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Research Article

Utility of Myelo peroxidase in Diagnosis, Prediction of Risk Factors and Prognosis of Acute Coronary Syndrome and Myocardial Infarction

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Abstract: ST elevated myocardial infarction (STEMI), non-ST elevated myocardial infarction (NSTEMI) and unstable anginas (UA) are continual spectrum of coronary artery disease (CAD). These are terminal events arising as a result of coronary artery atherosclerosis and superimposed thrombosis. In patients with acute coronary syndrome (ACS) and myocardial infarction (MI), it is desirable to identify a sensitive serum marker that is closely related to the degree of myocardial damage, provides prognostic information and can be measured rapidly. In our study, a total of 91 patients of either sex aged 20 to 60 years are recruited for this study, of which 30 are STEMI, 31 are NSTEMI / unstable angina and 30 are age and sex matched healthy controls. Of the total 91 subjects 30 were of STEMI (Group 1), 15 were of NSTEMI (Group 2), 16 were of unstable angina (Group 3) and 30 were controls (Group 4). In this study , out of total 30 cases of STEMI 11 had inferior wall Myocardial Infarction (MI), 5 had Antero septal wall MI, 11 had Anterior wall MI, 2 had Anterolateral wall MI and 1 had Apical wall MI. Of the total 59 patients of CAD (STEMI, NSTEMI, and UA) in which MPO determination was done, 17 had complications. In these patients MPO level was higher as compared to 42 patients in whom complications were absent. In patients in whom complications were present MPO level was 17.86±5.75 EU/ml, which was significantly higher, as compared to patients in whom complications were absent. This correlation was statistically significant. In complicated ACS, irrespective of other risk factors, MPO is significantly raised as compared to controls & can be used to predict immediate clinical complication. MPO is an early marker of plaque, destabilization in the overall spectrum of atherogenesis, it was postulated that it will be extremely useful in risk stratification of patients with chest pain, thereby preventing complications with help of timely intervention.
Keywords: Coronary Artery Disease (CAD), Acute Coronary Syndrome (ACS), Myelo peroxidase (MPO), Myocardial Infarction (MI), STEMI, Unstable Angina (UA), Troponin.

INTRODUCTION

ST elevated myocardial infarction (STEMI), non-ST elevated myocardial infarction (NSTEMI) and unstable anginas (UA) are continual spectrum of coronary artery disease (CAD). These are terminal events arising as a result of coronary artery atherosclerosis and superimposed thrombosis. In patients with acute coronary syndrome (ACS) and myocardial infarction (MI), it is desirable to identify a sensitive serum marker that is closely related to the degree of myocardial damage, provides prognostic information and can be measured rapidly. In patients with ACS the traditional markers being used are CPK and Troponin-T (Trop-T) & Troponin-I (Trop-I). Trop-T & I are very sensitive marker to detect myocardial damage. Its level in blood as low as 0.08 ng/ml can be easily detected by conventional quantative assay. Its level in the blood gives information about degree of myocardial damage, prognosis and can be measured easily within the time frame of at least 6 hours. Elliott *et al* [1] have showed that rise in levels of Trop I is directly proportional to the risk of complications in patients with ACS. Other marker that we are using is CK-MB. It rises earlier than Trop-T and remains elevated for 3-4 days. It is useful in detecting re-infraction because of its short life as compared to Troponins, which remains elevated for 10-14 days. Other than heart muscle CK is also released, from kidney brain and skeletal muscle so higher levels of MB isoform is needed for diagnosis of MI. Thus it is not specific as well as sensitive enough to detect micro-infraction and not provides much information regarding prognosis as Trop-T and I does. Other well known traditional marker used in diagnosis, prognosis and in determining line of management in ACS patients is CRP. It is basically a marker of coronary artery inflammation. It gives information regarding both ongoing coronary artery atherosclerosis as well as acute damage to coronary arteries as results of thrombosis and subsequent myocardial infection. It also gives information regarding prognosis in case of acute MI, NSTEMI or UA. It serves both as an upstream marker

