A STUDY OF PREVALENCE OF METABOLIC SYNDROME IN YOUNG PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

DISSERTATION SUBMITTED FOR

M.D GENERAL MEDICINE

BRANCH – I

APRIL 2017

THE TAMILNADU

DR.M.G.R. MEDICAL UNIVERSITY

CHENNAI, TAMILNADU, INDIA

CERTIFICATE

This is to certify that the dissertation entitled "A STUDY OF PREVALENCE OF METABOLIC SYNDROME IN YOUNG PATIENTS WITH ACUTE MYOCARDIAL INFARCTION**"** is the bonafide work of **Dr. B. SURESH KUMAR** in partial fulfilment of the university regulations of the Tamil Nadu Dr.M.G.R Medical University, Chennai, for **M.D General Medicine Branch I** examination to be held in **April 2017**.

Dr.V. T. Premkumar, M.D.
Professor and HOD,
Department of General Medicine,
Government Rajaji Hospital,
Madurai Medical College,
Madurai.

Dr.R.Balajinathan, M.D.
Professor,
Department of General medicine
Government Rajaji Hospital,
Madurai Medical College,
Madurai.

Dean
Govt Rajaji Hospital,
Madurai.

DECLARATION

I **Dr.B. SURESH KUMAR,** solemnly declare that, this dissertation "A STUDY OF PREVALENCE OF METABOLIC SYNDROME IN YOUNG PATIENTS WITH ACUTE MYOCARDIAL INFARCTION" is a bonafide record of work done by me at the Department of General Medicine, Govt. Rajaji Hospital, Madurai, under the guidance of **Dr.R. BALAJINATHAN,M.D**, Professor, Department of General Medicine, Madurai Medical College, Madurai.

This dissertation is submitted to The Tamil Nadu Dr. M.G.R Medical University, Chennai in partial fulfilment of the rules and regulations for the award of **M.D Degree General Medicine Branch-I;** examination to be held in **April 2017.**

Place: Madurai

Date:

Dr.B. SURESH KUMAR

ACKNOWLEDGEMENT

I would like to thank **Dr.M.R.VAIRAMUTHU RAJU,MD ,** Dean, Madurai Medical College, for permitting me to utilize the facilities of Madurai Medical College and Government Rajaji Hospital for this dissertation.

I wish to express my respect and sincere gratitude to my beloved teacher and head of department, **Prof. Dr.V.T.PREMKUMAR,M.D.,** professor of medicine for his valuable guidance and encouragement during the study and also throughout my course period.

I would like to express my deep sense of gratitude, respect and thanks to my beloved Unit Chief and Professor of Medicine **Prof.Dr.R.BALAJINATHAN, M.D.,** for his valuable suggestions, guidance and support throughout the study and also throughout my course period.

I am greatly indebted to my beloved Professors, **Dr.V.T.PREMKUMAR, M.D., Dr.M.NATARAJAN, M.D., Dr.G.BAGHYALAKSHMI, M.D., Dr.J.SANGUMANI, M.D., Dr.C.DHARMARAJ, M.D., and Dr.R.PRABHAKARAN, M.D.** and **DR.S.RAVINDRAN,MD** for their valuable suggestions throughout the course of study.

I express my special thanks to **Dr.BALASUBRAMANIAN M.D**, **D.M**., Professor and HOD, Department of Cardiology for permitting me to utilize the facilities in the Department, for the purpose of this study and guiding me with enthusiasm throughout the study period.

I am extremely thankful to Assistant Professors of Medicine of my Unit, **Dr.V.N.ALAGAVENKATESAN,M.D**., and **Dr.P.V.BALAMURUGAN,**M**D**, for their valid comments and suggestions.

I sincerely thank all the staffs of Department of Medicine and Department of Cardiology and Department of Biochemistry for their timely help rendered to me, whenever and wherever needed.

I extend my love and express my gratitude to my family and friends for their constant support during my study period in times of need.

Finally, I thank all the patients, who form the most vital part of my work, for their extreme patience and co-operation without whom this project would have been a distant dream and I pray God, for their speedy recovery.

CONTENTS

S.NO	CONTENTS	PAGE NO
1	INTRODUCTION	1
2	AIM OF STUDY	2
3	REVIEW OF LITERATURE	3
4	MATERIALS AND METHODS	56
5	RESULTS AND INTERPRETATION	61
6	DISCUSSION	69
7	CONCLUSION	74
8	SUMMARY	75
9	ANNEXURES	
	BIBLIOGRAPHY PROFORMA ABBREVATIONS MASTER CHART ETHICAL COMMITTEE APPROVAL LETTER ANTI PLAGIARISM CERTIFICATE	

Introduction

Coronary artery disease (CAD) is one of the commonest causes of death in developing and developed world. Metabolic syndrome has become a major public health problem. Globally the prevalence of metabolic syndrome is increasing. The metabolic syndrome is a group of risk factors for cardiovascular disease and diabetes mellitus. It includes abdominal obesity, dyslipidemia, raised blood pressure, insulin resistance, and an inflammatory state. Metabolic syndrome is present in nearly one quarter of all adults and in 40% of adults over 60 years of age. It is now recognised as a secondary target for intervention in the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III recommendation. Most studies show that 4–10% of patients with acute myocardial infarction (AMI) are below 45 years of age. There are limited data on the risks associated with the metabolic syndrome in the increasingly large group of young patients who have sustained an AMI. The aim of this study, therefore, is to assess the prevalence of the metabolic syndrome in young patients with AMI, by using the IDF definitions.

AIM OF THE STUDY

1. To study the prevalence of metabolic syndrome in young patients with acute myocardial infarction.
2. To find the prevalence of individual components of metabolic syndrome in the study population.

REVIEW OF LITERATURE

The metabolic syndrome also called as syndrome X is a collection of metabolic abnormalities that confer a person with it to high danger of cardiovascular disease and diabetes.

PREVALENCE OF THE METABOLIC SYNDROME

The metabolic syndrome is increasing in prevalence as result of rapid urbanisation. In Sub-Saharan Africa, a study done by International Diabetes Federation to diagnose metabolic syndrome, found the low prevalence of metabolic syndrome in rural population compared with a higher prevalence in urban population. Equally, using ATP III definition of metabolic syndrome, there was significant absence of the metabolic syndrome in rural men and rural women, and very low prevalence of MS in urban men (0.5%) and in urban women (0.2%). Higher rates were found when the WHO criteria are used, being 1.8% (rural) and (5.9%) urban women and 1.9% (rural) 7.3 % (urban) men.

With any of both the criteria's i.e. WHO and IDF, urban rates were higher, both in women and men compared to rural rates. The reason for the lower occurrence of metabolic syndrome in rural areas was the high level of physical activity in Saharan African countries.

Analysing the prevalence of individual risk factors in Sub-Saharan Africa revealed that, the elevated serum triglyceride was the least frequent for both women (0.3%) and men (1.4 %). The most common abnormality was hypertension.

In a study done among Zimbabwe in type 2 diabetic patients, to determine the prevalence of Metabolic syndrome revealed that 43% of the patients had metabolic syndrome.

Metabolic syndrome was also seen in 25.2% of type 2 diabetic patients in Nigeria. However the systemic hypertension was found to be the commonest component of metabolic syndrome by 38.5%. This study concluded that metabolic syndrome is associated with very high risk of stroke, peripheral vascular disease and microalbuminuria and kidney disease.

In a study conducted in Eastern India by D.S. Prasad et al, the prevalence rates of MS were 33.5% of which 24.9 % were males and 42.3% were females.

In another study conducted by Gupta R et al, MS was present in 31.6% subjects overall ; among which men contributed 22.9% and women about 39.9%.

THE RISK FACTORS FOR METABOLIC SYNDROME

I. Overweight and Obesity

Obesity is an important risk factor for both metabolic syndrome and coronary artery disease. Majority of patients with CAD are obese. Severity of CAD is higher among obese individuals when compared to non obese individuals. Obesity is a cumulative risk factor for diabetes, CAD, hypertension and lipid abnormalities.

II. Physical inactivity

Physical inactivity is one of paramount risk factors for the development of metabolic syndrome. Physical inactivity is an essential contributing factor for obesity, hypertension, and hyper-lipidaemia. Physical activity is an important interventional component, in terms of treatment and prevention of MS.

III. Aging and sex

As the age increases, the prevalence of metabolic syndrome also increases. Metabolic syndrome is present in nearly half of the US population over the age of 50years. After 60years the incidence is more in women than men.

IV. Glucose intolerance

A large proportion of men with type 2 diabetes will have MS. Hypo-adiponectinemia increases insulin resistance and is an important risk factor for development of metabolic syndrome.

V. Dyslipidemia

Dyslipidemia comprises of greatly elevated level triglyceride levels , lower concentration of HDL cholesterol and higher levels of small and dense LDL. This abnormality of lipids leads to a insulin resistance, which predisposes a person to develop CVD. Lower HDL-C and higher levels of triglycerides are the constituents which are included in the various definitions of metabolic syndrome.

VI. Lipodystrophy

Lipodystrophic disorders are associated with the metabolic syndrome. Both genetic syndromes (e.g., Berardinelli-Seip congenital lipodystrophy & Dunnigan familial partial lipodystrophy) and acquired causes (e.g., HIV-related lipodystrophy in patients treated withHAART) forms of lipodystrophy can lead to severe insulin resistance and metabolic syndrome.

VII. Smoking

Smoking is a significant risk factor for the progression of coronary heart disease (CHD). Smoking incites insulin resistance. Insulin resistance is the underlying metabolic abnormality for the development of metabolic syndrome.

Smoking leads to increase in the levels of hormones which counter the effects of insulin. GH, adrenaline is some mediators of this action.

The process of how cigarette smoking causes MS is not yet clear.

Fat oxidation controls the body adipose stores. Smoking increases the oxidation of FFA. So, upon smoking cessation the rate of fatty acid oxidation decreases which may lead to weight gain and development of MS. This can be prevented by decreasing the caloric consumption.

Constituents of Metabolic Syndrome

The constituents of syndrome X are:

- Visceral adiposity
- Dyslipidemia
- Systemic hypertension
- Insulin resistance
- Increased waist circumference

Each component is defined as follows:

- *Visceral adiposity*: visceral adiposity is a powerful risk factor for the development of metabolic syndrome.

BMI (body mass index) is defined as weight in kilogram divided by height in metre square. BMI is an important parameter to measure of obesity.

Classification of overweight and obesity by BMI

BMI	CLASSIFICATION
< 18.5	Underweight
18.5-24.9	Normal
25.0-29.9	Overweight
30.0-34.9	Obesity (Class I)
35.0-39.9	Obesity (Class II)
>40	Extreme Obesity (Class III)

the main disadvantage of BMI is it does not convey information about the distribution of body fat. South Asians have higher levels of abdominal fat in viscera and a greater degree of insulin resistance at comparably lower levels of BMI, which reveals that BMI alone cannot be relied upon t estimate the correct risk in Indian population. Now the obesity cut off for Indian population is reduced from BMI >30 to BMI >25.

BMI CUT OFF VALUES FOR ADULTS		
		Asians/Indians 2000
• Underweight	< 18.5	< 18.5
• Normal range	18.5 – 24.9	18.5 – 22.9
• Overweight (pre-obese)	25.0 – 29.9	23.0 – 24.9
• Obese class I	30.0 – 34.9	25.0 – 29.9
• Obese class II	35.0 – 39.9	≥ 30.0
• Obese class III	≥ 40.0	

CLASSIFICATION OF OBESITY

Android obesity: it is the collection of adipose tissue in the abdomen above the waist. It is also called central obesity or apple type obesity and is linked to high prevalence of CAD, DM, and hypertension.

Gynoid obesity : it is the collection of adipose tissue in the hips and buttocks, that is, below the waist. It is also called as pear shaped obesity. This type of obesity confers less risk of DM, HT but more to mechanical disorders like varicose veins and arthritis.

Measurement of central obesity

Waist hip ratio

Most common measure of central obesity is waist hip ratio. Since the excess fat is distributed in the hp in women and waist in men, the optimum value for waist hip ratio is lower in women than in men. In Indians the mean waist hip ratio is 0.93 in men and 0.84 in women.

Waist hip ratio >1.0 in men and >0.9 in women is abnormal. It carries a high risk for coronary artery disease.

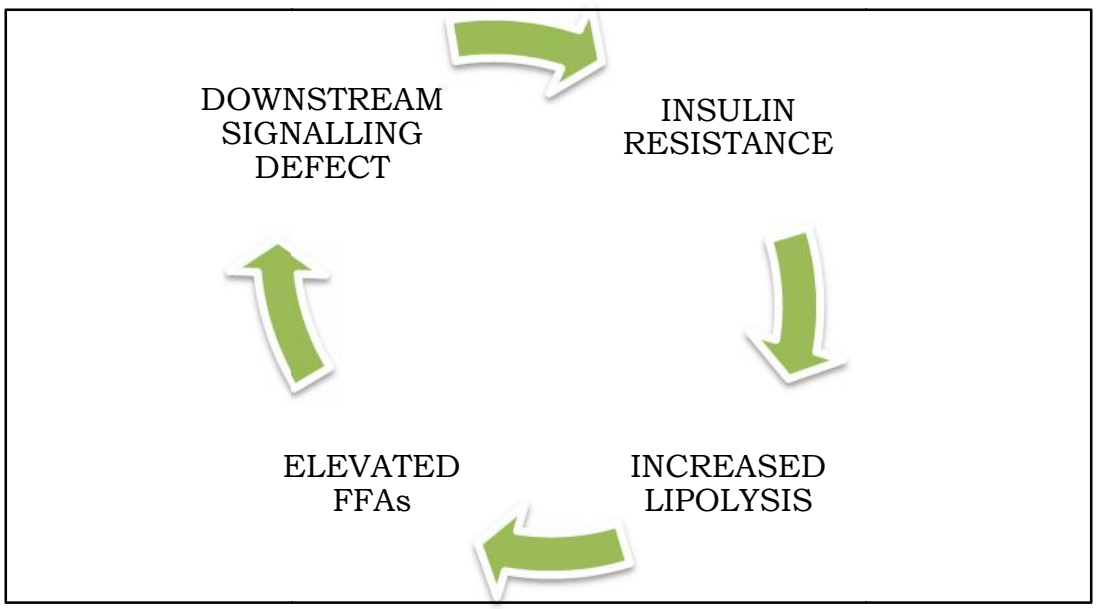
PATHOGENESIS OF METABOLIC SYNDROME

"The metabolic syndrome seems to have 3 potential etiological categories:

a. Obesity and disorders of adipose tissue;
b. Insulin resistance; and
c. A constellation of independent factors (eg, molecules of hepatic, vascular, and immunologic origin) that mediate specific constituents of the metabolic syndrome.
d. Other factors—aging, proinflammatory state, and hormonal changes—have been implicated as contributors as well."

INSULIN RESISTANCE

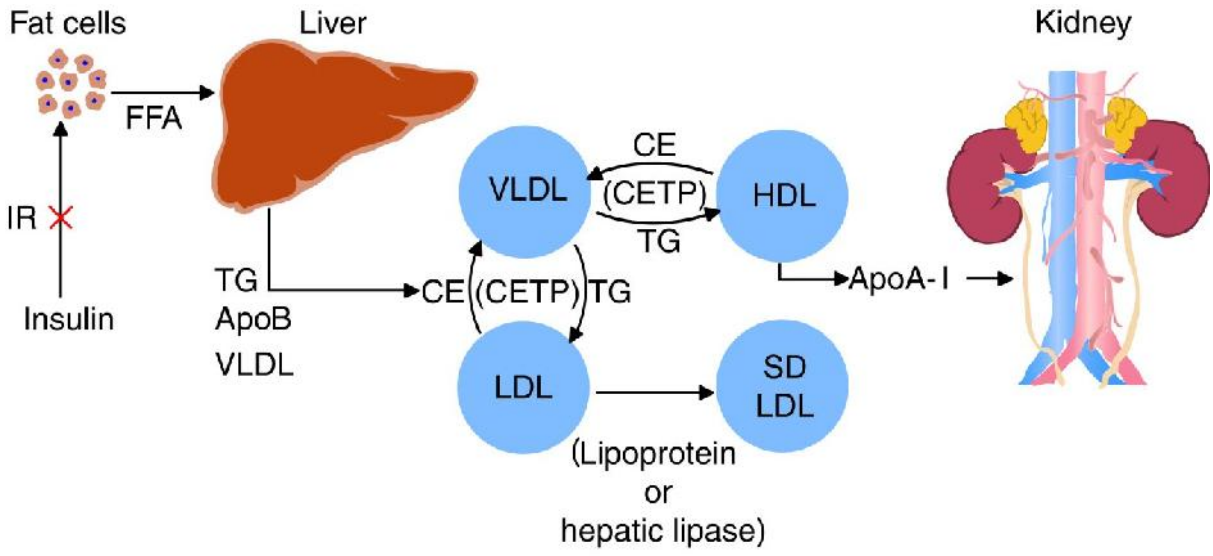
The most accepted theory for the development of syndrome X is insulin resistance. Defect in the action of insulin causes insulin resistance. Initially this will manifest as post prandial hyperinsulinemia which will proress to preprandial elevated insulin levels. As the defect progresses, eventually elevated blood glucose develop and may lead to diabetes. The base metabolic abnormality responsible for the causation of insulin resistance is elevated free fatty acids. The source of circulating free fatty acids is the adipose tissue and circulating lipoproteins. Free fatty acids released from adipose tissue are released into portal circulation and act directly on the liver. increased free fatty acids cause insulin resistance and insulin resistane further increase the free fatty acid level thereby leading to a vicious cycle.



Insulin normally inhibits lipolysis in the adipose tissue and increases the activity of Hormone sensitive lipase . Final effect is t decrease the FFA output from fat tissue. In insulin resistance, loss of inhibition of lipolysis leads to increased FFA levels, which act on liver and lead to increased VLDL production. Triglycerides also accumulate in the liver which may lead to the development of fatty liver. As the syndrome advances, fatty liver may progress to steatohepatitis , fibrosis and finally cirrhosis.

Excess FFA further cause propagation of insulin resistance by affecting downstream signalling in insulin pathway.

MECHANISM OF INSULIN RESISTANCE AND DYSLIPIDEMIA



Mechanism of insulin resistance and dyslipidemia
Insulin resistance leads to increased elease of FFA in circulation, which acts on liver and cause ncresased production of VLDL causing elevated TGL. VLDL stimulates cholesterol esters exchange with LDL and HDL. Apo A 1 dislodges from TGL rich HDL and deplete HDL. TGL rich LDL undergo lypolysis leading to elevated small dense LDL.

This loss of insulin sensitivity leads to defective insulin mediated glucose uptake which cause hyperglycemia. FFA also accumulate in various organs like muscle and liver.

Hyperleptinemia is commonly associated with MS. Studies indicate leptin resistance may play a role in the development of MS. Leptin suppress appetite and increases the basal metabolic rate and improves the peripheral action of insulin.

Oxidative stress also has been proposed to play a role as aging increases the prevalence of MS.

