		33	F	87	110	52	120/80	86	NO	no	yes	1+	no		nil
POOVIZHI		39	F	86	117	68	134/62	87	NO	no	no	nil	yes		2
REKHAPRIYA		36	F	79	99	62	130/92	88	NO	yes	no	nil	no		nil
SOMI		34	F	78	96	61	130/80	89	NO	no	no	nil	no		nil
NANDHIN		3	F	76	95	5	15	9	NO	no	y	1	no		nil

I		3				4	0/86	0			es	+			
SMRITHI		32	F	82	92	52	140/86	91	NO	yes	yes	1+	yes		1
CHANDRIKA		39	F	86	93	59	140/90	92	NO	no	no	nil	no		nil
DWANI		32	F	81	142	56	150/92	93	NO	no	no	nil	no		nil
SUMALATHA		39	F	82	126	54	152/88	94	NO	yes	no	nil	no		nil
RATHNAM		30	F	86	135	58	140/84	95	NO	no	yes	trace	yes		2
AANDAL		34	F	87	139	62	136/86	96	NO	no	yes	trace	no		nil
RAGJAVI		39	F	82	142	59	130/92	97	NO	yes	no	nil	no		nil
SUMA		30	F	80	136	53	130/90	98	NO	no	no	nil	no		nil
AMBIKA		30	F	83	102	50	140/88	99	NO	no	no	nil	yes		1
ANJALY		39	F	85	110	52	110/80	100	NO	yes	yes	1+	no		nil
RANI		39	F	87	120	54	130/90	77	NO	no	yes	1+	no		nil
RAMYA		39	F	82	146	53	130/90	78	NO	no	no	nil	no		nil
MARY		30	F	83	152	59	150/92	79	NO	yes	no	nil	yes		1
LOVELY		33	F	86	145	56	130/90	80	NO	no	no	nil	no		nil
GLORY		36	F	87	136	52	140/92	81	NO	no	yes	1+	no		nil
NAMITHA		37	F	81	103	50	130/9	82	NO	yes	ye	trac	no		nil

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JENNIFER		37	F	82	100	58	142/80	83	NO	no	no	nil	yes		1
AMAL		39	F	80	142	56	136/80	84	NO	no	no	nil	no		nil
RITHU		36	F	87	149	53	150/88	85	NO	yes	no	nil	no		nil
DEVI		39	F	85	122	54	120/80	86	NO	no	yes	trace	no		nil
RITHIKA		35	F	87	135	52	140/92	87	NO	no	yes	trace	yes		1
CHANDRA		34	F	85	104	59	152/88	88	NO	yes	no	nil	no		nil
GEETHA		39	F	82	106	54	130/90	89	NO	no	no	nil	no		nil
LAKSHMI		36	F	86	132	63	130/80	90	NO	no	no	nil	no		nil
RATHNAKUMARI		39	F	86	140	62	150/88	91	NO	yes	yes	trace	yes		1
PONNAMMA		36	F	87	114	51	140/90	92	NO	no	no	nil	no		nil
CHANDRIKA		37	F	87	96	53	130/90	93	NO	no	no	nil	no		nil
THANGAM		35	F	87	135	56	130/80	94	NO	yes	no	nil	no		nil
KANNU		33	F	81	143	62	120/80	95	NO	no	yes	1+	yes		1
AANDAL		33	F	82	100	60	110/80	96	NO	no	no	nil	no		nil
DARSHANA		36	F	86	135	63	150/88	97	NO	yes	yes	1+	no		nil
EZHIL		37	F	84	124	56	120/80	98	NO	no	no	nil	no		nil