as well as a downstream marker. Various studies have showed that in patients of CAD high levels of CRP is associated with poor prognosis. The traditional markers that we are using presently are downstream markers, i.e., they are released at the end stage of coronary artery atherosclerosis and superimposed thrombosis due to ischemia induced necrosis of myocardial cells. Hence, they do not give much information initially when pathogenesis of atherosclerosis was going on. Many a times, patient with chest pain admitted in emergency have normal ECG and unfortunately normal levels of cardiac enzymes and thus they are discharged. These patients may have fatal outcome, thus a negative cardiac marker value (Trop T, I or CK-MB) does not necessarily confer a low risk complication in patients presenting with acute chest pain to emergency department. Elevated level of Trop T, I, CK-MB, CRP each is associated with higher rates of death and recurrent ischemic events. Little is known about the utility of these biomarkers in combination. Recent investigations have further indicated that increase in upstream biomarkers like myeloperoxidase(MPO), Inter Cellular Adhesion Molecule(ICAM), Vascular Cell Adhesion Molecule (VCAM), Interleukin-1 (IL-1), CD34 as compared to biomarkers of necrosis like Trop T, CK-MB, may provide earlier assessment of overall patient risk and aid in identifying patients with higher risk of an adverse event. Several new cardiac biomarkers have emerged as strong predictors of risk among patients presenting with ACS and work is going on to make it routinely available to clinicians. Limited data are available regarding the predicting value of this new marker (myeloperoxidase) in patients of chest pain. This study is designed to assess the predictive value of MPO in prognosis of ACS and acute MI.

AIMS AND OBJECTIVES

1. To estimate the level of myeloperoxidase in healthy controls
2. To estimate the level of myeloperoxidase in acute coronary syndrome patients (STEMI and NSTEMI/unstable angina)
3. To correlate the level of myeloperoxidase with complications in acute coronary syndrome (STEMI and NSTEMI/ unstable angina).
4. To find correlation, if any between serum myeloperoxidase, hs-CRP and CPK-MB in diagnosis and prognosis of acute coronary syndrome (STEMI and NSTEMI/ unstable angina).

MATERIALS AND METHODS

This prospective study is conducted in the Departments of Medicine, Pathology and Microbiology, University College of Medical Sciences (University of Delhi) and Guru Teg Bahadur Hospital, Delhi. A total of 91 patients of either sex aged 20 to 60 years are recruited for this study, of which 30 are STEMI, 31 are NSTEMI / unstable angina and 30 are age and sex matched healthy controls. Patients with following complaints of maximum 24 hours duration are registered in the emergency department and are included in the study (ACC/AHA Guidelines, 2002).Chief Complaints considered were 1) Chest pain or severe epigastric pain, non-traumatic in origin with components typical of myocardial ischemia or MI. 2) Central or substernal compression or crushing chest pain, pressure, tightness, heaviness, cramping, burning achy sensation. 3) Unexplained indigestion, belching, epigastric pain. 4) Radiating pain in neck, jaw, shoulders, back, one or both arms. 5) Associated dyspnoea. 6) Associated nausea / vomiting. 7) Associated diaphoresis. Special Considerations were noted in Women who may present more frequently than men with atypical chest pain and symptoms, Diabetes patients may have atypical presentation due to associated autonomic dysfunction, Elderly patients may have atypical symptoms such as generalised weakness, stroke, syncope or a change in mental status.

Complete clinical history with particular reference to coronary risk factors like hypertension (HTN), Diabetes Mellitus (DM), smoking, alcohol intake, dyslipidemia, truncal obesity, family history and cardiovascular system are taken. Complete physical examination with special reference to Blood Pressure, Heart Rate, basal crepts, S3, S4, Jugular Venous Pressure (JVP), etc. were done. Complete cardiac assessment was done for the entire patients registered and treatment was started as per ACC/AHA guidelines.

