www.jmscr.igmpublication.org
Impact Factor (SJIF): 6.379
Index Copernicus Value: 79.54
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossrefDOI: https://dx.doi.org/10.18535/jmscr/v6i12.14

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Role of lipoprotein (A) as a Nonconventional Risk Factor in Patients of Acute Myocardial Infarction in Tertiary Centre of North India

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Abstract
Objective: *The study the levels of Liporotein (a) as a nonconventional risk factor in patients with acute myocardial infarction.*
Methods: *The present study was conducted in the P.G. Dept. of Medicine in the Cardiology Unit, S.N. Medical College, Agra. Patients of any age group willing to take part in the study. Patients who meets the criteria for diagnosing acute myocardial infarction. Determination of Lp(a) levels was done by Immunoturbidimetric test. This test has measuring range from 3-150 mg/dl.*
Results: *Clinical outcome was judged by mortality at the end of 24 hours, 48 hours and 1 week and a total of 38% of patients succumbed to their illness by the end of the above period. Highest mortality was seen within 24 hours period. Higher LpA values (>20mg/dl)were present in 68.42% of expired patients.63.64% of the patients with mortality within 24 hours had high Lp (a) values while amongst those who died within 48 hours and 1 week, 75% and 75% had high values respectively. There was significant difference in the mean LpA values of patients within 24 hours (T values = 2.183, p value = 0.002) and within 24-48 hours (t values = 1.771, p value = 0.004), 48 hours to 7 days (t value = 1.630, p value = 0.003).*
Conclusion: *In the search of non-conventional risk factor to explain the present CAD epidemic in north Indian population. Lp(a) is important non-conventional risk factor however other non-conventional risk factors like Apo A1, A2, fibrinogen level are also need to be investigated and explain CAD burden in north Indian population.*
Keywords: *Lipoprotein (a), acute MI, nonconventional risk factor.*

Introduction

Lipoprotein-A was first described by Berg in 1963[1]. Lipoprotein-(a) is a cholesterol rich lipoprotein particle composed of an LDL particle and a large glycoprotein, apolipoprotein a. A number of recent studies have shown that increased concentration of Lipoprotein(a) are associated with coronary atherosclerosis and also the evolution of acute myocardial infarction (AMI)[2-5].This Lipoprotein has been shown to be

an independent risk factor for the development of cardiovascular and cerebrovascular disease.

As compared to that of western countries there is an epidemic of CAD (coronary artery disease) in Indian patients and there are some peculiar features of CAD in Indian patients known as Indian Pattern of Coronary Diseases. First of all as noticed by *Enas a Enas* (2004) and subsequently confirmed by various other authors also, that presence of conventional risk factors probably does not explain the present epidemic of CAD in Indian patients. Unfortunately there is a paucity of data regarding non-conventional risk factors in Indian patients with different demographic profile especially north India.

Present study is undertaken to find out significance of a very noble non-conventional risk factor, Lipoprotein a in North Indian CAD patients especially in AMI.

Lipoprotein A has now been reconfirmed as an independent risk factor in CAD in many retrospective case control study and in some prospective studies in western population, few case control studies among Indians have shown significant higher level of lipoprotein a levels patient with CAD. David J. Moliterno et al showed that elevated plasma concentration of Lp a are associated with coronary atherosclerosis in Caucasians. Theyalso showed that although African- Americans have a higher mean plasma Lp(a) concentrations than Caucasians, they do not have a greater incidence of coronary atherosclerosis[6].

Significant relationship of lipoprotein (a) with CAD is noted in South Indian studies. Lp(a) levels correlate with both early and advanced atherosclerosis. Lp(a) excess accelerates the risk of premature CAD. Numerous studies in several continents within the past decade confirm and extend the previous evidence that Lp(a) is one of the top seven major risk factor for cardiovascular diseases[7-17].

Materials & Methods

Present study was conducted in Post Graduation Department of Medicine in Cardiology Unit, wards, OPD and patients admitted in Medicine ward as well as Emergency ward were included in the study. Present study comprises of fifty cases and twenty controls, the cases and controls were matched for age and sex, cases who had shown clinically ischemic symptoms. ECG changes and typical rise and fall of cardiac biomarkers like Troponin-T and CPK-MB were included in the study, while the patients who had taken drugs which can affect the LpA levels like Niacin and Fibrates, estrogen, patients with chronic illness like CKD, CLD and chronic inflammation were excluded from the study.

Determination of Lp a levels was done by Immunoturbidimetric test. This test has measuring range from 3-150 mg/dl. Patients of case and control groups were subjected to routine tests like hemogram, LFT, KFT, ECG and urine culture.

Observation

In present study conventional risk factors observed were Diabetes, Hypertension, smoking, previous history of CAD, obesity, hyperlipidemia. Diabetes was observed in around half of the population in MI. Hypertension was observed in 56% of population, smoking was observed in 64% of population and hyperlipidemia was observed in 42% of population and obesity was observed in 20% of population.

Table-1 Risk factors in study and control populations

Risk factors	No. of patients in control population	No. of patients in study population
Diabetes mellitus	4	26
Hypertension	6	28
Smoking	5	32
Obesity	3	14
Dyslipidemia	4	21

The mean Lpa level in the patients group was 21.6 whereas in control group mean Lp(a) level were 19. There was as such no significant difference in mean Lp(a) level of study and control population.

