To Study the Prevalence and Profile of Metabolic Syndrome, Levels of hs-CRP, Lp(a) and Serum Ferritin in Young Indian Patients (≤45 years) with Acute Myocardial Infarction

A Wadhwa*, R Avasthi**, JK Ghambhir***, S Dwivedi****

Abstract

Objective: To study the prevalence and profile of metabolic syndrome, levels of hs-CRP, Lp(a) and serum ferritin in young Indian patients (≤45 years) with acute MI.

Methods: A total of 80 subjects in two groups (40 cases and 40 controls) of age ≤45 years were studied. Diagnosis of MI was made using the American College of Cardiology and European Society of Cardiology guidelines for acute MI. Patients were assessed for presence of MetS, diagnosed as per modified ATP III criteria. The anthropometric measurements (including height, weight, waist circumference) and sample collection for lipid profile, fasting blood sugar, hs-CRP, Lp(a) and serum ferritin were done after seventy two hours of admission.

Results: The mean age for cases was 39.23±4.80 years and for controls it was 38.9±4.23 years. 19 (47.5%) patients out of 40 in group 1 fulfilled ≥3/5 criteria for MetS while only 8 (20%) subjects in control group had MetS. Among five components of metabolic syndrome, increased waist circumference was most predominant factor followed by decreased HDL, increased TG, increased blood pressure and impaired fasting glucose. The mean value of serum ferritin was 279.33±46.69 mg in case group as compared to 245.15±56.94 in control group. hs-CRP (16.048±10.27 mg/l vs 1.8±1.6 mg/l) and Lp(a) (38.74±26.15 mg/dl vs 20.54±16.27 mg/dl) levels were significantly raised in cases as compared to control subjects.

Conclusion: The present study revealed high prevalence of metabolic syndrome (47.5%) in young patients with acute MI. Serum hsCRP, a diagnostic and prognostic novel marker of inflammation was also significantly elevated in cases. Its relationship with metabolic syndrome is also well established. Lp(a) and serum ferritin were also raised in cases.

Introduction

Coronary artery disease (CAD) is one of the commonest causes of death in developing and developed world. Various studies have revealed a consistent increase in prevalence of CAD in urban and rural population. It has been known for several decades that risk factors for atherosclerotic cardiovascular disease often cluster together. At its simplest, the metabolic syndrome is a cluster of inter-related risk factors for cardiovascular disease and diabetes mellitus, which coincides more often than by chance alone. It consists of a constellation of metabolic abnormalities namely, abdominal obesity, atherogenic dyslipidemia, raised blood pressure, insulin resistance, proinflammatory state, prothrombotic state. Though the role of these individual components in posing a risk for future CVD is unequivocal, the optimal cut off levels for these markers in different ethnic groups has been a subject of constant research and revision. The presence of MetS in patients with CAD in general and younger age groups in particular and its impact on morbidity and mortality are not well worked out in Indian subjects. In the present study, we determined the prevalence and profile of metabolic syndrome along with serum ferritin, Lp(a) and hs-CRP levels in young Indian patients with acute myocardial infarction (≤45 years).

Materials and Methods

The study was conducted at UCMS and GTB Hospital, Delhi. A total of 80 subjects (40 cases and 40 controls) were studied over a span of one year. Diagnosis of acute MI was made using the American College of Cardiology and European Society of Cardiology guidelines for acute MI.

At the time of admission, proforma for detailed clinical history, including presenting complaints, risk factors, family history and clinical examination with special reference to cardiovascular system was recorded. Various anthropometric measurements (including height, weight, waist circumference, hip circumference) were done and details of ECG were recorded. Fasting blood sample was collected for blood sugar, Lp(a), hs-CRP and other routine investigations.

Patients were assessed for presence of MetS, diagnosed as per modified ATP III criteria (at least 3/5 features). The criteria included were waist circumference ≥90 cm in males and ≥80 in females, serum HDL-C ≤40 for males, and ≤50 for females, serum TG ≥150 mg/dl, blood pressure ≥130/≥85 mmHg, fasting blood glucose ≥110 mg/dl. Only criteria for waist circumference was modified as per IDF guidelines for South East Asian Region. Serum ferritin, Lp(a) and hs-CRP levels were determined using...
sandwich ELISA technique. All patients were managed as per AHA guidelines and followed for at least one month.

Data for all groups was expressed as means±SD. For calculating difference of significance of mean values unpaired t-test was used. For studying the prevalence of metabolic syndrome in patients with early onset CAD, Chi-square test was applied.

### Results

There were 35 (87.5%) males and 5 (12.5%) females in each group. Both the groups were age and sex matched. The mean age was 39.23±4.80 years in patients with acute MI and 38.9±4.23 years in control subjects. There was a positive family history of CAD in 15 (37.5%) patients in case group while in the control group 6 (15%) subjects had a family history of CAD. 32 (80%) cases were found to be smokers as compared to 7 (17.5%) in group 2. The number of patients with raised hsCRP and Lp(a) were significantly more in group 1 (Table 2).

It was seen that waist circumference had the highest positive predictive value for acute MI followed by HDL, TG, blood pressure and impaired fasting glucose (Figure 1).