Patients with unstable angina / NSTEMI

1. Patients with angina pectoris (or equivalent type of ischemic discomfort) with at least one of three features (reporting within 12 hours):
2. Occurs at rest or with minimal exertion usually last more than 20 minutes (if not interrupted by NTG)
3. Severe and described as a new onset pain (i.e. within 1 month)
4. Crescendo pattern

Patients are considered to have unstable angina or NSTEMI on the basis of serial electrocardiogram and determination of CK-MB. If markers are negative, with a reference limit of the 99th percentile of the normal population, the patient with ACS may be considered to have experienced unstable angina. The diagnosis of NSTEMI is established when the marker is released. In the latter condition, ECG, ST segment or T wave changes may be persistent, whereas they may or may not occur in patients with unstable angina and if they do, they are usually transient. Markers of myocardial injury may be detected in the blood stream hours after the onset of ischemic chest pain, which allows the differentiation between unstable angina (i.e. no markers in circulation, usually transient, if any, ECG changes of ischemia) and NSTEMI (i.e. elevated biochemical markers). Patients with myocardial infarction

The diagnosis of acute MI is based on the presence of at least two of the following criteria:

- Typical ischemic chest pain lasting for more than 30 minutes for the first time with no such history of similar episode.
- New appearance of abnormal Q waves with evolutionary ST and T wave changes in serial ECG tracings.
- Enzymatic evidence i.e., a rise in CK-MB to at least twice the upper limit of normal values.

Exclusion criteria

Treatable cause of angina like thyro toxicosis or anaemia , Abnormal Liver Function Test, Abnormal Kidney Function Test (end stage renal disease, creatinine > 2 mg/dl),Bone marrow transplantation, Acute inflammatory reaction, Congenital Heart Disease, aortic stenosis or other valvular lesions, Malignancy, Septicemia and other infections, Pheochromocytoma, Polycythemia, Malignant hypertension, Fever, Congenital myopathy, Connective tissue disorder and Vasculitis.

For testing of myelopeoxidase (MPO), 3 ml of venous blood sample was collected in plain vial from which serum was separated and stored at –20°C. MPO was determined by ImmuLisa Anti-Myelo peroxidase (MPO) Antibody ELISA method. 24 hours continuous ECG monitoring in Cardiac intensive Care Unit was done immediately after admission, patients were watched for complications like arrhythmia, asystole, bradycardia etc. Patients were observed for 7 days and followed up for next 3 months for identification of complications which could have arisen during follow up. Data was collected for establishing the level of myeloperoxidase which could assess the prognosis.

RESULTS

In the present study, 91 subjects were recruited from medical emergency during the period from November 2005 to January 2007. All of the subjects were meeting the inclusion criteria. Of the total 91 subjects 30 were of STEMI (Group 1), 15 were of NSTEMI (Group 2), 16 were of unstable angina (Group 3) and 30 were controls (Group 4).

In group 1 out of 30 cases 26 were males and 4 were female **(Fig. 1).** In Group 2 out of 15 cases 13 were males and 2 were females, in Group 3 out of 16, 13 were males and 3 females, in group 4 of total 30 controls 25 were males and 5 females (p=0.976).

