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A STUDY ON CLINICAL PROFILE OF METABOLIC SYNDROME AND ITS IMPACT ON MYOCARDIAL INFARCTION AT A TERTIARY CARE HOSPITAL IN KERALA

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ABSTRACT: Background: Metabolic syndrome has a significant impact on the severity and prognosis of various risk factors that may contribute to cardiovascular events. We examined the clinical profile and prevalence of MetS among MI patients along with the estimation of associated risk factors and determined the components of the MetS which conferred the paramount cardiovascular risk. **Methods:** A prospective observational study was conducted for duration of 10 months on a total of 117 MI patients who were further categorized based on IDF criteria for MetS at a tertiary care hospital in India. Statistical analysis of collected data was done using SPSS 22 for windows version. **Results:** Among all the parameters used for defining MetS, positive predictive value was highest for fasting blood sugar (p=0.001) followed by high blood pressure (p=0.005) and elevated triglycerides (p=0.850). MetS was significantly more prevalent in MI patients with a prevalence of 51.28% (p<0.001). **Conclusion:** The study depicted high prevalence of MetS among MI patients which implies greater risk of developing cardiovascular diseases. A systematic approach in identifying components of Mets and provision of appropriate management strategies remains a vital step in preventing further cardiovascular complications and improving quality of life of individuals.

INTRODUCTION: Metabolic syndrome is a constellation of interconnected metabolic disorders that represent risk factors for cardiovascular disease (CVD), atherosclerosis and diabetes mellitus type 2 (DM-2). Excessive lipid accumulation in various tissues, including adipose tissue results in insulin resistance, which triggers metabolic inflammation and acts as a substantive component in the development of metabolic syndrome along with other risk factors such as hypertension, dyslipidemia, central obesity and glucose intolerance [1]. With the increasing prevalence of obesity associated oxidative stress and other cardio metabolic risk factors, early identification of high risk patients is pertinent for proposing preventive strategies [2].

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In the current clinical scenario, metabolic syndrome serves as a tool for guiding the physician in forecast of the risk with respect to diabetes mellitus and cardiovascular diseases. Several definitions have been proposed by World Health Organization (WHO), the European Group for the study of Insulin Resistance (EGIR), the National Cholesterol Education Program-Adult Treatment Panel III (NCEP–ATP III) and the International Diabetes Federation (IDF), which share common modalities such as hyperglycemia, obesity, dys-lipidaemia and hypertension in recognizing the clinical components or risk factors, even though they differ in the subtle details and criterias [3, 4, 5, 6].

MetS is a state characterized by inflammation which occurs as an outcome of interaction between diverse factors with pervading systemic effects. Various environmental and genetic factors lead to adipose tissue hyperplasia and hypertrophy which results in altered free fatty acid metabolism and adipokine release which ultimately results in MetS [7].

Inflammation which occurs as a consequence of obesity plays a major causative role in generating insulin resistance, defective insulin secretion, and disruption of other aspects of energy homeostasis[8]. Furthermore, an elevated production of prothrombin activator inhibitor-1 leads to a pro-coagulant state along with endothelial dysfunction that result in increased risk of atherothrombosis, hypertension and CVD [9]. It is estimated that around 20 - 25 % of the world's adult population have MetS, its prevalence further depending on the diagnostic criteria used, age, gender, socioeconomic status, and the ethnic background [10, 6].

The prevalence of MetS is considerably low in rural areas when compared to urban areas and recent estimates suggest a prevalence of 29.7% in the South Indian urban region [11]. A high prevalence of the metabolic syndrome in urban Asian Indians shows that it is more prevalent in subjects with higher socioeconomic status, sedentary lifestyle, high fat diet and obesity [12]. Overall prevalence of MetS is rising in India and other developing countries which confer to increasing obesity, surplus energy intake, sedentary life styles and unhealthy nutrition. Coexistence of multiple cardiometabolic risk factors such as diabetes, dyslipidemia, hypertension and obesity in patients with metabolic syndrome makes them more prone to develop cardiovascular disorders. The diagnosis, prophylaxis, and adoption of appropriate treatment strategies to manage the individual components of metabolic syndrome is an essential approach for reduction of cardiovascular disease burden [13].

Knowledge of the impact of metabolic syndrome according to standard definitions on cardiovascular and overall mortality in the general population is crucial for developing public health policy and clinical guidelines for its prevention and treatment. The importance of the metabolic syndrome from a clinical and public health perspective may be greatest in the earlier stages before development of CVD or diabetes.

The current study aimed at evaluating the clinical profile of MetS and estimating the prevalence of MetS among myocardial infarction (MI) patients, whether CVD occurrence rates were influenced by the metabolic syndrome as defined by IDF criteria, investigating the risk factors and to determine the component(s) of the metabolic syndrome which conferred the highest cardiovascular risk.

