A STUDY ON THE PREVALENCE AND IMPACT OF METABOLIC SYNDROME ON HOSPITAL OUTCOMES IN ACUTE MYOCARDIAL INFARCTION

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CERTIFICATE

This is to certify that the dissertation titled "A study on the prevalence and impact of metabolic syndrome on hospital outcomes in acute myocardial infarction " is the bonafide original work of DR. R. ARUN in partial fulfillment of the requirements for M.D. Branch – I (General Medicine) Examination of the Tamilnadu DR. M.G.R Medical University to be held in September, 2006. The Period of study was from february 2005 to february 2006.

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DECLARATION

I solemnly declare that the dissertation titled "A study on the prevalence and impact of metabolic syndrome on hospital outcomes in acute myocardial infarction" was done at Government Stanley Medical college and Hospital during the period february 2005-february 2006 under the guidance and supervision of Professor Dr.S.NATARAJAN, M.D., Head of the department and Professor of Medicine, Government Stanley Medical college and Hospital, Chennai.

This dissertation is being submitted to the Tamil Nadu Dr.M.G.R. Medical University towards partial fulfillment of requirement for the award of M.D.Degree, Branch I, General Medicine – September, 2006.

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CONTENTS

INTRODUCTION

Metabolic syndrome is a constellation of interrelated risk factors of metabolic origin – metabolic risk factors – that appear to directly promote the development of atherosclerotic cardio vascular disease and type 2 diabetes mellitus by two to three fold[8].

It has variously been referred as the insulin resistance syndrome. Insulin resistance is the key pathologic feature of the syndrome, since its components are either causes or consequences of impaired insulin action.

The constellation of dyslipidemia (hypertriglyceridemia and low levels of high-density lipoprotein cholesterol), elevated blood pressure, impaired glucose tolerance, and central obesity is identified now as metabolic syndrome.It is also a prothrombotic and proinflammatory state.

Soon, metabolic syndrome will overtake cigarette smoking as the number one risk factor for heart disease . The National Cholesterol

Education Program[1]-Adult Treatment Panel III has identified metabolic syndrome as an indication for vigorous lifestyle intervention.

Studies based on populations at high risk for cardiovascular disease have shown a very high prevalence of metabolic syndrome.

In this study the prevalence of metabolic syndrome in acute myocardial infarction and its impact on hospital outcomes like heart failure, length of ICCU stay, case fatality have been studied. The relative influence of each of the 5 components of NCEP ATP III definition of metabolic syndrome on various hospital outcomes like risk of death and heart failure was also studied. In this study, metabolic syndrome was defined according to the criteria of the National Cholesterol Education Program's Adult Treatment Panel III (NCEP-ATP III).

AIM OF THE STUDY

1. To ascertain the prevalence of metabolic syndrome in acute myocardial infarction patients

2. To study the impact of metabolic syndrome on hospital outcomes, in particular, death and heart failure in acute myocardial infarction patients

3. To assess the relative influence of each of the 5 components of NCEP ATP III definition of metabolic syndrome on the risk of death and heart failure

4. To identify and treat the components of metabolic syndrome in acute myocardial infarction patients.

REVIEW OF LITERATURE

A report[1] from the National Cholesterol Education Program- Adult Treatment Panel (NCEP-ATP III) identified metabolic syndrome as an independent risk factor for cardiovascular disease and considered it an indication for intensive lifestyle modification.

The predominant underlying risk factors for the syndrome appear to be abdominal obesity and insulin resistance[5,6]other associated conditions can be physical inactivity,[3,7]aging,[8] and hormonal imbalance.

Metabolic syndrome can lead to serious medical problems, including type 2

diabetes, high blood pressure, heart disease and stroke.

Other associated diseases are:

Fatty liver

Non-alcoholic steatohepatitis

Acanthosis nigricans

Hemochromatosis

Polycystic ovarian syndrome

Several recent reports [25, 26, 27, 28] indicate that the presence of the metabolic syndrome is associated with increased risk for both ASCVD and type 2 diabetes. Persons with the metabolic syndrome have at least a 2-fold increase in risk for ASCVD[9], compared with those without metabolic syndrome. Risk for

type 2 diabetes in both men and women is increased about 5-fold [9]. The risk for diabetes is highest in those with impaired fasting glucose or IGT.

Other metabolic abnormalities that are associated with this syndrome are obesity, microalbuminuria, and abnormalities in fibrinolysis and coagulation [13–16]. In 1998, WHO[3] proposed a unifying definition for the syndrome and chose to call it the metabolic syndrome rather than the insulin resistance syndrome [17]. This name was chosen primarily because it was not established that insulin resistance was the cause of all the components of the syndrome.

Nomenclature

Other names for metabolic syndrome,[100] are

Syndrome X[101]

Metabolic syndrome X

Plurimetabolic syndrome

Insulin resistance syndrome[103,104]

"deadly quartet,"[102]

hypertriglyceridemic waist.[105]

Reaven's Syndrome

CHAOS (Australia)

Wohlstandssyndrom (German).

History

The term "metabolic syndrome" dates back to at least the late 1950's, but came into common usage in the late 1970's to describe various associations of risk factors with diabetes.

Multiple cardiovascular risk factors of endogenous origin commonly aggregate in one individual. This aggregation was originally observed many years ago[10,19]

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The history of metabolic syndrome dates back to postmortem descriptions by Morgagni[18] of both atherosclerosis and visceral obesity in noble persons whose lifestyle was characterized by “literary studies, sedentary life-style and abundant meals”

In 1988, Stanford University endocrinologist Dr. Gerald Reaven[8], in his Banting lecture, named after Sir Frederick Banting, reintroduced the concept of syndrome X for the clustering of cardiovascular risk factors like hypertension, glucose intolerance, high triglycerides, and low HDL cholesterol concentrations. Reaven did not include abdominal obesity, which has also been hypothesized as the underlying factor, as part of the condition.

The syndrome is, however, much older, having been already observed in 1923 by Kylin, who described the clustering of hypertension, hyperglycemia, and gout as a syndrome [10]

The Marseilles physician, Dr. Jean Vague[19,20] made the interesting observation that upper body obesity appeared to predispose to diabetes, atherosclerosis, gout, and calculi. He classified obesity into those with "gynoid" and those with "android" obesity.

Avogaro, Crepaldi and co-workers described six moderately obese patients with diabetes, hypercholesterolemia, and marked hypertriglyceridemia all of which improved when the patients were put on a hypocaloric, low carbohydrate diet.

In 1977, Haller used the term "metabolic syndrome" for associations of obesity, diabetes mellitus, hyperlipoproteinemia, hyperuricemia and steatosis hepatitis when describing the additive effects of risk factors on atherosclerosis.

The same year, Singer used the term for associations of obesity, gout, diabetes mellitus, and hypertension with hyperlipoprotenemia

Epidemiology and prevalence

Metabolic syndrome is prevalent in 25% using WHO[3] and 24% using ATP[1] III definitions in individuals aged 20 years[2] or above.the prevalence is equal among both the sexes. In-patients with diabetes the prevalence was 86%.

The prevalence of metabolic syndrome in coronary artery disease is 51% and the number of its metabolic features increases with the severity of angiographic coronary artery disease[21].

The prevalence of metabolic syndrome ranges from 35% to 80% in patients with hypertension or type 2 diabetes melliltus[22,25].

It is also associated with an increase in mean carotid intima media thickness and decrease in ankle brachial pressure index. The prevalence of metabolic syndrome correlated with the extent of vascular damage[23].