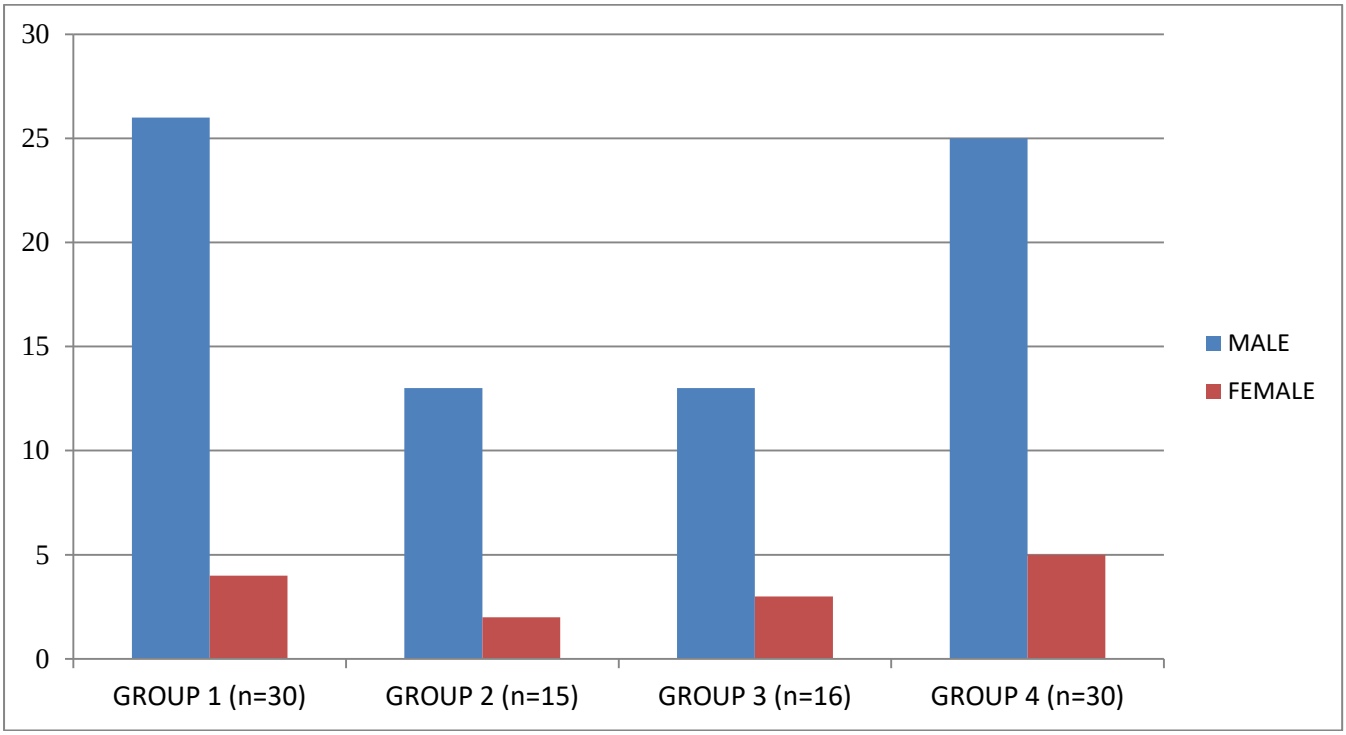

Fig-1: Sex Distribution In Study Groups. (Groups on X- Axis, Number of patients on Y-Axis.)

Mean age in Group 1 was 52.73±10.22 years, mean age in Group 2 was 55.80±11.40 years, mean age in Group 3 is 59.40±8.55 years, and in Group 4 mean age was 56.60±13.24 years (p=0.265).

BASELINE CHARACTERISTICS OF STUDY SUBJECTS

Table 1: Baseline Characteristics of Study Subjects

Variables	Group 1	Group 2	Group 3	Group 4	Significance (one way ANOVA)
Age (yrs)	52.73±10.22	55.80±11.40	59.40±8.55	56.60±13.24	0.265
Duration of chest pain (hrs)	8.07±3.46	8.67±11.50	9.75±5.85		0.731
Framingham risk score (% risk in 10 yrs)	13.20±10.21	17.87±10.21	13.38±7.72	7.63±1.33	0.282
Pulse rate (/min)	97.73±12.71	83.47±11.75	83.00±8.67	70.00±8.79	<0.001*
SBP (mmHg)	118.27±25.82	143.53±25.53	134.88±23.95	131.73±7.64	0.002*
DBP (mmHg)	79.07±14.57	86.53±9.21	83.69±8.00	83.23±8.05	0.151
Hb (gm/dl)	14.33±1.55	13.75±1.04	13.82±0.81	13.53±0.93	0.024*
TLC (n/dl)	10312±4481	8524±3572	5632±1266	5214±868	<0.001*
Blood sugar fasting (mg/dl)	97.53±31.84	97.13±32.28	92.06±23.17	83.07±11.57	0.132
Blood sugar postprandial (mg/dl)	141.33±53.62	145.67±63.96	138.56±72.21	129.87±9.88	0.74

