Association of metabolic syndrome and level of hs-CRP, Lp(a), and serum ferritin in young Asian patients (≤45 years) with acute myocardial infarction

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Abstract: *Aims:* This study was aimed to determine the levels of hs-CRP, serum ferritin, and Lp(a) and to study the prevalence of metabolic syndrome (MetS) in young patients (≤45 years) with and without acute myocardial infarction (AMI). *Methods:* This was a cross-sectional, case–control study conducted at a tertiary care center in India. Equal number of patients with matched age and sex ($n = 51$) were included in case group (with AMI) and in control group (without AMI). Subjects were assessed for the presence of MetS as per modified ATP III criteria. The hs-CRP, Lp(a), and serum ferritin were also measured. *Results:* The prevalence of MetS was found to be 62.74% in case group, whereas 33.33% in control group with decreased HDL level as the most prevalent parameter. The hs-CRP level was found to be 15.35 ± 8.27 mg/dl in case group and 1.85 ± 1.05 mg/dl in control group and Lp(a) was 33.84 ± 23.69 mg/dl in case group and 19.68 ± 10.39 mg/dl in control group. No significant difference was observed in the serum ferritin level in case (264.2 ± 40.6 ng/dl) and control (225.51 ± 45.35 ng/dl) groups. *Conclusion:* From this study, we can conclude that the assessment of these novel risk factors [hs-CRP, Lp(a), and MetS] may be used for the risk estimation and can help to prevent future mortality and morbidity due to CVD.

Keywords: metabolic syndrome, C-reactive protein, lipoprotein (a), serum ferritin, acute myocardial infarction

Introduction

Cardiovascular diseases (CVDs) have now become the leading cause of mortality in developing countries including India [1]. Compared with whites, individuals of South Asia demonstrate onset of coronary heart disease (CHD) at a younger age and are often diagnosed with CHD before the age of 40 years [2]. Metabolic syndrome (MetS) is a major risk factor for the development of CVD and is a growing health issue globally. The term MetS (syndrome X and insulin-resistance syndrome) is the cluster of related factors, such as insulin resistance, abdominal obesity, hypertension, and lipid abnormalities [elevated levels of triglycerides (TG) and low level of high-density lipoproteins (HDLs)], which is associated with a twofold increase in cardiovascular outcomes [3–5]. Although the role of each component of MetS is clear, the level of these markers is a point for further continuous research in different population.

Inflammatory mechanisms play a central role in the pathogenesis of various CVD and its complications. C-reactive protein (CRP) is a non-specific inflammatory marker, which is a strong independent predictor for cardiovascular risk and events. High-sensitivity CRP (hs-CRP) rises acutely after tissue injury, including myocardial infarction (MI), and its measurement is the strongest correlative factor for future clinical events due to arterial inflammation, MI, unstable angina, stroke, and

peripheral vascular disease in both diseased and apparently healthy asymptomatic patients [6].

Furthermore, serum ferritin is also an acute phase reactant and has positive correlation with hs-CRP [6]. There are number of studies suggesting strong association of serum ferritin and coronary artery diseases (CAD) with conflicting and contradictory results [7, 8].

Many observations have demonstrated that lipoprotein (a) [Lp(a)] levels could also be a risk factor for CVD [9]. Lp(a) significantly stimulated the growth of human vascular smooth muscle cells in a dose-dependent manner. Furthermore, Lp(a) levels constitute as a marker of restenosis after percutaneous transluminal coronary angioplasty and ischemic stroke [10].

Thus, as all these factors affect MI directly or indirectly, this study was aimed to determine the levels of novel risk factors, such as hs-CRP, serum ferritin, and Lp(a), and to study the prevalence and profile of MetS in young patients (≤45 years) with and without acute myocardial infarction (AMI).

Materials and Methods

This was a cross-sectional, case–control study conducted at Department of General Medicine, a tertiary care center in India between the period October 2013 and November 2015. Patients with AMI were included in case group and patients with matched age and sex without AMI were included in the control group. The study was approved by the Institutional Ethics Committee of the hospital and written informed consent was obtained from the total of 102 patients (51 cases and 51 controls).

Patients with ≤45 years of age and diagnosed with AMI (for case group) were included in the study. Patients with any recent illness, tissue injury, inflammatory arthritis, chronic kidney disease, iron deficiency anemia, hemochromatosis, liver disease (cirrhosis or hepatitis), Hodgkin's disease, leukemia, infection, on non-steroidal anti-inflammatory drugs (e.g., aspirin, ibuprofen, and naproxen) or statins or niacin use, and women on hormone replacement therapy were not included in the study.

Data were collected using a semi-structured questionnaire, clinical examination, and investigations. Diagnosis of MI was made using the guidelines given by the Joint ESC/ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction [11]. Subjects were assessed for the presence of MetS as per the modified Adult Treatment Panel III (ATP III) criteria *(Table I)* and minimum three out of five should be satisfied to be labeled as having MetS [12].

The anthropometric measurements (including height, weight, and waist circumference) and blood samples collection for lipid profile, fasting blood sugar, hs-CRP, Lp(a), and serum ferritin were carried out within 72 h of admission.

