Association of Serum Lipoprotein(a) with Left Ventricular Hypertrophy and Left Ventricular ejection Fraction in End-Stage Renal Failure Patients Under Hemodialysis

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Abstract

Background: The contribution of cardiovascular events to the extraordinary high mortality in end-stage-renal disease (ESRD) has generated some interest in non traditional athero sclerotic cardiovascular diseaserisk factors that are prevalent in ESRD , such as Lipoprotein(a) [Lp(a)]. In this study we aimed to consider the association of serum lipoproein(a)) with left ventricular hypertrophy (LVH) and hypertention (HTN) in ESRD patients under regular hemodialysis .

Methods and patients: 61 unselected patients with end-stage renal disease (ESRD), undergoing maintenance hemodialysis treatment were studied. Lipoprotein (a) was measured by enzyme immuno assay (ELISA) test, all patients were echographied for left ventricular hypertrophy and left ventricular (LV) ejection fraction (EF). Hypertensive patients were stratified into no HTN, stage one to three HTN, as well as LVH was stratified to normal, mild, moderate and severe.

Results: The total number of patients was 61(F=23 M=38). They consisted 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 all patients was 58.5±19mg/dl. Mean±SD of LP(a) of the diabetic group was 62±12.3 mg/dl and for the nondiabetic group it was 57.7±20 mg/dl. There was a significant positive relationship between stages of LVH and stages of HTN, significant positive correlation between presence of chest pain and stages of LVH, significant reverse correlation of Lp(a) with percent of LV ejection fraction, as well as positive correlation of serum LP(a) with stages of HTN. A significant correlation between stages of LVH with serum LP(a) was observed this study.

Conclusions: Lipoprotein(a) has an adverse effect on left ventricular hyperthrophy and hypertention of hemodialysis patients and needs more attention.

INTRODUCTION

The contribution of cardiovascular events to the extraordinary high mortality in end-stage-renal disease (ESRD) has generated some interest in non traditional athero sclerotic 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 unknown. Both proathengenic 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. Ts indicates that elevated Lp(a) levels in these patients are not due to genetic origin ([4,5]). Trefore, it has been suggested that kidneys have an important role in Lp(a) metabolism, decrease Lp(a) catabolism or increase of liver production ([4,5,6,7,8]). Cardiovascular disease is the principal cause of morbidly and mortality in dialysis patients ([9]). A principle findings of cardiovascular disease is left ventricular hypertrophy (LVH) determined by echocardiography ([9]). Left ventricular hypertrophy (LVH) is common and as LVH by itself is indepenclent risk factor for cardiovascular disease in hemodialysis (HD) patients ([10]).

HD Patients have been associated with elevation of Serum Lp(a) levels([7,11]) However, relatively little has been published on the link between Lp(a) and cardiovascular disease respectively LVH and LV ejection fraction in HD patients. We therefore sough to evaluate the association of serum level of Lp(a) with left ventricular hypertrophy, LV ejection fraction and chest pain in a group of ESRD-hemodialyzed patients consisting of diabetics and nondiabetics.

PATIENTS AND METHODS

This is a cross-sectional study. It was performed on 61 patients with end-stage renal disease (ESRD), undergoing maintenance hemodialysis treatment between September 2002 and December 2003. Patient selection 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) was measured by enzyme immuno assay (ELISA) by Immuno-Biological laboratories (IBL) kit (Germany). According to the sixth and seventh report of the joint national committee on prevention, detection, evaluation and treatment of high blood pressure we stratified hypertensive patients from stage one to three ([12,13]), (stage of zero equal to no HTN). Stages of the hypertension of HD patients were considered before treatment and at the first start of hemodialysis treatment. I regard to heart echocardiography (B-mode) one single cardiologist who was unaware of the patients data performed all echographies for left ventricular hypertrophy, 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). LVH measurements were done at the end diastolic phase. LV ejection fraction between 55 and 75% was considered normal. For statistical analysis descriptive data were expressed as mean± SD. Comparison between groups were performed using chi-square(χ^2 test), Mann Whitney as well as Kruskal & Wallis and Fisher 's exact tests. For correlations we used spearman`rho tes, partial correlation with adjustment for age, Phi & Cramer's V test and Eta test were used. All statistical analysis was performed by using the statisticall analysis system (SPSS 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 shows the mean± SD of data of patients , table 2,3 and 4 show the frequency distribution of chest pain, stages of HTN, and stages of LVH of patients. Mean±SD of ages of subjects was 46.5±16 years . Mean±SD of length of the time patients had been on hemodialysis was 32 ± 31 months. Mean±SD of LV fraction (EF%) was 51±8.9 percent and 39.3% of patients had chest pain. Mean±SD of LP (a) of total patients was 58.5±19mg/dl. Mean±SD of LP (a) of diabetic group was 62±12.3 mg/dl and for nondiabetic group 57.7±20 mg/dl. In this study there were no significant differences of ages, 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 (χ^2 test) (P>0.05). There was no significant difference in the presence of chest pain and also no significant difference of DM between two sexes (Fisher ? s exact test)(p>0.05). No significant difference between sex of the subjects and stages of hypertension (P>0.05) was found (χ^2 test). In this study, there was a significant positive correlation between stages of LVH and duration of hemodialysis treatment (p<0.01), no significant difference between stages of LVH and ages of the patients (p>0.005)(kruskal-wallis statistical analytic test). There was a significant positive correlation between stages of LVH and stages of HTN (r= 0.580 p<0.001) as well as no significant correlation between DM and LVH (P>0.05) (Phi & Cramer's V test). We found a significant positive correlation between presence of chest pain and DM (P<0.001). Tthe association between the presence of DM with presence of HTN as well as sex and DM was negative (p>0.005)(Phi & Cramer's V test). No correlation between DM with percent of LV ejection fraction was found (P>0.005)(Eta test). No significant different of duration of hemodialysis treatment as well as serum lipoprorein (a), ages of patients and percent of LV ejection fraction between diabetic and non diabetic group (P> 0.05)(Mann-Whitney test) was found. No significant correlation of ejection fraction with duration of hemodialysis treatment (P>0.05) (Spearman test) was found. A significant correlation between presence of chest pain and stages of LVH (P<0.001))(Phi & Cramer's V test) was observed. Regarding HTN there was no difference between stages of HTN with chest pain (P> 0.05) (χ^2 test). Partial correlation test with adjustment for age showed a significant