CHARACTERISTICS OF CASES OF MI/UA/NSTEMI

Table 2: Distribution of cases of MI

ECG DIAGNOSIS	NUMBER OF CASES
Anterior wall MI	11
Anterolateral wall MI	2
Antero septal wall MI	5
Apical wall MI	1
Inferior wall MI	11

In this study , out of total 30 cases of STEMI 11 had inferior wall Myocardial Infarction (MI), 5 had Antero septal wall MI, 11 had Anterior wall MI, 2 had Anterolateral wall MI and 1 had Apical wall MI.

Table 3: Distribution of ECG changes in cases of NSTEMI / unstable angina (UA)

ECG CHANGES	NUMBER OF CASES	
No Changes Seen, ECG normal	5	
ST depression of 1 mm and T wave inversion in V1-V6	4 (persistent abnormality)	
T inversion in V5, V6	3 (fresh change)	2 (persistent abnormality)
T inversion in lead II , III aVF	5 (persistent abnormality)	
LAHB	3 (New change)	
ST depression of 2mm & T inversion in II, III aVF	5 (persistent abnormality)	
ST depression of 1.5mm & T inversion in V1-V4	4 (persistent abnormality)	

Of 31 patients with NSTEMI / UA, 26 patients had abnormal ECG, and 5 patients had no ECG changes. Of 26 patients with abnormal ECG, 6 patients had fresh changes; rest of the 20 patients had old abnormal ECG changes. All the 30 cases of STEMI were thromoblysed, as there were no contraindications for its use. In NSTEMI / UA, STK was not given and all the three groups were given treatment as per ACC / AHA 2002 guidelines.

CORRELATION BETWEEN MPO AND TOTAL LEUKOCYTE COUNT (TLC)

TABLE 4: Correlation between MPO and TLC

Groups	N	Attribute	r-value	p-value
Group 1	30	MPO, TLC	0.112	0.555
Group 2	13	MPO, TLC	-0.227	0.457
Group 3	16	MPO, TLC	-0.216	0.423
Group 4	27	MPO, TLC	0.108	0.590

As MPO levels can be found to be elevated in various conditions in which TLC is raised e.g. leukemoid reaction, septicemia etc. Correlation test was applied to find whether there is any correlation between MPO and TLC. In our study there is no correlation between TLC and MPO levels. There is no correlation between TLC and MPO levels.

LEVELS OF MYELOPEROXIDASE IN STUDY GROUPS

Table 5: Level of Myelo Peroxidase (MPO)

Groups	**Myeloperoxdiase (EU/ml) (Mean±SD)**	**Significance**
Group 1 (n=30/30)	13.51±4.63	<0.001*
Group 2 (n=13/15)	15.60±7.07	<0.001*
Group 3 (n=16/16)	11.40±5.92	0.250
Group 4 (n=27/30)	8.80±1.67	<0.001*

MPO level in group 1 was 13.51±4.63 EU/ml ($p<0.001$), in group 2 it was 15.6±7.07 EU/ml ($p<0.001$), in group 3 it was 11.40±7.07 EU/ml ($p=0.250$), in group 4 it was 8.80±1.67 EU/ml ($p<0.001$). Thus MPO levels in STEMI, NSTEMI and UA was higher as compared to controls. This was statistically significant in case of STEMI / NSETMI and in controls. This was not statically significant in case of unstable angina. When STEMI, NSTEMI and UA were taken as a one group, MPO value was statistically significant as compared to controls.