Significantly more number of patients (65%) had deranged HDL-C as compared to controls (32.5%). High TG and LDL-C levels were seen in 21 (52.5%) and 20 (50%) patients and the difference with controls was significant. Low HDL-C was seen in both patients 26 (65%) and control 13 (32.5%) subjects.

The mean value of serum ferritin was 279.33±46.69 mg in case group as compared to 245.15±56.94 in control group.

hsCRP and Lp(a) levels were significantly raised in cases as compared to controls. The mean values for hsCRP were 16.04±10.27 mg/L (group 1) and 1.8±1.6 (group 2), while mean values for Lp(a) were 38.74±26.15 (group 1) and 20.54±16.27 (group 2). The number of patients with raised hsCRP and Lp(a) were significantly more in group 1 (Table 2).

### Discussion

In the present study, metabolic syndrome was present in 47.5% of cases as compared to 20% of controls. Among the five components of metabolic syndrome, waist circumference had the highest PPV (70%) for acute MI followed by a low HDL-C (65%), increased triglycerides (52.5%), raised blood pressure (35%) and impaired fasting glucose (IFG) (27.5%).

The prevalence of metabolic syndrome in our study population of patients is similar to those seen in recent studies. In a study of 582 patients aged ≤45 years who were newly diagnosed with coronary artery disease by elective coronary angiography, the prevalence of metabolic syndrome was 37%, women had twice the prevalence compared with men. In a similar study conducted by Chung et al., the prevalence of MetS was found to be 47%, determined in 223 patients aged ≤ 45 years, who presented with AMI and underwent primary PCI. MetS was diagnosed by NCEP ATP III guidelines (modified by substituting BMI ≥28.8 for waist circumference).

Although smoking continues to be a predominant risk factor in Indians, other factors of cardiovascular risk profile might be changing with a maximum contribution from increased waist circumference and decreased HDL-C levels, especially for young Indian subjects. The ATP III recommends waist circumference as a marker of adiposity rather than BMI because abdominal obesity correlates more closely with metabolic risk factors and insulin resistance than an elevated BMI. A raised waist circumference was found in 28 patients (70%) in our study.

The mean HDL-C for our patients was 39.75±4.93 mg/dl. A less than desired HDL-C is an exceedingly common abnormality in Indian context. Significantly more number of patients in the case group (65%) had decreased HDL-C cholesterol levels. Although causal role of triglycerides in the atherogenesis remains controversial, in view of tight link of TG levels with known risk factors (low HDL-C, uncontrolled diabetes), the finding of elevated TG should enter into overall risk assessment for an individual. ATP-III includes a TG level of ≥150 mg/dl as a
criterion for metabolic syndrome. In our study, level of TGs was significantly raised in cases as compared to controls.

Solonen et al first reported a significant association between the serum ferritin level and the risk of MI in a Finnish Kuopio Ischaemic Heart Disease Risk factor study (KIHD) of 1931 middle-aged men during an average follow-up of 3 years. They found that Finnish men with a serum ferritin ≥200 µg/L had a 2.2 higher risk of MI than did men with lower serum ferritin. In our study serum ferritin level was significantly increased in cases as compared to controls with a mean value of 238.9±12.8 ng/ml for case group and 126.8±58.33 ng/ml for control group.

Genetically determined elevations in Lp(a) play an important role in accelerating atherosclerosis that results in premature MI and stroke. Whereas earlier studies focused primarily on the role of Lp(a) as an independent risk factor in the absence of other risk factors, more recent studies have high lighted the important role of Lp(a) in accentuating the risk associated with virtually all conventional and emerging risk factors. The risk which appears to be limited to premature vascular disease is highest before age 45, declines after age 55 and often disappears after age 65. The higher the Lp(a) level the lower the age of first heart attack, and most affected individuals develop MI by the third to fifth decade of life.10

hsCRP adds prognostic value as an acute phase marker for cardiac risk: (i) Predicts the prognosis in ACS,11 stable angina, unstable angina (UA) and acute myocardial infarction (AMI), (ii) Adds independent and additive prognostic value to troponin, and (iii) Provides additional prognostic value in patients with negative cardiac troponin results.

Levels of hs-CRP start rising and may reach peak up to 24-48 hrs after acute MI. Levels may increase up to 5 times (>15 mg/L) the normal values during acute inflammatory phase after acute MI.12 hs-CRP has prognostic usefulness in cases of acute ischemia, even without troponin levels suggesting that enhanced inflammatory response at time of hospital admission can determine subsequent plaque rupture.13 Our study showed significantly high levels of hs-CRP with a mean value of 16.04±10.27 in cases as compared to 1.8±1.6 in controls.

In our study, the mean values of systolic and diastolic blood pressure were not analyzed as all patients were put on antihypertensives. For all these patients, a baseline blood pressure completely free of drug effect was difficult to ascertain.

Conclusion
It will be wrong to assume that the younger patients lack conventional risk factors. As has been demonstrated in this study, there was a high prevalence of metabolic syndrome (47.5%), with maximum contribution from increased waist circumference and decreased HDL, in patients with early onset coronary artery disease. hs-CRP levels might have prognostic usefulness in predicting plaque rupture in cases of acute ischemia.

Hence, cardiovascular risk profile particularly in young subjects might be evolving as a consequence of increasing prevalence of central obesity.

References
2. Enas EA. How to beat Heart disease epidemic among South Asians; 2008:76-79.