Central obesity has a key role in the pathogenesis of metabolic syndrome. Visceral adipose tissue (VAT) refers to fat cells located within the abdominal cavity and it includes omental , mesenteric retroperitoneal and perinephric adipose tissue .In lean individuals VAT represents 20% of fat in men and 6% of fat in women . Obese individuals have an expanded fat cell mass characterized by visceral adiposity. The increase in insulin resistance with weight gain is directly related to the amount of VAT.

NORMAL INSULIN ACTION:

In the fasting state approximately 85% of glucose production is derived from the liver with remainder produced by the kidney.

Metabolism of glucose by muscle requires insulin .In the fed state, carbohydrate ingestion leads an increase in the plasma glucose concentration and stimulates insulin release from the pancreatic beta cell. The resultant elevation in the plasma insulin

1. Suppress hepatic glucose production
2. Stimulates glucose uptake by peripheral tissues

The majority of glucose that is taken up by peripheral tissues is disposed in muscle, with only a small amount (4-5%) being metabolized by adiposities.

Although the fat tissue is responsible for only a small amount of total body glucose disposed, it plays a very important role in the maintenance of body glucose homeostasis through the release of free fatty acids (FFA) .Small increments in plasma insulin exert a potent antilipolytic effect, leading to a marked reduction in the plasma FFA level .The decline in the plasma FFA levels results in increased glucose uptake in muscle and reduces hepatic glucose production.

Visceral fat cells have a high lipolytic rate which is especially refractory to insulin .Increased lipolysis of fat results in elevation of plasma FFAs and cause insulin resistance in muscle and liver and impairs insulin secretion. Obese individuals have increased FFA levels in their blood. FFAs are stored as triglycerides in muscle and liver and the increased fat content correlates closely with insulin resistance in

these tissues .Finally FFA released into the portal circulation drain into the liver where they stimulate production of VLDL particles .

Visceral fat cells are active endocrine cells producing many cytokines including leptin, interleukin 6, tumor necrosis factor alpha, plasminogen activator inhibitor -1 (PAI-1) angiotensinogen, resistin and CRP .These adipokines drain into portal circulation and reduce insulin sensitivity in peripheral tissues.

VAT is also the source of anti inflammatory, anti atherosclerotic adipokines known as adiponectin ,a hormone associated with increased insulin sensitivity. obesity is associated with decreased levels of adiponectin studies have abnormalities in adiponectin –insulin sensitivity axis in non diabetic south Asians, which may be an important to atherogenisis in this population. Raji et al showed lower levels of adiponectin in Asian Indians.

Increased VAT may also leads to elevated level of cortisol, which would increase insulin resistance .

Fat cells size is an important predictor of diabetes. Small newly differentiated adipocytes are more insulin sensitive than large, lipid rich fat cells. The smaller cells are able to take up glucose and store lipid . In contrast, the larger cells have low rates of insulin stimulated glucose uptake, less suppression of lipolysis and a higher rate of cytokine

production .Visceral fat cells tend to be larger and more metabolically active than subcutaneous fat cells.

Dyslipidemia

Increased FFA act on liver and enhance VLDL production which lead to hypertriglyceridemia. Hypertriglyceridemia is a perfect marker for insulin resistance. As the degree of insulin defect increases, the triglyceride levels increase proportionally. Apo CIII levels increase in VLDL molecules which inhibit the peripheral lipoprotein lipase which further increase the TGL levels.

Increased TGL is commonly associated with decreased HDL and increased LDL. TGL cause abnormality in the function of Cholesterol Ester Transfer Protein - CETP, which normally is responsible for exchanging cholesterol and triglycerides between HDL, LDL and VLDL. This abnormality leased to decrease in cholesterol content of HDL and increased triglyceride content, which makes t highly sensitive to hepatic lipase. This process leads to the production of small HDL which is rapidly cleared by renal metabolism, ultimately leading to reduced HDL.

In addition, LDL metabolism is also altered. Hypertriglceridemia leads to predominance of small dense LDL which have more atherosclerotic properties.

Glucose intolerance

Defect in insulin action leads to increased hepatic and renal glycogenolysis and gluconeogenesis. In addition impaired insulin mediated glucose uptake by cells lead to hyerglycemia. Hyperglycemia stimulates hyperinsulinemia, which compensates for insulin resistance. As the abnormality progresses, compensatory mechanisms fail and defective pancreatic beta cells action may lead to development of frank diabetes which further increase the CAD risk.

HYPERTENSION

There is a definite relationship between insulin resistance and MS.

Insulin is a normal endogenous vasodilator. This mechanism is lost in insulin resistance leading to vasoconstriction. Insulin also increases salt resorption in the kidney thereby contributing to hypertension.

NADPH oxidase action in the adipose tissue releases oxygen free radicals which may play a role in hypertension.

Increased proinflammatory cytokines in metabolic syndrome may also contribute to hypertension

Hyperuricemia commonly seen in insulin resistance causes endothelial dysfunction, decreased Nitric oxide levels which may further lead to hypertension.

CRITERIA FOR DIAGNOSING METABOLIC SYNDROME

There are three different criteria for diagnosing metabolic syndrome.

The National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATPIII)

"According to the third report of the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATPIII), adults to be diagnosed with metabolic syndrome must have three or more of the following:

1. Waist circumference >102 cm (40.2 in) in men and >88 cm (35.6 in) in women
2. Serum triglycerides ≥150 mg/dl
3. Blood pressure ≥130/85 mmHg
4. HDL cholesterol <40 mg/dl in men and <50 mg/dl in women
5. Fasting plasma glucose >6.1mmol/l (≥100 mg/dl)"

The World Health Organization (WHO)

"On the other hand, definition of metabolic syndrome by the World Health Organization (WHO), the individual has to either be diabetic, or have , impaired fasting glucose (IFG) >5.6mmol/l, impaired glucose tolerance (IGT), or insulin resistance and then have **at least two** of the following:

1. Waist-to-hip ratio >0.90 in men or >0.80 in women or BMI> 30kg/m2

2. Serum triglycerides ≥150 mg/dl or HDL cholesterol <35 mg/dl in men and <39 mg/dl in women

3. Blood pressure ≥140/90 mmHg

4. Urinary albumin excretion rate >20 mg/min or albumin-to-creatinine ratio≥30 mg/g. (Microalbuminuria).

International Diabetes Federation (IDF) [75]

"Central obesity (defined as waist circumference with ethnicity specific values, if BMI is >30kg/m², central obesity can be assumed and waist circumference does not need to be measured) AND any two of the following:

1. Raised triglycerides : >150 mg/dL (1.7 mmol/L), or specific treatment for this lipid abnormality.
2. Reduced HDL cholesterol: < 40 mg/dL (1.03 mmol/L) in males, < 50 mg/dL (1.29 mmol/L) in females, or specific treatment for lipid abnormality
3. Raised blood pressure: systolic BP >130 or diastolic BP >85 mm Hg, or treatment of previously diagnosed hypertension.
4. Raised fasting plasma glucose :(FPG)>100 mg/dL (5.6 mmol/L), or previously diagnosed type 2 diabetes. If FPG >5.6 mmol/L or 100 mg/dL, OGTT Glucose tolerance test is strongly recommended but is not necessary to define presence of the Syndrome."

Ethinic specific values for cut off for waist circumference:

Country/ethnic group	Waist circumference value	
	Male	Female
Europids*	≥94 cm	≥80 cm
South Asians‡	≥90 cm	≥80 cm
Chinese	≥90 cm	≥80 cm
Japanese	≥85 cm	≥90 cm
Ethnic South and Central Americans	Use South Asian recommendations until more specific data are available	
Sub-Saharan Africans	Use European data until more specific data are available	
Eastern Mediterranean and Middle East (Arab) populations	Use European data until more specific data are available	

*In the USA, the ATP III values (102 cm male; 88 cm female) are likely to continue to be used for clinical purposes, ‡Based on Chinese, Malay and Asian-Indians populations

Metabolic Syndrome as a Predictor of CVD

People with metabolic syndrome are at expanded danger for CHD. In Framingham, the metabolic syndrome alone anticipated ≈25% of all new-onset CVD. Without diabetes, the metabolic syndrome by and large did not raise 10-year hazard for CHD to >20%; this is the edge for ATP III's CHD hazard comparable. Ten-year hazard in men with metabolic syndrome for the most part went from 10% to 20%. Framingham ladies with metabolic syndrome had moderately few CHD occasions over the span of the 8-year development; this was expected to some extent to the high extent of ladies who were under 50 years old. In spite of the fact that the metabolic syndrome in these ladies had all the earmarks of being

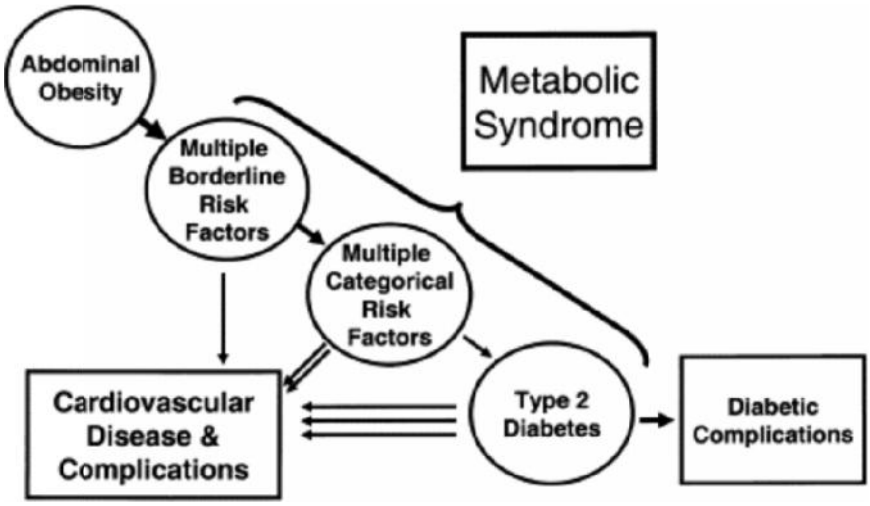
joined by higher danger for CVD/CHD, the certainty interim was wide, and contrasts between those with and without metabolic syndrome were not factually critical. Of note, the 10-year hazard for CHD in most ladies did not surpass 10%.

Framingham investigators then examined whether the metabolic syndrome carries incremental risk beyond the usual risk factors of the Framingham algorithm. Analyses were carried out both including and excluding patients with diabetes. Several models were tested. Results were compared as *C* statistics. The *C* statistic is the probability that the model used will place a person in the right order, giving the higher probability to the one who develops the disease than to the one who does not. Some investigators consider this approach to have limitations, particularly because of the high contribution of age alone to the *C* statistic. Nonetheless, this is a standard method for evaluating the power of adding new risk factors to multiple–risk factor equations.

A late meta-analysis by Gami et al. that included 36 distinct reports found that the general relative risk for CVD and demise for people with the Metabolic syndrome was 1.78 (95% CI, 1.58–2.00). In another report, U.S. grown-ups without earlier CVD from the NHANES were taken after for roughly 13 yr. For those with the metabolic syndrome, the danger variable balanced corresponding risks relapse for CHD mortality

was multiplied. Utilizing the Framingham database, the age-balanced relative dangers for CVD and CHD in men with the Metabolic syndrome were 2.88 and 2.54, individually, with those in ladies being somewhat lower (2.25 and 1.54, separately). The nearness of the metabolic syndrome in patients with prior CHD is likewise connected with an expanded danger for CVD occasions and mortality. Obese people and those with prior diabetes additionally have a multiplying of CVD danger when the Metabolic syndrome is available. McNeil et al. found that more established people (mean age, 72 yr) with the Metabolic syndrome were 20–30% more prone to encounter a CVD occasion than those without.. As one would expect, the more constituents or components of the Metabolic syndrome that are available, the more prominent the CVD hazard. There are only a couple of special cases to these discoveries.. The Prospective Study of Pravastatin in the Elderly at Risk (PROSPER), another investigation of more established people matured 70–82 yr, likewise neglected to demonstrate a relationship between the Metabolic syndrome and expanded danger of CVD. WC, in any case, was not measured in PROSPER, and HDL-C and diastolic pulse (unobtrusively) were the main constituents that anticipated occurrence CVD; neither BMI, nor systolic circulatory strain, LDL-C, or triglycerides were connected with CVD hazard. Since the prevalence of Metabolic syndrome levels in the 60s, this may not be a study that determines the

Metabolic syndrome/CVD result discussion. A study in an accomplice of non diabetic American Indians. CAD rates were entirely low by and large in this companion, as has been appeared in different investigations of American Indians, possibly affecting the ability to recognize contrasts. At long last, in an investigation of people with known stable CHD, the Metabolic syndrome was connected with expanded aggregate mortality and CVD mortality in ladies yet did not give off an impression of being connected with overabundance danger of CVD mortality in men. The meta-analysis by Gami *et al*. found the WHO definition to be associated with slightly greater risk than the NCEP:ATPIII definition (2.06 *vs.* 1.67).



Type 2 diabetes mellitus

The prevalence of T2D has tripled in the last 30 yr. In spite of the fact that insulin resistance is viewed as the sign of prediabetes, deformities in insulin emission are viewed as the key pathophysiological normal for T2D. In spite of the fact that T2D is a heterogeneous disorder, most patients with T2D have insulin resistance and the Metabolic syndromebefore onset of T2D. Actually, insulin resistance, hyperinsulinemia, dyslipidemia, and obesity go before the movement to T2D in 75 to 85% of patients.

CONDITIONS SEEN IN ASSOCIATION WITH METABOLIC SYNDROME:

NONALCOHOLIC FATTY LIVER DISEASE

Nonalcoholic fatty liver disease (NAFLD) range from mild steatosis to NASH to cirrhosis. A diagnosis of NAFLD can be made in patients with raised liver enzymes and/or fatty liver by imaging without different reasons for liver sickness, despite the fact that a conclusive determination must be made by liver biopsy. The prevalence of NAFLD extents from 3 to 36% of the overall public, contingent upon how it is characterized. It has been recommended that 95% of corpulent people

and up to 70% of those with T2D have some type of NAFLD. The prevalence of NAFLD is additionally expanded in youngsters with obesity and insulin resistance . In those patients with the Metabolic syndrome, liver fat substance is essentially expanded up to 4-fold higher than those without the Metabolic syndrome, and the frequency of NAFLD has appeared to be expanded 4-fold in men and 11-fold in ladies with the Metabolic syndrome

POLYCYSTIC OVARIAN SYNDROME (PCOS) :

It is a clinical syndrome that is connected with anovulation, androgen abundance, and insulin resistance. These patients are at increased risk for T2D and CVD.. There have been civil arguments on whether PCOS may in certainty be in the continuum with the Metabolic syndrome. The Metabolic syndrome is normal in ladies, particularly corpulent ladies, with PCOS. The prevalence of PCOS is likewise ascending, with rates reported as high as 28% in overweight/stout ladies.. The ovary, hypothalamic-pituitary pivot, and insulin resistance all are thought to have a part in this condition. Ladies with PCOS unmistakably have a higher prevalence of CVD danger elements.

OBSTRUCTIVE SLEEP APNEA

Obstructive sleep apnea (OSA) is a potentially serious consequence of obesity and is associated with increasing BMI. There is also an association between insulin resistance and OSA. OSA has also been shown to be associated with increased inflammation and reduced adiponectin concentrations. Individuals with OSA are more likely to have the features of the Metabolic syndrome than those without OSA, even when adjusted for obesity. In addition, disordered sleep in general is associated with weight gain and insulin resistance. Some have even suggested that OSA should be considered as a manifestation of the Metabolic syndrome.

HYPOGONADISM

There is a relationship between the Metabolic syndrome and male gonadal and erectile dysfunction. Men with the Metabolic syndrome seem to have a more prominent prevalence of hypogonadism. Moreover, components of the Metabolic syndrome enhance with testosterone substitution. The Metabolic syndrome has additionally been appeared to be autonomously connected with a more prominent prevalence of erectile dysfunction.

LIPODYSTROPHY

Lipodystrophies are a group of conditions characterised by fat wasting. The pathogenesis is complicated. Patients with this condition have extreme insulin resistance, making these people at danger for diabetes, fatty liver, cardiovascular disease. Anti retroviral therapy has been shown to dramatically reduce the prevalence of lipodystrophy corrects the deranged metabolic parameters.

MICROVASCULAR DISEASE

Patients with the Metabolic syndrome are at more serious danger for microvascular disease free of diabetes. Around 8–10% of people with IFG and IGT yet without diabetes, a large portion of whom have the Metabolic syndrome, have retinopathy. The Metabolic syndrome has additionally been appeared to be connected with an expanded danger of kidney dysfunction and microalbuminuria. Besides, the Metabolic syndrome has been observed to be connected with expanded danger for neuropathy. For those people with diabetes, the Metabolic syndrome seems, by all accounts, to be connected with expanded danger for a wide range of microvascular infection despite the fact that a late post hoc investigation of the United Kingdom Perspective Diabetes Study did not observe the Metabolic syndrome to be connected with a more serious danger for microvascular illness in people with T2D.

TREATMENT

Obesity And Adipose Tissue - Targets For Treatment

ATP III prescribed that obesity be the essential focus of intercession for metabolic syndrome. In the first place treatment ought to be weight reduction fortified with expanded physical action. Weight reduction brings down serum cholesterol and triglycerides, raises HDL cholesterol, brings down circulatory strain and glucose, and diminishes insulin resistance. Weight lessening can diminish serum levels of CRP and PAI- 1.Obesity contributes altogether to improvement of the metabolic syndrome in the all inclusive community.

Insulin Resistance as Target of Therapy

On the off chance that insulin resistance, whether primary or secondary to obesity, is in the chain of causation of metabolic syndrome, it would be an appealing target. Surely, weight decrease and expanded physical action will diminish insulin resistance. Two classes of medications are right now accessible that decrease insulin resistance. These are metformin and insulin sensitizers, for example, thiazolidinediones (TZDs).

Metformin has for some time been utilized for treatment of type 2 diabetes. In UKPDS, metformin clearly lessened new-onset CHD in corpulent patients with diabetes. In the Diabetes Prevention Program, metformin treatment forestalled (or postponed) onset of type 2 diabetes in people with IGT. At present, metformin can't be suggested diminishing danger for CVD in people with the metabolic syndrome.

TZDs right now are endorsed for treatment of type 2 diabetes. They lessen insulin resistance, positively alter a few metabolic danger elements. In this manner, regardless of guarantee, TZDs can't be prescribed at present for anticipating CVD in patients with either metabolic syndrome or diabetes.

THERAPEUTIC INTERVENTIONS

Diet.

a. Carbohydrate.

Currently, the United States Department of Agriculture (USDA) recommend a carbohydrate intake of 45–65% of total caloric intake (USDA, 2005). This recommendation is appropriate for most populations because total carbohydrate consumption has not been shown to be associated with the development of T2D or the Metabolic

syndrome. Due in part to the recent rise in the popularity of low-carbohydrate diets, there has been interest in the effect of carbohydrate intake on serum lipid levels. Investigations into this question have consistently reported that carbohydrate intake is positively associated with total cholesterol, LDL-C, and triglycerides and negatively associated with HDL-C. In addition, lower carbohydrate diets have been associated with improved carbohydrate metabolism in those with insulin resistance and/or T2D. Although weight loss has been shown to be greater with lower carbohydrate diets in the short term, the effects on long-term weight loss have been mixed.