CORRELATION OF MPO LEVELS WITH COMPLICATIONS IN ACS

Table 6: Correlation of MPO levels with complications in ACS

Complications	**Number of patients**	**Mean±SD**	**p-value (one way ANOVA)**	**Regression equation**
Present	17	17.86±5.75	<0.001*	C = 0.41 x MPO – 0.252
Absent	42	11.48±4.47		

Of the total 59 patients of CAD (STEMI, NSTEMI, and UA) in which MPO determination was done, 17 had complications. In these patients MPO level was higher as compared to 42 patients in whom complications were absent. In patients in whom complications were present MPO level was 17.86±5.75 EU/ml, which was significantly higher, as compared to patients in whom complications were absent. MPO level in these patients was 11.48±4.47 EU/ml. This correlation was statistically significant ($p<0.001$).

CORRELATION BETWEEN MPO, HS-CRP AND CPKMB IN PROGNOSIS OF ACS

Table 7: Correlation between MPO, HS-CRP and CPKMB in prognosis of ACS

Dependent factor	**Independent factor**	**r-value**	**Significant factor**	**p-value (t-test)**
Complications	MPO, hs-CRP, CKMB	0.508	MPO	<0.001*

In our study hs CRP levels, though moderately elevated as compared to controls, showed no association with clinical complications arising within 7 days. Similarly CK-MB levels were not associated with complications. Stepwise multiple regression analysis of complications on MPO, hs-CRP and CK MB showed that MPO is the only significant factor contributes to predict complications.

Correlation test showed that:

1) MPO, hs-CRP and CK-MB are not related to each other
2) Hs-CRP and CPKMB independently have no correlation with prognosis

Step-wise multiple regression gives the relationship between MPO and complications as 0.41 x MPO – 0.252. If 0 – complications absent, If 1 – complications present

DISCUSSION

Although new markers such as cardiac troponins have tremendously increased our ability to detect and/or exclude cardiac injury, a normal level does not totally exclude the risk. In such a scenario, there are many unnecessary admissions to expensive hospital areas where discharge may be equally appropriate. A mis-diagnosis of ACS carries considerable risk for patient and many can have serious

adverse event, myocardial infarction, sudden cardiac death etc. A biomarker which can define the risk will lessen the burden of admission in crowded and expensive emergency and coronary care department as well as provide an early assessment of overall patient risk and identify patient with higher risk of having an adverse event, will definitely be a big weapon in the armaterium of health care providers. Myelo peroxidase (MPO) and activated leucocytes, a marker of plaque destabilization an early event in the pathophysiology of atherosclerosis may be the ideal investigation.

Myelo peroxidase is a hemoprotein (molecular mass of 140 kDa) consists of a pair of heavy and light chains. It is stored in azurophilic granules of polymorphonuclear neutrophils and macrophages and functions to catalyse the conversion of chloride and H_2O_2 to hypochlorite. Myelo peroxidase is released into the extracellular fluid and general circulation during inflammatory conditions. This enzyme has been implicated in the oxidation of lipids contained within LDL.

Several studies support potential links between MPO and the development of CAD. Myelo peroxidase has been implicated as a participant in atherosclerosis through mechanisms related to its role in inflammation [2, 3], LDL oxidation [4-10] and nitric oxide consumption leading to endothelial dysfunction [8]. Myelo peroxidase generates an array of diffusible oxidants [2] and is capable of initiating lipid peroxidation and promoting protein nitration and corss linking [11] processes known to occur during the evolution of atherosclerosis [2, 12-16]. Myelo peroxidase also binds to LDL in plasma and promotes site-specific oxidation of the lipoprotein. Both immuno histo chemical and mass spectrometry studies demonstrate that MPO is present in, and promotes oxidative modification of targets within human atheroma at all stages of lesion development. Furthermore, LDL recovered from human atherosclerotic lesions is enriched in multiple oxidation products formed specifically by MPO, such as chlorotyrosine and Schiff base adducts of p-hydroxy phenyl acetaldehyde (a tyrosine oxidation product) with both a polipoprotein B100 lysine residues and amino phospholipids. There are several clues to the potential functional consequences of MPO catalysed oxidation in the artery wall. Isolated human monocytes use MPO to oxidatively convert LDL into an atherogenic particle capable of promoting cholesterol accumulation and foam cell formation. Uptake occurs via the scavenger receptor CD36, a receptor that appears to play a major role in foam cell formation in vivo. Myelo peroxidase may thus be involved in the atherosclerotic process direct by promoting lesion development.