METHODOLOGY: A prospective study was conducted at the division of cardiology, nephrology and general medicine in a multi-specialty tertiary care referral hospital located in Malappuram district at the State of Kerala, India. The study was approved and certified by the Institutional Ethical Committee as per letter no IEC/ASH/2014/PP/101 and informed consent was obtained from all the study subjects prior to the conduct of the study.

Data on patient's demographics, co morbidities, past histories, ECG findings, relevant lab investigation data, use of medications (on admission in hospital and on discharge) and use of invasive cardiac procedures were gathered from a total of 117 patients during a period of 10 months commencing from November 2016 to September 2017. Data's were collected from case reports, medication charts, and in-depth interviews with the patients and their by-standers. Information regarding diabetes, hypertension, hyperlipidemia, family history of coronary artery disease, smoking, alcohol consumption and other risk factors had been prospectively recorded.

The waist circumference was measured according to WHO stepwise approach to surveillance protocol where measurement should be made at the approximate midpoint between the lower margin of the last palpable rib and the top of the iliac crest using a tape, by maintaining the patient's upright posture. The International Diabetes Federation consensus worldwide definition of the metabolic syndrome (2006) was used to diagnose MetS. Central obesity (defined as waist circumference with ethnicity-specific values) and any two of the following criteria are required for the diagnosis of MetS:

- Raised triglycerides: >150mg/dL (1.7 mmol/L), or specific treatment for this lipid abnormality.
- 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 this lipid abnormality.
- Raised blood pressure (BP): systolic BP > 130 or diastolic BP >85 mm Hg, or treatment of previously diagnosed hypertension.

- Raised fasting plasma glucose (FPG): >100 mg/dL (5.6 mmol/L), or previously diagnosed type 2 diabetes If FPG is >5.6 mmol/L or 100 mg/dL, an oral glucose tolerance test is strongly recommended, but is not necessary to define presence of the syndrome.

If BMI is >30 kg/m², central obesity can be assumed and waist circumference does not need to be measured. The pilot study conducted on a sample of 20 patients evidenced that the prevalence of metabolic syndrome among the MI patients was 46%. On applying the sample size calculating equation $n = 4\ pq/d^2$, where n = minimum required sample size, p = 46%, q = 1 - p and d is the precision (taken as 20% of p) the minimum required sample size was estimated to be 117.

All statistical analysis was done using Statistical Package for Social Sciences (SPSS) software version 22.0 for windows. Level of significance was set at 5% with p value <0.05 being considered as statistically significant. Descriptive statistical analysis was performed and categorical variables were described by frequencies and percentages and continuous variables were described by means and standard deviations. Chi-square test was used to study differences between groups for variables of age, gender and risk factors.

RESULTS: A total of 117 MI patients were included in the study. The mean age of the patients was 58.37 years. In the total population under study, 77% (n= 90) were males and 23 % (n= 27) were females. Most of the study subjects were coming under the age group of 60 - 70 years. The minimum and maximum ages of the patients were 35 and 70 respectively.

Out of 23 female patients, 44.68% were adults while 8.57 % were geriatrics. At the same time out of 90 male patients, majority (91.43%) were geriatrics. Age and gender wise distribution of patients of MI patients revealed a statistical significance with a P value of 0.0001 **Table 1**.

60.68% subjects were obtained from cardiology department, 29.91 % from nephrology department and 9.41% from general medicine department. Among 117 patients, 64.96% were having non ST segment elevation myocardial infarction (NSTEMI) and 35.04% were having ST segment elevation myocardial infarction (STEMI).

Out of 76 NSTEMI patients, 78.94% were male and 21.05% were females. Similarly out of 41 STEMI patients, 73.14% were males while 26.83% were females **Table 2**.

TABLE 1: AGE WISE DISTRIBUTION OF MetS AMONG MI PATIENTS

Age		Sex			Chi square	P value
		Male	Female	Total		
35-59 years	n	26	21	47		
	%	55.32%	44.68%	100.0%		
60-70 years	n	64	6	70		
	%	91.43%	8.57%	100.0%	20.64	0.0001
Total	n	90	27	117		
	%	76.92%	23.07%	100.0%		

TABLE 2: TYPE OF MI AND GENDER WISE DISTRIBUTION

Type of MI	Sex			Chi square	P value
	Male	Female	Total		
NSTEMI	16	60	76	20.64	0.0001
	21.05%	78.94%	100.0%		
STEMI	11	30	41		
	26.83%	73.17%	100.0%		
Total	27	90	117		

Chi-square concluded no statistical significance (p value = 0.332) between the type of MI and sex wise distribution. 62.5% of NSTEMI patients and 61.16% of STEMI patients represented an age group of greater than 60 years. However there was no significant correlation between the type of MI and age wise distribution. (p= 0.65).