Dietary carbohydrate can be placed into two categories: simple and complex. It is the latter that should comprise the bulk of the carbohydrate intake, whereas simple carbohydrates, especially in the form of added sugars, should be limited (USDA, 2005). Common sources of added sugars in the diet include soft drinks, cakes, cookies, pies, fruit drinks, dairy desserts, and candy. Although added sugars are chemically identical to naturally occurring simple sugars (*e.g.*, sugars found in fruit), concern is warranted regarding the lack of nutrients found in foods laden with added sugars. It has been shown that individuals who consume a greater percentage of calories as added sugars consume significantly less vitamins and minerals.

b. Protein.

Information in regards to proper protein admissions for patients with the Metabolic syndrome are scanty. The ARIC concentrate, in any case, as of late found that meat admission was connected with Metabolic syndrome frequency. Except for patients with nephropathy, a protein admission inside the proposals for the overall public is satisfactory: a protein admission of 10–35% of aggregate caloric admission is suggested by the IOM.

c. Fat.

Saturated fat has reliably been appeared to be emphatically connected with fasting insulin levels. The substitution of unsaturated fats for saturated fats in the eating routine has been indicated either to have no impact on or to enhance insulin affectability. Given the watched relationship between saturated fat admission and insulin levels, it is judicious to prescribe a decrease in saturated fat admission (<7% of caloric admission) and in increment in the unsaturated fats, particularly linoleic (5–10% of caloric admission) and α-linolenic (0.7–1.6% of caloric admission), as is advanced by the 2005 USDA Dietary Guidelines. Both serum cholesterol and general CVD hazard have been appeared to be enhanced by kind of dietary fat, i.e., a lessening in soaked

fat and an expansion in unsaturated fat, more so than aggregate fat admission. The Nurses' Health Study agents reported that a 5% expansion in saturated fat admission was connected with a 17% increment in coronary danger, while monounsaturated and polyunsaturated fat admissions were contrarily identified with coronary disease.

d. Sodium.

Notwithstanding the impacts of eating regimen on weight reduction, other life changes can significantly affect blood presssure. An unmistakable positive affiliation has been appeared between sodium admission and circulatory strain, with intemperate sodium consumption connected with hypertension. Sodium limitation has been appeared to be a critical system in the prevention and treatment of hypertension. The Dietary Approaches to Stop Hypertension (DASH) diet demonstrated that lower sodium admission diminished circulatory strain in patients with high-ordinary pulse and mellow hypertension. Besides, sodium limitation has likewise been connected with diminished CVD occasions and congestive heart disappointment. Rules in this manner suggest that day by day sodium admission ought to be confined to close to 65–100 mmol. Notwithstanding sodium limitation, expanded potassium admission has additionally been appeared to enhance circulatory strain,

particularly in the setting of high sodium consumption. Rules have prescribed the admission of nourishments advanced with potassium, for example, products of the soil, with an objective of 90–120 mmol of potassium for every day.

Dietary admission obviously affects the greater part of the constituents of the Metabolic syndrome. Albeit every case ought to be dealt with exclusively, it is reasonable to suggest an eating routine low in saturated fat, higher in unsaturated fats, high in complex sugars, and low in sodium.

It is entrenched that weight reduction is advantageous for treating the majority of the constituents of the Metabolic syndrome, including unreasonable adiposity, dyslipidemia, hypertension, insulin resistance, and hyperglycemia. The greatness of weight reduction need not be intense; the Finnish Diabetes Prevention Study demonstrated that way of life mediation with humble weight reduction essentially diminished the prevalence of the Metabolic syndrome(OR, 0.62; 95% CI, 0.40–0.95) contrasted and the control bunch. A 41% decrease in the frequency of the Metabolic syndromewas likewise seen with the escalated way of lifestyle intervention of the DPP[121]. Furthermore, a weight reduction as little as 5–10% of body weight can fundamentally diminish triglycerides and increment HDL-C. Moreover, both hypertensive people and people at

danger for hypertension can see a noteworthy decrease in pulse with an unassuming weight reduction. Fasting blood glucose, insulin, and hemoglobin A1c can likewise be diminished with humble weight reduction; Strikingly, the DPP exhibited that weight reduction was the number 1 indicator of diminishment in the rate of diabetes. For each kilogram of weight reduction, the danger of diabetes advancement was diminished by 16%.

Aerobic Exercise And Insulin Resistance.

Exercise enhances glucose metabolism by improving glucose transport and insulin activity in working skeletal muscle. This intense impact of activity on insulin-mediated glucose uptake does not seem to hold on past 24 h after the last episode of activity. American College of Sports Medicine suggestion to practice no less than 30 min/d most days of the week. There is proof to recommend that maybe oxygen consuming activity preparing ought to be joined by weight reduction for a determined impact on glucose resilience and insulin activity past the prompt post exercise impacts.

Aerobic Exercise And Dyslipidemia.

Current NCEP:ATPIII guidelines recommend LDL-C reduction as the primary treatment goal for CVD risk reduction, Although aerobic

exercise training increase HDL-C and to decrease triglycerides, results are mixed for an effect on LDL-C.

Aerobic Exercise And Hypertension.

It is well known that aerobic exercise decrease the mean blood pressure both in obese and non obese individuals and is beneficial in patients with metabolic syndrome

CORONARY ARTERY DISEASE

Coronary artery disease is an important cause of mortality all over the world, in fact it is the leading cause of mortality. The rate of CAD varies widely among different populations. The CAD prevalence among Asian Indians who are staying overseas are 50 to 400% higher than the people of other ethnicity. India is now facing a huge epidemic of coronary artery disease and the CAD prevalence in Indians is more than fourfold higher than that of Americans.

Prevalence of CAD

In India the prevalence of CAD was 1.17 million in the year 1990. It was 1.59 million in 2000. By the year 2010, the prevalence rose to 2.03 million

The prevalence of CAD is twice in urban areas than in rural areas. It is higher in southern India than northern India. There is a higher rate of

abdominal adiposity among urban areas than rural areas. This increased prevalence of CAD in Asians is because of inherited hereditary factors.

CORONARY CIRCULATION

Anatomy of coronary arteries

The heart derives its blood supply from the two coronary arteries namely the right and the left.

Right coronary artery originates from the anterior aortic sinus and then it passes behind the right atrial appendage and the right ventricular infundibulum. It gives branches to both the atria and the ventricles as it passes downwards vertically in the atrio-ventricular groove. The marginal branch, a the inferior border of heart, passes to the left along the right ventricle and the main artery runs posteriorly. The inferior inter-ventricular branch arises from the inferior surface. This large artery runs along the posterior inter-ventricular groove in the posterior surface.

The left coronary artery originates from the left posterior sinus of aorta and divides immediately as anterior descending artery and circumflex artery which run into anterior inter-ventricular groove and the atrio-ventricular sulcus, respectively. The left circumflex passes through the lateral wall of the heart and supplies the posterior ventricle.

Distribution of the coronaries

Right coronary artery supplies anterior anterior right atrium and the right ventricle except at the upper margin of anterior surface, where it is supplied by anterior interventricular arteries.

Left ventricle is supplied by the LCA except for a narrow strip of the diaphragmatic surface which is supplied by inferior interventricular artery. It supplies left atrium and its appendage also with the posterior surface of right atrium.

SA node and AV node is supplied by the right coronary artery in 60% and 90% respectively. The left coronary supplies the remaining percentage of cases. The inferior interventricular artery supplies the AV node and His Bundle.

Dominant arteries

In 67% cases, right coronary artery is dominant while in 15%, the left coronary is dominant. In another 18% there is a balanced coronary arterial pattern.

Normal coronary blood flow

The coronary circulation receives about 4.5% of the cardiac output at rest. During exercise it increases y four to five fold.

Physiology of coronary circulation

Physiologically both the coronary arteries are end arteries, inspite of anastomoses. The innermost 75- 100 microns of endocardium obtains nutrition directly from blood in the cardiac chambers.

Control of coronary blood flow

1. Prime controller - local myocardial metabolism
2. Neuronal control

Local myocardial metabolism : the rate of blood flow increases with increase in vigour of contraction. The factors responsible are : Oxygen demand

As oxygen extraction is complete in resting state of heart, increase in oxygen demand has to be met with by increasing the coronary flow. This is achieved by

- ✓ Vasodilator theory : hypoxia will release several vasodilator substances from cardiac myocyte which increases the blood flow rate
    - Adenosine from ATP
    - Hydrogen ion
    - Carbon dioxide
    - Potassium ion
    - Bradykinin and
    - Prostaglandins

- ✓ Arterial smooth muscle relaxation theory: decrease in oxygen supply leads to anoxia of coronary arterial smooth muscle cells, which lose the tone leading to dilatation. Oxygen consumption depends upon following factors
    - Greater the work, the greater is consumption of oxygen, within physiological limits
    - Oxygen consumption is directly proportional to peak myocardial muscle tension which depends upon arterial pressure and size of the ventricular cavity

Neuronal control

Indirect:

Sympathetic stimulation of heart increases the rate and cardiac contractility, through the local metabolic mechanisms and hence increases the coronary flow. Parasympathetic stimulation decreases the heart rate and causes coronary vasoconstriction.

Direct effect:

Epinephrine and nor epinephrine directly act on their receptors in the coronary vessels an d cause vasoconstriction.

EPIDEMIOLOGY OF CORONARY HEART DISEASE

Coronary artery disease (CAD) is the foremost cause of mortality in individuals above 40 years of age throughout the world.

In the America it is estimates reveal that individuals above 30years of age have a prevalence of CAD of 213 per 100,000 people.

Accurate data on the prevalence of CAD in India are not available. Recent surveys in small population groups in different geographical areas estimate a prevalence of about 5% in urban and a much lower prevalence in rural population.

The pattern of CAD (India) is reported to as follows:

1. Males are more affected than females
2. Hypertension and diabetes accounts for 40% of all cases
3. Heavy smoking is particularly prevalent.
4. Other factors like high fat diet and sedentary lifestyle.
5. Alcohol consumption in large quantities increases the risk of atherosclerosis.

The prevalence of CAD in India has increased greatly in the last three decades and younger persons are also prone to the disease.

RISK FACTORS FOR CAD:

Risk factors for CAD can be broadly divided into modifiable and non modifiable risk factors .Modifiable risk factor can also be divided into lipid and non lipid factors.

NON MODIFIABLE RISK FACTORS:

1. AGE:

   Male > 45 years

   Females >55 years

2. FAMILY HISTORY OF PREMATURE CAD:

   Male first degree relative <55 years

   Female first degree relative <65 years

3. Male sex

MODIFIABLE-NONLIPID RISK FACTORS :

1. Diabetes

2. Smoking

3. Lifestyle risk factors –obesity –BMI>30kg/meter square

   - Physical inactivity

   -Atherogenic diet

4. Hypertension

MODIFIABLE –LIPID RISK FACTORS:

a) Total cholesterol > 200 mg/dl

b) Triglyceride >150 mg/dl

c) 3 Apo b >100mg/dl

d) HDL<40mg/dl in males and <50mg/dl in females

e) LDL >100 mg/dl

NEW EMERGING RISK FACTORS:

1. Impaired fasting glucose
2. Homocysteine >15
3. Prothrombotic factors
4. Proinflammatory factors

LIPID ABNORMALITIES OF CAD :

HDL is the only known carrier of cholesterol from peripheral tissues to liver i.e. reverse cholesterol transport ,which is a protective mechanism against atherogenesis .Each 1mg HDL cholesterol is estimated to decrease CAD by 2-4% .HDL >60 is a "negative "coronary risk factor. A low HDL is associated with increased risk of CAD even if TGL and TC levels are not elevated .A 10 mg /dl fall in HDL confers the same risk for CAD as 30mg/dl increase in LDL .In general Indians had HDL level > 5 mg /dl lower than Europeans and American whites .A study on Asian Indians living in the united states

found that 54% of men had an HDL level below 40 mg/dl and 68% of women had levels below 50 mg/dl .South Asians not only have HDL level lower but also have higher concentration of small ,less protective HDL particles ,which suggests impaired reverse cholesterol transport .

HIGH TRIGLYCERIDE:

About 95% of TG in body is stored in adipose tissue as glycerol fatty acids and monoglycerides. An 88mg/dl increase the relative risk of CAD by 30% in men and 75% in women .Paris prospective study and NCEP ATP III guideline has accepted TG as an important risk factor for CAD .Johnson SL et all .In STRIDE had noticed higher significance of TG in female CAD .The same was noted by Gupta et all and Acarteik et all. Low TG and high HDL level have a lower risk of CAD, but this profile is uncommon among Asian Indians.

TOTAL CHOLESTEROL:

It is a strong risk factor for CAD .At any given total cholesterol or LDL level, Asian Indians had more risk than whites. Recent study shown that 8 fold higher CAD mortality with increase in TC from 160 to >280mg/dl .Therefore Asian Indians should be treated aggressively .The optimum level of total cholesterol appears to be 150mg/dl for Asian Indians.

TC/HDL >4.5 has a higher risk, ratio < 3.5 is a clinical goal for CAD prevention.

LDL CHOLESTEROL:

Although LDL levels of south Indians tends to be higher, the particle size tends to be smaller. Small particles through increased susceptibility to oxidation are more atherogenic than larger particles.

LIPOPROTEIN (a) :

Is a variable of LDL and a strong risk factor. It appears to be the link between the atherosclerosis and thrombosis. It is highly thrombogenic and antifibrinolytic .It is denoted as" deadly cholesterol"

Their levels are governed by age, gender, diet, and other environmental factors childhood levels of Lp (a) is a future marker of CAD. Threshold level is >30 mg/dl and the risk increases with the level between 15-20 mg/dl.

PHYSICAL INACTIVITY:

Regular physical exercise reduces myocardial oxygen demand and increases the exercise capacity.

Benefits include

-Enhances insulin sensitivity

-decreases adiposity and diabetes

- lowers blood pressure

-improvement of dyslipidemia, plasma rrheology , vascular inflammations.

TOBACCO ABUSE:

Single most important risk factor .Smoking >10 Cigarettes or beedi per day is associated with high risk of MI .It affects atherothrombosis ,enhance oxidation of LDL and impairs coronary artery dilatation .It has adverse hemostatic and inflammatory activity including increased levels of hs CRP ,intercellular adhesion molecule -1 (ICAM-1) ,Fibrinogen ,homocysteine ,and spontaneous platelet aggregation .Smokers have increased risk for coronary spasm and ventricular arrhythmias ,Women are affected by passive smoking .The risk of CAD begins to decline with the cessation of smoking within 3-5 years .

PSYCHOSOCIAL FACTORS:

Depression, hostility, and anger and low social support are associated with CAD. Type A personality is not associated with CAD.

EMERGING CARDIC RISK FACTORS:

Lipoprotein (a), apo lipoprotein B, homocysteine, plasminogen activator inhibitor 1, pro inflammatory

adipokines levels tend to be high in south Asian .Micro albuminuria is considered as a independent risk factor .

ASIAN INDIAN PARADOX:

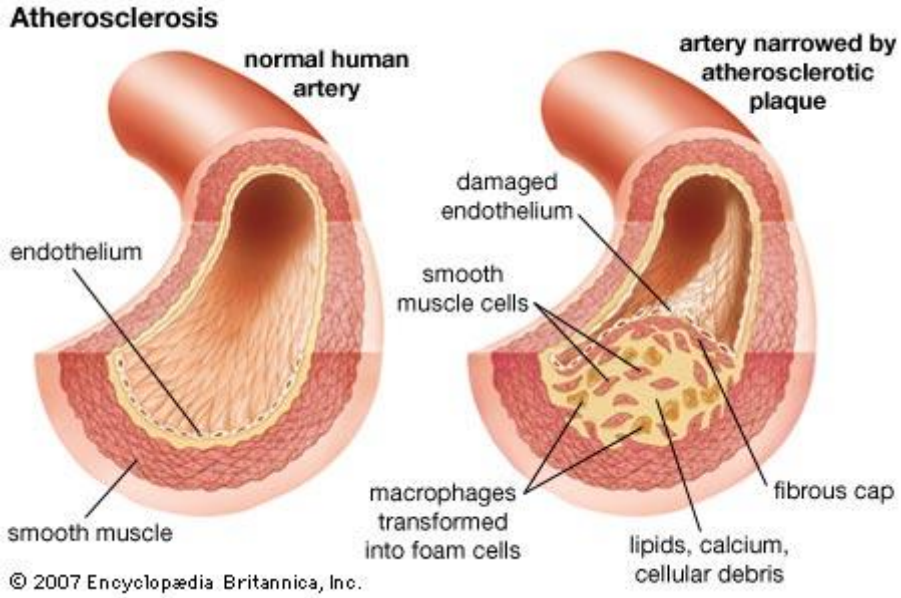
High rates of CAD in Asian Indians are accompanied by low rates of conventional risk factor except for diabetes. For Asian Indians physical activity was high and saturated fat consumption was low.

PATHOGENESIS

Atherosclerosis is a disease primarily affecting the intimal layer of the elastic arteries. Some arterial beds are more affected than others, for unknown reasons. Coronary, carotid and renal arteries are more commonly involved. The arteries of the lower limb also commonly involved leading to peripheral vascular disease.

Atherosclerotic pass through several stages and evolve slowly through several years. Histologically the earliest lesion to develop is the subendothelial accumulation of foam cells, which are lipid laden macrophages and associated T cell lymphocytes. This lesion is known as Fatty Streak. Fatty streaks are usually asymptomatic and do not lead to stenosis.