The results were statistically analyzed using SPSS (Chicago, IL, USA; version 15) and comparisons were made using *t*-test. Quantitative data like age, vital signs, and investigations are expressed as mean and standard deviation with 95% confidence interval and qualitative data like sex, symptoms, and clinical findings as frequency and percentages.

Table I ATP III criteria for diagnosis of metabolic syndrome

Waist circumference*	≥90 cm for males and ≥80 cm for females
Serum HDL	≤40 mg/dl for males and ≤50 mg/dl for females
Serum TG	≥150 mg/dl
Blood pressure	≥130/≥85 mmHg
Fasting blood glucose	≥110 mg/dl

The symbol "*" indicates that only criteria for waist circumference was modified as per IDF guidelines for South East Asian Region. ATP III: Adult Treatment Panel III; HDL: high-density lipoprotein; TG: triglycerides

Results

A total of 51 patients with AMI as case group and 51 patients without AMI as control group were collected as age and sex matched for this study. Mean age was found to be 42 ± 2.91 years. The study included 84.3% male and 15.7% female in each group. Demographic details of both the groups along with prevalence of diabetes mellitus, hypertension, and dyslipidemia are depicted in *Table II*.

The prevalence of MetS was found in 32 patients (62.74%) in case group, whereas in 17 patients (33.33%) in control group.

It was found that HDL-C level was decreased in 32 (62.74%) cases compared with 22 (43.13%) in control group. TG level was increased in 31 (60.78%) cases compared with 19 (37.25%) in control group. Waist circumference and fasting blood glucose level were found to increase in 30 (58.82%) and 22 (43.13%) cases compared with 22 (43.13%) and 20 (39.21%) in control group, respectively *(Fig. 1)* and *(Table III)*.

Table II Baseline characteristics of patients

Characteristics	Cases ($n = 51$)	Controls ($n = 51$)
Age (mean ± SD, years)	42 ± 2.91	42 ± 2.91
Male		
≤40 years, *n* (%)	13 (25.5%)	13 (25.5%)
41–45 years, *n* (%)	30 (58.8%)	30 (58.8%)
Smoker, *n* (%)	12 (23.52%)	13 (24.49%)
Diabetes mellitus, *n* (%)	17 (33.33%)	12 (23.52%)
Hypertension, *n* (%)	14 (27.45%)	10 (19.60%)
Dyslipidemia, *n* (%)	10 (19.60%)	11 (21.56%)
Metabolic syndrome, *n* (%)	32 (62.74%)	17 (33.33%)

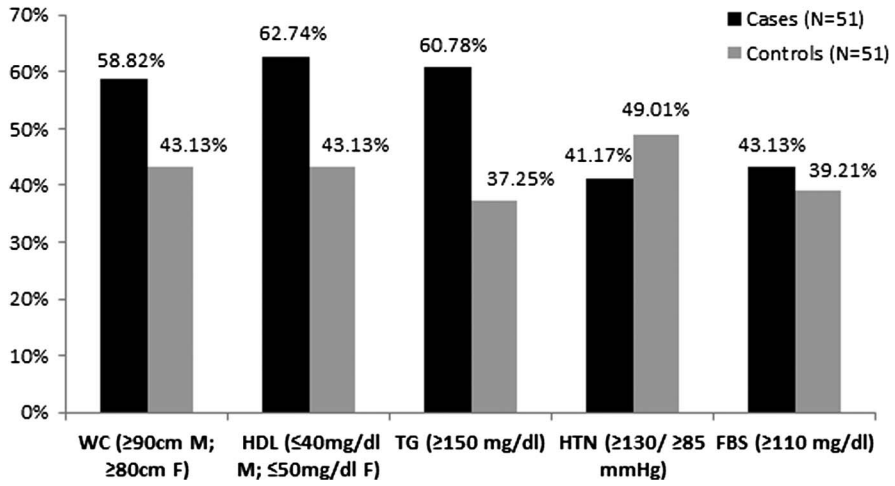

Fig. 1. Prevalence of individual parameter of metabolic syndrome in cases and controls

Table III Prevalence of individual parameter of metabolic syndrome among cases and controls

Parameters	Cases ($n = 51$)	Controls ($n = 51$)
Increased waist circumference, *n* (%)	30 (58.82%)	22 (43.13%)
Decreased HDL, *n* (%)	32 (62.74%)	22 (43.13%)
Increased triglycerides, *n* (%)	31 (60.78%)	19 (37.25%)
Hypertension, *n* (%)	21 (41.17%)	25 (49.01%)
High fasting blood sugar, *n* (%)	22 (43.13%)	20 (39.21%)

HDL: high-density lipoprotein

The most prevalent factor for MetS was found to be decreased HDL level followed by elevated TG level, increased waist circumference, impaired fasting glucose level, and hypertension.