Table-2 Levels of Lipoprotein-a

	Mean LpA levels(mg/dl)	Standard deviation
Study group	21.60	2.962
Control group	19	3.026

In the study population 76% of the subject had high Lpa values, there is no significant difference in the number of subjects with high Lpa values between the study and control population (t value=1.409), p value=0.165)

Table-3 Lpa levels and clinical complications in study population

	No. of patient	Patients with Lpa>20mg/dl	Patients with Lpa≤20mg/dl
Arrhythmias	15	14	1
Shock	6	5	1
Others viz infection	4	3	1

The most common complication overall was arrhythmias of the study population .Arrhythmias was the most common complication in the group with high Lp(a) values while in the patients with Lp(a) values in the normal range the arrhythmias was zero.

Thus, from above table it is clearly mentioned that high Lpa more than 20mg/dl have also a prognostic value Lpa level also can be correlated high LpA level can also be correlated with clinical outcome in patient of Acute myocardial infarction.

Table-4 Lpa levels in relation to in hospital mortality in study population

	No. of patients	No. of patients with Lpa>30 mg/dl
Mortality within 24 hours	11	7
Mortality 24- 48 hours	4	3
Mortality 48 hrs–7d	4	3

Clinical outcome was judged by mortality at the end of 24 hours, 48 hours and 1 week and a total of 38% of patients succumbed to their illness by the end of the above period. Highest mortality was seen within 24 hours period. Higher Lpa values (>20mg/dl)were present in 68.42% of expired patients.63.64% of the patients with mortality within 24 hours had high Lpa values while amongst those who died within 48 hours and 1 week, 75% and 75% had high values respectively. The mean Lpa levels in the mortality groups were 21.68.

Table-5 Association of In Hospital mortality with Lp(a) values in study population

	No. of patients	Mean LpA	T value	p value
Mortality within 24 hours	11	21.45	2.183	0.002
Mortality within 24-48 hours	4	21.7	1.771	0.004
Mortality in 48 hours – 7 days	4	22.5	1.63	0.003
Total mortality	19	21.68	1.861	0.003

There was significant difference in the mean Lpa values of patients within 24 hours (T values = 2.183, p value = 0.002) and within 24-48 hours (t values = 1.771, p value = 0.004), 48 hours to 7 days (t value = 1.630, p value = 0.003). Overall there was significant difference in the mean Lpa of patients with and those without mortality (t value = 1.861 and p value = 0.003).

Discussions

The mean Lp(a) values seen in the patient group was 21.60±2.962 whereas in the control group mean Lp(a) values were 19.0+- 3.026. On applying these values to statistical analysis we observed the difference between them to be significant (p= 0.001). High Lp(a) values >20mg/dl were seen in 76% of the study population and 45% of the control population. The correlation of number of years with diabetes and Lp(a) was found to be significant (Pearson's R= .463, significance 0.002)

The correlation of number of years with hypertension and Lp(a) was also found to be significant (Pearson's R = .490, significance 0.023). There was no significant difference in the mean Lp(a) between patients of acute myocardial infarction with hypertension and those without hypertension (t value = 1.550, p value = 0.132)

High Lpa values were associated with clinical complications. 50% of both patients with high values and those without the same had complications during the hospital stay. 84% of arrhythmias and 86.67% of cardiogenic shock were seen in the high Lpa group. There was a

significant difference in the mean Lpa of patients who developed complications of arrhythmias and shock and those who did not. There was however no significant difference in means with regard to other complications. Overall, there was a significant difference when the mean Lp(a) of patients who developed some complication and those who did not, were compared. This is in agreement with previous literature on this subject. Kim showed that elevated Lp(a) levels in patients with acute myocardial infarction seems to be a valuable prognostic factor for the development of cardiac complication within 1 month after admission. In their study, peak CRP value was one of the predictive parameter for development of cardiac complications in patients with acute myocardial infarction.

Higher Lp(a) values (>20mg/dl) were present in 80.77% of expired patients. There was a significant difference in the mean Lp(a) values of patients with mortality within 24 hours, within 24-48 hours and mortality within 48 hours to 7 days vs. those without mortality during these periods. Overall, there was a significant difference in the mean Lp(a) of patients with and without mortality. Highest mortality was seen within 24 hour period which is supported by the fact that the early 30 day mortality rate from AMI is 30% with more than half of these deaths occurring before the stricken individual reaches the hospital (Braunwald). These findings are similar to previous studies which have found LpA level to be a reliable marker of mortality marker of mortality in patients of acute coronary syndrome. Benjamin M Morrow their study showed that increased baseline concentrations of Lp(a) are strongly associated with mortality and helpful in identifying patients at high risk for AMI.

Conclusion

In present study it is noted that in the patient of acute MI, Patients who have a higher Lp(a) values develops the complications of arrhythmias and shock there Lp(a) has a good prognostic value. Higher Lp(a) value more than 20 mg/dl were present in most expired patients the mean Lp(a) level in the mortality group was 21.68%higher mortality was seven in within the 24hrs period and younger patients with AMI has a higher Lp(a) values.

In the search of non-conventional risk factor to explain the present CAD epidemic in north Indian population. Lp(a) is important non-conventional risk factor however other non-conventional risk factors like Apo A1, A2, fibrinogen level are also need to be investigated and explain CAD burden in north Indian population.

Limitations of our study is small size probably a multicentre analysis is needed to explain the role of Lp(a) in north Indian population.

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