Atherosclerotic plaque



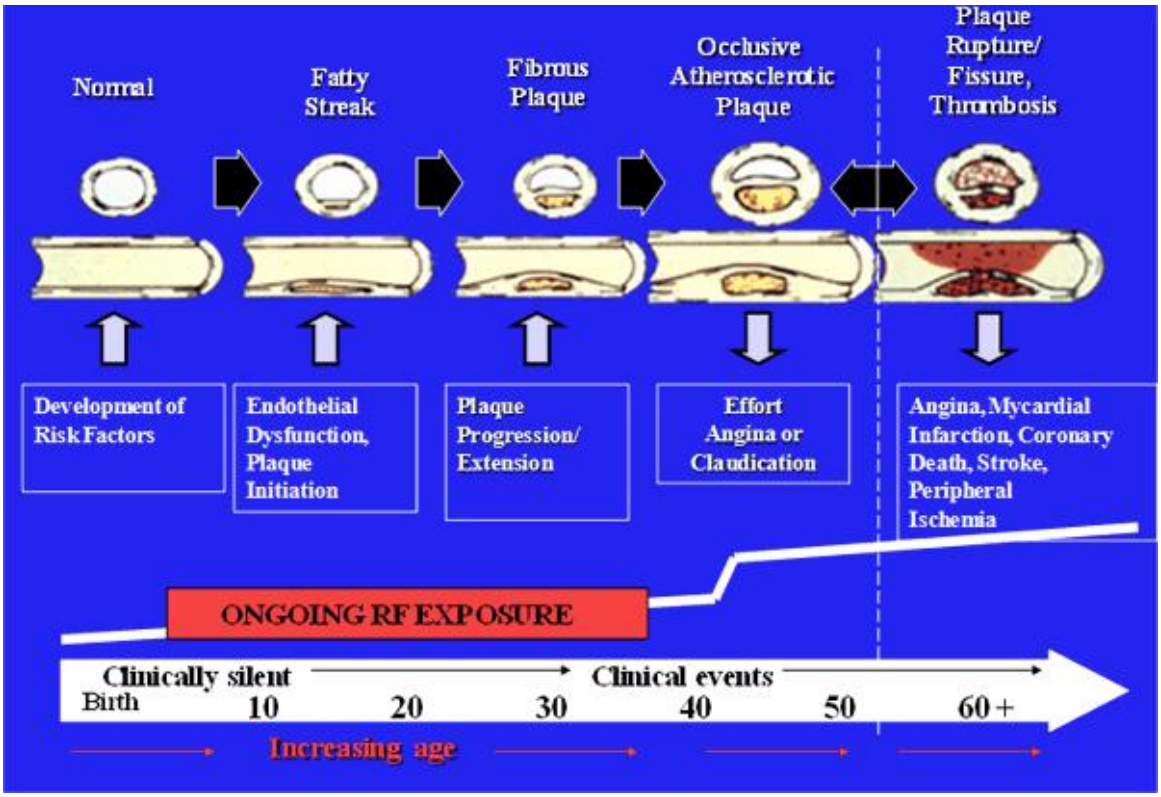
EVOLUTION OF THE ATHEROSCLEROTIC LESION

Autopsy studies have revealed that fatty streaks arise in the aorta at the end of the first decade of life. They appear in the coronaries by the the second decade and start to appear in the cerebral blood vessels by the third decade. With time, these lesions gradually progress and the core of the lesion become necrotic, containing cellular debris, cholesterol crystals and inflammatory cells, particularly lipid laden foam cells. This necrotic core gets surrounded on the luminal aspect by a fibrous cap

which is lined by endothelium. The fibrous cap is made up of vascular smooth muscle cells with extensive collagen and matrix. Inflammatory cells are also present in the cap especially at the shoulder region, where t cells, mast cells, macrophages tend to accumulate. As the lesions advance they become increasingly complex with evidence of calcification, new vessel formation, erosion and ulceration. The composition of the atheromatous plaque is thus complex and the progression and outcome depends on the interaction between various types of cells in the plaque.

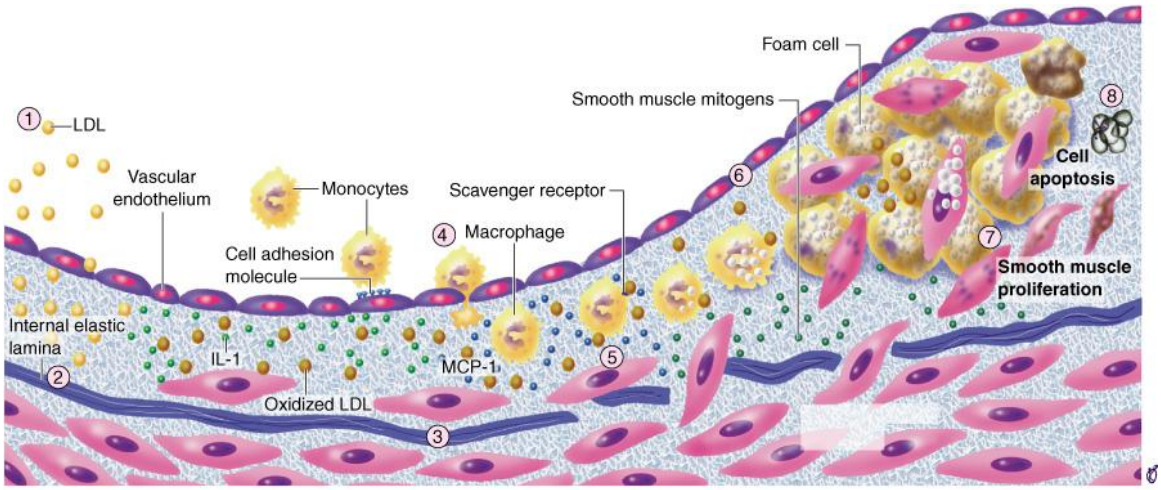
Atherosclerosis is regarded as a dynamic disease which is progressive and a result of combination of endothelial dysfunction and inflammation. The vascular endothelium has the ability to sense any change in the shear stress and respond by synthesising and releasing mediators of vascular tone. Vascular homeostasis depends upon the balance between endothelium derived relaxing factor and vasoconstricting agents. When this balance is disturbed by inflammation and other traditional cardiovascular risk factors, the vessels become susceptible to atherosclerosis. Inflammatory mediators play a critical role in the initiation, propagation and ultimate rupture of the atherosclerotic lesion.

Evolution of atherosclerotic plaque



Endothelial cell activation is an important feature of atherosclerosis. The activated endothelial cells express Vascular cell Adhesion Molecule 1 (VCAM 1), which cause leukocyte attachment and migration. Monocyte adhesion is a critical event for atherosclerosis. Cytokines oxidised low density lipoproteins present in the extracellular matrix and infectious agents like Chlamydia and cytomegalovirus cause endothelial cell activation.

Steps in the formation of atherosclerotic plaque



Endothelial dysfunction

There is a correlation between atherosclerotic risk factors and endothelial function. LDL, especially oxidised LDL is potent endothelial cell inhibitor of nitric oxide release and causes NO inactivation and superoxide production. Endothelial dysfunction is characteristically seen with elevated serum cholesterol. Cholesterol reduction improves the endothelial function and decrease cardiac mortality and morbidity in several studies. Increasing age, elevated bood pressure, diabetes mellitus, smoking and estrogen therapy all modify the endothelial function.

Inflammation and atherothrombosis

There is growing evidence of a link between inflammation and atherothrombosis. The endothelial cells express increased adhesion molecules like VCAM 1 which lead to increased leukocyte influx. Inflammatory processes all lead to initiation and evolution into advance atherosclerotic plaques which lead to thrombotic complications. The activated macrophages produce proteolytic enzymes which degrade the collagen of the fibrin cap, rendering the cap weak , thin and susceptible to erosion and rupture.

Cellular interaction and lesion stabilisation

Atherosclerotic plaque can manifest in one of two ways. Foamy macrophages undergo apoptosis in the presence of high concentration of oxidized LDL. The cellular remnant become incorporated into the lipid rich core. As the plaque size increases, it leads to reduction in the luminal area. At times of increased demand for blood flow, this may lead to cardiac ischemia such as angina. More dangerous, if the fibrous cap of the lesion disrupts, exposure of the thrombogenic matrix lead to thrombosis of the vessel. Depending on the factors like collateral blood flow, extent of the thrombus and degree of fibrinolytic activity, the end result may be arterial occlusion and myocardial necrosis.

Characteristics that are predictive of high risk for plaque rupture are

1. Thin fibrous cap
2. High inflammatory cells to vascular smooth muscle cells
3. Lipid core that occupies >50% of plaque volume

Inflammatory cells in the plaque promote plaque rupture by numerous mechanisms. Activated T cells produce pro- inflammatory cytokines like IFN that stimulate VSMC proliferation and inhibit matrix synthesis. Macrophage derived inflammatory mediators like IL -1, and TNF alpha cause depletion of VSMC due to their cytotoxic effects, leading to unstable plaque formation.

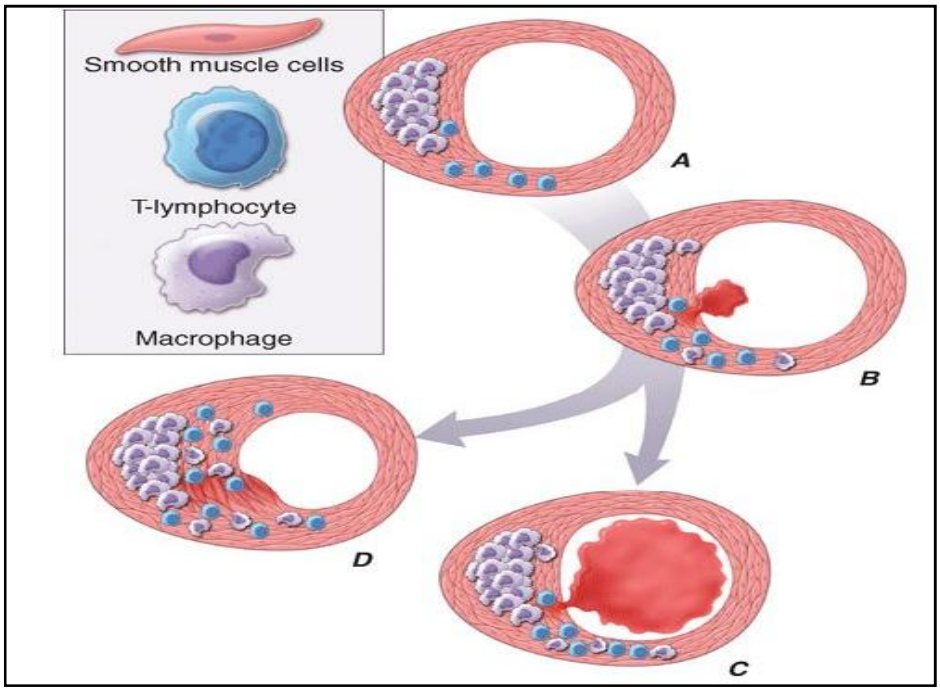
Activated macrophages can induce apoptosis of VSMC by direct cytopathic effects, due to the secretion of variety of matrix metallo-proteinases that degrade the matrix component of the fibrous cap by proteolysis of matrix. The production of these enzymes is up regulated by inflammatory mediators.

Plaque disruption

Atherosclerotic plaque when ruptured can lead to thrombus formation and lumen occlusion. This can be due to either erosion of endothelial cells lining the fibrous cap or rupture of the plaque with exposure of

thrombogenic matrix, leading to the formation of a platelet rich thrombus. Platelet activation may lead to triggering of the clotting cascade, thrombus formation and occlusion of the vessel. Upto 70% of the plaques may cause high grade stenosis and may contain histological evidence of previous subclinical rupture and subsequent healing.

Plaque rupture, thrombosis, and healing



PREVENTION OF CAD IN ASIAN INDIANS:

i. Lifestyle modification such as increased physical activity and reduced calorie intake particularly saturated fat should begin early in life.

ii. Consumption of all tobacco products should be eliminated.

iii. Screening methods such as waist circumference should be measured rather than WHR, BMI.

iv. Assessment of fasting glucose and lipid profile are essential.

v. Reduction of abdominal obesity through lifestyle measures can improve all components of the metabolic syndrome and likely delay the development of both diabetes and atherosclerosis.

vi. Appropriate drug therapy should be considered for all lipid abnormalities for the risk factors abnormalities which do not respond to lifestyle modification.

MATERIALS AND METHODS:

STUDY POPULATION:

The present study is conducted on patients admitted with a diagnosis of AMI to the Coronary Care Unit (CCU) of Government Rajaji Hospital, Madurai during the period of February 2016 to July 2016.

INCLUSION CRITERIA:

1. All patients admitted with a diagnosis of AMI to the Coronary Care Unit (CCU) of Government Rajaji Hospital with
2. Age < 45 years
3. Acute myocardial infarction is defined as at least two of the following: prolonged chest discomfort, typical electrocardiographic changes, or elevated cardiac troponin levels, as outlined by the Joint European Society of Cardiology/American College of Cardiology Committee

Exclusion criteria:

1. Rheumatic heart disease
2. Congenital heart disease
3. Severe anemia/ chronic kidney and liver disease
4. Cocaine abuse
5. Lack of definitive MI criteria
6. Age > 45 years

ANTICIPATED OUTCOME:

High prevalence of metabolic syndrome in young patients with acute myocardial infarction

DATA COLLECTION:

A previously designed proforma is used to collect the demographic and clinical details of the patients. A complete clinical examination will be done.

Demographic data obtained from all patients include age, gender, weight, height, waist circumference, and information on risk factors such as diabetes, hypertension, smoking status, and a family history of vascular disease. Smoking status was documented. The presence of previously diagnosed diabetes was noted, as well as the mode of therapy (diet alone, oral hypoglycaemic agents or insulin)

Blood pressure is measured twice in the supine position from right hand, using a mercury sphygmomanometer. Waist circumference (WC) is measured at the widest diameter between the xiphoid process of the sternum and the iliac crest. Serum lipids and blood sugar were measured by taking a sample of 5 mL blood from the right brachial vein after 12 h overnight fasting. The blood samples were sent to central lab of Government Rajaji Hospital.

Additional clinical data on complications encountered from hospital admission until discharge were collected, and included events such as

sustained ventricular arrhythmias (ventricular tachycardia/ventricular fibrillation) requiring intervention, complete heart block, cardiac failure, cardiogenic shock, recurrence of angina or MI and death, as well as information on angiographic results and revascularisation procedures such as angioplasty.

According to the new IDF definition, the metabolic syndrome is defined as :

"Central obesity (defined as waist circumference ≥ 90cm for Asian Indian men and ≥ 80cm for Asian Indian women)

Plus any two of the following four factors:

• **Raised TG Level**: ≥ 150 mg/dL (1.7 mmol/L), or specific treatment for this lipid abnormality

• **Reduced HDL Cholesterol**: < 40 mg/dL in males and < 50 mg/dL in females, or specific treatment for this lipid abnormality

• **Raised Blood Pressure**: systolic BP ≥ 130 or diastolic BP ≥ 85 mm Hg, or treatment of previously diagnosed hypertension

• **Raised Fasting Plasma Glucose** (FPG) ≥ 100 mg/dL, or previously diagnosed type 2 diabetes."

DESIGN OF STUDY:

Cross sectional study

PERIOD OF STUDY:

February 2016 to July 2016 (6 months)

COLLABORATING DEPARTMENTS:

Department Of Cardiology

Department Of Biochemistry

ETHICAL CLEARANCE: Applied for

CONSENT: Individual written and informed consent.

ANALYSIS: STATISTICAL ANALYSIS.

CONFLICT OF INTEREST: NIL

FINANCIAL SUPPORT: SELF

PARTICIPANTS:

Patients with age< 45years, admitted with a diagnosis of AMI to the Coronary Care Unit (CCU) of Government Rajaji Hospital, Madurai during the period of February 2016 To July 2016.

LABORATORY INVESTIGATIONS :

Overnight fasting blood sugar, and lipid profile were measured. The blood sugar was measured using the glucose oxidase and peroxidase method. In lipid profile total cholesterol was measured using the cholesterol oxidase peroxidase method. The triglyceride was measured using the glucose 3 phosphate oxidase-peroxidase method. Cholesterol in the supernatant is measured after precipitation of apo-B containing lipoprotein by polyethylene glycol to determine the HDL cholesterol. LDL cholesterol is estimated by using the Friedewald formula and this formula appears to be the most practical and reliable method for determining LDL-cholesterol in clinical practice.

LDL- cholesterol=Total cholesterol-[HDL+(Triglyceride/5)]

VLDL is estimated by dividing the plasma triglyceride by 5 reflecting the ratio of cholesterol to triglyceride in VLDL particles.

Limitations of the study:

1. Small number of subjects.

2. Single centre study.

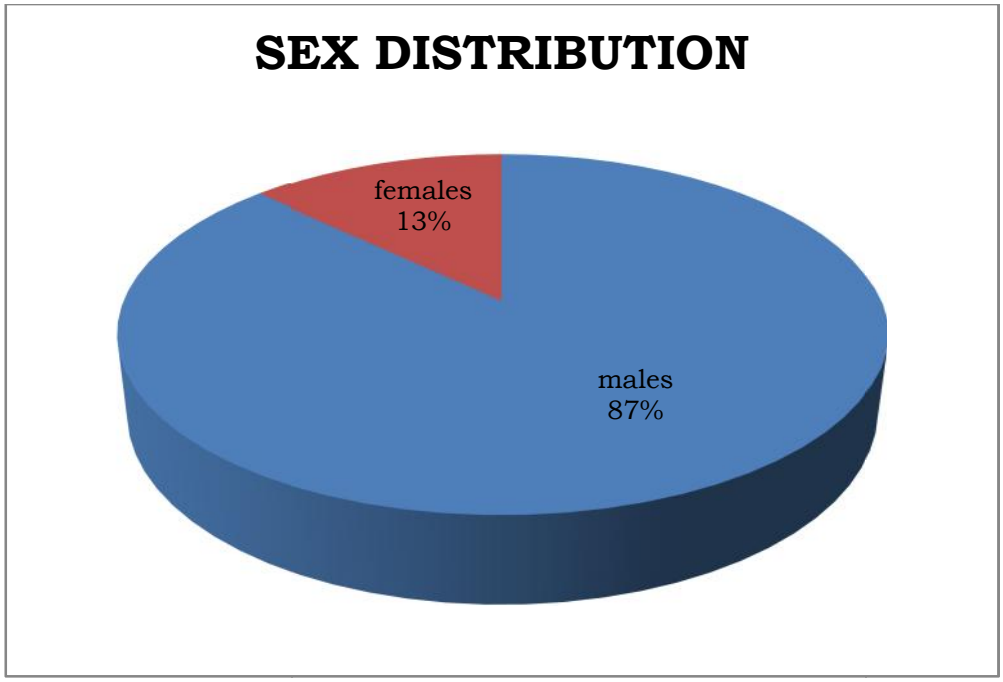
3. Only the one timed blood pressure was measured.

4. Direct LDL measurement was not done, measured only by Friedwald formula.

RESULTS AND INTERPRETATION

After applying the inclusion and exclusion criteria 62 cases were selected for the study. The age distribution is as follows,

GRAPH 1: SHOWING THE SEX DISTRIBUTION OF THE STUDY POPULATION



GRAPH 2: SHOWING THE AGE DISTRIBUTION OF THE STUDY POPULATION

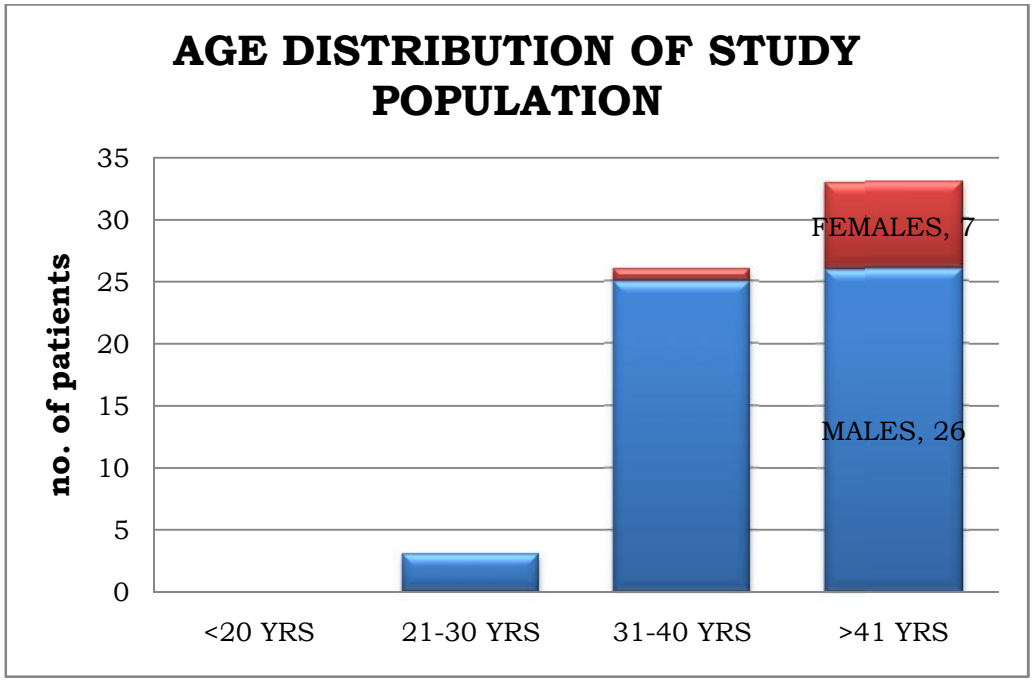


TABLE 1: SHOWING THE COMPARISION OF AGE DISTRIBUTION OF THE STUDY POPULATION, IN PATIENTS WTH AND WITHOUT METABOLIC SYNDROME.