Definitions of Metabolic syndrome

There are various definitions for metabolic syndrome. The widely used definitions are

I. WORLD HEALTH ORGANISATION (WHO)[3]

Clinical Measure	**WHO (1988)**
Insulin resistance	IGT,IFT,T2DM, or lowered Insulin sensitivity plus Any 2 of the following
Body weight	Men: waist to hip ratio>0.90 Women: waist to hip ratio>0.85 And/ or BMI>30 kg/ sq. m
Lipid	TG >=150 mg/dL HDL cholesterol <40 mg/dL for men, <50 mg/dL for women
Blood pressure	>=140/90 mmHg.
Glucose	IGT,IFG or T2DM
OTHER	**microalbuminuria (Urinary albumin to creatinine** ratio: 30 mg per g, or albumin excretion rate: 20 mcg per minute)

II. INTERNATIONAL DIABETIC FEDERATION[12]

Clinical Measure	**IDF (2005)**
Insulin resistance	None
Body weight	Increased waist circumference(population specific) Plus any 2 of the following
Lipid	TG >=150 mg/dL or on R/ HDL cholesterol <40 mg/dL for men, <50 mg/dL for women or on R/
Blood pressure	>=130/85 mmHg or on R/
Glucose	>=100 mg/dL(including diabetes)

III. THE ADULT TREATMENT PANEL[1] III OF THE

NATIONAL CHOLESTEROL EDUCATION PROGRAM (2001, 2005)

It defined the diagnosis as three or more of the following five

1. Increased waist circumference (>=102 cm in men and >=88 cm in women)
2. Elevated triglycerides (>=150 mg/dL or 1.7 mmol/l)
3. Decreased HDL cholesterol (<40 mg/dL for men, <50 mg/dL for women)
4. Blood pressure above 130/85 or active treatment for hypertension
5. Glucose levels above 100 mg/dL or active treatment for hyperglycemia

IV. AMERICAN HEART ASSOCIATION ,

NATAIONAL HEART , LUNG AND BLOOD INSTITUTE[9], JULY 2005

SCIENTIFIC STATEMENT

Metabolic syndrome was defined according to the AHA/NHLBI statement maintaining NCEP ATP III[1] criteria with minor modifications. Patients received a diagnosis of metabolic syndrome if they had any 3 of the following 5 criteria:

1. Abdominal obesity (waist circumference men >102 cm and in women >88 cm for western population and > 90 cm in men and > 80 cm in women of Asian origin)

2. High triglyceride levels >=150mg/dL

3. Low HDL Cholesterol level <40 mg/dL in men and <50 mg/dL in women

4. High blood pressure (treated hypertension, systolic blood pressure >=130 mm Hg, or diastolic blood pressure >= 85 mm Hg)

5. Fasting glucose >= 100 mg/dL or on treatment for diabetes mellitus

In accordance with a 2003 recommendation from the American Diabetes Association[11], in the last three definitions of IDF, Adult Treatment Panel III of the National Cholesterol Education Program (2001, 2005) and AHA/NHLBI statement the value of impaired fasting glucose was reduced from 110 mg/dL to 100 mg/dL.

When the waist circumference is 90 cm or more in men or 80 cm or more in women, the term abdominal obesity can be applied. The advantage of measuring waist circumference is that an excess abdominal fat is correlated more closely with the presence of metabolic risk factors than total body fat.

GENETICS

A "thrifty genotype hypothesis" implicates the evolutionary selection of metabolic genes in the development of the metabolic syndrome in the setting of a modern environment of physical inactivity and dietary excess. Family studies suggest a complex but significant genetic basis to individual components of the metabolic syndrome. However, identifying a genetic profile that defines an increased risk of developing a complex disease trait, such as the metabolic syndrome or atherosclerosis, remains difficult.

PATHOPHYSIOLOGY -MECHANISTIC LINKS BETWEEN COMPONENTS

INSULIN RESISTANCE

Insulin resistance per se is independently atherogenic. Insulin resistance is the pathophysiological process underlying the clustering of cardiovascular risk factors in the metabolic syndrome.[2,31] . In prospective studies, the presence of insulin resistance is associated with increased ASCVD risk [40].

Some of the risk factors that are hallmarks of insulin resistance—for example, abnormal lipid levels, glucose intolerance, and high blood insulin levels—appear to provide a fertile ground for the development of serious chronic diseases such as diabetes, heart disease, and fatty liver. For instance, high blood insulin levels have been linked to hypertension, while insulin resistance appears to promote atherosclerosis.

Multiple metabolic pathways have been proposed to link insulin resistance and compensatory hyperinsulinemia to the other metabolic risk factors[31,32]. This is true for many individuals of South Asian ethnicity.[33,34]. Although insulin-resistant individuals need not be clinically obese, they have an abnormal fat distribution that is characterized by predominant upper body fat.

Asymmetric dimethylarginine (ADMA), a naturally occurring substance, is increased in metabolic syndrome . It inhibits the synthesis of nitric oxide, a potent dilator of blood vessels. ADMA also increases the binding of white blood cells to the endothelial lining of arteries, which may contribute to atherosclerosis.

Indices of insulin resistance predict atherosclerosis and cardiovascular events independent of other risk factors including fasting glucose and lipid levels[35]. Many subjects with normal fasting glucose levels have insulin resistance.[2]The hyperinsulinemic clamp is considered the gold standard to define insulin sensitivity but requires prolonged insulin infusion and repeated blood sampling. Surrogate measures of insulin sensitivity, including the Homeostasis Model Assessment (HOMA) and Quantitative Insulin Sensitivity Check Index (QUICKI), have been developed that can be applied to single measurements of fasting insulin and glucose. These surrogates are useful in defining the MetSyn and in predicting the development of cardiovascular disease and type 2 diabetes mellitus[35,37].

Insulin resistance is thought to contribute to the accumulation of fatty deposits in the liver. Insulin resistance also has been implicated in polycystic ovary syndrome [54]and nonalcoholic steatohepatitis (NASH).

Innate immunity and inflammation play a role in the development of insulin resistance and predict the development of type 2diabetes mellitus[38,39]. Thus, the pathophysiology of insulin resistance and atherosclerotic cardiovascular events may have a common proximal inflammatory basis.

DYSGLYCEMIA

In cross-sectional and prospective studies, fasting and postprandial glucose and insulin concentrations are positively correlated. The increase in insulin

concentrations is paralleled by a decrease in insulin sensitivity. Decreased insulin sensitivity leads to defects in the ability of insulin to inhibit hepatic glucose production and to stimulate glucose uptake in peripheral tissues and thereby leading to hyperglycemia.

Increased FFA concentrations and resistance to the antilipolytic effect of insulin may contribute to worsening of hyperglycemia[41] because of multiple interactions between FFA and glucose metabolism both in the liver and in skeletal muscle.

A variety of mechanisms to explain how elevated plasma glucose may promote atherosclerosis are postulated[42].

A variety of mechanisms have been proposed whereby hyperglycemia might promote atherosclerosis [42]. Examples include nonenzymatic glycosylation of lipids and proteins, pathogenic effects of advanced glycation products, increased oxidative stress, activation of protein kinase C, and microvascular disease of the vasa vasorum of the coronary arteries.

OBESITY AND ABDOMINAL OBESITY

Obesity is related to insulin resistance[43,44] Obesity is associated with impaired insulin stimulation of glucose uptake and defect in the ability of insulin to inhibit endogenous glucose production and lipolysis in adipose tissue. These defects appear more severe in individuals with android (abdominal fat distribution) as compared to gynoid obesity.

Upper-body obesity correlates strongly with insulin resistance. Excess visceral fat is strongly associated with insulin resistance[24,35,36,37].Excess subcutaneous

abdominal (or truncal) fat also carries a significant association with insulin resistance.[45-50]An interesting feature of upper-body obesity is a high release of nonesterified fatty acids[61] from adipose tissue[51]; this contributes to accumulation of lipid in sites other than adipose tissue. Ectopic lipid accumulation in muscle and liver seemingly predisposes to insulin resistance[52] and dyslipidemia[53].

The foremost physical consequence of obesity is atherosclerotic cardiovascular disease (ASCVD) [1,9] . The majority of obese persons who develop ASCVD typically have metabolic syndrome.

Body mass index is a relatively insensitive indicator for metabolic and cardiovascular complications of obesity, as compared with measures of central or abdominal adiposity.[54] Waist circumference reflects both abdominal subcutaneous adipose tissue (SAT) and abdominal visceral adipose tissue (VAT) and is a general index of central (trunk) fat mass. So, waist circumference is preferred for measuring abdominal obesity. VAT has been proposed as the major determinant of metabolic and cardiovascular complications of obesity[55].

Our understanding of the relation between obesity and metabolic risk factors is growing rapidly. This understanding is based on the discovery of multiple products released from adipocytes[60].

Nonesterified fatty acids (NEFAs)

Inflammatory cytokines

PAI-1

Adiponectin

Leptin

Resistin

Circulating cytokines have systemic effects, *i.e*. promoting insulin resistance in muscle [63], increased synthesis of acute-phase reactants in the liver (CRP and fibrinogen), or activation of macrophages in atheromatous plaques [68].

Excessive influx of NEFAs into muscle leads to insulin resistance. Randle et al[62] postulated that excess fatty acids in muscle inhibit glucose oxidation (glucose-fatty acid cycle). Recent research [63]suggests that muscle levels of diacylglycerol are raised, which stimulates the serine phosphorylation of the insulin receptors and thereby inhibits normal insulin signaling. Other mechanisms also may play a role in insulin resistance in muscle[64].