The hs-CRP and Lp(a) levels displayed significant elevation in case group compared with control group ($p < 0.001$). The mean level of hs-CRP was found to be 15.35 ± 8.27 mg/dl in case group and 1.85 ± 1.05 mg/dl in control group, whereas the mean level of Lp(a) was 33.84 ± 23.69 mg/dl in case group and 19.68 ± 10.39 mg/dl in control group *(Table IV)*.

The mean level of serum ferritin in case group was 264.2 ± 40.6 ng/dl, whereas in control group, it was 225.51 ± 45.35 ng/dl. No significant difference was observed between both the groups ($p = 0.436$) *(Table IV)*.

Discussion

Asian Indians have known to be at a high risk for CVD and MetS [13]. As the prevalence of MetS and levels of hs-CRP, Lp(a), and serum ferritin in CVD have not been well explored in different Indian population, this work is an attempt to study all these novel risk factors in young South Indian subjects (≤45 years) with and without AMI.

In this study, the subjects were examined for the presence of MetS using the National Cholesterol Education Program (NCEP)–ATP III criteria. The prevalence of MetS was found higher than that observed in previous studies, i.e., 62.47% in cases compared with 33.33% in controls. Among all five parameters of MetS, low HDL-C level (62.74%) showed highest prevalence for AMI followed by increased TG (60.78%), increased waist

Table IV Levels of hs-CRP, Lp(a), and serum ferritin in case and control groups

Components	Cases ($n = 51$)	Controls ($n = 51$)	*p* value
hs-CRP (mean ± SD, mg/dl)	15.35 ± 8.27	1.85 ± 1.05	<0.001
Lp(a) (mean ± SD, mg/dl)	33.84 ± 23.69	19.68 ± 10.39	<0.001
Serum ferritin (mean ± SD, ng/dl)	264.2 ± 40.60	225.51 ± 45.35	0.436

hs-CRP: high-sensitivity C-reactive protein; Lp(a): lipoprotein (a)

circumference (58.82%), impaired fasting glucose (43.13%), and raised blood pressure (41.17%). In a similar study conducted by Wadhwa et al. [14], the prevalence of MetS was found to be 47.5% in cases and waist circumference was the most prevalent parameter for AMI. In another study conducted by Deepa et al. [15] on the South Indian population, the prevalence of MetS was estimated to be 23.2% as per NCEP–ATP III definition. The variation in the results of different studies might be due to regional difference and also because of difference in the characteristics of study groups, as this study includes below poverty line population.

Previous studies stated that the prevalence of MetS was higher in populations with acute coronary syndrome than in the general population; the exact mechanism by which the component of MetS increases the risk of CVD has not been clear, but various hypotheses have been established, which state that the involvement of pro-inflammatory responses leads to endothelial dysfunction [3].

It has been clear that acute phase inflammatory response is an important factor in AMI. This response is induced by pro-inflammatory cytokines, which are released from the inflamed tissue by inflammatory and parenchyma cells and stimulates the liver to synthesize a number of acute phase proteins. The hs-CRP is one of the classical acute phase reactants and various studies proved that serum level of hs-CRP increases in AMI. Recent studies have also shown that elevated hs-CRP levels have been associated with MetS [1, 6, 13].

The results obtained in the present study showed significant rise in hs-CRP level of 15.35 ± 8.27 mg/dl in cases compared with 1.85 ± 1.05 mg/dl in controls, which are analogous to the results of Wadhwa et al. [14], Wu et al. [16], and Chatterjee et al. [13]. The hs-CRP has prognostic usefulness in cases of acute ischemia, even without troponin levels, which indicate a significant association between high levels of hs-CRP and AMI [1].

The correlation between serum levels of ferritin and CVD has still been controversial and requires further investigation. Various previous studies stated that mean serum ferritin was significantly higher in patients of AMI [7, 14, 17–19]. On the other hand, the findings of Galan et al. [20] and Sempos et al. [21] failed to find a positive correlation between serum ferritin and AMI. Similarly, in this study, statistically significant difference ($p = 0.436$) was not observed in the serum ferritin level of case group (264.2 ± 40.60 ng/dl) and control group (225.51 ± 45.35 ng/dl). Hence, there is need of more researches and investigations to establish the association of serum ferritin level and CVDs.

Elevated serum Lp(a) is an independent predictor of CAD and MI. The result from this study showed significant increase in Lp(a) level of 33.84 ± 23.69 mg/dl in case group compared with 19.68 ± 10.39 mg/dl in control group and this result is equivalent to the findings of Wadhwa et al. [14], Chatterjee et al. [13], Mirzaei et al. [9], Boston et al. [22], and Pineda et al. [23]. A study by Goliasch et al. [24] showed elevated Lp(a) level even after premature MI. Thus, increased Lp(a) level might have some usefulness in risk estimation of AMI.

Conclusions

In this study, we found a significant association of novel risk factors namely MetS and levels of hs-CRP and Lp(a) with AMI, which stated that they have high prevalence of developing CVD in young individuals (≤45 years). Thus, we can conclude that assessment of these novel risk factors may be used for the risk estimation of CVD and can help to prevent future mortality and morbidity due to CVD.

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Conflict of interest: The authors declare no conflict of interest.

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