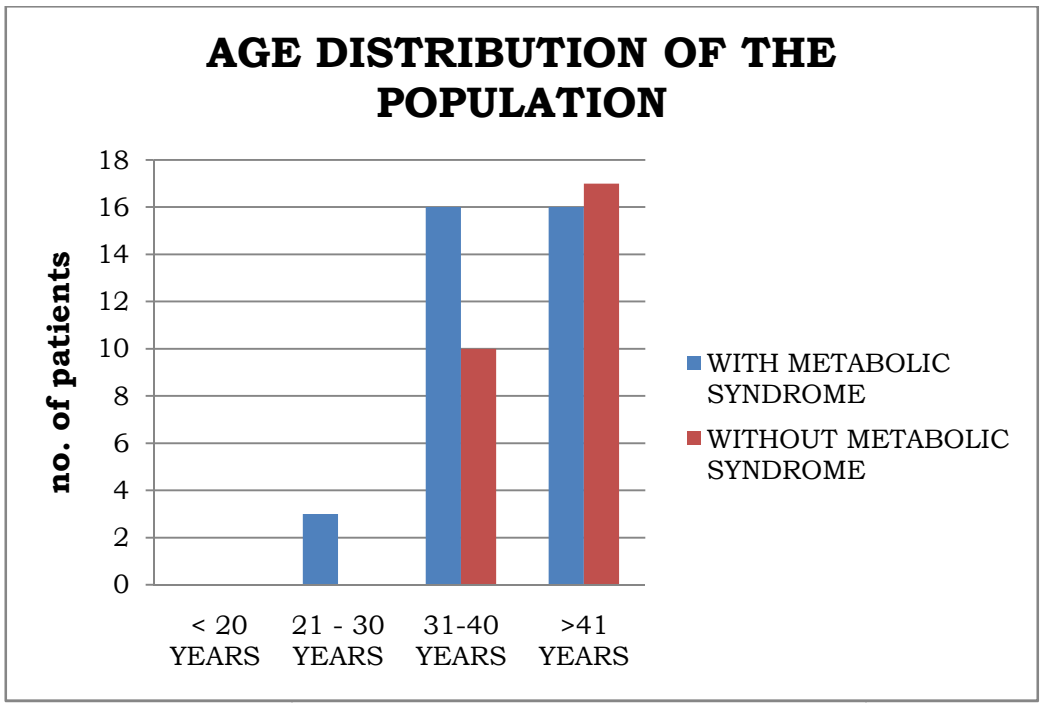
AGE GROUP	TOTAL (n = 62)	PATIENTS WITH METABOLIC SYNDROME (n = 35)	PATIENTS WITHOUT METABOLIC SYNDROME (n = 27)	PREVALENCE OF METABOLIC SYNDROME
<20 YEARS	0	0	0	0
21 – 30 YEARS	3	3	0	100%
31 – 40 YEARS	26	16	10	61%
>41 YEARS	33	16	17	48%
TOTAL	62	35	27	56%

MEAN AGE : 39.98 S.D. : 4.73

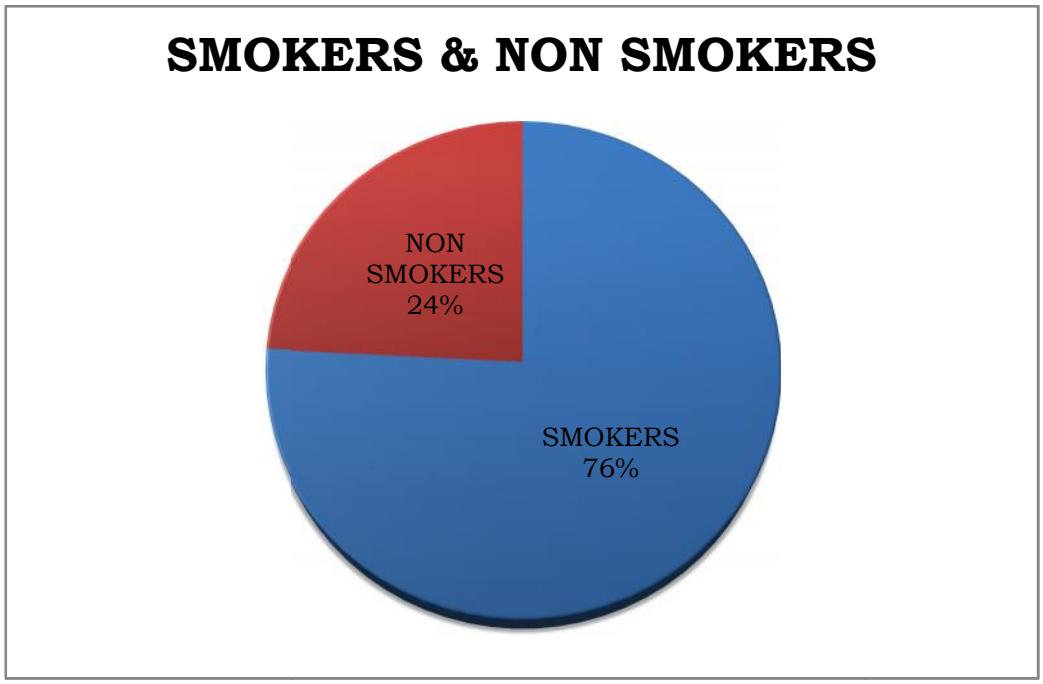
MINUMUM AGE: 27 YEARS

MAXIMUM AGE: 45 YEARS

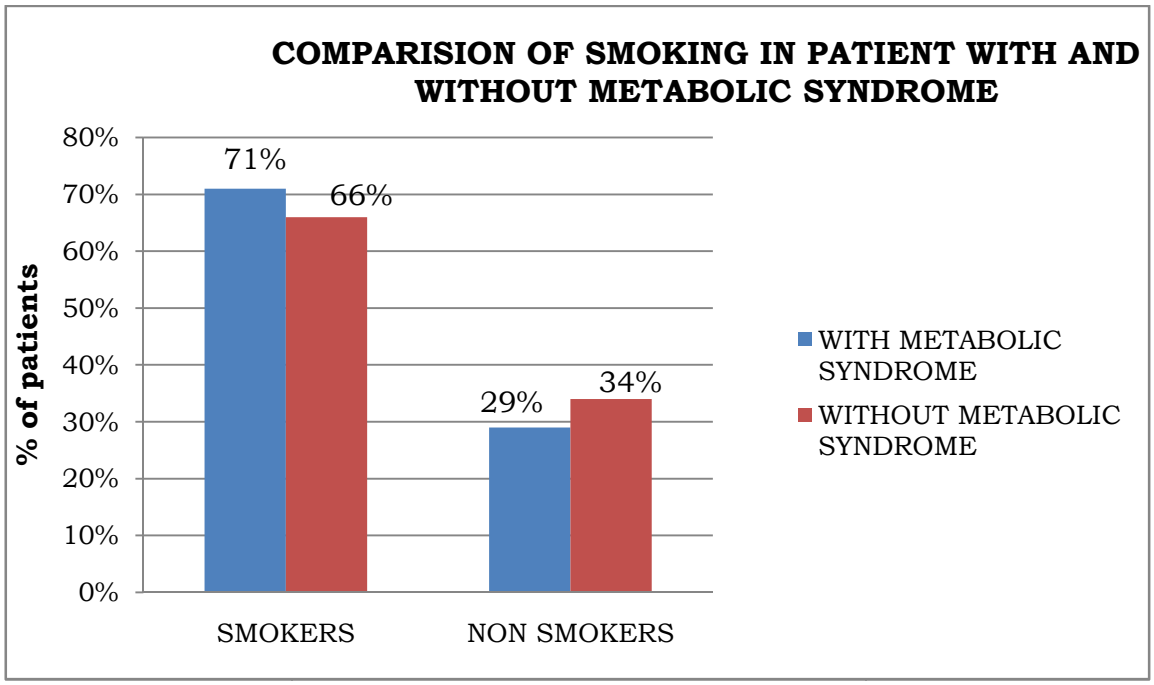
GRAPH 3: SHOWING THE COMPARISION OF AGE DISTRIBUTION IN PATIENTS WITH AND WITHOUT METABOLIC SYNDROME



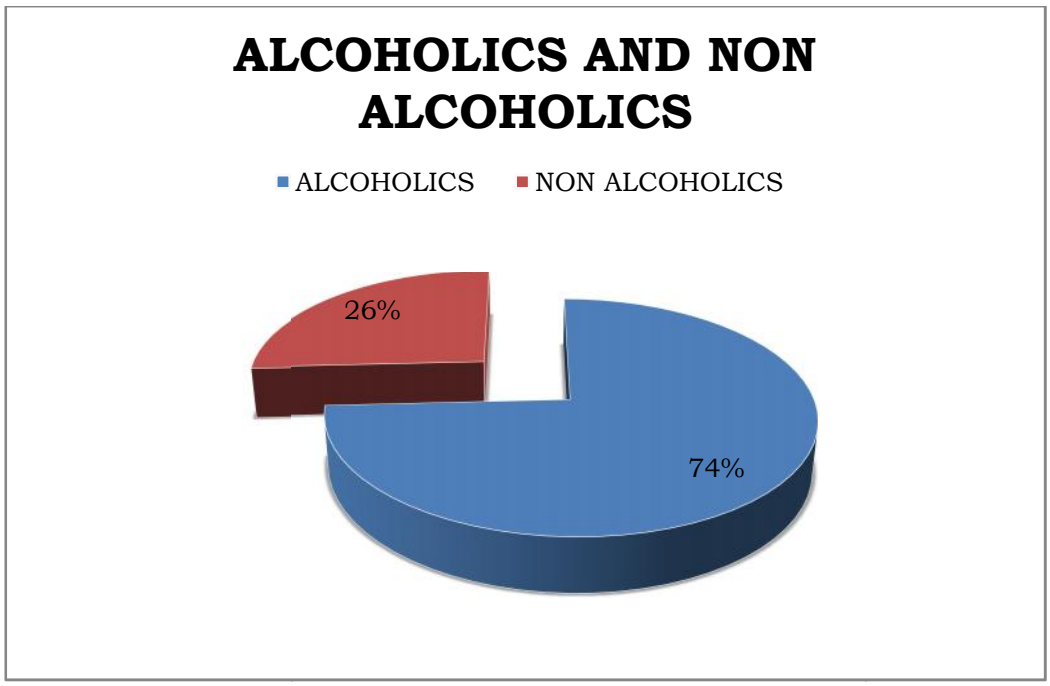
GRAPH 4: SHOWING THE PREVALENCE OF SMOKING AMONG STUDY POPULATION.



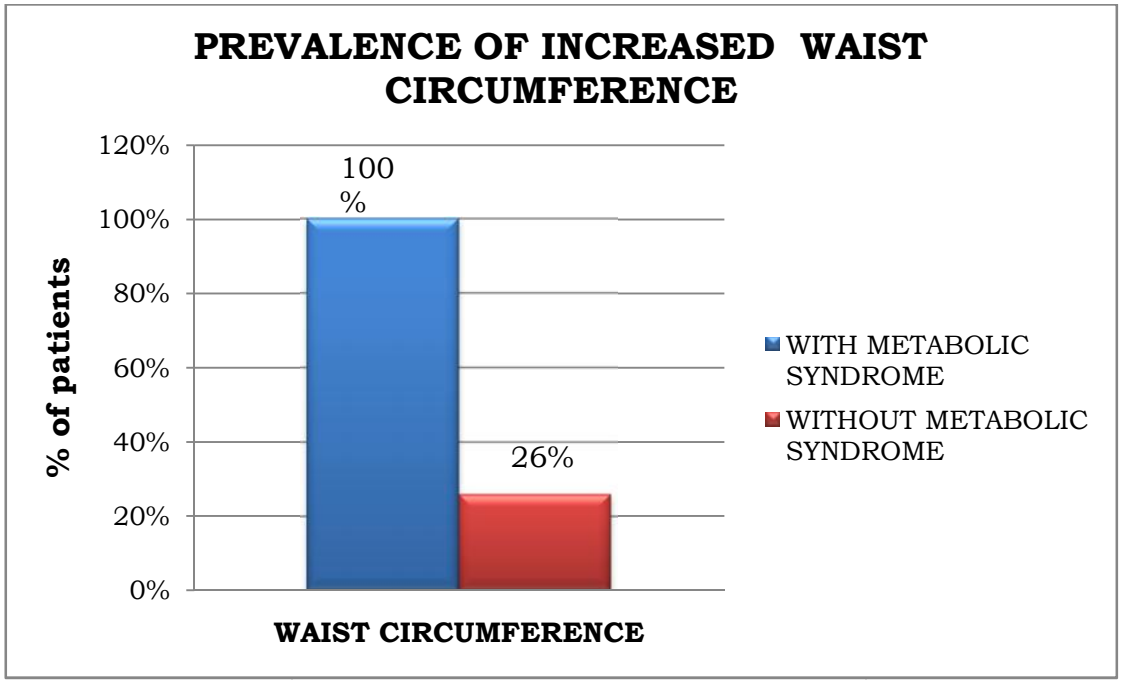
GRAPH5: SHOWING THE COMPARISION OF SMOKERS AND NON SMOKERS IN PATIENTS WITH AND WITHOUT METABOLIC SYNDROME



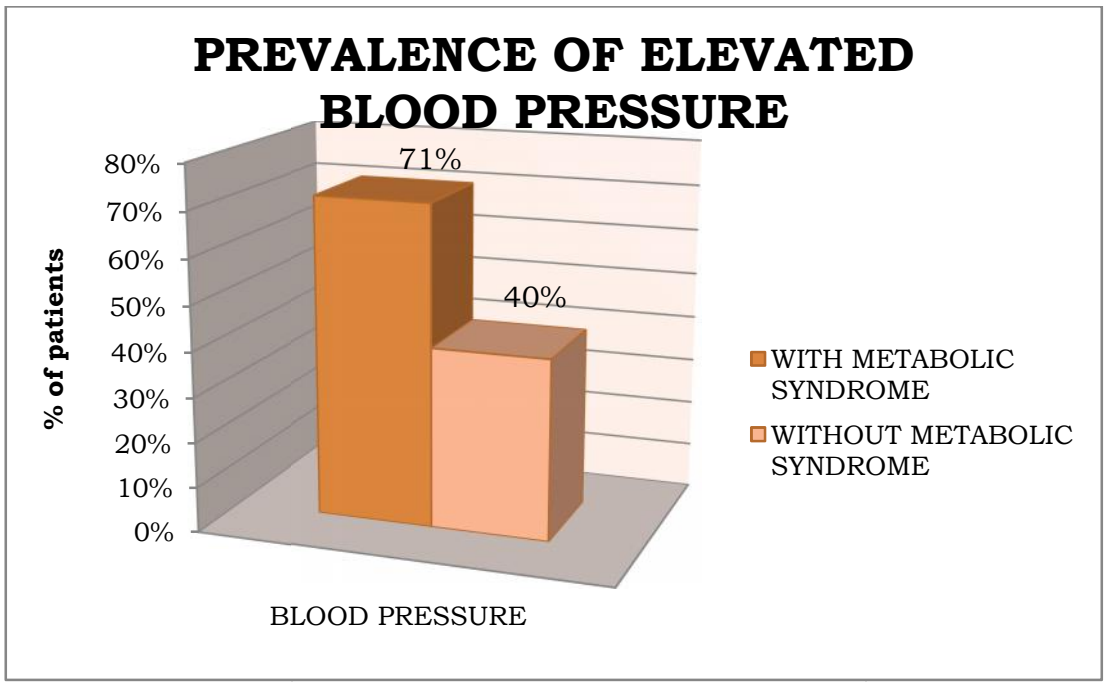
GRAPH 6: SHOWING THE PREVALENCE OF ALCOHOL INTAKE AMONG THE STUDY POPULATION



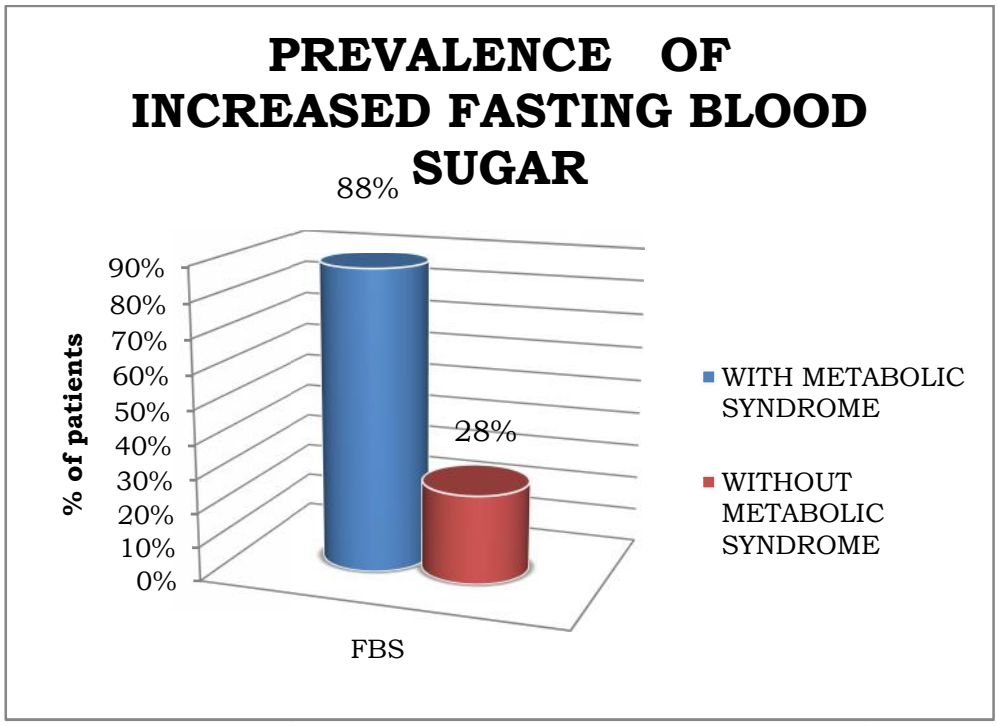
GRAPH 7: SHOWING THE COMPARISION OF INCREASED WAIST CIRCUMFERENCE AMONG PATIENTS WITH AND WITHOUT METABOLIC SYNDROME