Fat accumulation in the liver seemingly produces insulin resistance as it does in muscle. Reduction in insulin action in liver allows for enhanced gluconeogenesis and increased hepatic glucose output.

Hypotheses have been developed to link higher NEFA levels to higher blood pressures [66]. Accumulation of fat in the liver has been reported to be associated with increased hepatic synthesis of PAI-1, fibrinogen, and inflammatory cytokines, the key mediators of the prothrombotic and proinflammatory states [67].

Adipose tissue synthesizes PAI-1. A fatty liver may be another source of PAI-1. The resulting high PAI-1 levels in obese persons together with the high plasma fibrinogen observed in such persons contributes to a prothrombotic state.

Adiponectin[59] is reported to have antiinflammatory and antiatherogenic properties. Obese persons generally have low levels of adiponectin and hence may be deprived of its protective effects against the metabolic syndrome.

Leptin also may play a systemic role beyond being an adipose tissue-derived appetite suppressant. This hormone has been reported to have a beneficial effect on the liver to protect against fatty liver [57,58]. Its mechanism may be to enhance fatty acid oxidation in the liver. Finally, resistin is an adipose tissue-derived hormone that seemingly opposes the action of insulin [56].

DYSLIPIDEMIA

Dyslipidemia is a hallmark of the metabolic syndrome and is characterized by elevated triglycerides (TG) and low levels of HDL-C[45,46]. Increased fat in the liver provides a stimulus for increased formation and secretion of very LDL (VLDL) particles. The result is higher serum levels of triglyceride, apo B, and small LDL particles. High serum triglycerides reduce HDL-cholesterol concentrations through exchange of VLDL triglycerides with HDL cholesterol esters.

HYPERTRIGLYCERIDEMIA

Influx of excess NEFAs into the liver increases the triglyceride content of the liver (fatty liver) [65]. Increased flux of free fatty acids from the periphery to the liver in the insulin-resistant state drives hepatic TG synthesis, which in turn promotes the assembly and secretion of TG-containing VLDL[46].

Insulin normally suppresses the production of VLDL particles from the liver by directly inhibiting the assembly and production of VLDL particles[69]. In insulin resistance this action of Insulin is lost leading to increase in serum triglycerides[70].

Under hypertriglyceridemic conditions, there is excessive exchange of cholesterol esters and triglyceride-rich lipoproteins, mediated by cholesterol ester transfer protein.

LOW HDL CHOLESTEROL

Metabolic syndrome is associated with low HDL cholesterol. HDL particles become enriched with triglycerides[71] and act as good substrate for hepatic lipase which now removes HDL particles at an accelerated rate. This is mediated by mediated by the cholesteryl ester transfer protein.[45,46] Subnormal activity of lipoprotein lipase may further decrease level of HDL cholesterol.

Activation of innate immunity offers a potential unifying pathophysiology for insulin resistance and dyslipidemia in the metabolic syndrome. In animal models, activation of innate immunity leads to changes in lipoproteins, enzymes, transfer proteins, and receptors with an increase in atherogenic lipoprotein particles.[47]. One possible contributor to the changes in HDL during inflammation is the increased production of lipases that act on HDL phospholipids, thus reducing the lipid content of HDL and promoting its catabolism.[48].

A low HDL level is another characteristic of atherogenic dyslipidemia [1]. As a risk predictor, a low HDL rivals an elevated total apo B (or VLDL+LDL cholesterol). This fact has led to the concept that HDL is intimately involved in the atherogenic process.

The theories abound as to the mechanisms whereby HDL is antiatherogenic are enhanced reverse cholesterol transport, antiinflammatory properties, ability to protect against LDL modification. Although HDL in fact may be directly antiatherogenic, it also is a marker for the presence of other lipid and nonlipid risk factors.

SMALL DENSE LDL PARTICLES

In metabolic syndrome LDL particles are smaller and denser than normal[45,46].

Small dense LDL particles are known to be highly atherogenic[73] and provide a plausible link between insulin resistance and cardiovascular disease.

The increase in the triglyceride content of LDL particles[72] makes them a better substrate for hepatic lipase which hydrolyzes triglycerides in the LDL particles and so decrease their size.

High levels of circulating oxidised LDL, which is increased in metabolic syndrome are associated with a greater disposition to atherothrombotic coronary disease[74.]

A theory widely held is that smaller LDL particles are more atherogenic than larger

LDLs [75]. Small LDL particles are a surrogate for an increased LDL particle number [76].

A simple strategy for assessing the sum of atherogenic particles is measurement of either LDL+VLDL cholesterol (non-HDL cholesterol) or total apo B . In persons with metabolic syndrome, both LDL+VLDL cholesterol and total apo B typically are elevated. These measurements should be used increasingly both in risk assessment and as targets of therapy in persons with the metabolic

syndrome [77].

HYPERTENSION

The association between insulin resistance and hypertension is perhaps the most controversial. In insulin resistant patients with essential hypertension, basal intracellular calcium levels have been shown to be elevated and the normal ability of insulin to attenuate angiotensin II induced increases in intracellular calcium is blunted in skin fibroblasts[78].

The renal action of insulin to reabsorb sodium is similar in normo- and hypertensive insulin-resistant subjects. Such a preserved action of insulin could contribute to an increase in blood pressure in hyperinsulinemic subjects[79].

Insulin resistance has consistently been found to correlate with high sodium-lithium counter-transport in erythrocyte membranes: this is thought to parallel increased activity of the sodium hydrogen ion pump in the cell membrane of other tissues, which could raise intracellular sodium and calcium concentrations and enhance vascular muscle contractility. Such action could also contribute to the development of hypertension in non-diabetic, insulin resistant subjects.

A higher blood pressure is a strong risk factor for cardiovascular disease (CVD) [80]. Well-known complication of hypertension are CHD, stroke, left ventricular hypertrophy, heart failure, and chronic renal failure. hypertension is particularly dangerous to the cardiovascular system. This concept supported by the Framingham Heart Study [81].

Hyperuricemia

Within the non-diabetic range of glucose tolerance, serum uric acid concentrations are positively correlated with glucose and insulin concentrations and inversely with insulin resistance[82].

In normal subjects, insulin acutely reduces the renal clearance of both sodium and uric acid[87]. These actions are preserved in insulin resistant states such as obesity, diabetes and essential hypertension and so provide a potential mechanistic link for the clustering of insulin resistance with hyperuricemia[83].

ALTERATIONS IN COAGULATION, FIBRINOLYSIS AND PLATELET FUNCTION

Metabolic syndrome is associated with a proinflammatory/prothrombotic state that includes elevated levels of C-reactive protein, endothelial dysfunction, hyperfibrinogenemia, increased platelet aggregation, increased levels of plasminogen activator inhibitor 1, elevated uric acid levels, microalbuminuria

Pro-coagulant changes such as impaired fibrinolysis and increased levels of PAI-I and defects in platelets function are frequently associated with insulin resistance.

PAI-I, an inhibitor of fibrinolysis, is elevated in obesity associated insulin resistance[84].

Coagulation and fibrinolytic abnormalities cause endothelial dysfunction,which in turn is involved in the atherogenic process [90].

CHANGES IN INFLAMMATORY MARKERS

IL-6 , the main regulator of the synthesis of C-reactive protein in the liver[85] is increased in metabolic syndrome. Upto one third of circulating IL-6 originate from subcutaneous and visceral adipose tissue depots and circulating levels are increased in

obese subjects[86].Recently, this syndrome has been noted to be associated with a state of chronic, low-grade inflammation.[88,89.] It is of interest that obese persons [91]and particularly those with the metabolic syndrome [92] also have elevated levels of CRP.

MICROALBUMINURIA

The mechanisms underlying the clustering of insulin resistance and microalbuminuria are poorly understood. Insulin has been shown to increase urinary excretion of albumin and protein markers of proximal tubular function in diabetic patients but not in nondiabetic individuals[93].Microalbuminuria may also be a sign of preclinical endothelial or vascular damage[94].

ABNORMALITIES IN THE AUTONOMIC NERVOUS SYSTEM

In insulin resistant subjects, insulin can enter the hypothalamus and other parts of the brain, where insulin receptors are expressed at high levels, and it acts centrally to stimulate the SNS[95]. Insulin also regulates the autonomic control of heart rate by decreasing vagal tone, and increasing sympathetic drive[96].