In this study, the prevalence of MetS among MI patients was found to be 51.28%. Among the total

of 117 patients with MI followed for 10 month period, there were, 60 patients with MetS and 57 patients without MetS. According to IDF criteria, the waist circumference (> 90 cm for men, >80 cm for women) is an essential criteria for determining the MetS. In subjects with MetS, WC and FBS were found to be major factors followed by hypertension, cholesterol and triglyceride levels **Table 3**.

TABLE 3: PREVALENCE OF EACH COMPONENT OF METABOLIC SYNDROME

S. no.	Variables	MetS		t value	P value
		Yes	No		
1	WC	59	33	10.32	0.0001
2	TGL	39	10	0.190	0.850
3	HDL	31	17	0.345	0.731
4	FBS	58	33	4.95	0.0001
5	HTN	39	7	2.89	0.005

Among all parameters, positive predictive value was highest for fasting blood sugar (p=0.001) followed by high blood pressure (p=0.005) and triglycerides (p=0.850). Among 60 patients with metabolic syndrome, 70% of patients were seen in the age group of 61-70 years, showing a statistical significance with a p value of 0.001 **Fig. 1**.

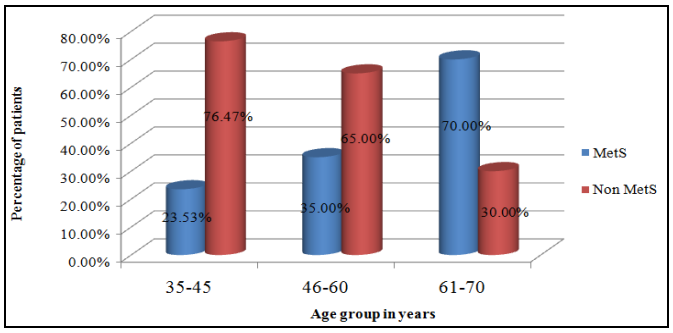

FIG. 1: AGE WISE DISTRIBUTION OF MetS AMONG MI PATIENTS

The prevalence of MetS was found to be higher in female patients (77.77%) and lower in male patients (43.33%) reflecting a statistical significance between gender and risk of MetS with a P value of 0.002 **Table 4**. Various clinical factors were evaluated for significance in the development of MetS among MI patients **Table 4**.

No statistical significance was found between food habits and MetS even though majority of the patients were non vegetarians. Both alcohol consumption and smoking also had no significant relation with the occurrence of MetS. The present study has delineated several unique characteristics that influence the cardiovascular health of the patients, including a low degree of control of high blood pressure and elevated sugar level, a fairly high rate of dyslipidaemia and overweight.

TABLE 4: BASELINE DEMOGRAPHIC AND BEHAVIOURAL CHARACTERISTICS OF THE PARTICIPANTS

Variable	Metabolic syndrome		Total	Chi square	P value
	Yes	No			
Age					
35-45	4 (23.53%)	13 (76.47%)	17 (100%)	17.9	0.001
46-60	14 (35.00%)	26 (65.00%)	40 (100%)		
61-70	42 (70.00%)	18 (30.00%)	60 (100%)		
Gender					
Male	39 (43.33%)	51 (56.66%)	90 (100%)	9.86	0.002
Female	21 (77.77%)	6 (22.22%)	27(100%)		
Food habits					
Vegetarian	7 (46.67%)	8 (53.33%)	15 (100%)	0.14	0.702
Non vegetarian	53 (51.96%)	49 (48.03%)	102 (100%)		
Alcohol habit					
Alcoholic	40 (53.34%)	35 (46.67%)	75 (100%)	0.35	0.55
Non alcoholic	20 (47.61%)	22 (52.38%)	42 (100%)		
Smoking habit					
Smoker	31 (52.54%)	28 (47.45%)	59 (100%)	0.076	0.738
Non smoker	29 (50.00%)	29 (50.00%)	58 (100%)		

DISCUSSION: In the current prospective study conducted to evaluate the impact of MetS on MI, prevalence of MetS was found to be 51.28%. Diabetes mellitus, hypertension, central obesity and hyperlipidemia are found to be the most important risk factors in the development of MetS.

Substantial increase of MetS in developing countries is attributed to surplus energy intake, improving economic situations and sedentary lifestyle leading to increased mortality and morbidity due to various complications including life threatening cardiovascular diseases. Appropriate research needs to be conducted to explore the absolute risk factors of MetS and investigate new treatment regimen and adequate prevention strategies. The estimates of prevalence varied among various studies. In our study IDF criteria was used for defining MetS among the study population, which has shown a high level of agreement in predicting cardiovascular risk and a relatively high prevalence was obtained.

As per estimated evidence, the prevalence of MetS, as defined by ATPIII, IDF and WHO classifications, was relatively higher, especially for those with existing hypertension [14]. Comparison in prevalence of MetS obtained from different studies with varied ethnicities is difficult because various definitions are being used.