HARINI		39	F	85	95	59	150/92	78	NO	no	no	nil	yes		1
REKHA		34	F	86	96	65	140/88	79	NO	yes	no	nil	no		nil
AMALA		33	F	83	125	54	126/80	80	NO	no	no	nil	no		nil
SAFA		39	F	87	142	53	130/80	81	NO	no	yes	2+	yes		1
DEVI		36	F	85	136	56	130/90	82	NO	yes	no	nil	no		nil
RASHIA		39	F	87	100	56	134/62	83	NO	no	yes	2+	no		nil
HGEETHA		36	F	83	140	62	126/80	84	NO	no	no	nil	no		nil
NISHA		33	F	86	128	63	140/90	85	NO	yes	no	nil	yes		1
RENU		35	F	84	139	54	136/86	86	NO	no	no	nil	no		nil
ANJALI		30	F	82	107	59	120/80	87	NO	no	no	nil	no		nil
ANN		40	F	86	124	58	130/90	88	NO	yes	yes	1+	no		nil
SINDHU		35	F	85	136	56	140/86	89	NO	no	no	nil	yes		1
CHANDRA		34	F	87	105	54	126/80	90	NO	no	yes	1+	no		nil
ARATHY		33	F	82	119	58	126/80	91	NO	yes	no	nil	no		nil
MALINI		32	F	83	121	52	120/80	92	NO	no	no	nil	no		nil
DEVADHARSHINI		39	F	80	114	59	140/88	93	NO	no	no	nil	yes		1
SUJATHA		3	F	79	135	5	13	9	NO	yes	n	ni	no		nil

		9				6	0/90	4			o	l			
CHANDRA		36	F	78	120	51	130/90	95	NO	no	yes	1+	no		nil
LAKSHMI		36	F	77	106	52	140/86	96	NO	no	no	nil	no		nil
SUPRIYA		34	F	85	108	56	140/90	97	NO	yes	yes	1+	yes		1
KAVYA		4O	F	86	148	57	120/80	78	NO	no	no	nil	no		nil
YOGAMBINI		39	F	85	426	52	130/90	79	NO	no	no	nil	no		nil
BBEEYATRIS		39	F	86	129	59	130/92	80	NO	yes	no	nil	no		nil
DIVYAKUMARI		30	F	82	123	53	140/92	81	NO	no	no	nil	yes		1
ASHA		34	F	82	110	54	150/92	82	NO	no	yes	1+	no		nil
DURGA		40	F	87	125	52	136/86	83	NO	yes	no	nil	no		nil
RAHEEMA		30	F	80	135	50	130/90	84	NO	no	yes	1+	no		nil
SHRUTHI		40	F	83	142	59	140/88	85	NO	no	no	nil	yes		1
REKHA		35	F	84	116	56	136/86	86	NO	yes	no	nil	no		nil
SAHANA		39	F	86	108	62	140/90	87	NO	no	no	nil	no		nil
VIDYA		35	F	87	100	63	136/88	88	NO	no	no	nil	no		nil
SHILA		36	F	82	135	60	120/80	89	NO	yes	yes	trace	yes		1
ANANDHUSHREE		39	F	84	106	54	130/9	90	NO	no	no	nil	no		nil

							0								
KOTHAI		35	F	85	122	53	126/80	91	NO	no	yes	trace	no		nil
ANJUSHA		30	F	81	149	59	140/86	92	NO	yes	no	nil	no		nil
RUMA		40	F	80	124	56	130/92	93	NO	no	no	nil	yes		1
ANURADHA		30	F	79	94	53	130/90	94	NO	no	no	nil	no		nil
PRERANA		40	F	78	130	54	150/88	95	NO	yes	no	nil	no		nil
APOORVA		40	F	82	106	59	140/90	96	NO	no	yes	trace	no		nil
APARNA		40	F	86	129	57	140/92	97	NO	no	no	nil	yes		2
BINDHYA		39	F	82	122	52	136/86	98	NO	yes	yes	trace	no		nil
NITI		39	F	79	124	53	140/92	99	NO	no	no	nil	no		nil
NIKITHA		40	F	82	134	56	152/80	78	NO	no	no	nil	no		nil
NAME		AGE	SEX	WAIST	S.TRIGLY	HDL	BP	FPG	MET.SYN	ECHO-LVHU.ALB		dipstick	RETINOPATHY		grade