ACUTE MYOCARDIAL INFARCTION AND METABOLIC SYNDROME

In prospective epidemiologic studies, hyperinsulinemia is an independent risk factor for CHD in non-diabetic men after adjusting for body weight,blood pressure and dyslipidemia[97].This study reveals that patients with an AMI and no previous diagnosis of diabetes have a high prevalence of insulin resistance[108 ·] There has been consistent relationship of metabolic syndrome with prevalent MI and stroke[109]

In men participating in the West of Scotland Coronary prevention Study[40], the insulin resistance syndrome defined according to NCEP criteria increased the risk for a CHD

event by 1.76 fold. Men with four to five features of the syndrome had a 3.7 fold increase in risk for CHD.

OTHER MARKERS OF METABOLIC SYNDROME AS PREDICTORS OF CARDIOVASCULAR DISEASE

C-reactive protein has predicted cardiovascular disease independent of other risk factors[98].Hyperuricemia is associated with increased mortality from all causes of cardiovascular disease in the NHANES I^2 epidemiologic survey in women but not in men[99].PAI-I has been found predictive for cardiovascular disease in several studies[106]. Microalbuminuria increased the relative risk of CHD death eightfold and of all CHD events threefold even after adjusting for gender, smoking, blood pressure and HDL cholesterol[107].

All these predictors of cardiovascular disease namely CRP, hyperuricemia, PAI-I and microalbuminuria are strongly associated with metabolic syndrome.

MANAGEMENT OF METABOLIC SYNDROME

Metabolic syndrome is the secondary target for reducing cardiovascular events. Smoking cessation, lowering the levels of LDL-C, and blood pressure management are primary target for risk reduction. Lifestyle modifications are the initial therapies recommended for treatment of metabolic syndrome. If lifestyle change is not sufficient, then drug therapies may be indicated. To date, there is insufficient evidence for primary use of drugs that target the underlying causes of metabolic syndrome.

SUBJECTS AND METHODS

STUDY POPULATION

Patients admitted with acute myocardial infarction in Intensive Coronary Care unit in Government Stanley Hospital, between February, 2005 and February, 2006 constitute the study population. A total of 85 patients were studied. Patients were initially studied when they were in ICCU and they were followed up till their discharge. They were examined and investigated personally. The detailed clinical study was made as per proforma. The emphasis of this study is mainly to ascertain the prevalence of metabolic syndrome in acute MI patients and to study the impact of metabolic syndrome

on hospital outcomes especially heart failure. The relatively influence of each of the components of metabolic syndrome was analysed. . No patient had been counted twice if he or she got admitted again after discharge during the period.

INCLUSION CRITERIA

1. Patients admitted with acute ST elevation MI in ICCU

2. All age groups were included

3. Both sexes were included

EXCLUSION CRITERIA

Patients with non- STEMI, unstable angina were excluded.

DIAGNOSIS OF ACUTE MYOCARDIAL INFARCTION:

Acute STEMI was diagnosed based on typical chest pain, ECG showing ST elevation or new onset or suspected left bundle branch block as defined by the Joint Committee of the European Society of Cardiology and the American College of Cardiology[110]

DIAGNOSIS OF METABOLIC SYNDROME

Metabolic syndrome was defined according to the AHA/NHLBI[9] statement maintaining NCEP ATP III[1] criteria with minor modifications. Patients

received a diagnosis of metabolic syndrome if they had any 3 of the following 5 criteria:

1.Abdominal obesity (waist circumference > 90 cm in men and > 80 cm in women[9])

2. High triglyceride levels >=150mg/dL

3. Low HDL Cholesterol level <40 mg/dL in men and <50 mg/dL in women

4. High blood pressure (treated hypertension, systolic blood pressure >=130 mm Hg, or diastolic blood pressure >= 85 mm Hg)

5. Fasting glucose >= 100 mg/dL or on treatment for diabetes mellitus

DATA COLLECTION

Informed consent was obtained from all patients who fit in the inclusion criteria.

A detailed history was taken. The onset, duration, character, radiation of chestpain were taken. Past history of CAHD, diabetes, hypertension, dyslipidemia, smoking, alcoholism were taken. Special emphasis was given to family history of CAHD. Family history of coronary artery disease was defined by a history of premature coronary artery disease in first degree relatives (having occured in those relatives at age < 55 years for men and <65 years for women). Data concerning long term therapy before admission including

aspirin, beta blockers, angiotensin converting enzyme inhibitors and statins were also collected.

Body height and weight were measured. Waist circumference was measured on admission midway between the last rib and iliac crest and the average of 2 measures was recorded to the nearest 0.1 cm[111].

A complete examination was done, looking for anemia, jaundice, cyanosis, clubbing, oedema and lymphadenopathy. Vital parameters, namely, temperature, respiratory rate, Pulse rate, blood pressure were recorded

Electrocardiogram was taken at the time of admission and subsequent ECGs were taken as required. Acute STEMI was diagnosed based on typical chest pain , ECG showing ST elevation or new onset or suspected left bundle branch block.

The blood pressure values used in the study were those collected on the day before discharge. For the patients who died, the value recorded on the eve of death was used. JNC 7[80] was applied for staging blood pressure. At each participating site, echocardiography was performed on day and all ECHO parameters were studied including wall motion abnormalities, LVEF etc.,

DEFINITION OF HEART FAILURE

Heart failure was defined as the highest killip class[127] reached during hospitalisation. Severe heart failure was defined as killip class greater than II.. Cardiogenic shock was defined as a systolic blood pressure less than 90 mm Hg persisting for longer than 1 hour despite fluid challenge and associated with clinical signs of hypoperfusion[125]. Features of heart failure were looked for and killips classification was done.

During the hospital stay, data regarding ventricular arrhythmia (ventricular tachycardia or fibrillation), stroke, recurrent MI, cardiogenic shock and death were collected.

Patients who had one exclusion criteria were excluded.

The following investigations were done.

At the time of admission,

Blood sugar

Blood urea, serum creatinine

Blood total count, differential count, platelet count

CPK MB, SGOT, SGPT

Lipid profile including total cholesterol, LDL, HDL, Triglycerides[122] was done at admission or within 24 hours.

On day 4 and 5 fasting glucose was taken and the average was taken as fasting glucose[111.]

STUDY SAMPLE

Study sample constitutes the patients who were admitted in ICCU with acute STEMI. 85 patients were studied and the criteria for metabolic syndrome were applied on these patients.

STUDY METHODS

These patients were divided into two groups

(1)patients with metabolic syndrome and

(2) patients without metabolic syndrome. They were followed up during their hospital stay.

The relative influence of each component of metabolic syndrome in both the groups and with respect to hospital outcomes and various parameters like VT/VF, heart failure, duration of stay in ICCU, recurrent MI, death were studied.

STUDY VARIABLES

The variables in the study were waist circumference, blood pressure, fasting glucose, HDL and triglycerides. The other variables include hospital outcomes like heart failure, ventricular arrhythmias, recurrent MI, length of stay in ICCU

and case fatality. The following variable like admission glucose , total cholesterol, LDL cholesterol were also studied.

STATISTICAL ANALYSIS

All the 85 patients were analysed and criteria for metabolic syndrome were applied.Continuous data were expressed as medians and mean +- SD.

Chi square test was applied to analyse data and to test for significance. All the components of metabolic syndrome waist circumference, blood pressure, fasting glucose, HDL and Triglycerides have shown a significant p value on applying the chi square test. A p value less than 0.05 is statistically significant. Apart from this, a significant p value also resulted in heart failure, ICCU stay and smoking history.

RESULTS

PREVALENCE OF METABOLIC SYNDROME IN ACUTE MI PATIENTS

A total of 85 patients with acute STEMI were studied. Of these 42 patients fulfilled the criteria for metabolic syndrome. The remaining 43 patients did not have metabolic syndrome.

Metabolic syndrome	N	Mean	Std. Deviation
No	43	53.58	10.658
yes	42	56.64	11.155

The prevalence of metabolic syndrome in acute MI was 49%. This showed the high prevalence of metabolic syndrome in acute myocardial infarction patients.

The mean in the metabolic syndrome group was 56.6 years whereas in the non-metabolic syndrome group the mean was 53.5 years. So, the mean age of prevalence was found to be high in the MS group.

