Original article

Serum Lp(a) levels in patients with liver disease

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Abstract

Objective: The study was conducted to evaluate the effect of liver diseases on serum Lp(a) levels and also to study the relationship between Lp(a) levels with other lipid parameters and liver function tests in 32 hyperbilirubinemia patients with total bilirubin >3mg/dL. The results were compared with 20 healthy age matched individuals. **Methods**: Serum obtained from venous blood sample are used for estimating total cholesterol (TC), triglyceride(TG), high density lipoprotein cholesterol(HDL-c), low density lipoprotein cholesterol(LDL-c), very low density lipoprotein cholesterol(VLDL-c), total protein(TP), albumin(ALB), total bilirubin, direct bilirubin, aspartate amino tranferase(AST), alanine amino transferase(ALT), alkaline phosphatase(ALP), gamma glutamyl transferase (GGT), lipoprotein (a) [Lp(a)], serum phospholipids. **Results**: There was significant decrease in serum Lp(a) levels in liver disease patients and the decrease was directly correlated with reduced serum albumin levels and inversely with liver function parameters. **Conclusion**: Thus the present study indicates hepatic synthetic damage has possible biochemical basis for the reduction of serum Lp(a) levels

Keywords: Liver disease; Lipoprotein (a); Phospholipids; Lipid profile

INTRODUCTION

Lipoprotein (a) [Lp(a)] is a circulating particle closely related to low density lipoprotein(LDL). It is a genetic variant of LDL and consists of covalent association of the unique and enigmatic apolipoprotein(a) to apolipoprotein B-100 by a single disulphide bridge [1]. The metabolism of Lp(a), from synthesis to catabolism is not clear. More than 90 percent of Lp(a) level is under genetic regulation and greater part is accounted by size polymorphism in the sequence of apo(a) gene [2]. Besides, metabolic abnormalities such as the acute phase response [3,4], hormone disorders [5,6], diabetes [7], liver and renal disease [8-10] have strong influence on Lp(a) levels in plasma, suggesting that factors other than genetic may also play a central role in the intricate metabolism of the lipoprotein.

It has been reported that raised Lp (a) concentrations have relation with genesis, progression and complication of both atherosclerosis and thrombosis[11]. These findings caused an interest among researchers to correlate serum/plasma Lp (a) level with clinical information and use this parameter to predict the risk of cardiovascular or thrombotic diseases in patients belonging to various other disease groups. The present study was planned to evaluate the effect of liver diseases on serum Lp (a) levels and its relationship with other parameters of liver function.

MATERIALS AND METHODS

The study included 32 patients with hyperbilirubenemia (total bilirubin > 3 mg/dL) attending kasturba teaching hospital, manipal, India. Age and sex matched healthy individuals were taken as controls after obtaining proper consent. Serums obtained from venous blood sample are used for various biochemi-

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cal estimation. The following biochemical parameters were estimated in all the patients and controls. total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-c), low density lipoprotein cholesterol (LDL-c), very low density lipoprotein cholesterol (VLDL-c), total protein (TP), albumin (ALB), total bilirubin, direct bilirubin, aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatase (ALP), gamma glutamyl transferase (GGT) by HITACHI Auto analyzer 912 (Bausch and lomb). Lp(a) level in serum samples was estimated by a specific and sensitive immunoturbidometric assay, by using auto analyzer HITACHI - 912 Japan using tests kits from randox laboratories, UK. Serum phospholipids are estimated by method of [12].

All parameters were expressed as mean ± standard deviation (SD). A P value less than 0.05 is considered as significant. Statistical analysis was done using SPSS (statistical package for social sciences, SPSS-10, Chikago, USA). Independent sample t test was used to compare between cases and controls. Pearson's correlation test used to correlate between the parameters.

