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SERUM MALONDIALDEHYDE (MDA) LEVELS AND LIPID PROFILE PATTERN IN THE PATIENTS WITH ACUTE MYOCARDIAL INFARCTION (AMI)

Biological Science

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ABSTRACT

Acute Myocardial Infarction (AMI) is one of the critical emergencies of cardiovascular events leading to increased mortality rate and sudden deaths. Multiple arrays of biomarkers are required for its diagnosis and prognosis. To investigate serum Malondialdehyde (MDA) levels as an indicative of oxidative stress and comparison of lipid profile pattern in AMI patients. This is a prospective case- control study carried out in a tertiary care hospital between July and December 2017. The study recruited 100 consecutive AMI patients from the department of cardiology and 100 control subjects were recruited without the history of MI. Fasting (12 hours) blood samples was collected from all the subjects from ante-cubital vein and aliquated in to vials. MDA was measured using thio-barbituric acid method. Total cholesterol (TC) was estimated by Triender CHOD/POD end point method, triglycerides (TG) by GPO/POD enzymatic colorimetric method. High density lipoprotein (HDL) cholesterol was estimated using PEG-CHO-POD end point method. Low density lipoprotein (LDL) cholesterol was assessed by using the Friedewald formula. We observed notably higher levels of MDA in AMI patients (607±76nmol/dl) than in control subjects (230 ± 26nmol/dl) ($p< 0.05$). The lipid profile including serum triglycerides(TG), total cholesterol(TC), low-density lipoproteins (LDL), very-low density lipoproteins(VLDL) cholesterols were also significantly higher compared to controls ($p<0.001$). The High-density lipoproteins (HDL) levels are significantly lower in MI patients than in controls. Oxidative stress contributes in the pathogenesis of AMI. Therefore, oxidative stress biomarkers like malondialdehyde can be of good predictors for risk of AMI.

KEYWORDS

Malondialdehyde, Oxidative stress, Acute myocardial infarction, Lipid profile.

1.INTRODUCTION

Acute myocardial infarction (AMI) is a critical component of cardiovascular disease with high risk mortality rate.[1] It is mainly attributed to multi-factorial chronic inflammatory atherosclerosis process. Research suggests that reactive oxygen species (ROS) plays an important role in the pathogenesis of myocardial infarction.[2] Following an ischemic event, ROS are produced during reperfusion phase.[3, 4] and it can react with unsaturated lipids and initiates the self-perpetuating chain of reactions of lipid peroxidation in the cell membranes.[5,6] Consequently ischemic and reperfusion injury can result in impairment of mitochondrial function in heart cells.[7] Decreased antioxidant defense after reperfusion has been known to be associated with impaired myocardial perfusion.[8] Oxidative stress and resultant ROS can lead to the progress of major complications like left ventricular remodeling may be followed by AMI event.[9] There are various studies reporting lipid profile pattern among myocardial infarction patients to date. A study Kumar et al[10] recorded that there was significance in presence of higher levels of total cholesterol, triglycerides and reduced high-density lipoprotein levels in AMI patients. Whereas lower concentrations of serum HDL and higher serum TG were found to be independent risk factors of AMI[11] but, there are few studies, Lehto et al[12] reporting no significant differences in mean serum TC levels between the AMI patients and controls. The management of hyperlipidemia has been vital feature of post-myocardial infarction care[13]. However, LDL reduction alone cannot afford the overall risk reduction with statin treatment after acute coronary syndrome. [14] In recent years, there is growing focus on markers of oxidative stress that can aid in treatment of AMI patients. Thus, we hypothesized that MDA and lipid profile pattern might have relation and varies significantly among AMI patients. Therefore, we intended to study the oxidative stress marker like Malondialdehyde (MDA) levels and lipid profile between AMI patients and control subjects. Further, we attempted to study the correlation between patient's MDA levels, lipid.

2. MATERIALS AND METHODS

2.1 Study Design

This is a single centered, prospective case - control study carried out in a tertiary care hospital, NRI General Hospital, Guntur district, A.P. from July to December 2017. We recruited one hundred consecutive patients diagnosed with AMI aged between 35 and 65years of both the genders. Subsequently, age and sex matched 100 patients without the history of MI were recruited as control subjects. Patients with recent surgeries, active infection, diabetes, impaired hepatic or renal or thyroid dysfunction, malignancy, pregnancy and lactating women, patients with age below 35 and above 65 years were excluded from the study. The proposed study was approved by Institutional Ethics Committee and it was carried out in harmony fulfilling ethical standards of the institutional committee on human experimentation and with the Helsinki. An informed consent to participate in study was obtained from all the study participants after explaining the details of the study.

2.2 Sample size calculation

Sample size was calculated through online sample calculator; the survey system (https://www.surveysystem.com/sscalc.htm#one) by taking average of AMI patients attending hospital with 95% confidence level and 7.11 confidence interval and population size of 210.The resultant sample size required for the study was 100 patients and the control subjects were in 1:1 ratio.

