ASSOCIATION OF SERUM LIPOPROTEIN(A) WITH LEFT VENTRICULAR HYPERTROPHY AND EJECTION FRACTION IN MAINTENANCE HEMODIALYSIS PATIENTS

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ABSTRACT

Objective: To investigate the association of serum lipoproein(a) elevation with left ventricular hypertrophy(LVH) and hypertention(HTN) in patients with end-stage renal failure under regular hemodialysis .

Material and Methods: Sixty-one patients with end-stage renal disease (ESRD), undergoing maintenance hemodialysis treatment were studied. Serum lipoprotein (a) measured by enzyme immuno assay (ELISA) test. For all patients echocardiography for left ventricular hypertrophy and LV ejection fraction were performed. Hypertensive patients stratified into no hypertention, stage one to three HTN and LVH categorized to normal, mild, moderate and severe hypertrophy.

Results: Total patients were 61(F=23 M=38), consisting of 50 non diabetic hemodialysis patients (F=20 M=30) and 11 diabetic hemodialysis patients (F=3 M=8). Mean±SD of LP(a) of total patients were 58.5±19mg/dl.Mean±SD of LP(a) of diabetic group and nondiabetic group were 62±12.3 mg/dl and 57.7±20 mg/dl respectively.Significant positive correlation between presence of chest pain and diabetes mellitus was seen .There was a positive relation between stages of LVH and stages of HTN. A significant positive correlation between presence of chest pain and stages of LVH was demostrated. Also significant linear inverse correlation of serum Lp(a) with the percent of LV ejection fraction and positive correlation of serum LP(a) with stages of HTN were found . Significant correlation between stages of LVH with serum LP(a) was found too.

Conclusion: In hemodialysis patients the relationship of serum lipoprotein(a) with left ventricular hyperthrophy and ejection fraction and also with hypertention accelerate the cardiovascular disease in there patients , needs more attention.

Keywords: Lipoprotein(a), Left Ventricular Hypertrophy, Hemodialysis, Atherosclerosis.

INTRODUCTION

The contribution of cardiovascular events to the extraordinary high mortality in end-stage-renal disease (ESRD) has generated some interest in non traditional atherosclerotic cardiovascular disease (ASCVD) risk factors that are prevalent in ESRD, such as Lipoprotein(a) [Lp(a)][1]. Lp(a) which is the most complex and polymorphic of the Lipoprotein particles is formed by an LDL moiety and a unique protein, apo (a) linked to apolipoprotein (apo) B-100 of LDL[2] Lp(a) is an independent risk factor for coronary heart disease(CAD) by inducing premature atherosclerosis but the exact mechanism by which Lp(a) confers cardiovasular risk is un known. Both proatherogenic and prothrombogenic effects have been hypothesized[3]. Elevated plasma Lp(a) levels in chronic renal failure patients have been associated with a frequency distribution of apolipoprotein(a) [apo(a)] isoforms, similar to those found in general population. This indicates that elevated Lp(a) levels in these patients are not due to genetic origin[4,5]. Therefore, it has been suggested that kidneys have an important role in Lp(a) metabolism, decrease Lp(a) catabolism or increase of liver production[4-8]. Cardiovascular disease is the principal cause of morbidly and mortality in dialysis patients[9]. Principle findings of cardiovascular disease is left ventricular hypertrophy(LVH) as determined by

echocardiography[9]. Left ventricular hypertrophy(LVH) is common and as LVH by itself is indepenclent risk factor for cardiovascular disease[10] in hemodialysis (HD) patients and HD patients have been associated with elevation of serum Lp(a) levels[7,11].But relatively little has been published on the link between Lp(a) and cardiovascular disease respectively HD patients. This study was conducted to evaluate the association of serum level of Lp(a) with left ventricular hypertrophy and ejection fraction in a group of HD patients consisting of diabetics and nondiabetics.