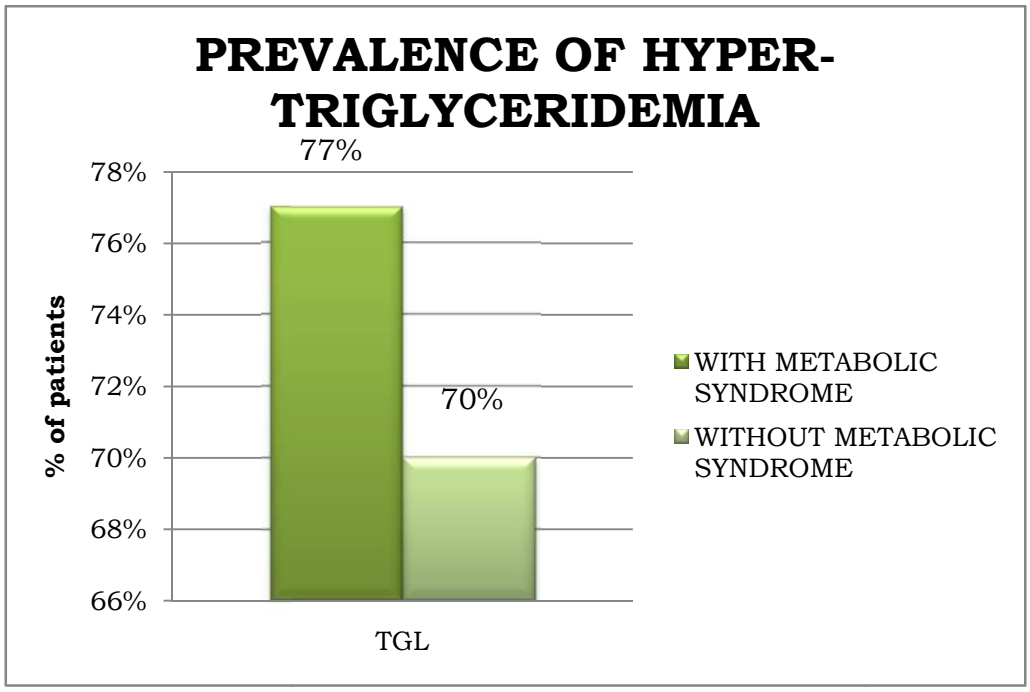
GRAPH 8: SHOWING THE COMPARISION OF ELEVATED BLOOD PRESSURE AMONG PATIENTS WITH AND WITHOUT METABOLIC SYNDROME



GRAPH 9: SHOWING THE COMPARISION OF ELEVATED FASTING BLOOD SUGAR AMONG PATIENTS WITH AND WITHOUT METABOLIC SYNDROME



GRAPH 10: SHOWING THE COMPARISION OF HYPERTRIGLYCERIDEMIA AMONG PATIENTS WITH AND WITHOUT METABOLIC SYNDROME



GRAPH 11: SHOWING THE COMPARISION OF DECREASED HDL AMONG PATIENTS WITH AND WITHOUT METABOLIC SYNDROME

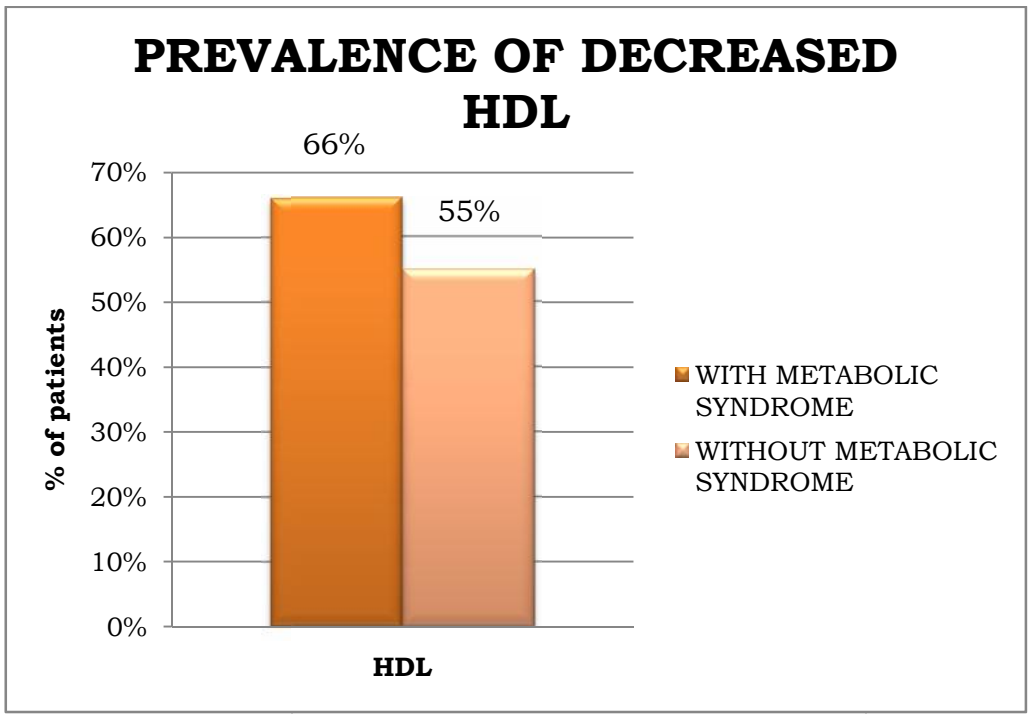


TABLE 2: SHOWING THE CLINICAL CHARACTERISTICS OF THE STUDY POPULATION

CHARACTERISTICS	PATIENTS WITH METABOLIC SYNDROME (n = 35)	PATIENTS WITHOUT METABOLIC SYNDROME (n = 27)	P VALUE
DEMOGRAPHIC FACTORS AGE	38.6±5.45	41.5±3.1	NS
MALE	32	25	NS
FEMALE	6	2	NS
POST MENOPAUSAL	3	-	
SMOKER	25	22	NS
NON SMOKER	10	5	NS
ALCOHOLIC	24	22	NS
NON ALCOHOLIC	11	5	NS
VEGETARIAN DIET	3	1	NS
NON VEGETARIAN DIET	32	26	NS
COMPONENTS INCREASED WAIST CIRCUMFERENCE	35	7	NS
HIGH BLOOD PRESSURE	25	11	NS
ELEVATED TRIGLYCERIDES	27	19	p<0.001
LOW HDL	23	15	p<0.001
ELEVATED FASTING GLUCOSE	31	7	p<0.001

DISCUSSION

This study is conducted on patients admitted to the Coronary Care Unit (CCU) of Government Rajaji Hospital, Madurai during the period of February 2016 to July 2016. All patients admitted with a diagnosis of AMI with age less than 45 years to the Coronary Care Unit (CCU) are included in the study. Acute myocardial infarction is defined as at least two of the following: prolonged chest discomfort, typical electrocardiographic changes, or elevated

Cardiac troponin levels, as outlined by the Joint European Society of Cardiology/American College of Cardiology Committee. Patients with Rheumatic heart disease, congenital heart disease, severe anemia, chronic kidney and liver disease, cocaine abuse, lack of definitive MI criteria and Age > 45 years are excluded from the study. A total of about 62 patients were studied during the given period after satisfying the inclusion criteria and obtaining written consent from the patients. Patients who satisfied the international diabetes federation criteria were diagnosed to have metabolic syndrome.

Age distribution

A total of about sixty two patients were studied, of which 35 (56%) of the patients fulfilled the criteria for metabolic syndrome.

Remaining patients with age <45 years and Acute myocardial infarction without metabolic syndrome constituted 44% (n= 27).

The mean age for patients with metabolic syndrome is 38.6 with a standard deviation of ±5.45. The mean age for patients without metabolic syndrome is 41.51, with a standard deviation of ±3.13

There were no patients below 20 years of age. Between 21 and 30 years, there were 3 patients all of whom were males. Between 31 and 40 years there were 26 patients, of whom 25 were males and one female. More than 41 years, there were 33 patients, oh who 26 were males and 7 females.(graph 2)

All the 3 patients between 21 and 30 years had metabolic syndrome. Between 31 and 40 years (n=26), 16 patients (61/%) of them satisfied the criteria for metabolic syndrome (graph 3). In the age group of > 41 years (n=33), 16 patients (48%) had metabolic syndrome. The overall prevalence of metabolic syndrome (n=62), was 56% (n=35). From the table 1, it is obvious that younger age groups had higher prevalence of metabolic syndrome than older age groups.

Sex distribution

Data from graph 1 reveals that out of 62 patients, 87% (n=54) of the patients were males and 13% (n=8) females.

Prevalence of smokers

The prevalence of smokers was 76% among the study population, as seen in the graph 4. Among patients who satisfied the criteria for metabolic syndrome, 71% (n=25) of the patients were smokers and remaining 29% were non smokers. Among patients without metabolic syndrome 66% (n=8) were smokers and remaining 34% non-smokers. However the p value is not significant in our study to say that smoking increases the prevalence of metabolic syndrome or myocardial infarction.

Prevalence of alcoholism

In our study, the prevalence of alcoholics was 74% and non alcoholics 26%. (graph6)

PREVALENCE OF INDIVIDUAL COMPONENTS OF METABOLIC SYNDROME

WAIST CIRCUMFERENCE

Increased waist circumference >80 for female and> 90 for males is the mandatory criteria to diagnose metabolic syndrome according to IDF criteria. In our study 42 patients had increased waist circumference of which 35 patients satisfied the remaining criteria for metabolic syndrome. Of the 27 patients without MS, 7 patients (26%) had increased waist circumference. (Graph 7). In a study done by N Ranjith

et al in department of cardiology at Nelson Mandela School of medicine, increased waist circumference was present in 16% of the young MI patients without metabolic syndrome.

ELEVATED BLOOD PRESSURE

Elevated blood pressure >130/80 is an important criteria for diagnosing metabolic syndrome. It is present in about 71% (n=25) of the patients with metabolic syndrome and 40% (n=11) of patients without metabolic syndrome (Graph8). In a study done by N Ranjith et al in Department Of Cardiology at Nelson Mandela School of medicine, elevated blood pressure was present in about 51% of patients with metabolic syndrome and 29% of patients without metabolic syndrome.

FASTING BOOD SUGAR

Elevated fasting blood sugar >100mg/dl is present in about 88% of patients with metabolic syndrome and 28% of patients without metabolic syndrome (graph 9). In a study done by N Ranjith et al in department of cardiology at Nelson Mandela School of medicine, elevated fasting glucose is present n 91% of patients with metabolic syndrome and 71% of patients without metabolic syndrome.

HYPERTRIGLYCERIDEMIA

Increased levels of fasting triglyceride is seen in about 77 % (n=27) of patients with metabolic syndrome and 70% (n=19) of the patients without metabolic syndrome(graph 10). In a study done by N Ranjith et

al in department of cardiology at Nelson Mandela School of medicine, elevated TGL was present in about 78% of patients with metabolic syndrome and 42% of patients without metabolic syndrome.

DECREASED HDL

Decreased HDL in seen in about 66% (n=23) of patients with metabolic syndrome and 55% (n=15) of the patients without metabolic syndrome (graph11). In a study done by N Ranjith et al in department of cardiology at Nelson Mandela School of medicine, decreased HDL is present in 67% of patients with metabolic syndrome and 54% of patients without metabolic syndrome.

Our study shows a strong relationship of metabolic syndrome with myocardial infarction in young patients <45years.Of the individual components of metabolic syndrome, elevated fasting blood sugar has the highest positive predictive value of 88% followed by increased triglyceride levels in 77% , elevated blood pressure in 71% and decreased HDL in 66% of the patients.

CONCLUSION

Metabolic syndrome is highly prevalent in young patients with acute myocardial infarction. Hence all measures must be undertaken to prevent the cardiovascular events in these patients.

SUMMARY

- ✓ The metabolic syndrome also is a collection of systemic abnormalities that confer a person with it to high risk of cardiovascular disease (CVD).
- ✓ Each component of metabolic syndrome is an independent risk factor for cardiovascular and cerebrovascular disease.
- ✓ The metabolic syndrome is increasing in prevalence as result of rapid urbanisation
- ✓ Obesity, sedentary lifestyle, smoking and insulin resistance are important risk factors for metabolic syndrome
- ✓ Metabolic syndrome is diagnosed by various criteria like ATP III criteria, WHO criteria and IDF criteria.
- ✓ Indians have a higher risk for CAD at comparatively lower waist circumference than western people.
- ✓ Indians have a lower cutoff for waist circumference for diagnosing metabolic syndrome (>80cm for females and > 90cm for males)
- ✓ Increasing prevalence of myocardial infarction in young individuals is mainly due to increased in prevalence of metabolic syndrome.

BIBLIOGRAPHY

1. WHO (2008) (2008-2013). Action plan for global strategic for prevention and control of non-communicable diseases. WHO, Geneva

2. Reaven G.M: The metabolic syndrome: Requiescat in pace.Clin Chem 51:931–938,
   2005
3. Lohsoonthorn V, Dhanamun B, Williams M A. Prevalence of Metabolic syndrome & its relationship to white blood cell count in population of Thai men &women receiving routine health examinations. Am J Hypertens2006; 19: 339-45

4. Feng Y, Hong X, Li Z, Zhang W, Jin D, Li UX, Zhang Y, Hu FB, Wei LJ, Zang T,
   Xux.Prevalence of metabolic syndrome & its relation to body composition in a
   Chinese rural population obesity.silver spring, med 2006;2089-98

5. Makuyana D, Gomo Zar, Munyombwe T, Matenga JA, Hakim JG. Metabolic syndrome disorders in urban black Zimbabweans with type 2 Diabetes mellitus. Cent Afr J Med. 2004 Mar–Apr; 50(3-4):24–29.

6. Alebiosu Christopher Olutayo, Odusan B Olatunde. Metabolic syndrome in subjects with type-2 diabetes mellitus. J Natl Med Assoc. 2004 Jun; 96(6):817–821.

7. Poulsen, P.; Vaag, A.; Kyvik, K.; Beck-nielsen, H. (2001), "Genetic versus environmental aetiology of the metabolic syndrome among male and female twins", Diabetologia 44 (5): 537–54

8. Groop, Leif, Genetics of the metabolic syndrome, British Journal of Nutrition 2000;83:S39–S48

9. Bouchard, G. (1995), "Genetics and the metabolic syndrome", International journal of obesity 1995;19: 52–59
10. DI, Block ER, Herrera-Acosta J, Patel JM, Johnson RJ (2006). "A causal role for uric acid in fructose-induced metabolic syndrome". Am J Phys Renal Phys 2006;290: F625–F631

11. Hallfrisch J Metabolic effects of dietary fructose Faseb J 1990; 9: 2652–2660.

12. Reiser, Powell AS, Scholfield DJ, Panda P, Ellwood KC, Canary S JJ (1989). "Blood lipids, lipoproteins, apoproteins, and uric acid in men fed diets containing fructose or high-amylose cornstarch". Am J Clin Nutr 1989; 49: 832–839

13. Fukuchi S, Hamaguchi K, Seike M, Himeno K, Sakata T, Yoshimatsu H. Role of Fatty Acid Composition in the Development of Metabolic Disorders in Sucrose- Induced Obese Rats. Exp Biol Med 2004;229:486–493

14. 14. Motala A, Mbanya JC, Ramaiya K, Metabolic Syndrome in Sub- Saharan Africa. Ethn Dis. 2009;Suppl 2:S2-8-S2-10

15. Kelliny C, William J, Riesen W, Paccaud F, Bovet P,"Metabolic syndrome according to different definitions in a rapidly developing country of the African region Cardiovasc J S Afr 2007; 93(1):70-6

16. Fezeu L, Balkau B Kengne A P,et al. Metabolic syndrome in a sub Saharan African setting Atherosclerosis 2007; 93: 70-6

17. Fauci, Anthony S. Harrison's principles of internal medicine. McGraw-Hill Medical.2008; 1102-1103 ISBN 0-07-147692-X

18. Xu T, Zhang Y, Yu L, Tong W Prevalence of the metabolic syndrome and its risk factors in Inner Mongolia, China Acta Cardiol 2009;64: 397-404

19. Groop, Leif, Genetics of the metabolic syndrome, British Journal of Nutrition
2000;83:S39–S48

20. 20. Kahn R, Buse J, Ferrannini E, et al.The metabolic syndrome: Time for a critical appraisal: Joint statement from the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 2005;28:2289–2304

21. Renaldi O, Pramono B, Sinorita H, Purnomo LB, Asdie RH, Asdie AH Hypoadiponectinemia: a risk factor for metabolic syndrome. Acta Med Indones2009; 41: 20–4

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

23. Attvall S, Fowelin J, Lager I, Von Schenck H, Smith U. Smoking induces insulin resistance - a potential link with the insulin resistance syndrome. J Intern Med 1993; 233:327–32.

24. Rönnemaa T, Rönnemaa EM, Puukka P, Pyörälä K, Laakso M. Smoking is independently associated with high plasma insulin levels in nondiabetic men. Diabetes Care 1996; 19: 1229–32.

25. Nakanishi N, Nakamura K, Matsuo Y, Suzuki K, TataraK. Cigarette smoking and risk for impaired fasting glucose and type 2 diabetes in middle-aged Japanese men. Ann Intern Med 2000; 133: 183–91.

26. Liese AD, Mayer-Davis EJ, Haffner SM. Development of the multiple metabolic syndromes: an epidemiologic perspective. Epidemiol Rev 1998; 20: 157–72.

27. Reaven G Metabolic syndrome: pathophysiology and implications for management of cardiovascular disease. Circulation 2002;106: 286–8

28. Cryer PE, Haymond MW, Santiago JV, Shah SD. Norepinephrine and epinephrine release and adrenergic mediation of smoking-associated hemodynamic and metabolic events. N Engl J Med 1976; 295: 573–7.

29. Kirschbaum C, Wust S, Strasburger CJ (1992) 'Normal' cigarette smoking increases free cortisol in habitual smokers. Life Sci 1992; 50: 435–42.

30. Wilkins JN, Carlson HE, Van Vunakis H, Hill MA, Gritz E, Jarvik ME (1982) Nicotine from cigarette smoking increases circulating levels of cortisol, growth hormone, and prolactin in male chronic smokers. Psychopharmacology (Berl) 1982; 78: 305–8.

31. Bergman RN, Ader M. Free fatty acids and pathogenesis of type 2 diabetes mellitus. Trends Endocrinol Metab 2000; 11: 351–6.

32. Moffatt RJ, Owens SG. Cessation from cigarette smoking: changes in body weight, body composition, resting metabolism, and energy consumption. Metabolism 1991; 40: 465–70.

33. Stamford BA, Matter S, Fell RD, Papanek P. Effects of smoking cessation on weight gain, metabolic rate, caloric consumption, and blood lipids. Am J Clin Nutr 1986; 43: 486–94.