PREVALENCE OF METABOLIC SYNDROME – Age group

Agegroup		Met syn		Total
		no	yes	
	20-29	1	1	2

	30-39	**2**	**2**	**4**
	40-49	**12**	**6**	**18**
	50-59	**13**	**14**	**27**
	60-69	**13**	**15**	**28**
	70-79	**1**	**3**	**4**
	80-89	**1**	**1**	**2**
Total		**43**	**42**	**85**

The lowest age in the study group was 27 years and the highest age was 86 years. The incidence of acute myocardial infarction was high in the age group between 50-69 years. The prevalence of metabolic syndrome tend to increase as age increases, otherwise the incidence of MI is almost similar in both the study groups.

SEX PREVALENCE

Metabolic syndrome				
	NO		YES	
	n	%	n	%
male	40	57.1 %	30	42.9%
female	3	20.0 %	12	80.0%

Among the 85 acute MI patients studied, 70 patients were male and 15 were female.

Of these, 30 male patients and 12 female patients had metabolic syndrome and the other 40 male and 3 female patients did not have metabolic syndrome.

The study showed that the prevalence of metabolic syndrome in male patients and female patients were 42.9% and 80% respectively indicating a higher prevalence in the female sex.

Age group	No Metabolic syndrome		Metabolic syndrome	
	Male	Female	**Male**	**Female**
20-29	1	0	1	0
30-39	2	0	2	0
40-49	12	0	6	0
50-59	12	1	9	5
60-69	12	1	9	6
70-79	0	1	2	1
80-89	1	0	1	0

The prevalence of metabolic syndrome tend to increase in both sexes as age increases. But the prevalence in age group 50- 70 years in females was more,

indicating that metabolic syndrome was more prevalent in older age in females.i.e., patients with metabolic syndrome were older more likely to be women.

The components of metabolic syndrome, abdominal obesity (waist circumference), blood pressure, fasting glucose, triglycerides were increased and HDL decreased in the metabolic syndrome group. All the five components showed statistical significance ($p<0.05$).

components		Metabolic syndrome			
		no		yes	
		n	%	n	%
Waist Circumference cms	Male <90 female <80	38	90.5%	4	9.5%
	Male >90 female >80	5	11.6%	38	88.4%
Blood pressure Mm Hg	< 130/85	22	73.3%	8	26.7%
	>130/85	21	38.2%	34	61.8%
Fasting glucose Mg/dL	< 100	34	89.5%	4	10.5%
	>100	9	19.1%	38	80.9%
HDL Mg/dL	Male > 40,female > 50	42	57.5%	31	42.5%
	Male < 40,female < 50	1	8.3%	11	91.7%
TGL Mg/dL	<150	36	63.2%	21	36.8%
	>150	7	25.0%	21	75.0%

Parameter	Chi-square	p value
Waist circumference	52.85	0.001
Blood pressure	11.76	0.008
Fasting glucose	42.57	0.001
HDL	9.98	0.002
TGL	10.94	0.001

Waist circumference of more than 90 cms in male and > 80 cms in female was prevalent in 88.4% of the metabolic syndrome group and it showed statistical significance (p=0.001)

Hypertension was more prevalent in the metabolic syndrome group (61.8%). On applying chi-square test it showed statistical significance (p= 0.008)

Fasting glucose was prevalent to the extent of 80.9% in the metabolic syndrome group and it was statistically significant (p= 0.001).

To an extent of 91.7% HDL was decreased in the metabolic syndrome group and its p value 0.002 was significant.

Triglycerides were elevated to 75% in the metabolic syndrome group and this also showed a significance of p= 0.001.

The admission glucose was increased in both the groups (49.3% and 51.7%) and this was not statistically significant. The total and LDL cholesterol were increased in both the groups and there was no significance in both the groups.

Only two patients in the study gave a family history of CAHD and they showed metabolic syndrome but this was not significant statistically. Though smoking was more prevalent in the non-metabolic syndrome group there was statistical significance in the metabolic syndrome group (p=0.001).

The various parameters that were studied in both the groups namely patients with metabolic syndrome and without metabolic syndrome are tabulated below.

Parameters		Met syn			
		no		yes	
		n	%	n	%
Admission glucose	<110	5	62.5 %	3	37.5%

mg/dL	>110	38	49.3%	39	50.7%
Total cholesterol mg/dL	<200	16	59.3%	11	40.7%
	200-239	24	50.0%	24	50.0%
	>240	3	30.0%	7	70.0%
LDL mg/dL	<100	-	-	5	100.0%
	100-129	9	40.9%	13	59.1%
	>130	34	58.6%	24	41.4%
FH CAHD	No	43	51.8%	40	48.2%
	yes	-	-	2	100.0%
smoking	No	8	26.7%	22	73.3%
	Yes	35	63.6%	20	36.4%
Case fatality	No	42	51.2%	40	48.8%
	yes	1	33.3%	2	66.7%
Recurrent MI	No	37	52.1%	34	47.9%
	yes	6	42.9%	8	57.1%
VT/VF	No	41	53.9%	35	46.1%
	yes	2	22.2%	7	77.8%
Heart failure Killips class	1	32	94.1%	2	5.9%
	>2	11	21.6%	40	78.4%
days CCU	1	37	74.0%	13	26.0%
	> 1	6	17.1%	29	82.9%

Parameter	Chi-square	p value
Admission glucose	6.86	0.07
Total cholesterol	2.51	0.28
LDL cholesterol	7.44	0.02
FH of CAHD	2.09	0.15
smoking	10.6	**0.001**
Recurrent MI	0.4	0.53
VT/VF	3.3	0.07
Heart failure	45.5	**0.001**
Case fatality	0.32	0.57
ICCU Days	27.5	**0.001**

Though recurrent MI (57.1%) and ventricular arrhythmias (77.8%) were more prevalent in the metabolic syndrome they did not show statistical significance in this study.

Severe heart failure, defined as Killips[127] class > =2 was more prevalent in the metabolic syndrome group (78.4%) and this was statistically significant (p=0.001).

The stay in ICCU was more in the patients of metabolic syndrome and this was also significant (p=0.001). The mean ICCU stay in the metabolic syndrome group was 1.8 day whereas it was 1.1 day in the non-metabolic syndrome group.

Group	Fasting glucose >100 mg/dL	Heart failure >= killips class 2
Metabolic syndrome	40	36
No metabolic syndrome	9	2

Hyperglycemia was strongly associated with severe heart failure in the metabolic syndrome group(90%) when compared to the non-metabolic syndrome (22%).

DISCUSSION

The metabolic syndrome is a constellation of interrelated risk factors of metabolic origin—*metabolic risk factors*—that appear to directly promote the development of atherosclerotic cardiovascular disease (ASCVD).[1] So, metabolic syndrome is a risk factor for the development of coronary artery diseases.

It has variously been referred as the insulin resistance syndrome. Insulin resistance is the key pathologic feature of the syndrome, since its components are either causes or consequences of impaired insulin action.

The constellation of dyslipidemia (hypertriglyceridemia and low levels of high-density lipoprotein cholesterol), elevated blood pressure, impaired glucose tolerance, and central obesity is identified now as metabolic

syndrome. It is also a prothrombotic and proinflammatory state. Soon, metabolic syndrome will overtake cigarette smoking as the number one risk factor for heart disease . The National Cholesterol Education Program-Adult Treatment Panel III[1] has identified metabolic syndrome as an indication for vigorous lifestyle intervention..

The predominant underlying risk factors for the syndrome appear to be abdominal obesity[2–4]insulin resistance[5,6]; other associated conditions can be physical inactivity,[3,7]aging,[8] and hormonal imbalance

The Adult Treatment Panel III of the National Cholesterol Education Program (2001, 2005) defined the diagnosis as three or more of the following five components

1. Increased waist circumference (>=102 cm in men and >=88 cm in women), indicating central obesity

2. Elevated triglycerides (>=150 mg/dL or 1.7 mmol/l)

3. Decreased HDL cholesterol (<40 mg/dL for men, <50 mg/dL for women)

4. Blood pressure above 130/85 or active treatment for hypertension

5. Glucose levels above 100 mg/dL or active treatment for hyperglycemia.

PREVALENCE OF METABOLIC SYNDROME

In this study metabolic syndrome was highly prevalent (49%) in acute MI patients.

Solymoss BC, Bourassa MG, Campeau L et al on their study on "Effect of increasing metabolic syndrome score on atherosclerotic risk profile[21] and coronary artery disease angiographic severity" have shown an increased prevalence of metabolic syndrome ,51% in their study. Similar prevalence rates was also shown by Mariam Zeller[111] and co workers in their studies.

