COMPARISON OF SERUM LIPOPROTEIN (A) LEVEL IN TYPE 2 DM AND NON-DIABETIC PATIENTS WITH ACUTE CORONARY SYNDROME

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ABSTRACT

BACKGROUND

Coronary artery disease has multifactorial origin including hereditary and acquired risk factors. Newer risk factors which are elevated in Indian population include Lp (a), CRP and homocysteine levels. Lipoprotein (a) levels are consistently elevated in Indian population compared to other ethnic groups.

The aim of this study is to estimate lipoprotein (a) level in type 2 diabetic and non-diabetic patients with acute coronary syndrome and to correlate its levels with severity of ACS.

MATERIALS AND METHODS

The present study was a case control study, conducted at MBS Hospital, Kota. The sample size was 50 in each group. 50 patients were type 2 diabetics and 50 patients were non-diabetics. They were categorised as Unstable Angina, NSTEMI and STEMI groups. Lp(a)-C estimation was performed with EDC Helena electrophoretic analyser. Lp(a) was calculated from Lp(a)-C by multiplying with 3.

RESULTS

Lp(a) level was significantly higher in type 2 diabetics compared with non-diabetic group (15.15 ± 5.3 vs 11.93 ± 5.7 , $p < 0.02$). More number of diabetics had Lp(a)-C level > 10 mg/dL than non-diabetic group. This difference was found to be significant (82% vs 38, $p < 0.05$). Lp(a)-C levels in all three subgroups of ACS (NSTEMI; 12.85 ± 4.57 vs 11.05 ± 5.3 , STEMI; 16.61 ± 3.11 vs 11.21 ± 5.8 , UA; 15.76 ± 7.39 vs 13.61 ± 6.2) were significantly more in diabetic group compared to non-diabetic group ($p < 0.05$). Further Lp(a)-C levels were more in STEMI group ($p < 0.001$) compared to NSTEMI ($p < 0.030$) and unstable angina group ($p < 0.002$). The diabetic group had a significantly higher BMI (27.37 ± 3.39 vs 22.90 ± 2.4 , $p < 0.05$) and Waist Circumference (97.14 ± 4.93 vs 92.28 ± 5.90 , $p < 0.04$) as non-diabetic group, in which males had a significantly higher waist circumference compared to females (90.64 ± 5.20 vs 85.54 ± 3.55 , $p < 0.05$). Cardiac biomarkers (CK-MB, 80.32 ± 57.55 vs 62.56 ± 44.81 ; Troponin T, 0.021 ± 0.020 vs 0.014 ± 0.0002 , $p < 0.05$) and random blood sugar (180.04 ± 46.75 vs 119.84 ± 18.99 , $p < 0.05$) were significantly higher in the diabetic as compared to non-diabetic group.

CONCLUSION

Type 2 diabetic patients had 2.15-fold higher chance of having Lp(a)-C > 10 mg/dL than non-diabetic individual. Lp(a) may contribute to the higher risk of having CAD in type 2 diabetics as compared to non-diabetics. Higher level of Lp(a) directly correlates with severity of myocardial injury.

KEY WORDS

Lipoprotein (a), Lipoprotein (a)-C, Acute Coronary Syndrome, Type 2 DM.

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BACKGROUND

Acute myocardial infarction is one of the most common diagnosis in hospitalised patients in industrialised countries.¹ Cardiovascular disease has emerged as major health problem worldwide. Coronary artery disease has multifactorial origin including hereditary and acquired risk factors.²

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The Lp(a) concentration was higher in patients who died from cardiovascular disease in comparison with those who remain alive or those who died from non-cardiovascular disease in a large 9-year prospective study in 1993 by Hernandez et al on 122 consecutive patients with type 2 DM attending diabetic unit in Barcelona.³

Type 2 DM is associated with significant cardiac morbidity and mortality with a more than three-fold increase risk of coronary artery disease. However, this increased cardiovascular risk is only partially explained by conventional risk factors like hypertension, lipid abnormalities, central obesity and glucose intolerance.⁴ Newer risk factors which are elevated in Indian population in a comparative study include Lp(a), CRP and Homocysteine levels.² Lipoprotein (a) levels were consistently elevated in Indian population compared to other ethnic group.⁵

Objective

The aim of this study is to estimate lipoprotein (a) level in type 2 diabetic and non-diabetic patients with acute coronary syndrome and to correlate its levels with severity of ACS.