linear inverse correlation between serum Lp(a) with LV ejection fraction (r = - 0.24 p=0.032)(figure 1) as well as positive correlation of serum LP(a) with stages of HTN (r = 0.245 p=0.029). No positive correlation between serum Lp(a) with duration of hemodialysis treatment (P>0.05) (spearmant test) was found . Significant correlation between stages of LVH with serum LP(a)(p<0.05) was found (kruskal-wallis test).

Figure 1

Figure 1: Reverse correlation of percent of LV ejection fraction with serum lipoprotein(a) (r = - 0.24 p=0.032)(partial correlation test with adjustment for age).

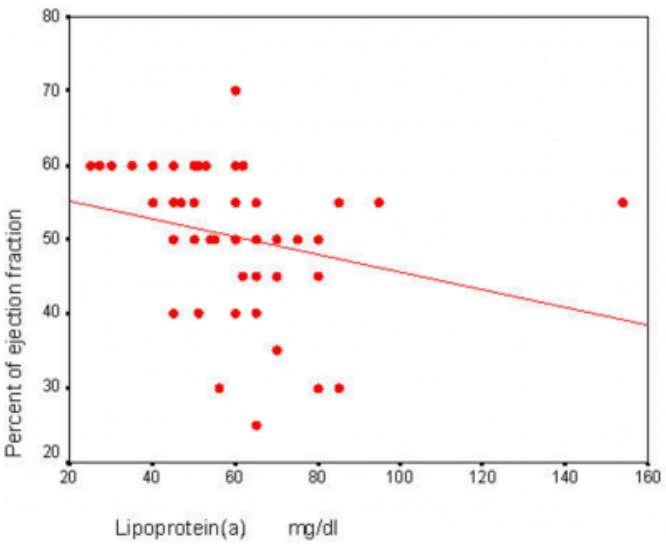

Figure 2

Table 1: Mean ±SD , Minimum and Maximum of data.

		Age years	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

*duration of hemodialysis treatment

**Cardiac ejection fraction.

Figure 3

Table 2 : Frequency distribution of stages of hypertension (HTN).

Stages of HTN	Total patients n=61		DM group* n=11		Non-DM group n=50	
	Number	Percent	Number	Percent	Number	Percent
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

*DM=Diabetes Mellitus.

Figure 4

Table 3: Frequency distribution of chest pain in hemodialysis patients.

Chest pain	Total patients n=61		Diabetic patients n=11		Non diabetic patients n=50	
	Number	Percent	Number	Percent	Number	Percent
Yes	24	39.3	9	81.8	15	30
No	34	60.7	2	18.2	35	70

Figure 5

Table 4 : Frequency distribution of Left ventricular hypertrophy(LVH) in hemodialysis patients.

	Total patients n=61		Diabetic patients n=11		Non diabetic patients n=50	
	Number	Percent	Number	Percent	Number	Percent
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

Discussion: In this study, there was a positive correlation between stages of LVH with duration of hemodialysis treatment and positive correlation between stages of LVH with stages of hypertension. In addition, a positive correlation between stages of LVH with presence of chest pain, correlation of diabetes mellitus with the presence of chest pain as well as positive correlation of serum LP(a) with stages of HTN was found. Significant correlation between stages of LVH with serum LP(a) was observed. Strauman et al. in a study on 62 patients on maintenance hemodialysis observed 65% prevalence of LV hypertrophy. He showed that 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 the dialysis group ($_{14}$). De Lima et al. in a study of 103 HD patients showed that systolic 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

that Lp(a), age ,diabetic state were the only independent contributors of a sclerotic cardiovascular death ([7]). Ohashi et al. in an evaluation of 268 HD Patients observed that those who died of cardiovascular events had significantly higher serum Lp(a) levels than those who 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 ischemic heart disease (IHD) than non diabetic hemodialysis patients. We could show that the association of Lp(a) with HTN of hemodialysis patients as well as the association of Lp(a) with LVH that was shown in our study further highlights the importance of high serum lipoprotein(a) in HD patients. Another study by Fytili et al. previously showed that high serum lipoprotein(a) in HD patients could have an association with hypertention in hemodialysis ([19,20]) as we did in our study.. In the meantime, further clinical studies into this important aspect of hemodialysis patients is needed.

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