The prevalence of metabolic syndrome in coronary artery disease is 51% and the number of its metabolic features increases with the severity of angiographic coronary artery disease[21].The prevalence of metabolic syndrome ranges from 35% to 80% in patients with hypertension or type 2 diabetes melliltus[22,25].

PREVALENCE IN VARIOUS AGE GROUPS

In this study,the prevalence of metabolic syndrome increased as age increases. The incidence of acute myocardial infarction was high in the age group between 50-69 years. The mean in the metabolic syndrome group was 56.6 years whereas in the non-metabolic syndrome group the mean was 53.5 years. In a similar study conducted by Marianne Zeller[111] and co- workers the mean age was 70 years in the western population. Balkau B, Vernay M, Mhamdi L,

et al in their study "The incidence and persistence of the NCEP metabolic syndrome[112]" had shown similar features.

PREVALENCE IN BOTH SEXES

Of the 42 metabolic syndrome patients, 30 male patients and 12 female patients had metabolic syndrome. It is prevalent in both sexes but the incidence in females increases as ages increases than in males. Patients with metabolic syndrome were older more likely to be women.

In the Marianne Zeller[111] Study, out of 290 metabolic syndrome patients ,108 patients were female. Whereas in the non-metabolic syndrome group, females constituted 50 out of 343 patients.

COMPONENTS OF METABOLIC SYNDROME

WAIST CIRCUMFERENCE

The rationale for the use of waist criteria arises partly from data showing that measures of overall obesity, such as body mass index, are relatively insensitive indicators of the risk for metabolic and cardiovascular complications of obesity, as compared with measures of central or abdominal adiposity.[54] Apridonidze T[54] study on the "Prevalence and characteristics of the metabolic syndrome in women with polycystic ovary syndrome", it has been suggested to use waist circumference as an indicator for abdominal obesity.

Body fat distribution, particularly excess abdominal fat, plays an important role in the etiology of the syndrome.

Waist circumference (88.4%) in the metabolic syndrome group was increased in the study and it showed statistical significance (p=0.001). In the Zeller study [111], out of 290 patients of MS group had high waist circumference when compared to 94 out of 343 non-MS patients.

FASTING GLUCOSE

Increased fasting glucose is seen in patients with metabolic syndrome which is shown by studies done by Marianne Zeller[111] and co-workers. In their study 55 out of 290 MS patients had increased fasting glucose in contrast to 20 out of 343 non-MS patients.

Fasting glucose was prevalent to the extent of 80.9% in the metabolic syndrome group and it was statistically significant (p= 0.001).

HYPERTENSION

High blood pressure is a strong risk factor for cardiovascular disease (CVD) [80]

Hypertension is particularly dangerous to the cardiovascular system. This concept is supported by the Framingham Heart Study [81.]

Hypertension was more prevalent in the metabolic syndrome group (61.8%). On applying chi-square test it showed statistical significance (p= 0.008) which

is consistent with Zeller[111] study which shows 228/290 in the MS group having hypertension as that of to 99/343 non-MS patients.

HYPERTRIGLYCERIDEMIA

Dyslipidemia is a hallmark of the MetSyn and is characterized by elevated triglycerides (TG) and low levels of HDL-C.[45.46] Triglycerides were elevated to 75% in the metabolic syndrome group and this also showed a significance of p= 0.001.

In the Zeller[111] study elevated triglycerides was found in57% of MS patients to that of 14% in the non-MS group.

LOW HDL

A low HDL level is another characteristic of atherogenic dyslipidemia [1]. To an extent of 91.7% HDL was decreased in the metabolic syndrome group and its p value=0.002 was significant. So, low HDL is a significant risk factor for myocardial infarction as shown by Zeller[111] Study,in which 80% in MS group and 22% in the non-MS group had myocardial infarction.

OTHER PARAMETERS

ADMISSION GLUCOSE

A variety of mechanisms have been proposed whereby hyperglycemia might promote atherosclerosis [42]. Examples include nonenzymatic glycosylation of lipids and proteins, pathogenic effects of advanced glycation products,

increased oxidative stress, activation of protein kinase C, and microvascular disease of the vasa vasorum of the coronary arteries.

The admission glucose was increased in both the groups (49.3% and 51.7%) and but this was not statistically significant. But in the Zeller[111] study admission glucose was increased in 52% of MS group and 35% of non-MS group

TOTAL CHOLESTEROL AND LDL CHOLESTEROL

The total and LDL cholesterol were increased in both the groups and there was no significance in both the groups which is consistent with Zeller[111] study

SIGNIFICANCE OF FAMILY HISTORY

Family history of coronary artery disease was defined by a history of premature coronary artery disease in first degree relatives (having occured in those relatives at age < 55 years for men and <65 years for women)

Only two patients in the study gave a family history of CAHD and they showed metabolic syndrome but this was not significant statistically which is similar to Zeller[111] study.

HABIT OF SMOKING

Smoking is a modifiable risk factor. Smokers have increased levels of oxidised LDL[130], low HDL and increased vascular reactivity.Though smoking was more prevalent in the non-metabolic syndrome group(63%) than metabolic syndrome group(36%) there was statistical significance in the metabolic

syndrome group(p=0.001). In Zeller[111] study also smoking was more prevalent in the non- MS group (38%) than MS group(23%) and showed statistical significance.

INFLUENCE OF METABOLIC SYNDROME ON HOSPITAL OUTCOMES

HEART FAILURE

Heart failure was defined as the highest killip class[127] reached during hospitalisation.Severe heart failure, defined as Killips class > =2 was more prevalent in the metabolic syndrome group (78.4%) and this was statistically significant (p=0.001). In the Zeller[111] study 28% of MS group and 16% of non-MS group were found to have severe heart failure and this showed significant p value<0.001.

RECURRENT MI,VENTRICULAR ARRHYTHMIAS

Though recurrent MI (57.1%)and ventricular arrhythmias (77.8%) were more prevalent in the metabolic syndrome they did not show statistical significance in this study which is consistent with Zeller[111] study.

Metabolic syndrome did not appear to have an impact on ventricular tachyarrhythmias or recurrent myocardial infarction.

CASE FATALITY

Case fatality was high in MS group(2 patients died) than non MS group(one patient died) but this was statistically not significant. In Zeller[111] study case fatality was 11% in MS group and 4% in non-MS group.

Metabolic syndrome was associated with an increased case fatality rate though it was not an independent predictor of case fatality[25,111]

ICCU STAY

The stay in ICCU was more in the patients with metabolic syndrome and this was also significant (p=0.001). The mean ICCU stay in the metabolic syndrome group was 1.8 day whereas it was 1.1 day in the non-metabolic syndrome group. In Zeller[111] study the mean ICCU stay in both the groups was 4 days and it was statistically significant (p=0.03).

METABOLIC SYNDROME, HYPERGLYCEMIA, HEART FAILURE

Hyperglycemia was strongly associated with severe heart failure in the metabolic syndrome group(90%) when compared to the non-metabolic syndrome (22%).

There has been a consistent and marked increase in the incidence of heart failure in patients with metabolic syndrome. Among the components of metabolic syndrome hyperglycemia is strongly associated with heart failure and poor hospital outcomes which is consistent with other studies[113-117]

Likewise, low HDL cholesterol and elevated triglyceride levels appeared to have little impact on hospital outcomes confirming the data from the Aspirin Myocardial Infarction Study[111,119]

METABOLIC SYNDROME , A PREDICTOR OF MYOCARDIAL INFARCTION

In this study, statistically significant results are obtained with regard to the components of metabolic syndrome. They are strongly associated with acute myocardial infarction.

This is consistent with other studies [1,42,45,46,52,53,54,80,111]. Hence, metabolic syndrome is a major predictor for acute myocardial infarction.

METABOLIC SYNDROME AND PROGNOSIS

Large observational studies have shown that heart failure is a major determinant of hospital outcomes after acute coronary syndrome [127,128,129].Hyperglycemia is most strongly associated with poor outcomes[117,126.]

According to the study done by Marianne Zeller[111] and co-workers Metabolic syndrome is a strong and independent predictor of severe heart failure. Among the components of metabolic syndrome hyperglycemia is an independent predictor of heart failure . In this study, hyperglycemia has proved to be a strong predictor of heart failure.

Although abdominal obesity undoubtedly plays an important role in insulin resistance associated with metabolic syndrome, it does not seem to represent a major determinant of outcome[111,120]. In this study also waist circumference did not influence on hospital outcome.

Wahab et al[126] have shown that lipids have no role in predicting hospital outcomes which is consistent with this study.