MATERIALS AND METHODS

Study Design

This study is case control study.

All the subjects under study were recruited from MBS Hospital, Kota, in year 2017 after obtaining informed consent. All the patients in the diabetic group were confirmed diabetics, who were either diagnosed as per ADA criteria or were receiving treatment for diabetes mellitus. A detailed history was taken and examination and relevant investigations done.

Following Investigations were Conducted-

- Routine investigations (done for all cases): ECG in all 12 leads, Blood Sugar (BS) at the time of admission, Serum Lipoprotein (a) and other routine investigations done.
- Special investigations: HbA1c, Microalbuminuria.

The Study Population consisted of 50 Age and Sex Matched Cases and Controls-

- Type 2 Diabetics with acute coronary syndrome.
- Non-diabetic patients with acute coronary syndrome.

Patients with type 2 diabetes mellitus having ACS were taken as cases and non-diabetics with ACS considered as controls.

Selection of case and control was made on "first come and first find" basis. The patients who report first in hospital was included in the study after applying exclusion and inclusion criteria in year 2017 till sample size achieved in both groups.

Inclusion Criteria

Patients with angina of duration more than 30 minutes, but within 24 hours from onset of angina including both Type 2 diabetic and non-diabetic patients.

Exclusion Criteria

- Angina secondary to extracardiac causes, eg. Anaemia, thyrotoxicosis.
- Pre-diabetes (Impaired fasting glucose and impaired glucose tolerance) patients were excluded from both groups.
- Any type of renal failure.
- Nephrotic syndrome.
- Type 1 diabetes mellitus.
- Liver disease.
- Post-myocardial infarction angina.
- Treatment history of drug that alter serum LP(a) level, e.g. Aspirin, Hypolipidemic drugs, Oral contraceptive pill, Oestrogen replacement therapy and Antiepileptic drugs.
- Patients refused to give informed consent for the study.

Sample size was calculated by using online calculator for comparing two means by student's t-test, in which R Salehi et al study mean level for serum Lp(a)-Type 2 Diabetic 16.8 ± 4.4 and for non-diabetic 13.3 ± 5.1 was taken as μ_1 (mean for population 1) and μ_2 (mean for population 2) and 5.1 was taken as common standard deviation. By applying two-sided test using 90 percent power and 5 percent α error, sample

size was calculated as 45 in each group which was rounded off to 50 in each group.

Statistical Analysis

Statistical analysis was done by using percentages, mean values, standard deviation, chi-square test and student t-test. A p-value < 0.05 level was considered statistically significant and a p-value > 0.05 was considered as statistically insignificant. All statistical analysis was done using SPSS 16.0.

RESULTS

In diabetic patients, maximum value of Lp(a)-C was seen in 51 - 60 years age group, while minimum value of Lp(a)-C was seen in 31 - 40 years age group. 82% of diabetics had Lp(a)-C > 10 mg/dL ($p < 0.05$) (Table 1). In non-diabetic patients, minimum value of Lp(a)-C was seen in 61 - 70 years of age group and 38% of non-diabetics had Lp(a)-C > 10 mg/dL (Table 2). The diabetic group had a significantly higher mean BMI and Waist Circumference as compared to non-diabetic group ($p < 0.05$), in which males had a significantly higher Waist Circumference compared to females ($p < 0.05$) (Table 3). Cardiac biomarkers and random blood sugar were significantly higher in the diabetic as compared to the non-diabetic group ($p < 0.05$) (Table 4). Serum Lp(a)-C, Total Cholesterol, Triglyceride and VLDL were significantly higher in type 2 diabetic group when compared to non-diabetic group ($p < 0.05$) except HDL-C, which was significantly lower in type 2 diabetic group than non-diabetic group ($p < 0.05$), while LDL-C was higher in type 2 diabetics but not statistically significant (Table 5). Mean Lp(a)-C in all three subgroups of ACS were significantly more in diabetic group compared to non-diabetic group ($p < 0.05$). Lp(a)-C levels were more in STEMI ($p < 0.001$) group compared to NSTEMI and unstable angina group (Table 6).

