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Original Research Article

Assessment of Risk Stratification and Prognosis among Patients of AMI by Lipoprotein (A), Lipid Profile and Antioxidant Biomarkers

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Abstract

Introduction: Acute myocardial infarction (AMI) is one of the important reasons for morbidity and mortality in the world. Indians are more prone to coronary artery disease (CAD) at a much younger age. Lipoprotein (a) [Lp (a)] levels have revealed wide ethnic variations. Lp(a) levels show link with clinical variables and severity of AMI in Gwalior region of India population needed further studies. The aim is to study and evaluate the alteration of lipid profile and lipoprotein (a) in AMI and compare it with that of a healthy population mainly in Gwalior region in India.

Methodology: Case control studies involving 100 patients of AMI were taken as cases and 100healthy persons were used as controls almost same age and sex matched. They were analysed by measurement of various parameters like BP, biochemical parameters such as FBS, lipid profile, MDA, GPx, SOD and catalase enzymes and Lipoprotein (a). Serum Lp(a) estimation was performed by immunoturbidimetric method.

Results: Our findings and evaluation demonstrated that elevated values of FBS, total cholesterol, triglycerides, LDL-c, VLDL-c and Lp(a) level and decreased level of HDL-c and antioxidant enzymes (GPx, SOD and catalase) were observed in AMI subjects. Concentration of Lp(a) was significantly higher in AMI subjects (43.66±8.20) in comparison to control subjects (22.9±03.46).The values of all biochemical markers were found increased in AMI patients and the difference were found to be statically significant. The level of Lp (a) and Lipid profile were found positive correlation in AMI.

Conclusion: Our study showed the patients of acute myocardial infarction have increased levels of serum Lp(a) as compared to healthy individuals. The increased level of serum lipoprotein(a) is strongly linked with the risk of coronary heart disease.

Keywords: Lipoprotein (a) , Acute myocardial infarction, Lipid profile.

Introduction

Acute myocardial infarction (AMI) is a significant contributor to global morbidity and mortality. Risk factors for developing coronary artery disease (CAD) include gender, age, race, family history, and modifiable factors such as serum cholesterol,

hypertension, smoking, and diabetes mellitus [1]. CAD is prevalent in Indians, with MI rates 2.2 - 5 times higher and coronary artery mortality rate 1.5-3 times higher rates compared to other populations. Indians also experience MI at a younger age, with mortality rates for MI in the 30-39 age group being nearly 10 times higher than in the white population. Autopsies show more severe and extensive atherosclerosis, larger infarct size, and increased incidence of triple vessel disease in Indians [2].

Studies in expatriate Indians have identified lipoprotein (a) as a major risk factor for AMI. While some studies show divergent results, several studies suggest higher levels of Lp (a) levels in cases than in controls [3]. Elevated levels of Lp (a) increase the risk of premature AMI by 3 – 100 fold, depending on the presence or absence of associated risk factors [4]. Numerous epidemiological and genetic studies support Lp (a) as a significant risk factor for AMI. As India undergoes economic development and mechanization, the population is experiencing epidemic evolution.

There is evidence that elevated levels of total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and reduced levels of high-density lipoprotein cholesterol (HDL-C) contribute to the development of atherosclerotic disease encourage plaques [5-7]. This study aimed to investigate variations in lipoproteins and serum lipid profiles in patients with AMI in the Gwalior region of India and explore the relationship between the onset of AMI and various inflammatory factors.

Material and Methods

The study recruited 200 subjects between February 2022 to March 2023, from the Department of Medicine at a tertiary care teaching hospital and medical outpatient camps. The subjects were divided into two groups:

Group 1 comprised of 100 healthy individuals free from any complications of myocardial infarction (MI) and Coronary Heart Disease (CHD).

Group 2 comprised of 100 patients with acute myocardial infarction.

Written informed consent was obtained from all participants, and demographic data such as age, sex, height, body weight, duration of AMI, blood pressure, hypertension, kidney diseases, smoking habit, dietary habits, and family history related to AMI were recorded. The study was approved by the Institutional Ethics Committee, and followed the ethical guidelines set by the committee.

