**ORIGINAL ARTICLE**

# Serum Lipoprotein (A) and Symptomatic Peripheral Arterial Disease in Diabetic Patients

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## ABSTRACT

**Aim**: To determine the association between levels of lipoprotein (a) concentration and peripheral arterial disease in diabetic patients.

**Methods**: In this case control study, 159 diabetic patients were included. 53 subjects with peripheral arterial disease (PAD) selected as cases and 106 subjects without PAD selected randomly as control. Among them, 72 were males and 87 were females. Inclusion criteria was age forty years and above and confirmed diabetics with minimum duration of 5 years and exclusion criteria was coronary artery disease (CAD), Raynaud's disease, patient with acute illness, patients taking niacin and estrogen replacement therapy. Blood samples were taken after the written consent of participants. History was taken on prescribed Performa. Serum was separated and estimation of Lp(a) and serum glucose were determined immediately. Turbidometery immunoassay method was used for the detection of LP (a).

**Results**: There is decreased ABI in group A when comparing with Group B controls with significant difference. Lp(a) in Group A is increased as compared to Group B. There is week negative correlation between Lp(a) and ABI. There is negative correlation between ABI and Age.

**Conclusion:** It is concluded that lipoprotein (a) has association with peripheral arterial disease but statistically non significant (p>0.05).

**Keywords**: lipoprotein (a), peripheral arterial disease, Diabetes mellitus

## INTRODUCTION

Peripheral arterial disease (PAD) means poor blood circulation in the arteries, the arteries of lower limb in this study. PAD appears if there is considerable thickening of arteries distal to the arch of the aorta. Thickening of arteries is caused by atheroma formation within the walls of medium and large arteries[1]. The peripheral arterial disease may be symptomatic or asymptomatic. The symptoms of PAD include rest pain, pain on exertion (intermittent claudication), skin ulceration and ischemic necrosis (gangrene). A symptomatic PAD is diagnosed by reduced circulation in limbs measuring ankle brachial index[2]. PAD can be an expression of systemic atherosclerosis in addition to the limbs involving other major circulations like cerebral and coronary circulations[3]. True incidence in Pakistan is unknown however local observations show that incidence of disease is increasing each year. The incidence of disease increases with age, 5% of men and 2.5% women up to the age of sixty have symptoms of PAD. Prevalence of PAD in south Asian (people originating from India, Pakistan, Bangladesh) population in United Kingdom goes on increasing and is about 53% in minorities of UK[4,5] .

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Ankle-brachial index (ABI) is considered as a simple method used for screening PAD that involves more than five million adult Americans and results in significant morbidity and mortality[6]. ABI is calculated as, take systolic blood pressure of one side of leg and divide it by brachial systolic blood pressure of the same side. ABI <0.9 is considered as PAD[7]. Lp(a) is thought to be contributed in LDL- like Particle that induce atherogenesis. It is now established that increased plasma concentration of Lp (a) is an independent cause for coronary artery disease[8]. Elevated concentration of Lp(a) has also reported in association with intermittent claudication. PAD is a sign of systemic atherosclerosis. In a study conducted in Taiwan, Lp(a) was established as a strong risk factor (OR=3.0) for the development of PAD in type 2 diabetic patients[9].

## METHODOLOGY

All the confirmed cases of diabetes mellitus with PAD diagnosed by ABI during the study period were included. The controls were randomly selected from diabetic patients not having PAD at the same hospital as of cases. Inclusion criteria for Group A was age forty years and above, confirmed diabetics with minimum duration of 5 years and Patients having ABI <0.9. Inclusion criteria for Group B was age forty years and above, confirmed diabetics with minimum duration of 5 years and patients having ABI >0.9.

Exclusion Criteria for groups A and B was coronary artery disease (CAD), Raynaud's disease, patient with acute illness, patients taking niacin and estrogen replacement therapy. Data was collected by interviewing the patient using structured Performa. Information was sought on demographic characteristics and potential confounders. The diagnosis was made on the basis of ABI determined by palpatory method, and serum Lp(a) was determined by turbidometry method in both the cases and controls. The participation in the study was voluntary, and informed consent was obtained from all the subjects (Appendix I); only those who consent to participate were included in the study.

## RESULTS

In experimental group (A), out of 53 patients 24 (45.3%) are in age ranges of 51–60 years & 12 (22.6%) are in ranges >60 years. This shows that PAD is mostly in age limits of >51 years. In control group (B), out of 106 patients, 68 (64.2%) are in age ranges of 40– 50 years & 28 (26.3%) are in ranges of 51–60 years. In experimental group (A), 24 (45.3%) are males and 29(54.7%) are females while in control group (B), 48(45.3%) are males and 58(54.7% are females. In both groups, females are more involved than males. Mean±SD values of ABI in experimental group (A) & Control group (B) are 0.76±0.21 & 0.95±0.41 with ranges of 0.45–0.88 & 0.90–1.04 respectively. Comparison between group (A) with PAD and Group (B) without PAD showed that there is decreased ABI in group (A) and difference was significant statistically ($p<0.05$). Mean±SD values of LPa in experimental group (A) & Control group (B) are 36.02±4.19 & 34.3±3.27 mg/dl with ranges of 2 – 143 & 2–260mg/ml respectively. Comparison between group (A) with PAD and Group (B) without PAD showed that there is increased LPa in group (A) and difference was significant statistically ($p<0.05$).