LP(a)-C (mg/ dL)	21-30 Yrs.		31-40 Yrs.		41-50 Yrs.		51-60 Yrs.		61-70 Yrs.		> 70 Yrs.	
	N	%	N	%	N	%	N	%	N	%	N	%
0-5	0	0	1	10	0	0	0	0	0	0	0	0
>5-10	0	0	1	10	2	18	4	27	1	14	0	0
>10-15	1	25	3	30	1	9	6	40	4	57	1	33
>15-20	2	50	2	20	7	64	3	20	1	14	0	0
>20-25	1	25	3	30	1	9	0	0	1	14	2	67
>25-30	0	0	0	0	0	0	2	13	0	0	0	0
Total	4		10		11		15		7		3	

Table 1. Distribution of Lp (a)-C Levels in different age group of Diabetic Patients

LP(a)-C (mg/ dL)	21-30 yrs.		31-40 yrs.		41-50 yrs.		51-60 yrs.		61-70 yrs.		> 70 yrs	
	N	%	N	%	N	%	N	%	N	%	N	%
0-5	0	0	0	0	0	0	0	0	1	10	0	0
>5-10	2	67	4	40	7	64	8	61	6	50	3	75
>10-15	0	0	1	10	0	0	1	7.7	1	20	0	0
>15-20	0	0	2	20	2	18	3	23	1	10	0	0
>20-25	1	33	3	30	1	9	1	7.7	1	10	1	25
>25-30	0	0	0	0	0	0	0	0	0	0	0	0
Total	3		10		10		13		10		4	

Table 2. Age distribution of Lp (a)-C levels in Non-Diabetic Group

Parameter	Group I Mean $\pm$ SD	Group II Mean $\pm$ SD	P-Value
Mean BMI (kg/sq.m)	27.37 $\pm$ 3.39	22.90 $\pm$ 2.4	0.02
Mean Waist Circumference Males (cms)	97.14 $\pm$ 4.93	92.28 $\pm$ 5.90	0.04
Mean Waist Circumference Females (cms)	90.64 $\pm$ 5.20	85.54 $\pm$ 3.55	0.03

Table 3. Anthropometric Parameters

Parameters	Group I Mean $\pm$ SD	Group II Mean $\pm$ SD	P-value
Mean CK-MB (mg/dL)	80.32 $\pm$ 57.55	62.56 $\pm$ 44.81	0.04
Mean Troponin T (ng/mL)	0.021 $\pm$ 0.020	0.014 $\pm$ 0.0002	0.03
Random Blood Sugar (mg/dL)	180.04 $\pm$ 46.75	119.84 $\pm$ 18.99	0.02

Table 4. Biochemical Parameters

Parameters	Group I Mean $\pm$ SD (mg/dL)	Group II Mean $\pm$ SD (mg/dL)	P-value
Lp(a)-C	15.15 $\pm$ 5.3	11.93 $\pm$ 5.7	0.02
Total Cholesterol	211.19 $\pm$ 46.08	189.07 $\pm$ 44.43	0.024
LDL Cholesterol	140.84 $\pm$ 45.13	122.89 $\pm$ 45.79	0.22
HDL Cholesterol	31.84 $\pm$ 9.54	36.48 $\pm$ 9.20	0.035
Triglyceride	190.68 $\pm$ 62.70	149.31 $\pm$ 57.91	0.001
VLDL	38.53 $\pm$ 12.52	29.87 $\pm$ 11.12	0.002

Table 5. Lp (a)-C Levels and Lipid Profile in Both Groups

ACS Type	Group I		Group II		Total		P-value
	N	Lp(a)-C Mean $\pm$ SD (mg/dL)	N	Lp(a)-C Mean $\pm$ SD (mg/dL)	N	Lp(a)-C Mean $\pm$ SD (mg/dL)	
NSTEMI	15	12.85 $\pm$ 4.57	17	11.05 $\pm$ 5.3	32	13.5 $\pm$ 4.4	0.030
STEMI	14	16.61 $\pm$ 3.11	17	11.21 $\pm$ 5.8	31	13.1 $\pm$ 4.7	0.001
UA	21	15.76 $\pm$ 7.39	16	13.61 $\pm$ 6.2	37	15.9 $\pm$ 5.1	0.002