Peripheral venous blood samples were collected within 24 hours of admission to measure lipid profiles. The diagnosis of AMI was made by a combination of history, physical examination, ECG, and biochemical examinations such as fasting blood sugar (FBS), total cholesterol, triglycerides, LDL, HDL, VLDL, MDA, Lp (a) level, and antioxidant enzymes (GPx, SOD, and Catalase). The enzymatic method (glucose-oxidase peroxidase) was used to analyze fasting blood glucose concentration, while lipid profiles were determined according to the manufacturer's protocol. Serum total cholesterol and serum triglycerides were estimated by COD-POD and Tinder's GPO-POD method, respectively. Serum HDL-cholesterol was estimated by the phosphotungstate method, and serum VLDL and serum LDL-cholesterol values were determined by calculation through *Friedewald's formula.* Serum Lp(a) levels were estimated by Quantitative Latex-Enhanced immunoturbidimetric test using a human lipoprotein(a) kit (Human Gesellschaft, Weisbaden, Germany). All measurements were performed using a fully automated analyzer XL-1000 Erba Mannheim and ELISA reader Hydro flux (Tecan, Grödig, Austria).

Data collection and Analysis: Data were prospectively collected, such as Age, sex, obesity, hypertension, duration of diabetes, and family history.

Other medical complications in Diabetic patients were excluded from the study. The body mass index (BMI) was calculated through the formula, weight (Kg) divided by height (m) squared.

Healthy reference range of BMI is between 18.4–24.8kg/m^2

Grade I - obesity (overweight) – BMI 25–30 kg/m^2

Grade II - obesity – BMI > 30 kg/m^2

Grade III - morbid obesity – BMI > 40 kg/m^2

Obesity is associated with many health complications e.g. type II diabetes, CHD, hypertension, stroke, arthritis, gall bladder disease.

Results

The current investigation comprised of 100 acute myocardial infarction (AMI) subjects and 100 healthy subjects. The age-wise distribution of the patients was examined. The mean age of the patients was found to be 54.30 ± 10.12 years (ranging from 32 to 72 years).

Among the patient cohort, 6% (6/100) were aged 30-39 years, while 37% (37/100) were aged 40-49 years. The majority of AMI cases were observed in the age group of 50-60 years, accounting for 57% (57/100) of the patients.

Table 1: Distribution of AMI patients according to sex and age wise.

Age group (years)	Male	Female	Total
30-39	04	02	06
40-49	22	15	37
50->60	30	27	57
Total	56	44	100

Table 2: Comparison of laboratory abnormalities between healthy controls and AMI subjects.

Study Variables	Healthy controls n=100	AMI patients n=100
Age	51.62 ± 9.35	54.30 ± 10.12
BMI	22.8 ± 1.88	23.72±7.53
FBS (mg/dl)	90.46 ± 13.66	148.0±38.6*
Total cholesterol (mg/dl)	184.06 ± 48.76	258.3±42.09*
TG (mg/dl)	124.09 ± 19.49	142.78 ± 68.13
HDL (mg/dl)	42.47 ± 8.19	38.31 ± 7.05
LDL (mg/dl)	111.2 ± 28.23	161.8 ± 39.4*
VLDL (mg/dl)	25.61 ± 5.02	52.90 ± 11.5*
Total cholesterol/HDL ratio	4.38 ± 0.52	6.78 ± 0.68*
LDL/HDL cholesterol ratio	2.61 ± 0.24	3.05 ± 0.38*
Lipoprotein(a) (mg/dl)	22.9 ± 3.46	43.66 ± 8.20*
Malondialdehyde (nmol/ml)	2.76 ± 0.16	5.65 ± 0.18*
Glutathione Peroxidase (mg/dl)	68.44 ± 2.26	45.56 ± 1.2*
Superoxide dismutase (U/gmHb)	1128.1 ± 59.16	552.4 ± 44.08*
Catalase(nmol/ml)	35.3 ± 7.7	20.28 ± 10.35*

*Significant

Discussion

In the present study we found that (shown in Table-1) no significant differences in age or sex ratio between CAD cases and controls.

Our study showed FBS levels in AMI subjects' group (148.0±38.6) were slightly higher than healthy subjects (P value <0.0001).

In the present study we calculated in lipid profile- Serum total cholesterol (diabetic= 258.3±42.09 and controls=184.06±48.76), triglyceride (diabetic=142.78±68.13 and control=124.09±19.49), LDL-cholesterol (diabetic 161.7±39.3 and control 111.1±28.20) and HDL-cholesterol (diabetic=38.31±7.05and control= 42.47±8.19) found significant changes in AMI and control group and the results were statistically insignificant. The level of total-cholesterol and LDL- cholesterol were found significantly increased in cases than in controls [8-10].

Lp (a), a circulatory lipoprotein was discovered in 1963 by the Norwegian physician Kaare Berg [11] and the year 2013 marks the 50th years of its journey as a clinically applicable lipoprotein. Lp (a) has developed from an antigenic factor in blood type to the strongest genetically determined risk factor for myocardial infarction over the last 50 years, [12-14]

Lipoprotein(a) has been exposed to be an independent risk factor for atherosclerosis of coronary arteries and cerebral hence leads to AMI. It is known that in some patient's coronary artery spasm is known to play a significant role in the existence of AMI [15,16].