Myelo peroxidase also may play a role in the pathogenesis of acute coronary syndromes through plaque destabilization. Circulating leukocytes release MPO during acute coronary syndromes. Macrophages containing MPO and MPO dependent oxidation products are selectively enriched in atheromas that have undergone plaque rupture and ulceration. Moreover hypochlorous acid (HOCI) a primary oxidant generated by MPO, may promote extracellular matrix degradation in vivo. Myelo peroxidase-generated HOCI both activates latent matrix metalloproteinases and inactivates their physiological inhibitors (e.g. tissue in inhibitor of metalloproteinase 1). Myelo peroxidase thus may influence plaque stability and the propensity for provoking thrombosis.

Myelo peroxidase also may contribute to CAD through promoting endothelial dysfunction. Nitric oxide modulates MPO catalytic activity and serves as a physiological substrate for MPO. Myelo peroxidase attenuates nitric oxide-dependent smooth muscle relaxation and preliminary studies with preconstricted vascular rings show that MPO attenuates nitric oxide mediated vasorelaxant responses [17]. Thus, MPO may serve as a catalytic sink for nitric oxide, limiting its bioavailability and function [10, 18].

Although multiple lines of evidence suggest potential mechanisms for MPO in the development of cardiovascular disease, there are limited data in humans or animals. A cross-sectional study of 92 MPO deficient individuals reported that MPO deficiency (a genetic disorder that occurs in 1:2000 to 1:5000 individuals) is associated with a decreased prevalence of cardiovascular events [19]. A functional polymorphism in the promoter region of the gene for MPO resulting in decreased enzyme expression recently was reported to be associated with decreased risk of CAD [20]. Recent studies with MPO knockout mice demonstrated increased atherosclerotic lesion development [21]. However, further investigation demonstrated species-specific differences between mouse and human man, including the absence of MPO and its oxidation products within lesions among wild-type mice [21]. Previous studies have shown that MPO levels do not follow a gaussian distribution curve and its values is higher in male as compared to females. MPO level is also not affected by smoking, hypertension and other traditional risk factors for CAD except hyperlipidemia. Hyperlipidemia is associated with increased levels of MPO. MPO released from neutrophils have a tendency to bind to glycosoaminoglycans present in the endothelial wall, heparin causes release of MPO from endothelial wall. Thus MPO values can be higher in those patients of CAD treated with heparin and in patients with hyperlipidemia. A single initial measurement of plasma myeloperoxidase independently predicts the early risk of myocardial infarction, as well as the risk of major adverse cardiac events in the ensuing 20-day and 6-month periods. Myelo peroxidase levels, in contrast to troponin T, creatinine kinase MB isoform, and C-reactive protein levels, identified patients as risk for cardiac events in the absence of

myocardial necrosis, highlighting its potential usefulness for risk stratification among patients who present with chest pain [22].

