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SERUM LIPOPROTEIN (A) CONCENTRATION IS A BETTER PREDICTOR OF MYOCARDIAL INFARCTION THAN TRADITIONAL LIPID PROFILE AND LIPID RATIOS

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Abstract

Background- Lipoprotein (a) is a variant form of Low Density Lipoprotein (LDL) which comprises of an LDL like particle in which apo B-100 is firmly linked to apo-a glycoprotein. A large number of genetic and epidemiologic studies have identified Lipoprotein(a) as a risk factor for atherosclerotic diseases such as coronary heart disease and stroke. Based on our knowledge, this is the first study comparing Lipoprotein(a) with lipid profile and lipid ratios in Nepal. **Aim & Objective-** To compare the serum Lipoprotein(a) and Lipid panel concentrations in myocardial infarction patients and normal healthy control subjects. **Materials & Methods-** Study was carried out in 45 myocardial infarction patients as cases and 45 healthy subjects as controls. Lipoprotein(a) and Lipid profile tests were measured in serum using HumaStar 600 fully automated analyzer, Human, Germany. **Results-** Mean serum Lipoprotein(a) concentration in myocardial infarction group was significantly higher as compared to healthy controls. Lipid panel assays were not statistically significant among the groups. **Conclusion-** Our study revealed that myocardial infarction patients have elevated levels of serum Lipoprotein(a) as compared to healthy subjects. High concentration of serum Lipoprotein(a) is strongly associated with the risk of coronary heart disease.

Keywords: - Lipoprotein(a), low density lipoprotein, myocardial infarction, lipid panel

Introduction

Lipoprotein(a) [Lp(a)], a genetically determined lipoprotein is composed of Low Density Lipoprotein (LDL) particle whose apolipoprotein B is bound to a plasminogen-like glycoprotein named apolipoprotein(a) (Utermann et al., 2001). Apolipoprotein(a), a member of plasminogen-prothrombin family is found to interfere with the action of plasminogen and promotes thrombosis (Cobbaert et al., 1997). The prothrombotic nature of Lp(a) is supported by the studies that have shown the significant association of hyper-Lp(a) and venous thrombosis (Sofi et al., 2007) and atherogenesis (Scanu et al., 1991). Coronary thrombosis formation is nowadays regarded as the most important cause of Acute Myocardial Infarction (AMI) (DeWood et al., 1980). Different studies have established Lp(a) as the independent risk factor for the development of atherosclerosis, genesis of AMI (Nguyen et al., 1997) and cerebrovascular diseases (Schwartzman et al., 1998).

Serum Lp(a) is found to be higher in south Asians compared with Caucasians (Reddy et al., 1992) which is again confirmed by the finding that south Indian living in Britain had higher Lp(a) value than that of the white Europeans (Bhatnagar et al., 1995). These findings parallel with the increasing risk for myocardial infarction and cardiovascular death in migrants of south Asians than in other ethnic groups (Tuomilehto et al., 1984).

Considering the role of Lp(a) in evolution of Acute Myocardial Infarction (AMI) and increasing burden of Cardiovascular Disease in south Asians we in our present study tried to investigate the predictive value of Lp(a) for AMI compared with traditional Lipid panel and ratios.

Materials and Methods

Study population-

In this study a total number of 90 participants were included. 45 myocardial infarction (MI) positive participants (cases) admitted at Sahid Gangalal National Heart Center, Bansbari, Kathmandu, Nepal

and equal number of healthy participants (controls) aged above 30 years from Imadole and Gwarko communities of Lalitpur, Nepal were recruited. Patients with myocardial infarction were considered for our study after the confirmative diagnosis done by the cardiologist based on the findings of Electrocardiogram (ECG) and raised cardiac enzymes (Creatine Kinase – MB, Lactate Dehydrogenase (LDH), Serum Glutarate Pyruvate Transminase(SGPT), Serum Glutarate Oxaloacetate Transaminase (SGOT) and Troponin I). All the participants except cases were asked for the history of diabetes, hormonal disorders, liver diseases, renal diseases and other chronic diseases. Those suspected of any disorders as indicated above were excluded.

Sample Collection-

After an overnight fast of at least 12 hours, blood samples were collected from the ante-cubital vein of each participant. Samples were collected in plain vials, allowed to clot, centrifuged at 3000rpm for 10 minutes and serum separated. Separated serum samples were preserved at -20^{o} C until assays were run.

Biochemical Analysis-

The lipid profile was done using CHOD-PAP method (Systemic Reagent for Humastar 600, Human, Germany). The Low Density Lipoprotein (LDL) was calculated using the Friedewald Formula (Friedewald et al., 1972). All the biochemical tests were run in the fully autoanalyzer (Humastar 600, Human, Germany). The serodos and serodos plus were used as the quality control samples and autocal as the standard to calibrate the tests. Both internal and external quality assurance tools were employed routinely to ensure the quality of test results.

The Lp(a) concentration was measured using DRG ELISA Total Human Lipoprotein (a) (EIA- 4406), DRG International Inc., USA. The dynamic range of the Lp(a) ELISA assay kit was 3 µg/dL-405µg/dL.

Ethical Clearance-

Ethical clearance for the study was taken from Nepal Health Research Council, Nepal as per the Helsinki declaration of 1975.

Statistical Analysis-

All the statistical analysis were done using IBM SPSS Statistics (version 19) software. All tests of statistical significance were two sided with 95% confidence intervals (CI).

Results

A total of 90 subjects including equal numbers of MI cases and healthy normal controls were recruited in the study. The demographics of the study population are presented in Table-1.