2.3 Sample collection

Peripheral blood samples were collected after 24 hours of MI from all the patients. Fasting (12 hours) blood samples were obtained from ante-cubital vein. The samples were centrifuged at 3000 rpm for 10 minutes. Sera were separated for the analysis of marker (MDA) and lipid profile.

2.4 Biochemical Investigations

Serum Malondialdehyde (MDA) was measured using thio-barbituric acid reactive substances.[15] Total cholesterol was estimated by Triender CHOD/POD[16] end point method, TG by GPO/POD enzymatic colorimetric method[17] in which TGL are hydrolyzed by lipase to glycerol and free fatty acids. The intensity of color depends on amount of TGs and HDL cholesterol was estimated using PEG-CHO-POD end point method. LDL cholesterol was assessed using the formula of Friedewald equation [LDL = TC – (HDL + TG/5)]. Normal range cut off was taken as follows, TGL, ≥150 mg/dl; TC, ≥200 mg/dl; HDL-cholesterol, ≤60 mg/dl; and LDL–cholesterol, ≥130 mg/dl[18, 19]. All the clinical and laboratory data were collected from biochemistry department and medical records department of the hospital.

2.5 Statistics

All the obtained data were analyzed by using Statistical Package for Social Sciences (SPSS) (free version 7). Student's t-test was used to compare means of all the parameters among AMI patients and normal subjects. *P* value <0.05 were considered as statistically significant.

3. RESULTS

Among 100 patients included in our study, male gender was more

dominant than females indicating male gender as one the risk factors for cardiovascular events. Gender wise distribution of all the subjects was shown in figure 1. In different age groups, 51-55 years of age were more prone to AMI when compared to other groups (Figure 2). In our study, smokers and hypertensive patients are more among AMI cases than controls indicating that hypertension and smoking are one of the co- relating factors or risk factors for AMI (Figure 3). The serum lipid level of total cholesterol, triglycerides, VLDL and LDL cholesterol were higher in AMI patients when compared to controls subjects. Triglycerides were more among AMI cases and the difference is highly significant at $p < 0.001$.Total cholesterol, VLDL cholesterol were high among cases and the difference is significant at $p < 0.05$. The difference in LDL cholesterol between cases and controls is highly significant at $p < 0.001$ which is an important risk factor for various cardiovascular events. In this context, we observed positive correlation with LDL- C and MDA levels in the AMI patients (Figure 4). HDL cholesterol is a protective factor against various chronic and non-communicable disorders including myocardial infarction. We observed very low levels serum HDL cholesterol among cases compared to normal subjects. (table 1). We observed significantly higher levels of serum malondialdehyde in AMI patients compared to control subjects ($p<0.05$). The higher levels of MDA in patients are due to increased oxidative stress than in control (Figure 5).

5. DISCUSSION

Studies reported that oxidative stress in acute myocardial disease is due to reperfusion, an imbalance between antioxidants and pro-oxidants.[20,21] Oxidative stress is the key the process in the pathogenesis of several chronic diseases including myocardial infarction.[22] MDA is one of the more frequently intricated biological markers of oxidative stress.[23] It is capable to impair several pathways by its ability to react with organic molecules such as DNA and proteins. Based on these preliminary observations, we hypothesize that differences in MDA levels may correlate with lipid profile patterns in AMI patients.