Hypertension is not a major determinant of mortality and is only a moderate predictor of hospital outcome which is in agreement with other studies[111,118].Even in this study, hypertension had not influenced hospital outcomes.

According to Isomaa et al[25], the cardiovascular case fatality rate was markedly higher in patients with metabolic syndrome. In this study case fatality(2 patients died) was higher in patients with metabolic syndrome though it did not show statistical significance.

According to the study done by Marianne Zeller[111] , low HDL has a strong association with heart failure but in this study low HDL was a strong risk factor for acute MI and not for heart failure.

TREATMENT SIGNIFICANCE

Among the components of metabolic syndrome hyperglycemia was associated more with heart failure. This confirms the importance of evaluating glycemic

control during the acute phase of MI[124]. The other components of metabolic syndrome are also strong cardiovascular risk factors[1]and they should be treated.

CONCLUSION

1. There is a high prevalence of metabolic syndrome in patients with acute myocardial infarction.
2. The prevalence of metabolic syndrome increases as age increases
3. In women, metabolic syndrome is more prevalent in older age.
4. All the components of metabolic syndrome namely hyperglycemia, abdominal obesity, hypertension, hypertriglyceridemia and low HDL levels showed statistical significance ($p<0.05$) confirming strong association with myocardial infarction.

5. Admission glucose was increased in both the groups and it did not show statistical significance with the metabolic syndrome group.

6. Though, total and LDL cholesterol were increased in both the groups, there was no significance.

7. Only two patients in the study gave a family history of CAHD and they showed metabolic syndrome but this was not significant statistically.

8. Metabolic syndrome group had a number of cardiovascular risk factors and history of previous MI.

9. Though smoking was more prevalent in the non-metabolic syndrome group there was statistical significance in the metabolic syndrome group($p=0.001$).

10. Among the components of metabolic syndrome, hyperglycemia was associated more with heart failure. This confirms the importance of evaluating glycemic control during the acute phase of MI[124].

11. Though recurrent MI (57.1%)and ventricular arrhythmias (77.8%) were more prevalent in the metabolic syndrome they did not show statistical significance in this study.

12. Heart failure was present more in metabolic syndrome group. The incidence of heart failure at admission was high and also during

hospitalisation patients with metabolic syndrome developed severe heart failure (killip class > 2). It showed statistical significance.

13. Hyperglycemia was strongly associated in patients with severe heart failure.

14. Case fatality was high in MS group(2 patients died) than non MS group(one patient died) but this was not statistically significant.

15. The number of days in ICCU was high in the MS group when compared to NON-MS group and it was statistically significant.

LIMITATIONS

1. Acute metabolic stress due to MI may potentially affect blood glucose and lipid levels[121], both of which are criteria for metabolic syndrome, and therefore may lead to errors in the calculation of the prevalence of metabolic syndrome. However, the presence of fasting glycemia[111] at days 4 and 5 of AMI represents a

valid early marker of individuals at high risk of abnormal glucose metabolism.

2. Moreover, in studies evaluating the biological relevance of lipid assessment at the acute phase of MI, a gradual decrease in mean HDL cholesterol and triglyceride levels[122, 123] during hospital stay has been reported but is only minor during the first 24 hours. So, this decrease could weakly influence the calculation of the prevalence of metabolic syndrome.

3. Although the risk factors were assessed at the time of index event, the duration of risk factors before MI could not be assessed. Hb A_{1c} was not studied.

4. Other tests like microalbuminuria, which is a part of WHO criteria for diagnosing metabolic syndrome and a good predictor for cardiovascular diseases were not studied.

5. The study population was less, only 85 patients were studied. Though, statistical significance was obtained for all the components of metabolic syndrome.

6. **The study is subject to subject error, instrument error and investigator error.**

PROFORMA

CASE STUDY: PREVALENCE AND IMPACT OF METABOLIC SYNDROME ON HOSPITAL OUTCOMES IN ACUTE MYOCARDIAL INFARCTION

Name of the patient: Occup,Address:

Age: DOA: DOD:

Sex: Informant:

Presenting complaints: chest pain – onset,duration,site,character,duration
Breathlessness
Palpitations
Syncope

HOPC:

Yes/No/Duration

Past H: CAHD
DM
HT

Personal H: Smoking
Alcoholic

Family H: CAHD

Treatment H: Aspirin, beta blockers, ACE inhibitors, nitrates, statins, OHA.

GENERAL EXAMINATION:

BMI W/H2

Built vitals Temp

Nutrition

Pallor PR
Jaundice
Cyanosis RR
Clubbing
Pedal oedema BP
Lymphadenopathy

CVS

RS

ABD

CNS

INVESTIGATIONS

ECG

BLOOD TC CXR
DC
ESR
Hb
Platelet count

BLOOD Urea
Sugar
S.creatinine
S.electrolytes
Na
K

Cl

HCO3

SGOT

SGPT

CPK MB

URINE

Alb

Sug

Dep

Ketones

PRESENTING DATA

Door to needle time

PR

BP

KILLIPS CLASS

STEMI- AWMI

IWMI

RVMI

PWMI

Thrombolytic R/

MS CRITERIA

Waist circumference

BP

HDL

TGL

Fasting glucose

MS –yes or no

OUTCOMES

Case fatality

Non fatal rec. MI

VT/VF

Heart blocks

Stroke

HF

HF > K 1

Severe HF > k II

Cardiogenic shock K IV

ECHO

Wall motion abnormalities

LVEF

Days in ICCU

DIAGNOSIS

FINAL OUTCOME:

APPENDIX-I

MASTER

S. no	IP no	Name	age	sex	Wc cm	BP Mm Hg	FG Mg/dL	HDL Mg/dL	TGL Mg/dL	Met syn	TC Mg/dL	AG Mg/dL	FH CAH D	LDL Mg/dL	s
1	136071	Arif khan	60	M	78	110/70	120	41	52	N	183	140	N	132	
2	136098	Vijaya kumar	43	M	90	100/70	99	46	84	N	200	120	N	137	
3	123364	Chinnathambi	55	M	82	130/90	136	39	178	Y	175	120	N	100	
4	136093	Ravikumar	37	M	98	110/80	130	56	172	Y	233	112	N	143	
5	136083	Shakunthala	67	F	94	120/80	120	56	218	Y	225	130	N	113	
6	136105	Singaram	75	M	70	130/80	170	49	115	Y	200	200	N	121	
7	136107	Dharman	48	M	75	110/80	68	56	126	N	233	130	N	152	
8	136102	Abdullah	48	M	86	100/80	72	61	99	N	250	132	N	169	
9	136106	Sheikh munnar	40	M	80	110/70	160	54	90	N	217	170	N	145	
10	136097	Samson	44	M	98	130/90	110	41	93	Y	175	250	Y	115	
11	136533	Murugesan	55	M	94	120/70	140	39	210	Y	175	158	N	94	
12	136613	Chinnappan	86	M	82	140/90	120	54	98	N	217	160	N	143	
13	136109	Madhavan	45	m	101	160/100	110	68	102	Y	267	140	N	179	
14	136108	Rangamma	68	F	92	130/90	120	56	94	Y	233	138	N	158	
15	136100	Rukmani	55	F	97	140/90	120	51	100	Y	208	135	N	137	
16	137426	Bahadurkhan	68	M	76	160/100	110	46	59	Y	192	130	N	134	
17	137432	Mariambee	50	F	87	110/80	130	73	221	Y	292	500	N	175	
18	137580	Arunasingh	49	M	95	150/100	120	59	148	Y	233	120	N	144	
19	136082	Abdul ajeez	54	M	83	120/80	130	44	57	N	192	116	N	137	
20	137233	Saifudeen	65	M	91	150/100	180	46	142	Y	183	411	N	109	
21	136136	Kuttiappan	38	M	83	120/80	130	41	141	N	183	139	N	114	
22	136132	Alamelu	60	F	92	160/80	86	49	187	Y	200	154	N	114	
23	136898	Elizebeth	50	F	120	130/90	120	54	108	Y	217	171	Y	142	
24	136133	Amala	59	F	96	120/80	232	46	102	Y	225	384	N	149	
25	136139	Yesudoss	54	M	84	120/80	140	53	107	N	217	130	N	141	
26	136138	Kubendran	55	M	94	140/100	120	49	160	Y	200	160	N	119	
27	136144	Munusamy	46	M	93	130/90	176	63	194	Y	258	96	N	156	
28	136148	Saminathan	62	M	84	140/90	98	51	84	N	208	120	N	140	
29	136111	Janarthanan	28	M	83	120/80	120	37	72	N	158	110	N	107	
30	136118	Vedhachalam	50	M	80	170/120	130	41	83	N	183	155	N	225	
31	136120	Natarajan	67	M	84	110/80	90	56	88	N	217	136	N	150	
32	136142	Papammal	60	F	82	110/70	130	39	185	Y	158	145	N	82	