34. Ferrara CM, Kumar M, Nicklas B, McCrone S, Goldberg AP. Weight gain and adipose tissue metabolism after smoking cessation in women. Int J Obes Relat Metab Disord 2001; 25: 1322–6.

35. Perkins KA, Epstein LH, Marks BL, Stiller RL, Jacob RG. The effect of nicotine on energy expenditure during light physical activity. N Engl J Med 1989; 320:898–903.

36. Schutz Y, Tremblay A, Weinsier RL, Nelson K. Role of fat oxidation in the long-term stabilization of body weight in obese women. Am J Clin Nutr 1992; 55: 670–4.

37. Jensen EX, Fusch C, Jaeger P, Peheim E, Horber FF. Impact of chronic cigarette smoking on body composition and fuel metabolism. J Clin Endocrinol Metab 1995: 80: 2181–5.

38. 74. National Cholesterol Education Programme (NCEP) Adult Treatment Pannel III final report circulation 2002; 106:3143-3421

39. Third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). Final report. Circulation. 2002; 106: 3143–3421.

40. Reaven GM. Banting lecture 1988: role of insulin resistance in human disease. Diabetes. 1988; 37: 1595–1607.

41. Ferrannini E, Haffner SM, Mitchell BD, et al. Hyperinsulinaemia: the key feature of a cardiovascular and metabolic syndrome. Diabetologia. 1991; 34: 416–422.

42. Abbasi F, Brown BW, Lamendola C, et al. Relationship between obesity, insulin resistance, and coronary heart disease risk. J Am Coll Cardiol. 2002; 40: 937–943.

43. Bogardus C, Lillioja S, Mott DM, et al. Relationship between degree of obesity and in vivo insulin action in man. Am J Physiol. 1985; 248(3 pt 1): e286–e291.

44. Pacini G 2006 The hyperbolic equilibrium between insulin sensitivity and secretion. Nutr Metab Cardiovasc Dis 16 S22–S27

45. Bravata DM, Wells CK, Concato J, Kernan WN, Brass LM, Gulanski BI 2004 Two measures of insulin sensitivity provided similar information in a U.S. population. J Clin Epidemiol 57:1214–1217

46. Ginsberg HN 2000 Insulin resistance and cardiovascular disease. J Clin Invest 106:453–458 –

47. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, Gordon DJ, Krauss RM, Savage PJ, Smith Jr SC, Spertus JA, Costa F 2005 Diagnosis and management of the metabolic syndrome. An American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Executive summary. Cardiol Rev 13:322–327

48. Weir GC, Bonner-Weir S 2007 A dominant role for glucose in β-cell compensation of insulin resistance. J Clin Invest 117:81–83

49. Wajchenberg BL 2007 β-Cell failure in diabetes and preservation by clinical treatment. Endocr Rev 28:187–218

50. Kahn BB, Flier JS 2000 Obesity and insulin resistance. J Clin Invest 106:473–481

51. Eckel RH, Grundy SM, Zimmet PZ 2005 The metabolic syndrome. Lancet 365:1415–1428

52. Jocken JW, Langin D, Smit E, Saris WH, Valle C, Hul GB, Holm C, Arner P, Blaak EE 2007 Adipose triglyceride lipase and hormone-sensitive lipase protein expression is decreased in the obese insulin-resistant state. J Clin Endocrinol Metab 92:2292–2299

53. Kahn SE, Prigeon RL, Schwartz RS, Fujimoto WY, Knopp RH, Brunzell JD, Porte Jr D 2001 Obesity, body fat distribution, insulin sensitivity and Islet β-cell function as explanations for metabolic diversity. J Nutr 131:354S–360S

54. Weisberg SP, McCann D, Desai M, Rosenbaum M, Leibel RL, Ferrante Jr AW 2003 Obesity is associated with macrophage accumulation in adipose tissue. J Clin Invest 112:1796–1808

55. Sopasakis VR, Sandqvist M, Gustafson B, Hammarstedt A, Schmelz M, Yang X, Jansson PA, Smith U 2004 High local concentrations and effects on differentiation implicate interleukin-6 as a paracrine regulator. Obes Res 12:454–460

56. Hube F, Hauner H 1999 The role of TNF-α in human adipose tissue: prevention of weight gain at the expense of insulin resistance? Horm Metab Res 31:626–631

57. Lewis GF, Uffelman KD, Szeto LW, Steiner G 1993 Effects of acute hyperinsulinemia on VLDL triglyceride and VLDL apoB production in normal weight and obese individuals. Diabetes 42:833–842

58. Lewis GF, Steiner G 1996 Acute effects of insulin in the control of VLDL production in humans. Implications for the insulin-resistant state. Diabetes Care 19:390–393

59. Sniderman AD, Faraj M 2007 Apolipoprotein B, apolipoprotein A-I, insulin resistance and the metabolic syndrome. Curr Opin Lipidol 18:633–637

60. Murakami T, Michelagnoli S, Longhi R, Gianfranceschi G, Pazzucconi F, Calabresi L, Sirtori CR, Franceschini G 1995 Triglycerides are major determinants of cholesterol esterification/transfer and HDL remodeling in human plasma. Arterioscler Thromb Vasc Biol 15:1819–1828

61. Lewis GF, Rader DJ 2005 New insights into the regulation of HDL metabolism and reverse cholesterol transport. Circ Res 96:1221–1232

62. Jiang J, Torok N 2008 Nonalcoholic steatohepatitis and the metabolic syndrome. Metab Syndr Relat Disord 6:1–7

63. . Khashab M, Chalasani N 2007 Use of insulin sensitizers in NASH. Endocrinol Metab Clin North Am 36:1067–1087

64. 170. Frayn KN 2003 Metabolic regulation: a human perspective. Oxford, UK: Blackwell Science

65. Boden G, Chen X, Ruiz J, White JV, Rossetti L 1994 Mechanisms of fatty acid-induced inhibition of glucose uptake. J Clin Invest 93:2438–2446173.

66. Dresner A, Laurent D, Marcucci M, Griffin ME, Dufour S, Cline GW, Slezak LA, Andersen DK, Hundal RS, Rothman DL, Petersen KF, Shulman GI 1999 Effects of free fatty acids on glucose transport and IRS-1-associated phosphatidylinositol 3-kinase activity. J Clin Invest 103:253–259

67. Roden M, Krssak M, Stingl H, Gruber S, Hofer A, Furnsinn C, Moser E, Waldhausl W 1999 Rapid impairment of skeletal muscle glucose transport/phosphorylation by free fatty acids in humans. Diabetes 48:358–364

68. Pan DA, Lillioja S, Kriketos AD, Milner MR, Baur LA, Bogardus C, Jenkins AB, Storlien LH 1997 Skeletal muscle triglyceride levels are inversely related to insulin action. Diabetes 46:983–988

69. Summers SA 2006 Ceramides in insulin resistance and lipotoxicity. Prog Lipid Res 45:42–72

70. Bruce CR, Kriketos AD, Cooney GJ, Hawley JA 2004 Disassociation of muscle triglyceride content and insulin sensitivity after exercise training in patients with type 2 diabetes. Diabetologia 47:23–30

71. Sato F, Tamura Y, Watada H, Kumashiro N, Igarashi Y, Uchino H, Maehara T, Kyogoku S, Sunayama S, Sato H, Hirose T, Tanaka Y, Kawamori R 2007 Effects of diet-induced moderate weight reduction on intrahepatic and intramyocellular triglycerides and glucose metabolism in obese subjects. J Clin Endocrinol Metab 92:3326–3329

72. Takata Y, Osawa H, Kurata M, Kurokawa M, Yamauchi J, Ochi M, Nishida W, Okura T, Higaki J, Makino H 2008 Hyperresistinemia is associated with coexistence of hypertension and type 2 diabetes. Hypertension 51:534–539

73. Bernal-Mizrachi C, Weng S, Li B, Nolte LA, Feng C, Coleman T, Holloszy JO, Semenkovich CF 2002 Respiratory uncoupling lowers blood pressure through a leptin-dependent mechanism in genetically obese mice. Arterioscler Thromb Vasc Biol 22:961–968

74. Kim SP, Catalano KJ, Hsu IR, Chiu JD, Richey JM, Bergman RN 2007 Nocturnal free fatty acids are uniquely elevated in the longitudinal development of diet-induced insulin resistance and hyperinsulinemia. Am J Physiol Endocrinol Metab 292:E1590—E1598

75. Lakka HM, Laaksonen DE, Lakka TA, et al. The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. JAMA. 2002; 288: 2709–2716.

76. Wilson PW, D'Agostino RB, Levy D, et al. Prediction of coronary heart disease using risk factor categories. Circulation. 1998; 97: 1837–1847

77. Gami AS, Witt BJ, Howard DE, Erwin PJ, Gami LA, Somers VK, Montori VM 2007 Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and meta-analysis of longitudinal studies. J Am Coll Cardiol 49:403–414

78. Lakka HM, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E, Tuomilehto J, Salonen JT 2002 The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. JAMA 288:2709–2716

79. Malik S, Wong ND, Franklin SS, Kamath TV, L'Italien GJ, Pio JR, Williams GR 2004 Impact of the metabolic syndrome on mortality from coronary heart disease, cardiovascular disease, and all causes in United States adults. Circulation 110:1245–1250

80. Wilson PW, D'Agostino RB, Parise H, Sullivan L, Meigs JB 2005 Metabolic syndrome as a precursor of cardiovascular disease and type 2 diabetes mellitus. Circulation 112:3066–3072

81. Isomaa B, Almgren P, Tuomi T, Forsen B, Lahti K, Nissen M, Taskinen MR, Groop L 2001 Cardiovascular morbidity and mortality associated with the metabolic syndrome. Diabetes Care 24:683–689

82. Dekker JM, Girman C, Rhodes T, Nijpels G, Stehouwer CD, Bouter LM, Heine RJ 2005 Metabolic syndrome and 10-year cardiovascular disease risk in the Hoorn Study. Circulation 112:666–673

83. Daly CA, Hildebrandt P, Bertrand M, Ferrari R, Remme W, Simoons M, Fox KM 2007 Adverse prognosis associated with the metabolic syndrome in established coronary artery disease. Data from the EUROPA trial. Heart 93:1406–1411

84. McNeill AM, Katz R, Girman CJ, Rosamond WD, Wagenknecht LE, Barzilay JI, Tracy RP, Savage PJ, Jackson SA 2006 Metabolic syndrome and cardiovascular disease in older people: the Cardiovascular Health Study. J Am Geriatr Soc 54:1317–1324

85. 392. Klein BE, Klein R, Lee KE 2002 Components of the metabolic syndrome and risk of cardiovascular disease and diabetes in Beaver Dam. Diabetes Care 25:1790–1794

86. 393. Bruno G, Merletti F, Biggeri A, Bargero G, Ferrero S, Runzo C, Prina Cerai S, Pagano G, Cavallo-Perin P 2004 Metabolic syndrome as a predictor of all-cause and cardiovascular mortality in type 2 diabetes: the Casale Monferrato Study. Diabetes Care 27:2689–2694

87. 394. Sattar N, McConnachie A, Shaper AG, Blauw GJ, Buckley BM, de Craen AJ, Ford I, Forouhi NG, Freeman DJ, Jukema JW, Lennon L, Macfarlane PW, Murphy MB, Packard CJ, Stott DJ, Westendorp RG, Whincup PH, Shepherd J, Wannamethee SG 2008 Can metabolic syndrome usefully predict cardiovascular disease and diabetes? Outcome data from two prospective studies. Lancet 371:1927–1935

88. Resnick HE, Jones K, Ruotolo G, Jain AK, Henderson J, Lu W, Howard BV 2003 Insulin resistance, the metabolic syndrome, and risk of incident cardiovascular disease in nondiabetic American Indians: the Strong Heart Study. Diabetes Care 26:861–867

89. Kragelund C, Kober L, Faber J, Steffensen R, Hildebrandt P 2007 Metabolic syndrome and mortality in stable coronary heart disease: relation to gender. Int J Cardiol 121:62–67

90. . Kannel WB, Larson M 1993 Long-term epidemiologic prediction of coronary disease. The Framingham experience. Cardiology 82:137–152

91. McNeill AM, Rosamond WD, Girman CJ, Golden SH, Schmidt MI, East HE, Ballantyne CM, Heiss G 2005 The metabolic syndrome and 11-year risk of incident cardiovascular disease in the atherosclerosis risk in communities study. Diabetes Care 28:385–390

92. Wannamethee SG, Shaper AG, Lennon L, Morris RW 2005 Metabolic syndrome vs Framingham Risk Score for prediction of coronary heart disease, stroke, and type 2 diabetes mellitus. Arch Intern Med 165:2644–2650

93. Assmann G, Guerra R, Fox G, Cullen P, Schulte H, Willett D, Grundy SM 2007 Harmonizing the definition of the metabolic syndrome: comparison of the criteria of the Adult Treatment Panel III and the International Diabetes Federation in United States American and European populations. Am J Cardiol 99:541–548

94. Reaven GM 2005 Insulin resistance, the insulin resistance syndrome, and cardiovascular disease. Panminerva Med 47:201–210

95. Lebovitz HE 1999 Type 2 diabetes: an overview. Clin Chem 45:1339–1345

96. Meigs JB, Rutter MK, Sullivan LM, Fox CS, D'Agostino Sr RB, Wilson PW 2007 Impact of insulin resistance on risk of type 2 diabetes and cardiovascular disease in people with metabolic syndrome. Diabetes Care 30:1219–1225

97. Bonora E, Targher G, Formentini G, Calcaterra F, Lombardi S, Marini F, Zenari L, Saggiani F, Poli M, Perbellini S, Raffaelli A, Gemma L, Santi L, Bonadonna RC, Muggeo M 2004 The metabolic syndrome is an independent predictor of cardiovascular disease in type 2 diabetic subjects. Prospective data from the Verona Diabetes Complications Study. Diabet Med 21:52–58

98. Hanson RL, Imperatore G, Bennett PH, Knowler WC 2002 Components of the "metabolic syndrome" and incidence of type 2 diabetes. Diabetes 51:3120–3127

99. Hanley AJ, Karter AJ, Williams K, Festa A, D'Agostino Jr RB, Wagenknecht LE, Haffner SM 2005 Prediction of type 2 diabetes mellitus with alternative definitions of the metabolic syndrome: the Insulin Resistance Atherosclerosis Study. Circulation 112:3713–3721

100. Laaksonen DE, Lakka HM, Niskanen LK, Kaplan GA, Salonen JT, Lakka TA 2002 Metabolic syndrome and development of diabetes mellitus: application and validation of recently suggested definitions of the metabolic syndrome in a prospective cohort study. Am J Epidemiol 156:1070–1077

101. Lauenborg J, Mathiesen E, Hansen T, Glumer C, Jorgensen T, Borch-Johnsen K, Hornnes P, Pedersen O, Damm P 2005 The prevalence of the metabolic syndrome in a Danish population of women with previous gestational diabetes mellitus is three-fold higher than in the general population. J Clin Endocrinol Metab 90:4004–4010

102. Verma A, Boney CM, Tucker R, Vohr BR 2002 Insulin resistance syndrome in women with prior history of gestational diabetes mellitus. J Clin Endocrinol Metab 87:3227–3235

103. Bloomgarden ZT 2005 Second World Congress on the Insulin Resistance Syndrome: insulin resistance syndrome and nonalcoholic fatty liver disease. Diabetes Care 28:1518–1523

104. Hamaguchi M, Kojima T, Takeda N, Nakagawa T, Taniguchi H, Fujii K, Omatsu T, Nakajima T, Sarui H, Shimazaki M, Kato T, Okuda J, Ida K 2005 The metabolic syndrome as a predictor of nonalcoholic fatty liver disease. Ann Intern Med 143:722–728

105. Bugianesi E, Pagotto U, Manini R, Vanni E, Gastaldelli A, de Iasio R, Gentilcore E, Natale S, Cassader M, Rizzetto M, Pasquali R, Marchesini G 2005

Plasma adiponectin in nonalcoholic fatty liver is related to hepatic insulin resistance and hepatic fat content, not to liver disease severity. J Clin Endocrinol Metab 90:3498–3504

106. Ehrmann DA, Barnes RB, Rosenfield RL, Cavaghan MK, Imperial J 1999 Prevalence of impaired glucose tolerance and diabetes in women with polycystic ovary syndrome. Diabetes Care 22:141–146
107. Talbott EO, Guzick DS, Sutton-Tyrrell K, McHugh-Pemu KP, Zborowski JV, Remsberg KE, Kuller LH 2000 Evidence for association between polycystic ovary syndrome and premature carotid atherosclerosis in middle-aged women. Arterioscler Thromb Vasc Biol 20:2414–2421

108.. Orio Jr F, Palomba S, Spinelli L, Cascella T, Tauchmanova L, Zullo F, Lombardi G, Colao A 2004 The cardiovascular risk of young women with polycystic ovary syndrome: an observational, analytical, prospective case-control study. J Clin Endocrinol Metab 89:3696–3701

109. Christian RC, Dumesic DA, Behrenbeck T, Oberg AL, Sheedy 2nd PF, Fitzpatrick LA 2003 Prevalence and predictors of coronary artery calcification in women with polycystic ovary syndrome. J Clin Endocrinol Metab 88:2562–2568

110. Vgontzas AN, Bixler EO, Chrousos GP 2005 Sleep apnea is a manifestation of the metabolic syndrome. Sleep Med Rev 9:211–224

111. Wolk R, Somers VK 2007 Sleep and the metabolic syndrome. Exp Physiol 92:67–78

112. Ip MS, Lam B, Ng MM, Lam WK, Tsang KW, Lam KS 2002 Obstructive sleep apnea is independently associated with insulin resistance. Am J Respir Crit Care Med 165:670–676

113. Bansal TC, Guay AT, Jacobson J, Woods BO, Nesto RW 2005 Incidence of metabolic syndrome and insulin resistance in a population with organic erectile dysfunction. J Sex Med 2:96–103

114. Bal K, Oder M, Sahin AS, Karatas CT, Demir O, Can E, Gumus BH, Ozer K, Sahin O, Esen AA 2007 Prevalence of metabolic syndrome and its association with erectile dysfunction among urologic patients: metabolic backgrounds of erectile dysfunction. Urology 69:356–360

115. Carr MC 2003 The emergence of the metabolic syndrome with menopause. J Clin Endocrinol Metab 88:2404–2411

116. Margolis KL, Bonds DE, Rodabough RJ, Tinker L, Phillips LS, Allen C, Bassford T, Burke G, Torrens J, Howard BV 2004 Effect of oestrogen plus progestin on the incidence of diabetes in postmenopausal women: results from the Women's Health Initiative Hormone Trial. Diabetologia 47:1175–1187

117. Samaras K, Wand H, Law M, Emery S, Cooper D, Carr A 2007 Prevalence of metabolic syndrome in HIV-infected patients receiving highly active antiretroviral therapy using International Diabetes Foundation and Adult Treatment Panel III criteria: associations with insulin resistance, disturbed body fat compartmentalization, elevated C-reactive protein, and [corrected] hypoadiponectinemia. Diabetes Care 30:113–119