Table 1: Ages of experimental group A and control group B

| Age (Yrs) | Experimental group(A) (n=53) | Control group(B) (n=106) |
|---|---|---|
| 40-50 | 17 (32.1%) | 68(64.2%) |
| 51-60 | 24(45.3%) | 28(26.3%) |
| >60 | 12(22.6%) | 10(9.4%) |
| Total | 53(100%) | 106(100%) |

Table 2: Gender of Experimental Group (A) & Control Group (B)

| Gender | Experimental group(A) (n=53) | Control group(B) (n=106) |
|---|---|---|
| Males | 24 (45.3%) | 48(45.3%) |
| Females | 29(54.7%) | 58(54.7%) |
| Total subjects | 53(100%) | 106(100%) |

Table 3: ABI in experimental group A and control group B

| ABI | Experimental group(A) (n=53) | Control group(B) (n=106) |
|---|---|---|
| Mean ±SD | 0.76± 0.21 | 0.95±0.42 |
| Ranges | 0.45---0.88 | 0.90---1.04 |
| Total | 53 | 106 |

Table 4: Lipoprotein(a) In Experimental Group (A) And Control Group (B)

| Lipoprotein(a) (mg/dl) | Experimental group(A) (n=53) | Control group(B) (n=106) |
|---|---|---|
| Mean ±SD | *36.02±4.19 | 34.3±3.27 |
| Ranges | 2---143 | 2---260 |
| Total subjects | 53 | 106 |

Table 5: LPa in relation to ABI in experimental group A

| LPa(mg/dl) | n | LPa (Mean± SD) | ABI(Mean± SD) |
|---|---|---|---|
| <30 | 29 | 11.2±0.32 | 0.77±0.28 |
| 31-100 | 18 | 49.8±2.41 | 0.72±0.25 |
| >100 | 6 | 112.8±3.84 | 0.70±0.25 |
| Total | 53 | 57.9±2.61 | 0.72±0.26 |

## DISCUSSION

This study was done on diabetic patient keeping in view that lipoprotein (a) has association with PAD. Different results were described by researchers. This may be due to study design, collection and storage method, assays used, statistical analysis. A study was conducted in Turkish population to see the variation in Lp(a) levels. There is a significant difference in the concentrations of Lp (a) among individuals. Plasma lipoprotein (a) levels in type 2 DM with and without vascular diabetic complications were found to be higher in the type 2 DM as compared to healthy subjects .Lp (a) levels in type 2 DM with vascular complications were significantly higher than those of the type 2 DM without vascular complications[10].

A study conducted in Chinese population living in Taiwan confirmed the association between Lp(a) and PAD. Conventional cutoff of 30.0 mg/dl was used which corresponded to 80th percentile of their sample. Though, the optimal cutoff in Chinese type 2 diabetic patients in Taiwan seemed to be at a lower level (13.3 mg/dl), which gave the greatest correct predictions (60%) for patients with and without PAD and significantly increased the risk of PAD by 2.7-folds, signifying that some other risk factors were involved in the development of PAD in type 2 diabetic patients[9]. Age is a major determinant of Lp(a) in both sexes in general population of Taiwan and women tend to have slightly higher Lp(a) level than men. The proportion of people with Lp(a) $\geq$30.0 mg/dl is also higher in females (men versus women, 11.6 vs. 14.3%, $P< 0.05$). The correlation between Lp(a) and

age was only observed in the experimental group A in this study.. The diabetic men and women have similar levels of Lp(a), and similar proportions of Lp(a) ≥30.0mg/dl. This study suggests that a higher proportion of diabetic patients with PAD would have Lp(a) ≥30.0mg/dl than the general population without much influence by age or sex.

In our present study, Lp (a) levels are higher with PAD as compare to controls and the difference is non significant statistically. This may be due to ethnic variation or cut off values for Pakistani population may be lower than 30mg/dl as considered in this study. On the whole, these results are conclusive and suggest that the relationship between Lp(a) levels and incident of PAD should be further investigated in more detail.

In this study, palpatory method was used for ABI determination. Dorsalis Pedis artery was palpated for ankle systolic blood pressure determination. This method may not be as effective as Doppler ultrasound in determination of atherosclerosis by ABI method. In most of the studies, Doppler ultrasound probe is used for the determination of ankle systolic blood pressure. In a study done in Pakistan, palpatory method is equally effective[11]. Our study indicated a weak negative association between the Lp(a) levels and the ABI, because the levels of Lp(a) were found to be significantly higher in the study group as compared to the control group where levels of ABI are lower, but this correlation is statistically non significant ($p>0.05$). However, as the present study was performed on a population confined to a particular area these results do not necessarily applicable to the other racial groups. The small sample size and storage methods are also another restriction of our study. Lp(a) shows negative correlation with duration of DM in experimental group A and this correlation is statistically significant ($p< 0.05$). ABI in relation to duration of DM in group A also shows negative correlation. As duration of DM increases, ABI decreases significantly

## CONCLUSIONS

Lp(a) has association with diabetic macrovascular complications and it appears to be an independent risk factor for PAD. The other risk factors for PAD seen in the present study included age >51 years, longer duration of diabetes, smoking, and higher systolic and diastolic blood pressure. No gender difference regarding appearance of PAD.

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