MATERIAL AND METHODS

This cross-sectional study was carried-out on 61 patients with end-stage renal disease (ESRD), undergoing maintenance hemodialysis treatment between September 2002 and december 2003. Factors serve as exclusion criteria were cigarette smoking, body mass index (BMI) more than 25, anti lipid drugs taking, recent MI and vascular diseases as well as active or chronic infection and pericarditis or pericardial effusion in echocardiography. For all subjects lipoprotein (a) measured by enzyme immuno assay (ELISA) by Immuno-Biological laboratories (IBL) kit of Germany. For stratification of hypertensive patients, according to the sixth and seventh report of the Joint national committee on prevention, detection, evaluation and treatment of high blood pressure we categorized hypertensive patients from stage one to three,[12,13] (stage of zero means no HTN). For heart echocardiography one single cardiologist who was unaware of the patients data, performed all echocardiographies for left ventricular hypertrophy and LV ejection fraction. On the base of sepal thickness, we stratified the patients into no LVH (septal thickness between 6-11 mm), mild(septal thickness between 11-15 mm), moderate (septal thickness between 15-18 mm) and severe LVH(septal thickness >18 mm). LV measured at the end diastolic phase and LV ejection fraction between 55to 75% was considered normal. For statistical analysis descriptive data are expressed as Mean± SD. Comparison between groups were performed by using chi-square (x^2 test), Mann Whitney as well as Kruskal & Wallis and also Fisher ó s exact test. For correlations we used Spearman Rho test. Partial correlation with adjustment for age, Phi & Crameró s V test and Eta test were used too. All statistical analysis were performed by using the SPSS software (version 11.00). Statistical significance was inferred at a p value < 0.05.

RESULTS

Total patients were 61(F=23 M=38), consisting of 50 non diabetic hemodialysis patients (F=20 M=30), and 11 diabetic hemodialysis patients (F=3 M=8). Table 1 show the mean± SD of patients data. Table2 and 3 and 4 show the frequency distributionsof chest pain, stages of HTN and stages of LVH of patients. Mean±SD of ages of subjects were 46.5±16 years. Mean±SD of length of the time patients had been on hemodialysis were 32 ± 31 months. Mean±SD of cardiac ejection fraction(EF) were 51±8.9 percent and 39.3% of patients had chest pain. Mean±SD of serum LP(a) of total patients were 58.5±19mg/dl.Mean±SD of LP(a) of diabetic group and nondiabetic group were

Mean ± SD , Minimum and Maximum of data.

		AgeYears	D.H.T* months	EF** percent	LP(a) mg/dl
Total Patients n = 61	Mean±SD	46.5±16	32±31	51±8.9	58.5±19
	Min	15	2	25	25
	Max	78	108	70	154
Diabetic Group n = 11	Mean±SD	57±16	22.6±22.4	47.7±7	62±12.3
	Min	27	3	30	40
	Max	78	60	55	85
Non-diabetic Group n = 50	Mean±SD	47.8±16	34±33	51±9	57.7±20
	Min	15	2	25	25
	Max	78	108	70	154

Table 1

*duration of hemodialysis treatment
** LV ejection fraction

Frequency distribution of stages of hypertension (HTN).

Stages of HTN	Total patients		DM group*		Non-DM group	
	Number n=61	%	Number n=11	%	Number n=50	%
0	4	6.6	0	0	4	8
1	5	8.2	0	0	5	10
2	33	54.1	8	72.7	25	50
3	19	31.1	3	27.3	16	32

Table 2

*DM=Diabetes Mellitus.

62±12.3 mg/dl and 57.7±20 mg/dl respectively. No significant difference of duration of hemodialysis treatment as well as serum lipoprorein(a) , ages of patients and percent of heart ejection fraction between diabetic and non diabetic group(P> 0.05)(Mann-Whitney test) were existed.In this study there were no significant difference of age , percent of LV ejection fraction and duration of hemodialysis treatment between males and females (P>0.05) (Mann-Whitney U test).There was no significant difference of LVH between two sexes (x2 test) (P>0.05). There was not significant difference in the presence of chest pain and DM between two sexes (Fisher ó s exact test)(p>0.05). No significant association between sex of the subjects and stages of Hypertension (P>0.05) (x^2 test) was found. In this study, there was a positive association between stages of LVH and duration of hemodialysis treatment (p<0.01) .No significant correlation between stages of LVH and ages of the patients(p>0.05) (kruskal-wallis statistical analytic test) was existed. There was a positive relationship between stages of LVH and stages of HTN(r= 0.580 p<0.001). No significant correlation between presence of DM and LVH (P>0.05) (Phi & Crameró s V test) was seen. There was a significant positive correlation between presence of chest pain and presence of the DM (P<0.001). No significant association between the presence of DM and HTN was seen. Also association of sex and DM were negative(p>0.05)(Phi & Crameró s V test). No significant correlation between presence of DM and LV ejection fraction was found (P>0.05)(Eta test). No significant correlation of percent of LV ejection fraction with duration of hemodialysis treatment (P>0.05) (Spearman test) was found. In patients a significant positive correlation between presence of chest pain and stages of LVH (P<0.001) (Phi & Crameró s V test) was observed. About HTN there was not any association between stages of HTN with the presence of chest pain (P> 0.05) (x^2 test). Partial correlation test with adjustment for age showed a significant linear ineverse correlation of serum Lp(a) with percent of LV ejection fraction (r = -0.24 p=0.032)(figure 1). A positive correlation of serum LP(a) with stages of HTN(r = 0.245 p=0.029) was found too (Partial correlation test with adjustment for age). No positive correlation between serum Lp(a) and duration of hemodialysis treatment (P>0.05) (spearmant test) was demonstrated. Significant association between stages of LVH with serum LP(a)(p<0.05) was found (kruskal-wallis test).