33	136152	Kaurpusamy	53	M	92	140/90	252	54	184	Y	208	134	N	120	
34	136143	Jamal	55	M	98	110/80	90	49	122	N	200	112	N	127	
35	136117	Madhavan	48	M	78	140/90	90	44	90	N	200	120	N	138	
36	136159	Marimuthu	65	M	93	150/80	200	56	122	Y	233	180	N	153	
37	136142	Pandian	49	M	88	100/70	96	63	145	N	250	100	N	158	
38	134668	Ganesan	45	M	78	150/90	90	41	88	N	167	98	N	108	
39	136121	Sajudeen	72	M	100	130/100	84	46	158	Y	200	68	N	122	
40	136119	Abdul jaffer	62	M	92	130/80	120	56	142	Y	217	136	N	133	
41	135839	Kamala	75	F	108	160/100	88	46	114	Y	225	110	N	146	
42	136160	Selvam	50	M	90	170/110	151	66	184	Y	267	180	N	164	
43	131592	Sathyanathan	50	M	92	130/100	96	39	83	Y	167	90	N	111	
44	131129	Vijayan rao	45	M	98	150/90	70	41	132	N	175	68	N	108	
45	136162	Kumar	37	M	85	100/80	90	63	111	N	250	160	N	161	
46	136143	sakunthala	58	F	92	140/90	120	48	160	Y	218	136	N	146	
47	136095	ravikumar	38	M	106	130/90	110	56	172	Y	233	130	N	143	
48	130562	Damodharan	63	M	89	120/80	90	54	158	N	175	105	N	100	
49	136129	Jayakumar	27	M	94	130/90	128	59	178	Y	250	148	N	169	
50	136120	Indrani	64	F	106	160/100	130	45	187	Y	267	180	N	152	
51	136152	kupusamy	54	M	83	130/90	94	44	57	N	194	116	N	138	
52	136126	Ranganathan	48	M	84	120/80	99	41	141	N	184	139	N	114	
53	136140	veetabai	70	F	78	150/90	98	48	190	N	233	196	N	153	
54	136159	Marimuthu	66	M	83	130/90	90	58	90	N	210	180	N	145	
55	136092	Tulasiammal	68	F	78	110/80	96	45	170	N	208	185	N	157	
56	136134	Arunachalam	61	M	98	130/80	170	49	156	Y	200	200	N	121	
57	136096	Santhanam	54	M	84	130/90	96	54	109	N	218	130	N	142	
58	136098	Vijayakumar	44	M	80	110/70	92	54	90	N	218	170	N	142	
59	136084	Chandra	58	F	76	110/70	96	55	117	N	235	180	N	158	
60	136103	Subramani	53	M	95	120/70	96	59	148	N	233	120	N	144	
61	136107	Murugesan	52	M	104	160/100	110	68	102	Y	267	140	N	179	
62	136114	Thangasamy	54	M	87	130/90	120	51	100	N	192	140	N	137	
63	136134	Arunagiri	62	M	102	170/100	130	44	190	Y	250	186	N	170	
64	136153	Vijayan	43	M	90	100/70	94	46	84	N	200	120	N	137	
65	136116	Rajan	55	M	94	120/70	140	39	212	Y	175	148	N	96	
66	136124	Munirathinam	64	M	80	130/90	98	54	90	N	220	170	N	148	

67	135136	manikumar	66	M	84	140/90	98	51	84	N	208	120	N	140		
68	136432	Duraisamy	67	M	86	130/90	96	56	88	N	217	136	N	150		
69	136110	Venkataraman	83	M	94	140/100	254	56	188	Y	208	138	N	128		
70	137429	Mohan	49	M	78	150/90	70	41	132	N	175	68	N	108		
71	136148	Saminathan	54	M	88	120/70	90	58	98	N	178	140	N	134		
72	136168	Pannerselvam	62	M	84	130/90	98	54	96	N	210	176	N	148		
73	136696	Varadharajan	62	M	92	130/90	120	56	142	Y	217	136	N	133		
74	137426	Dhanasekaran	58	M	84	130/90	96	58	86	N	208	138	N	148		
75	137427	Jayaraman	65	M	78	100/70	90	44	90	N	233	160	N	153		
76	136761	Kamaludeen	54	M	87	130/90	96	51	100	N	194	140	N	137		
77	136073	Balu	59	M	78	130/90	96	56	98	N	178	140	N	137		
78	136091	Shanmugham	66	M	76	120/80	98	54	156	N	175	110	N	135		
79	136088	Munusamy	58	M	92	150/100	120	48	160	Y	220	139	N	146		
80	163089	Narayanasamy	68	M	84	130/90	98	54	108	N	218	130	N	145		
81	136086	Murali	64	M	93	140/90	110	54	156	Y	175	135	N	100		
82	136087	Mohammed faro	62	M	78	150/90	108	56	142	Y	235	160	N	155		
83	136080	chinnadurai	45	M	84	130/90	110	53	140	Y	200	136	N	120		
84	136533	Murugesan	50	M	98	140/90	120	37	132	Y	158	110	N	108		
85	136079	Shanmugham	68	M	104	150/100	138	40	188	Y	238	164	N	160		

KEY FOR MASTER CHART

WC- WAIST CIRCUMFERENCE

BP – BLOOD PRESSURE

FG – FASTING GLUCOSE

TGL – TRIGLYCERIDES

HDL- HIGH DENSITY LIPOPROTEIN

MET SYN – METABOLIC SYNDROME

TC- TOTAL CHOLESTEROL

LDL- LOW DENSITY LIPOPROTEIN

AG- ADMISSION GLUCOSE

FH CAHD- FAMILY HISTORY OF CORONARY ARTERY HEART DISEASE

SM- SMOKING

HF -HEART FAILURE

CF- CASE FATALITY

R MI – RECURRENT MI

VT/VF – VENTRICULAR TACHYCARDIA/VENTRICULAR FIBRILLATION

ICCU – INTENSIVE CORONARY CARE UNIT

APPENDIX-II

GLOSSARY

ADA	- AMERICAN DIABETES ASSOCIATION
ADMA	- ASYMMETRICAL DIMETHYL ARGININE
AHA	- AMERICAN HEART ASSOCIATION
AMI	- ACUTE MYOCARDIAL INFARCTION
APO B	– APO LIPOPROTEIN B
ASCVD	- ATHEROSCLEROTIC CARDIO VASCULAR DISEASE
ATP III	- ADULT TREATMENT PANEL III
BMI	– BODY MASS INDEX
CAD	– CORONARY ARTERY DISEASE
CAHD	- CORONARY ARTERY HEART DISEASE
CRP	- C-REACTIVE PROTEIN
HDL	- HIGH DENSITY LIPOPROTEIN
HOMA	- HOMEOSTASIS MODEL ASSESSMENT
ICCU	- INTENSIVE CORONARY CARE UNIT
IFG	- IMPAIRED FASTING GLUCOSE
IGT	- IMPAIRED GLUCOSE TOLERANCE
IHD	- ISCHEMIC HEART DISEASE
LDL	– LOW DENSITY LIPOPROTEIN
MS , MET SYN -	**METABOLIC SYNDROME**
NASH	- NON ALCOHOLIC STEATO HEPATITIS
NCEP	-NATIONAL CHOLESTEROL EDUCATION PROGRAM
NEFA	- NON ESTERIFIED FATTY ACID
NHLBI	- NATIONAL HEART,LUNG, BLOOD INSTITUTE
NON-MS	-NON METABOLIC SYNDROME
NON-STEMI	– NON ST ELEVATION MYOCARDIAL INFARCTION
PAI	- PLASMINOGEN ACTIVATOR INHIBITOR
SAT	– SUBCUTANEOUS ADIPOSE TISSUE
STEMI	– ST ELEVATION MYOCARDIAL INFARCTION
TGL,TG	- TRIGLYCERIDES
VAT	- VISCERAL ADIPOSE TISSUE
VF	– VENTRICULAR FIBRILLATION
VLDL	- VERY HIGH DENSITY LIPOPROTEIN
VT	- VENTRICULAR TACHYCARDIA
WC	- WAIST CIRCUMFERENCE

APPENDIX-III

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