Coronary artery spasm now established that intracoronary blood clot formation is usually an important occasion in the pathogenesis of AMI [17]. The level of the lipoprotein determines by the rate of secretion in the liver. Apo-lipoprotein(a) has a close homology with plasminogen, which makes this molecule important not only in the process of atherosclerosis but also in thrombosis.

The 34 different lipoproteins (a) isoforms are depending on the size the apo-lipoprotein (a). This has resulted in important variability in measured Lp (a) levels if assays used are sensitive to difference in number of repeat domain in Apo-lipoprotein(a) [18,19].

While Lp (a) promotes atherosclerosis by increasing smooth cell proliferation and enhancing LDL-C retention in the subintima, it promotes thrombosis by competitively inhibiting plasminogen and upregulating expression of plasminogen activator inhibitor (PAI).[20]

Lp (a) promotes atherosclerosis by various mechanisms.[21]

The very low-density lipoprotein (VLDL) receptors found on the macrophages present in atherosclerotic lesions can bind to and mediate the catabolism of Lp (a) by endocytosis, leading to its degradation within lysosomes. This would lead to a cellular accumulation of lipids within macrophages. Supporting this hypothesis is the observation that the Lp (a) is universal in human coronary atheroma, co-localizes with plaque macrophages, and is identified in excess amount in tissue from offender injuries in patients with unstable associated to stable CAD.

Binding to endothelium and components of the extra cellular matrix, leading to endothelial dysfunction due to selective impairment of vasodilators capacity of receptor mediated endothelial stimuli.

Enhancement of expression of intracellular adhesion molecule 1, resulting in the enrolment of monocytes to the vessel wall and attached to macrophages. This can

promote the localization of Lp (a) and foam cell formation in atherosclerotic plaque.

Prothrombotic mechanism: Given the extensive sequence homology between plasminogen and Apo (a), it has been recommended that much of the atherogenic-latent of Lp (a) originates from interference in common pathways of breakdown of RBCs (Thrombolysis), to predispose patients to acute thrombotic difficulties.[22]

In this study we found that lipoprotein (a) was suggestively increased in AMI younger in comparison of healthy subjects. These all data show that only Lp (a) is found significantly (99.9%) higher in compare to controls in patients of AMI, along with serum total cholesterol, serum triglyceride, and serum low density lipoprotein-C level were significantly increased. It means lipoprotein (a) has played role as autonomous risk factors for atherosclerosis and MI. Also, we observed that those patients who did not have high levels of serum total cholesterol (<200 mg/dl), the higher levels of serum Lp (a) triggered the CAD. Thus, Lp (a) level is not dependent on serum total cholesterol level. This again means that lipoprotein (a) may causatively risk factor for MI. Similar findings reported by Sandkamp and Funke.[23]

In healthy controls mean MDA level in this research was found 2.757±0.1623 nmol/ml, some studies were agreed with reported by Dey Sarkar and Shinde *et al*. [24-25]

The increased level of MDA in AMI patients was much significant as compared to controls. The present study has a fair correlation with findings of many workers [24,26,27].

Superoxide dismutase in whole blood was found suggestively decreased in cases in comparison of controls. [24,26]. SOD is the major antioxidant enzyme in the cell involved in the primary mechanism for clearance of superoxide anions. It catalyzes dismutation of superoxide anions to hydrogen peroxide and molecular oxygen [28]

Results of the present study show significantly decreased levels of GPx levels in AMI as compared to controls [29,30,31]

GPx is tetrameric enzyme which utilizes reduced form of glutathione as a hydrogen donor for the removal hydrogen peroxides and lipid hydroperoxides. GPx help in the inhibition of oxidative stress encouraged by cardiovascular risk factor which reduced it is an important anti-atherogenic enzyme.[24]

AMI exhibits disturbances in oxidants and antioxidants metabolism irrespective of the gender.

Conclusion

In the present study, it was found that there was a male predominance in young patients with MI. Elevated lipoprotein (a) levels are a compelling and independent analyst for MI and an independent risk factor for CAD. The Lp (a) level in the serum is not dependent on the total cholesterol level in the serum. In addition, our results support previous observations suggesting that the correlation between lipoprotein(a) and cardiovascular effects may be reduced in patients with lower LDL-cholesterol levels.

Limitation: Our study has some limitations. In our study, the diagnosis of AMI was based on ultrasound and exclusion of known causes of cardiac disease. Some clinical trials regarding use of other inflammatory markers also proving valuable.

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