118. Falasca K, Ucciferri C, Manzoli L, Mancino P, Pizzigallo E, Conti P, Vecchiet J 2007 Metabolic syndrome and cardiovascular risk in HIV-infected patients with lipodystrophy. Int J Immunopathol Pharmacol 20:519–527

119. Krentz AJ, Clough G, Byrne CD 2007 Interactions between microvascular and macrovascular disease in diabetes: pathophysiology and therapeutic implications. Diabetes Obes Metab 9:781–791

120. Cull CA, Jensen CC, Retnakaran R, Holman RR 2007 Impact of the metabolic syndrome on macrovascular and microvascular outcomes in type 2 diabetes mellitus: United Kingdom Prospective Diabetes Study 78. Circulation 116:2119–2126

121. Orchard TJ, Temprosa M, Goldberg R, Haffner S, Ratner R, Marcovina S, Fowler S 2005 The effect of metformin and intensive lifestyle intervention on the metabolic syndrome: the Diabetes Prevention Program Randomized Trial. Ann Intern Med 142:611–619

122. Hamman RF, Wing RR, Edelstein SL, Lachin JM, Bray GA, Delahanty L, Hoskin M, Kriska AM, Mayer-Davis EJ, Pi-Sunyer X, Regensteiner J, Venditti B, Wylie-Rosett J 2006 Effect of weight loss with lifestyle intervention on risk of diabetes. Diabetes Care 29:2102–2107

123. McKeown NM, Meigs JB, Liu S, Saltzman E, Wilson PW, Jacques PF 2004 Carbohydrate nutrition, insulin resistance, and the prevalence of the metabolic syndrome in the Framingham Offspring Cohort. Diabetes Care 27:538–546

124. Lutsey PL, Steffen LM, Stevens J 2008 Dietary intake and the development of the metabolic syndrome: the Atherosclerosis Risk in Communities study. Circulation 117:754–761

125. Liese AD, Gilliard T, Schulz M, D'Agostino Jr RB, Wolever TM 2007 Carbohydrate nutrition, glycaemic load, and plasma lipids: the Insulin Resistance Atherosclerosis Study. Eur Heart J 28:80–87

126. Stern L, Iqbal N, Seshadri P, Chicano KL, Daily DA, McGrory J, Williams M, Gracely EJ, Samaha FF 2004 The effects of low-carbohydrate versus conventional weight loss diets in severely obese adults: one-year follow-up of a randomized trial. Ann Intern Med 140:778–785 –

127. Lewis CJ, Park YK, Dexter PB, Yetley EA 1992 Nutrient intakes and body weights of persons consuming high and moderate levels of added sugars. J Am Diet Assoc 92:708–713

128. Jenkins DJ, Kendall CW, Augustin LS, Franceschi S, Hamidi M, Marchie A, Jenkins AL, Axelsen M 2002 Glycemic index: overview of implications in health and disease. Am J Clin Nutr 76:266S–273S

129. Appel LJ, Brands MW, Daniels SR, Karanja N, Elmer PJ, Sacks FM 2006 Dietary approaches to prevent and treat hypertension: a scientific statement from the American Heart Association. Hypertension 47:296–308

130. LaMonte MJ, Barlow CE, Jurca R, Kampert JB, Church TS, Blair SN 2005 Cardiorespiratory fitness is inversely associated with the incidence of metabolic syndrome: a prospective study of men and women. Circulation 112:505–512

131. Wing RR, Hill JO 2001 Successful weight loss maintenance. Annu Rev Nutr 21:323–341 578.

132. Katsanos CS 2006 Prescribing aerobic exercise for the regulation of postprandial lipid metabolism: current research and recommendations. Sports Med 36:547–560

133. Balducci S, Zanuso S, Massarini M, Corigliano G, Nicolucci A, Missori S, Cavallo S, Cardelli P, Alessi E, Pugliese G, Fallucca F 2007 The Italian Diabetes and Exercise Study (IDES): design and methods for a prospective Italian multicentre trial of intensive lifestyle intervention in people with type 2 diabetes and the metabolic syndrome. Nutr Metab Cardiovasc Dis 18:585–595

134. Alberti KG et al: Harmonizing the metabolic syndrome: A joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 120:1640, 2009[PMID: 19805654]

135. D'Agostino RB et al: General cardiovascular risk profile for use in primary care: The Framingham Heart Study. Circulation 117:743, 2008[PMID: 18212285]

136. Delahoy PJ et al: The relationship between reduction in low-density lipoprotein cholesterol by statins and reduction in risk of cardiovascular outcomes: An updated meta-analysis. Clin Ther 31:236, 2009[PMID: 19302897]

137. Hamsten A, Eriksson P: Identifying the susceptibility genes for coronary artery disease: From hyperbole through doubt to cautious optimism. J Intern Med 263:538, 2008[PMID: 18410597]

138. Libby P et al: Inflammation in atherosclerosis: From pathophysiology to practice. J Am Coll Cardiol 54:2129, 2009[PMID: 19942084]

139. Mosca L et al: Evidence-based guidelines for cardiovascular disease prevention in women: 2007 update. Circulation 115:1481, 2007[PMID: 17309915]

140. Ridker PM et al: C-reactive protein and parental history improve global cardiovascular risk prediction: The Reynolds Risk Score for men. Circulation 118:2243, 2008[PMID: 18997194]

141. Shao B, Heinecke JW: HDL, lipid peroxidation, and atherosclerosis. J Lipid Res 50:599, 2009[PMID: 19141435]

PROFORMA:

Name:

Age / Sex:

IP no:

Occupation:

Presenting complaints:

Past History:

h/o previous MI/ CAD

H/o DM, HT, CKD, CVD, DRUG INTAKE, Thyroid disorders, **Personal history**

cocaine abuse

smoker/ nonsmoker

alcoholic/ non alcoholic

vegetarian/ non vegetarian

Family H/o CAD

Clinical Examination:

General Examination:

Consciousness, Pallor, jaundice, Clubbing, Lymphadenopathy, hydration status

Vitals:

PR

BP

RR

SpO2

Anthropometry:

Waist circumference

Height

Weight

Systemic examination:

CVS:

RS:

ABDOMEN:

CNS:

Laboratory investigations:

Fasting lipid profile

Fasting plasma glucose

Diagnosis

MASTER CHART

name	sex	age	veg/NV	smoker	alcoholic	WC	BP	RBS	TGL	HDL	MS
kuppusamy	male	42	NV	Y	Y	96	N	112	157	44	y
kadhir	male		NV	Y	Y	92	N	105	195	42	y
alagappan	male	35	V	N	Y	99	N	142	157	46	y
mudaliyar	male	41	NV	Y	Y	102	N	132	157	42	y
karthik	male	28	NV	Y	Y	98	N	112	164	44	y
saravanan	male	38	V	N	Y	101	Y	109	168	44	y
joseph	male	44	NV	Y	N	96	Y	117	187	46	y
vasanthan	male	43	NV	Y	Y	92	Y	124	164	48	y
ramu	male	38	V	Y	Y	96	Y	124	157	44	y
keshavan	male	45	NV	N	Y	95	Y	108	153	42	y
muthu nadar	male	44	NV	Y	Y	99	Y	135	157	44	y
vaidhyanathan	male	43	NV	Y	Y	95	y	184	186	34	y
vikram	male	32	NV	Y	Y	94	y	104	185	36	y
selvam	male	38	NV	Y	N	91	y	119	157	36	y
murali	male	44	NV	N	Y	92	y	186	195	33	y
prabhu	male	41	NV	Y	Y	98	y	164	192	38	y
prakash	male	35	NV	Y	Y	106	y	148	132	34	y
suresh	male	34	NV	Y	Y	108	y	108	130	38	y
mahalingam	male	44	NV	Y	Y	96	y	157	126	36	y
velayutham	male	40	NV	Y	Y	103	y	154	124	34	y
venkatesan	male	40	NV	Y	Y	98	y	164	120	30	y
alagu	male	33	NV	Y	N	97	y	149	138	32	y
balamurugan	male	31	NV	Y	Y	99	y	147	144	38	y
mohan	male	44	NV	Y	Y	105	y	143	176	34	y
chandran	male	40	NV	Y	N	101	Y	84	178	36	y
sai saravana	male	27	NV	Y	Y	99	Y	86	194	38	y
chokkalingam	male	31	NV	Y	Y	94	N	95	175	38	y
marimuthu	male	28	NV	Y	N	98	Y	94	165	36	Y
lingesh	male	38	NV	Y	Y	101	y	102	140	44	y

MASTER CHART

kasi nathan	male	41	NV	N	Y	94	N	113	142	42	N
seekumar	male	40	NV	N	Y	99	N	118	134	46	N
jegan	male	44	NV	N	Y	95	N	116	132	48	N
anandan	male	45	NV	N	Y	99	N	124	124	42	N
manivannan	male	43	NV	Y	Y	95	N	134	134	42	N
mohankumar	male	41	NV	Y	Y	99	N	165	124	46	N
sivakesavan	male	41	NV	N	Y	85	N	124	140	38	N
mahalingam g	male	43	NV	Y	Y	84	Y	124	156	34	N
manoj	male	39	NV	Y	N	88	Y	154	165	36	N
syed akbar	male	40	NV	Y	Y	81	Y	134	186	36	N
vedathiyar	male	45	NV	Y	Y	80	Y	132	186	38	N
rathnavel	male	45	NV	Y	Y	86	Y	121	174	34	N
panner	male	43	NV	N	Y	81	Y	154	157	30	N
senthil	male	45	NV	Y	Y	88	Y	124	168	32	N
vijay	male	40	NV	Y	N	87	Y	120	154	34	N
anand kumar	male	39	V	Y	Y	79	Y	142	154	36	N
dhanush	male	40	NV	Y	Y	80	Y	154	185	38	N
bhaskaran	male	44	NV	Y	Y	82	Y	108	165	34	N
venkatachlapthy	male	41	NV	Y	Y	88	Y	115	187	36	N
senthilpandi	male	38	NV	Y	N	87	N	105	186	31	N
vairamuthu	male	34	NV	Y	Y	80	N	86	164	44	N
thirumoorthy	male	45	NV	Y	Y	82	N	72	168	42	N
kuppan	male	43	NV	Y	Y	87	N	75	186	44	N
sathyamurthy	male	34	NV	Y	Y	84	N	78	176	46	N
akshay	male	39	NV	Y	Y	86	N	89	162	44	N
rajathi	female	44	NV	N	N	99	N	112	165	44	y
rajammal	female	45	NV	N	N	104	N	110	158	42	y
lakshmi	female	44	NV	N	N	101	N	147	154	38	y
kumari	female	41	NV	N	N	98	Y	154	157	42	y
selvi	female	40	NV	N	N	99	Y	125	164	44	y
saraswathi	female	45	NV	N	N	78	Y	84	142	46	N
suseela	female	44	NV	N	N	98	Y	88	174	52	N
pothumponnu	female	43	NV	N	N	96	Y	140	154	42	y

ABBREVIATIONS

MS Metabolic Syndrome

HDL High Density Lipoprotein

LDL Low Density Lipoprotein

VLDL Very Low Density Lipoprotein

TGL Triglycerides

BP Blood Pressure

FBS Fasting Blood Sugar

CVD Cardio Vascular Disease

DM Diabetes Mellitus

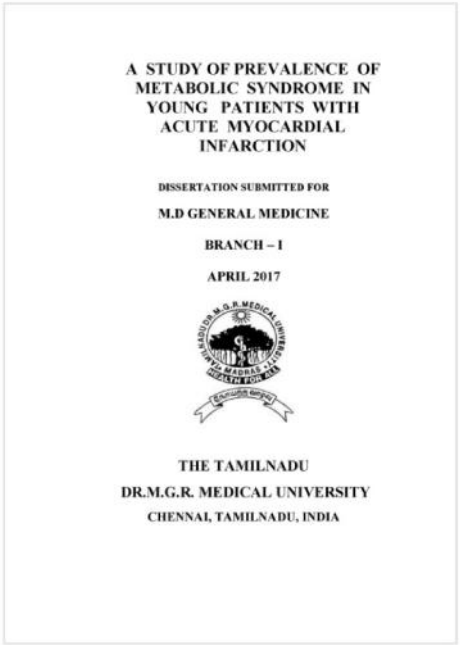
turnitin

Digital Receipt

This receipt acknowledges that Turnitin received your paper. Below you will find the receipt information regarding your submission.

The first page of your submissions is displayed below.

Submission author:	201411118 Md Genmed B.Suresh K..
Assignment title:	2015-2015 plagiarism
Submission title:	A STUDY OF PREVALENCE OF ME...
File name:	sk_desstatin.docx
File size:	934.25K
Page count:	85
Word count:	10,970
Character count:	62,547
Submission date:	18-Sep-2016 09:48PM
Submission ID:	705876307



A STUDY OF PREVALENCE OF METABOLIC SYNDROME IN YOUNG PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

DISSERTATION SUBMITTED FOR

M.D GENERAL MEDICINE

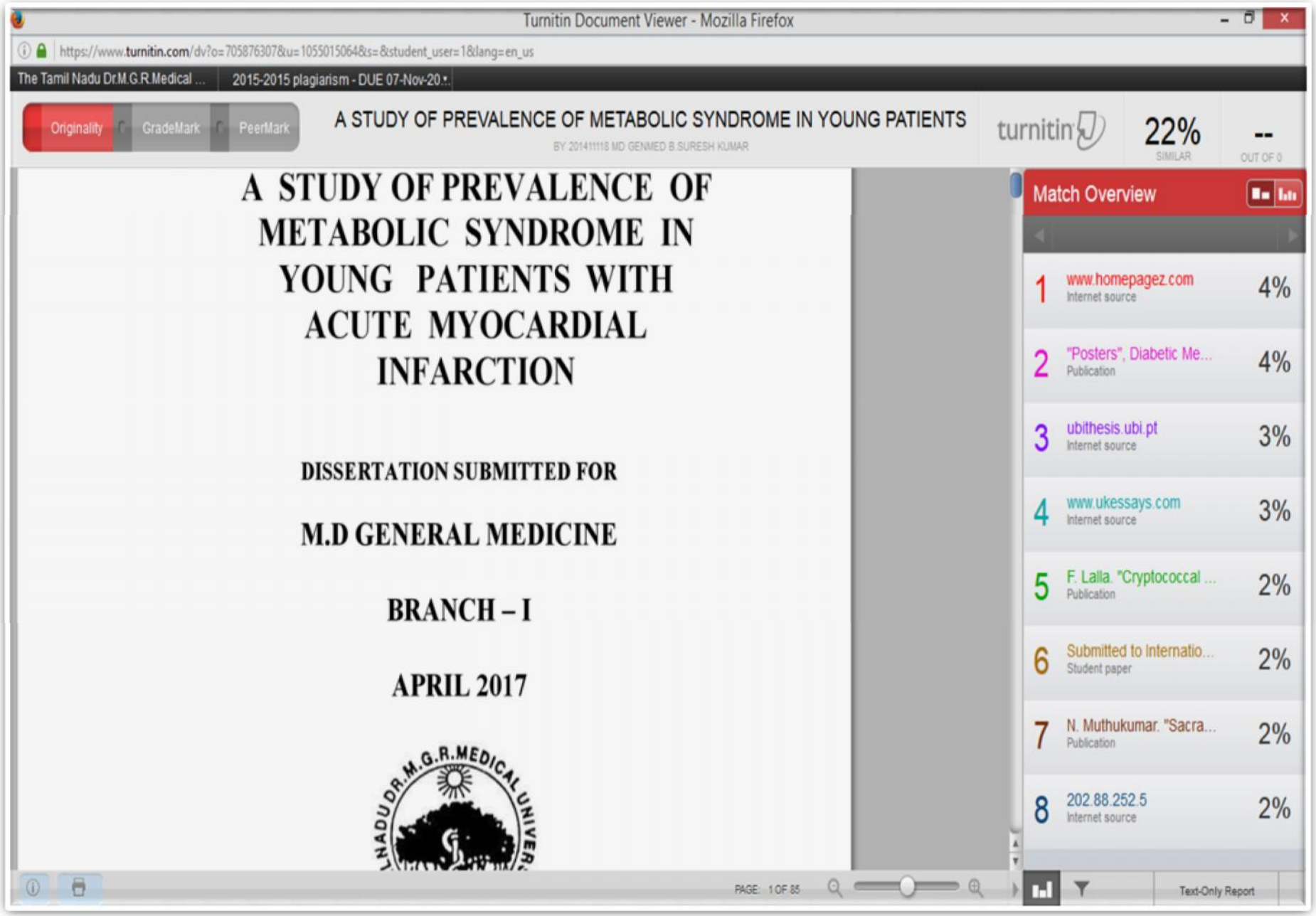
BRANCH – I

APRIL 2017

THE TAMILNADU

DR.M.G.R. MEDICAL UNIVERSITY

CHENNAI, TAMILNADU, INDIA


Turnitin Document Viewer - Mozilla Firefox
https://www.turnitin.com/dv?o=705876307&u=1055015064&s=&student_user=1&lang=en_us
The Tamil Nadu Dr.M.G.R.Medical ...
2015-2015 plagiarism - DUE 07-Nov-20.
Originality
GradeMark
PeerMark
A STUDY OF PREVALENCE OF METABOLIC SYNDROME IN YOUNG PATIENTS
BY 201411118 MD GENMED B.SURESH KUMAR
turnitin
22%
SIMILAR
--
OUT OF 0
A STUDY OF PREVALENCE OF METABOLIC SYNDROME IN YOUNG PATIENTS WITH ACUTE MYOCARDIAL INFARCTION
DISSERTATION SUBMITTED FOR
M.D GENERAL MEDICINE
BRANCH – I
APRIL 2017
Match Overview
1 www.homepagez.com Internet source 4%
2 "Posters", Diabetic Me... Publication 4%
3 ubithesis.ubi.pt Internet source 3%
4 www.ukessays.com Internet source 3%
5 F. Lalla. "Cryptococcal ... Publication 2%
6 Submitted to Internatio... Student paper 2%
7 N. Muthukumar. "Sacra... Publication 2%
8 202.88.252.5 Internet source 2%
PAGE: 1 OF 85
Text-Only Report

MADURAI MEDICAL COLLEGE
MADURAI, TAMILNADU, INDIA -625 020
(Affiliated to The Tamilnadu Dr.MGR Medical University, Chennai, Tamil Nadu)

ETHICS COMMITTEE CERTIFICATE

Name of the Candidate	:	Dr.B.SURESHKUMAR
Course	:	PG in MD GENERAL MEDICINE
Period of Study	:	2014-2017
College	:	MADURAI MEDICAL COLLEGE
Research Topic	:	A STUDY OF PREVALENCE OF METABOLIC SYNDROME IN YOUNG PATIENTS WITH ACUTE MYOCARDIAL INFARCTION
Ethical Committee as on	:	11.01.2016

The Ethics Committee, Madurai Medical College has decided to inform that your Research proposal is accepted.

R. Parameswari

Member Secretary — Chairman — Dean / Convenor

DEAN
Madurai Medical College
Madurai-20

11 JAN 2016
மதுரை - 625020