Plasma lipid profiles and Lipoprotein(a) of the groups are shown in Table-2. Lipid profile parameters were similar among the groups except for serum HDL Cholesterol which was significantly higher in normal controls (p= 0.026). Serum lipoprotein(a) value was significantly higher in MI cases (Figure-1) in comparison to the controls (p=0.004).

Table 1- Demographics of study population

	MI Cases (n=45)		Normal Controls (n=45)	
Sex	N	%	N	%
Male	28	62.23	20	37.77
Female	17	37.77	25	55.55
Age (inYears)	54.51±10.31		46.11±10.81	

N= number of subjects, n= population size

Table 2- Lipid panel parameters and Lp(a) levels of study population

Analyte	MI Cases	Normal Controls	T Test "P value"
Total Cholesterol (TC) (mmole/L)	4.314±1.155	4.267±0.658	0.827
Triglyceride (TG) (mmole/L)	1.793±0.948	1.708±0.920	0.683
HDL Cholesterol (mmole/L)	1.008±0.122	1.035±0.135	0.026*
LDL Cholesterol (mmole/L)	2.452±1.131	2.418±0.407	0.864
TC /HDL Ratio	4.288±1.162	4.184±0.518	0.626
LDL/ HDL Ratio	2.485±1.002	2.459±0.451	0.891
Non HDL Cholesterol (mmole/L)	3.288±1.162	3.187±0.523	0.636
Lp(a) (µg/dl)	38.450±19.132	28.056±14.048	0.004**

*Statistically significant **Statistically highly significant

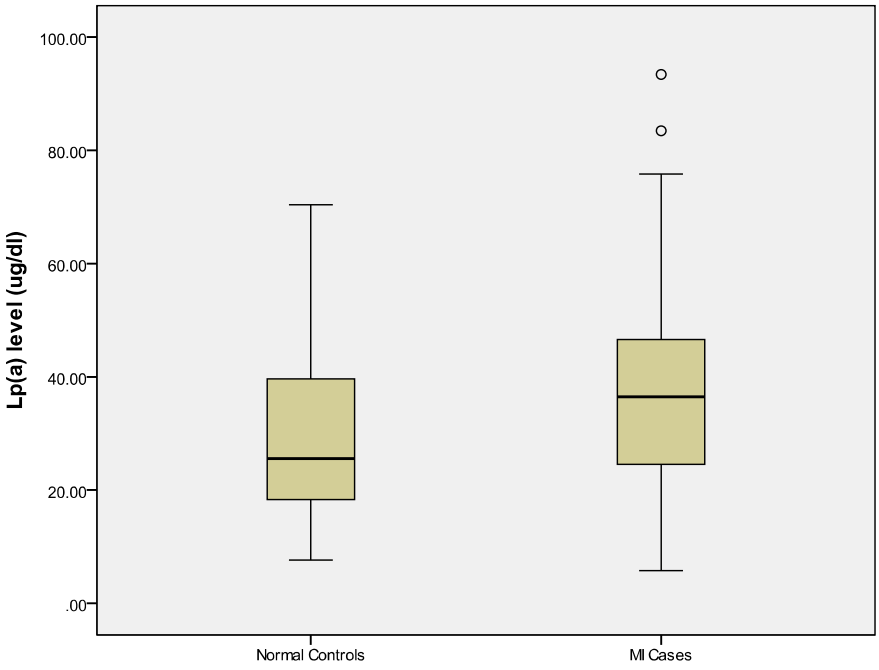

Fig. 1- Distribution of serum Lp(a) levels among the study groups

Discussion

Findings of this study showed no significant differences in Total Cholesterol (TC), Triglycerides (TG), LDL Cholesterol (LDL-C), TC/HDL ratio, LDL/HDL ratio and Non HDL-Cholesterol among the groups. Rather it showed the significant differences in Lp(a) level and HDL-C level among the group. Woo et al., (1993) observed higher mean TC, LDL-C and TG as well as lower mean HDL-C in AMI patients; high HDL-C was among the protective factors. Similarly Kumar et al., 2009 observed significantly higher TC and TG levels and lower HDL-C levels in AMI patients. Though in our study, the mean TC, TG, LDL-C, TC/HDL, LDL/HDL and non HDL-C were higher in AMI patients than that found in healthy participant, they were statistically not significant. In line with our findings, Lehto et al., 1993 did not find any difference in mean serum TC levels between the AMI patients and controls. The risk of AMI was associated with an increase in LDL-C and a decrease in HDL-C in both Asians and non-Asians (Karthikeyan et al., 2009). Lower concentrations of serum HDL-C and higher

serum TG were found to be independent risk factors while serum LDL-C was not associated with AMI (Tokuda, 2005).

Though different studies have shown lipid profile and lipid ratio to be promising in assessing the cardiovascular risk, there are some contradictory findings as mentioned above. Significantly higher value of Lp(a) and significantly lower value of HDL-C in AMI patients than in healthy participants indicate that Lp(a) is much better predictor of AMI than traditional lipid profile and lipid ratios.

Conclusion

Nowadays homocystein, hs-CRP, Apo B/Apo A1 ratio, Lp(a) and other emerging risk factors are considered to be superior cardiovascular risk assessment tools. Our study also indicated that Lp(a) can be the better predictor of AMI. Moreover, for lipid profile patient preparation is required (Patients are required to be on at least 12 hours fast). In addition, Friedwald formula for calculating LDL-C is not valid if TG level is more than 4.2 mmol/L (450 mg/dL). Lp(a) on other hand is genetically determined and it doesn't fluctuate with diet. Taking all these in consideration we from the current study would like to project Lp(a) as the better predictor of AMI though there still remain some questions that limit its dissemination in clinical practice as mentioned by Pischon et al., 2005. The central question focuses on the cost-benefit relation associated with a change in the traditional clinical approach.

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