DISCUSSION

In the present study there was positive correlation between stages of LVH with duration of hemodialysis treatment and positive correlation between stages of LVH with stages of hypertension was observed. Also positive correlation between stages of LVH with presence of chest pain was seen. Positive association of diabetes mellitus with the presence of chest pain and also positive correlation of serum LP(a) with stages of HTN

Frequency distribution of chest pain in hemodialysis patients.

Chest pain	Total patients		Diabetic patients		Non diabetic patients	
	Number	% age	Number	% age	Number	% age
Presence	24	39.3	9	81.8	15	30
Abscence	34	60.7	2	18.2	35	70

Table 3

*DM=Diabetes Mellitus.

Frequency distribution of Left ventricular hypertrophy(LVH) in hemodialysis patients.

	Total patients		Diabetic patients		Non diabetic patients	
	Number	% age	Number	% age	Number	% age
No LVH	9	14.8	1	9	8	16
Mild LVH	25	41	4	36.4	21	42
Modrate LVH	20	32.8	4	36.4	16	32
Severe LVH	7	11.5	2	18.2	5	10

Table 4

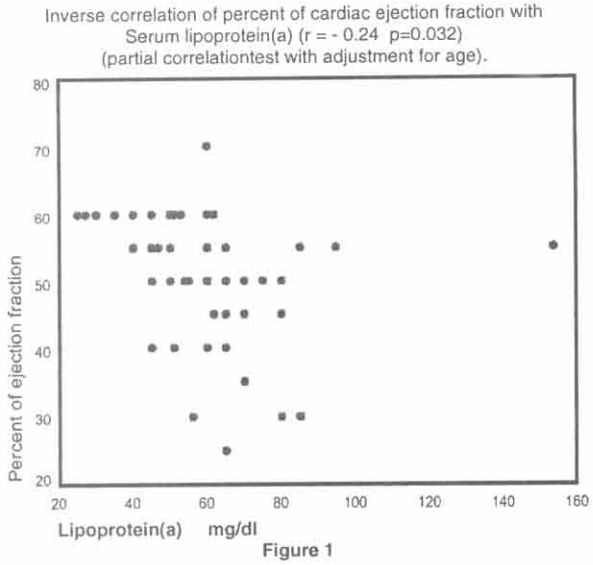

Figure 1

were demonstrated. Significant association between stages of LVH with serum LP were observed too. Strauman et al in a study on 62 patients on maintenance hemodialysis observed 65% prevalence of LV hypertrophy. He showed age, body mass index, and duration of HTN was associated with LV hypertrophy and asymmetric septal hypertrophy[13].Greaves et al in the evaluation of 30 HD patients and 54 patients under peritoneal dialysis compared with 38 ESRD patients not yet on dialysis demonstrated that left ventricular wall thickness was greater in dialysis group[14]. De Lima et al in the study of 103 HD patients showed that systoloc blood pressure was significantly associated with LV mass and was significantly and independently correlated with LVH and posterior wall hypertrophy[15]. Koda in a study on 390 HD Patients showed serum Lp(a) , age , diabetic state were the only independent contributors of atherosclerotic cardiovascular death[7] Ohashi et al in evaluation 268 HD Patients observed that, those who died of cardiovascular events has significantly higher serum Lp(a) levels than those died of non cardiovascular events[17]. During a follow-up of 48-month, Cressman et al showed that Lp(a)was an independent predictor of fatal events attributable to cardiovascular disease during the period of follow-up[18]. Our results provide the frist direct evidence that diabetic patients with ESRD undergoing hemodialysis treatment had more accelerated atherosclerosis and more involvement by ischemic heart disease(IHD) than non diabetic hemodialysis patients. We could show the positive association of serum Lp(a) with HTN of hemodialysis patients and also the association of Lp(a) with LVH was shown in our study, which further highlights the importance of high serum lipoprotein(a) in HD patients.

As previously shown that high serum lipoprotein(a) in HD patients could have an association with hypertention in hemodialysis by Fytili et al19,20. And we also could show this association, but in the meantime more studies needs for this importance aspect of hemodialysis patients .

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