Table 6. Lipoprotein (a)-C based on subtype of ACS

DISCUSSION

In the present study considering the optimal cut-off point as 10 mg/dL, 82 % of type 2 diabetic patients had Lp(a)-C > 10 mg/dL compared to 38% of non-diabetic patients. This is almost comparable with values of Salehi et al.⁶ (59% in diabetic group; 42% in non-diabetic group) and Neki et al.⁷ in acute myocardial infarction patients. Type 2 diabetic patients had 2.15-fold risk of having higher serum lipoprotein (a) compared to non-diabetic group during acute coronary syndrome. This phenomenon may be explained by two hypotheses-

- Diabetic group had a pre-existing high baseline serum lipoprotein (a). This might have contributed to the premature acute coronary syndrome.
- Diabetic group underwent an accelerated acute phase reaction to acute coronary syndrome and may be a prognostic marker in such situations.

Both these hypotheses require a long-term prospective study analysing serum lipoprotein (a) serially with other parameters like HbA1c, Plasma Insulin and C-peptide being analysed to find out the correlation between these.

Atherosclerotic risk increases steadily with the increased duration of diabetes. In the present study, mean BMI and waist circumference were significantly higher in type 2 diabetic group compared to the non-diabetic group ($p < 0.05$). This is consistent with findings of Mohan et al.⁸ In the present study, type 2 diabetic patients had a significantly higher peak level of CK-MB and Troponin T as compared to the non-diabetic group ($p < 0.05$). This is comparable to the results of Gusto IIb trial.⁹ The diabetic individuals were not only susceptible for wider area of infarction, but also to micro-infarction from repeated, multiple microemboli from a friable coronary artery thrombus. In this study serum total cholesterol, VLDL-C and triglyceride were significantly higher ($p < 0.05$) in the diabetic group. LDL-C levels were not significantly different in both groups ($p > 0.05$). This agrees with Haffner et al.¹⁰ In the present study all the three subgroups of ACS, there was significant difference between mean value of Lp(a)-C in the diabetic and non-diabetic groups ($p < 0.05$). Neki et al.,⁷ Salehi et al.⁶ and Tseng et al.¹¹ studies show no statistically significant difference between the means of the Lp(a)-C in UA, NSTEMI or STEMI group. Enas et al.¹² and several other studies have also documented this elevation in Lp(a) levels in people of Indian origin when compared to other ethnic groups. Similar to the present study, higher levels of Lp(a) have been associated with CAD, especially if there is concomitant elevation of LDL levels. Levels of Lp(a) are largely genetically determined and genetic factors account for over 70% of the variation in the Lp(a) levels in the population.

In the present study, mean Lp(a)-C was 13.54 $\pm$ 5.5 mg/dL. The range of values varied from 4.0 to 26.7 mg/dL. Type 2 diabetic patients had higher Lp(a)-C levels (Mean 15.15 $\pm$ 5.3 mg/dL) compared to non-diabetic patients (Mean 11.93 $\pm$ 5.7 mg/dL). The difference of means was statistically significant ($p < 0.05$). This was comparable with Mohan et al.⁸ Neki et al.⁷ and Salehi et al.⁶ This was because of similar patient sample and method used to measure serum Lp(a)-C.

CONCLUSION

Type 2 diabetic patients have 2.15-fold higher chance of having Lp(a)-C >10 mg/dL than non-diabetic individuals. Higher levels of Lp(a) directly correlate with severity of myocardial injury. Elevated serum lipoprotein (a) in type 2 diabetic patients may contribute to the accelerated atherogenic/ prothrombotic state causing major adverse cardiac events. Lp(a) may contribute to the higher risk of having CAD in type 2 diabetics as compared to non-diabetics. This requires a long-term prospective study to find out the magnitude of this contribution from lipoprotein (a).

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