In our study, we found male gender was predominant among AMI patients and control group. Consistently, a study reported by Deborah Zucker[24] et al also reported that male sex is more prone to myocardial infarction. Cigarette smoking is the most common and most modifiable risk factor in patients of myocardial infarction. In our study participants, 40% of patients had smoking history which is contradicting with results of Bennet et al[25] who reported 64% patients had smoking history from their study findings. Elevated serum malondialdehyde levels indicate the status of oxidative stress (higher MDA and lower antioxidant status) in MI patients. Our study further revealed the positive correlation between serum MDA levels and lipid profile levels in AMI patients. Our results showed higher levels of TC, LDL, and VLDL levels which are significant among AMI patients (Table 1). The study done by Gorecki et al[26] showed higher TC and LDL levels in patients mediate complicated infarction. Akosah et al[27] reported ideal LDL levels in a population of 183 young patients reporting AMI. Gaziano et al[13] found the average levels of TC and LDL were significantly lower in-hospital settings than after 2 to 3 months follow up. Thus, it is proposed to use the in-hospital levels as a guide to make decisions regarding lipid-lowering therapy, which can be started in early post-MI setting. Arun Kumar et al[28] have reported high cholesterol, LDL-C, low HDLC in cases compared to controls with significant p values. Rosoklija et al.[29] followed-up the HDL cholesterol levels from 24 hours to 3 months and concluded that the best time for determining the HDL is within 24 hours of the actual event. It might be possibly due to adoption of various life style changes or due to system changes during acute crisis. The study done by Al Aqeel et al[30] showed that low HDL seems to be one of the key risk factor for MI in Kuwaiti patients that recommends to prioritize the primary prevention strategies to enhance HDL levels. High Malondialdehyde levels also appear to be clearly associated with an increased risk of cardiovascular disease. This was also reported by Arun Kumar et al[24], Kaur et al[31], Rashmi Raghuvanshi et al.[32] In the present study, there is an significant association of MDA concentration and risk of MI. Lipid ratios have not been used to assess the risk of myocardial infarction. The ratio LDL/HDL was proposed to be an independent predictor of AMI in the Japanese rural population[33.] Go swami et al[34] reported that apo-B/apo-AI ratio is a good discriminator of myocardial infarction risk in pre-coronary artery disease patients compared to the conventional lipid ratios. The study done by Karthikeyan et al[35] found that there is strongest association between ApoB/ApoA1 and AMI. It was found that glutathione (GSH) protects the heart tissue against damage caused by free radicals. Low cellular levels of GSH would impair the recovery after myocardial ischemic event. The main limitation of this study is we have not evaluated the important oxidative marker, GSH levels due to financial constraints and lack of feasibility. Further, multi-centric studies are warranted to confirm the accurate prognostic value of these markers in AMI patients.

6. CONCLUSION

From the study findings, it is clear that prevalence of higher systematic inflammatory status in AMI patients is inversely correlated to protective HDL-levels. We observed significantly higher levels of serum MDA in MI patients compared to control group. Thus, low HDL and high LDL cholesterol levels can predispose the risky individuals to the event of AMI. However, multi-center studies on more number of patients with various associated co-morbid conditions must be done to draw more accurate and reliable conclusions.

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Tables and figures:

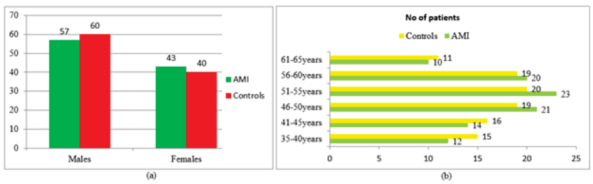

Figure 1. (a)Gender wise distribution of study participants, (b) Age group distribution

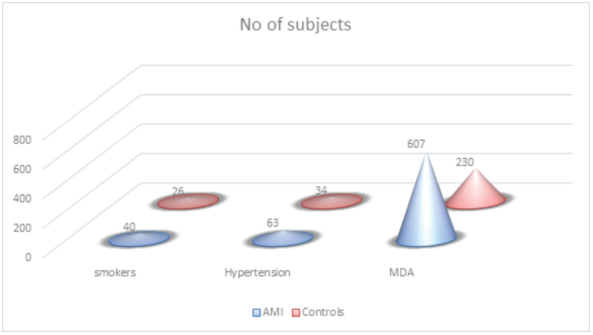

Figure 2: Distribution of smoking and hypertension among patients.

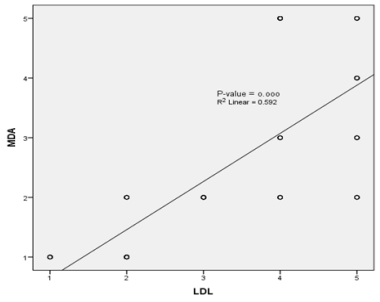

Figure 3. Correlation between MDA and LDL levels in AMI patients

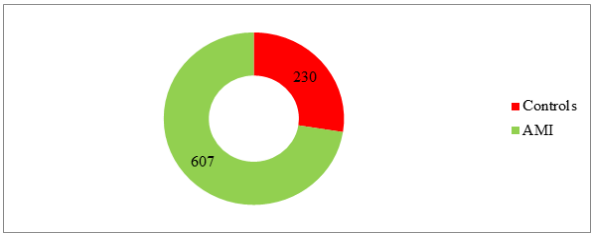

Figure 4: MDA level comparison among patients MDA in nmol/dl

Table 1: Lipid profile pattern comparision between 2 groups.

S. No.	Name of the parameter	Controls or normal subjects Mean ± S.D	Cases with Myocardial infarction Mean ± S.D	p value
1	Triglycerides (mg/dl)	110 ± 32	245 ± 60	< 0.0001
2	Total Cholesterol (mg/dl)	164 ± 32	276 ± 43	< 0.0001
3	VLDL Cholesterol (mg/dl)	25 ± 5	59 ±12	< 0.0001
4	HDL Cholesterol (mg/dl)	38 ± 8	28 ± 7	< 0.0001
5	LDL Cholesterol (mg/dl)	98 ± 8	190 ± 32	< 0.0001

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