A recent study of Alakkas Z *et al*., in 2016 conducted in line with our study estimated MetS in consensus with new IDF definition [15]. The study had similar investigation strategy to that of our research except in the fact the high rates of MetS was obtained across all segments of patients in the CCU and was not limited to patients with acute coronary syndrome. The prevalence was found to be higher among females with statistically significant correlation between gender and development of MetS in our study which was in line with the aforementioned study. Data regarding the significance of gender are conflicting with the majority of the studies that found the highest prevalence in women compared to men [16, 17].

The prevalence of obesity, hypertension, dyslipidaemia and hyperglycaemia may increase with age, thereby increasing the prevalence of metabolic syndrome also in consensus with age. In our study there was a preponderance of MetS among elderly patients, considerably in the age group of above 60 years of age. In a cross sectional study of 1369 patients, the prevalence of MS was 3 times higher in elderly subjects (>60 years) in relation to the group <60 years [18]. Thus individuals above 60 years of age are associated with increased risk of cardiovascular complications mainly pre-disposed due to insulin resistance, hormonal alterations, and increase in visceral adipose tissue.

Among the components of MetS, positive predictive value was highest for waist circumference (WC) fasting blood sugar (FBS) followed by blood pressure (BP) and low HDL cholesterol in our study. Waist circumference is a required component of the IDF definition, which may explain its lesser discrimination of risk in comparison with the harmonized version [14]. Previous studies concluded similar baseline characteristics of patients showing that they were older, precisely diabetic, and have a higher waist circumference, and waist-to-hip ratio [15, 18]. All these components of metabolic syndrome such as insulin resistance, increased waist circumference, hyper-tension, dyslipidemia, are all risk factors for endothelial dysfunction, which is an important factor in the pathophysiology of atherosclerosis and acute coronary syndromes. The initial indicator of a high-risk metabolic profile is central obesity, and our present study coherently points to the high priority of this risk factor in the elderly segment of the population, when focusing on preventing T2DM and CVD and in advancing efforts to regulate the obesity epidemic.

In the Suriname Health Study, a national survey designed according to the WHO Steps guidelines, prevalence of MetS and its components were determined for all ethnicities. The study estimated highest prevalence's for central obesity and low high-density lipoprotein cholesterol (HDL-C) [19]. In our study, there was a higher proportion of smoking and alcohol consumption among those with MetS [20]. A previous study observed significantly higher TG levels among excessive drinkers of male population [21]. Such high consumption of alcohol was associated with high risk of MS due to high BP, impaired fasting glucose, abdominal obesity and TG. On the other hand smoking can alter almost all components of MetS including waist circumference, high density lipids, fasting glucose, and triglycerides and predisposes them to development of MetS [22].

Thus smoking acts as a modifiable risk factor of MetS and may lead to chronic inflammatory states thereby, predisposing to atherosclerosis and other

cardiovascular complications. A systematic approach in identifying social habits such as alcohol consumption and smoking, thereby adopting appropriate cessation programs into the routine healthcare system should be made mandatory for equating those at risk of developing MetS.

In a previous study conducted by Mottillo S *et al*., in 2010 obtained consistently higher point estimates for cardiovascular outcomes and showed that the risk for cardiovascular disease mortality and stroke exceeds that of all-cause mortality [23]. The review identified an important gap in the literature and suggested the need of further studies to investigate whether the predictive significance of metabolic syndrome exceeds the risk associated with the totality of its individual components.

All the current studies highlight that there is importance of early diagnosis and treatment of major cardiac related risk factors, such as diabetes and MetS, when cardiac patients are being evaluated. There is a substantial need for more evidence based studies to investigate the cardiovascular risk associated with metabolic syndrome and to categorize the predictive value for each individual component consistent with the proposed definition. More efforts related to education and awareness should be encouraged among healthcare providers involved in providing pharmaceutical care to these patients. Public health education campaigns to educate high-risk populations about MetS and its complications are also considered important. Although there are currently no specific protocol proposed in the treatment of MetS as a whole, preference is to be sought at treating the individual components via lifestyle modifications, dietary changes, lipid correcting agents and hypoglycemic agents that have shown to slow the progression of MetS and reduce the risk of cardiovascular complications.

CONCLUSION: Metabolic syndrome acts as a significant prognostic tool in the identification of cardiovascular complications. The prophylaxis and management of metabolic syndrome in MI patients remains a vital step in preventing further complications and improving the quality of life of the individuals. Providing comprehensive care that will address both the admission of cardiac disease, as well as its risk factors, is key to improve patient outcomes. Despite different definitions proposed for metabolic syndrome, the individual components identified according to these diagnostic criteria's remains highly modifiable and can act simple tools for predicting the future societal risk of cardiovascular diseases.

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