In a case control prospective study by Zang *et al.;* [23] conducted from July to September 2000 in a US tertiary care referral centre, there were 158 patients with established CAD (Angiographic ally proven cases) and 175 patients without established CAD (Angiographic ally proven control). Main outcome measure was association of MPO levels per ml of neutrophils protein (Leukocyte MPO) and MPO levels per ml of blood (Blood MPO) with CAD risk. Results showed that leukocyte and blood MPO levels where both significantly greater in patients with CAD than in controls ($p<0.001$). In multivariate models adjusted for traditional risk factors, Framingham Risk Score and WBC counts, MPO levels was significantly associated with presence of CAD with an OR of 11.9 for the highest vs. lowest quartiles of leukocyte MPO and an OR of 20.4 for the highest vs. lowest quartiles of blood MPO. Thus, elevated levels of leukocyte and blood MPO were found to be associated with the presence of CAD. These findings supported a potential role of MPO as an inflammatory marker in CAD and have important implication for atherosclerosis diagnosis and risk assessment.

Brennan *et al.;* [22] assessed prognostic value of MPO, in patients with chest pain and its role as predictor of complications. They evaluated 604 patients presenting to emergency department with chest pain. Controls were young individuals of 20-25 year age groups selected from general population. Of the 604 patients 23.5% had MI, 17.1% had unstable angina, and 37.6% had suspected coronary syndrome and 21.5% had non cardiac chest pain. Plasma level of MPO in patients presenting with chest pain ranged from 0-4666 pM with a median of 198 pM and an inter quartile range of 119 to 394 pM. These levels were significantly higher than those observed in the 115 control subjects (median 120 pM, inter quartile range 97 to 146 pM; $p<0.001$). MPO levels in the patients were correlated weakly with peak troponin T levels ($r = 0.21$, $p<0.001$) CRP levels ($r = 0.10$, $p = 0.01$) and age ($r = 0.11$, $p = 0.01$) but not the white cell count ($p=0.11$). Median MPO levels were higher in men than in women (213 vs. 184 pm, $p = 0.05$). Initial MPO levels predicted the risk of MI even in patients who were negative for troponin T (<0.1 ng per ml) at baseline ($p <0.01$) further, MPO levels at presentation also predicted the risk of major adverse cardiac events (MI, the need for revascularization or death) within 30 days & 6 months after presentation.($p<0.001$). In patients without evidence of myocardial necrosis i.e. those who are negative for troponin T, the base line MPO levels independently predicted the risk of major adverse coronary events at 30 days and at 6 months. Those patients in whom trop T, hs-CRP and other traditional markers are negative, MPO independently predicted the risk of adverse outcome. When MPO was used in predicting outcome in patients of CAD along with trop T it increased the predictive value of trop T.

Baldus *et al.;* [24] enrolled 1265 patients with ACS (follow-up of CAPTURE Trial), all of whom had undergone angiography before randomisation and had shown significant CAD with a culprit lesion ≥ 70% suitable for angioplasty. These patients were randomly assigned to abciximab or placebo. Primary end points of study were mortality and non-fatal MI during the 30 days of the follow-up period. Serum samples were collected 8.7±4.9 hours after the last episode of chest pain. MPO serum levels were assessed in 1090 patients of ACS. MPO levels did not correlate with trop T, soluble CD40 ligand, CRP or with ST segment changes. However, patients with elevated MPO levels (>350 µg/l; 31.3%) experienced a markedly increase cardiac risk ($p=0.003$). In particular, MPO serum levels identified patients at risk who had trop T levels below 0.01 µg/l ($p=0.001$). In a multivariate model that included other biochemical markers trop T, CRP, VEGF, soluble CD40 ligand and MPO were all independent predictors of the patients six month outcome.

CONCLUSION

In this present study of 91 subjects we concluded that in patients of ACS, MPO is raised as compared to controls. Also in complicated ACS, irrespective of other risk factors, MPO is significantly raised as compared to controls & can be used to predict immediate clinical complication. There was no significant association between MPO, hs CRP & CK-MB when taken together to predict complications. MPO serves both as a marker of established CAD and as well as of plaque destabilization and subsequent complications. As MPO is an early marker of plaque, destabilization in the overall spectrum of atherogenesis, it was postulated that it will be extremely useful in risk stratification of patients with chest pain, thereby preventing complications with help of timely intervention.

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