RESULTS

As depicted in table 1 there was significant increase in levels of total bilirubin ($P<0.01$), direct bilirubin ($P<0.01$), AST ($P<0.01$), ALT ($P<0.01$), ALP ($P<0.01$) and GGT ($P<0.01$). Serum total protein and albumin level was decreased in the patients compared to the controls ($P<0.05$). Serum Lp(a) levels were significantly decreased in patients with liver disease compared to healthy controls ($P<0.01$). Serum Lp(a) levels were correlated negatively with total bilirubin ($r=-0.410$, $P<0.01$) (figure 1), direct bilirubin ($r=-0.320$, $P<0.01$) (figure 2), ALT ($r=-0.273$, $P<0.01$), ALP ($r=-0.346$, $P<0.01$) and positively with total protein ($r=0.417$, $P<0.01$) (figure 3), albumin ($r=0.473$, $P<0.01$) (figure 4), TC ($r=0.446$, $P<0.01$), phospholipids ($r=0.342$, $P<0.01$).

Table 1. Lp(a) and liver function test parameters in with hyperbilirubinemia and healthy controls(mean ± SD)

Parameters	Hyperbilirubinemia patients ($n=32$)	Healthy controls ($n=20$)
Total Bilirubin (mg/dL)	12.60 ± 8.39 *	0.97 ± 0.43
Direct Bilirubin (mg/dL)	12.25 ± 13.33 *	0.20 ± 0.08
Total Protein (g/dL)	5.12 ± 0.92 *	6.93 ± 0.66
Albumin (g/dL)	2.43 ± 0.53 *	4.06 ± 0.37
Globulin (g/dL)	2.68 ± 0.86	2.86 ± 0.61
AST (U/L)	358.48 ± 122.67 *	35.55 ± 12.57
ALT (U/L)	504.33 ± 111.40 *	42.00 ± 14.75
ALP (U/L)	377.96 ± 183.90 *	176.65 ± 28.96
GGT (U/L)	127.93 ± 28.83 *	36.90 ± 52.99
Total Cholesterol (mg/dL)	201.70 ± 35.71 *	100.00 ± 44.51
Triglycerides (md/dL)	168.18 ± 95.95	154.50 ± 46.70
VLDL (mg/dL)	31.67 ± 19.34	30.75 ± 9.23
HDL (mg/dL)	12.13 ± 6.69 *	41.55 ± 14.05
LDL (mg/dL)	112.70 ± 41.56 *	58.81 ± 43.71
Phospholipids (mg/dL)	163.33 ± 39.44 *	237.40 ± 33.57
Lipoprotein (a) (mg/dL)	5.12 ± 3.62 *	29.40 ± 20.21

* P value is <0.01 compared to healthy controls.

DISCUSSION

The liver plays a key role in the production and metabolism of plasma lipids and lipoproteins. Hepatocellular damage may cause significant alteration in lipid and protein metabolism due to its decreased synthesizing capacity. Apo (a) is the protein part of Lp(a) along with Apo-B100, so decrease in synthesizing capacity of hepatocytes may possibly decrease the levels of Lp(a) in liver disease patients. In our study we observed significant decrease in levels of Lp(a) in liver disease patients with significantly raised levels of bilirubin and elevated liver enzyme markers. Previous authors reported alterations in serum total cholesterol and triglyceride levels in liver disease patients [13] and also suggested that decrease was due to decrease in lysolecithin in these patients. They had also suggested that lysolecithin was lowest in patients with the greatest degree of liver damage, and the low lysolecithin with markedly elevated lecithin in the patients with obstructive jaundice. We have observed decreased levels of total cholesterol along with phospholipids in patients with liver disease. The significant correlation between liver function parameters and serum Lp (a) levels suggests the degree of hepatic damage and its relation to Lp (a) levels in serum. An earlier study reported low Lp (a) concentration in heavy drinkers (more than 200 grams alcohol/day) for several years [14] and suggested that alcohol lowered serum Lp (a) concentration. Possibly the low Lp (a) concentration found in drinkers was partly mediated through hepatic damage and reduced synthesis. The present study supports this view by showing significant correlation of Lp (a) with serum albumin levels. A decreased synthesis rate of Apo B-100 could also be responsible for a defective Lp (a) assembly as some authors have suggested. Further research is needed to verify whether Apo B-100 or other intracellular pool of cholesterol plays a role in Lp (a) assembly and in its serum concentration. The lipid and lipoprotein changes of liver disease may be of practical importance which helps to understand pathological process and to design certain treatment modalities for these patients.

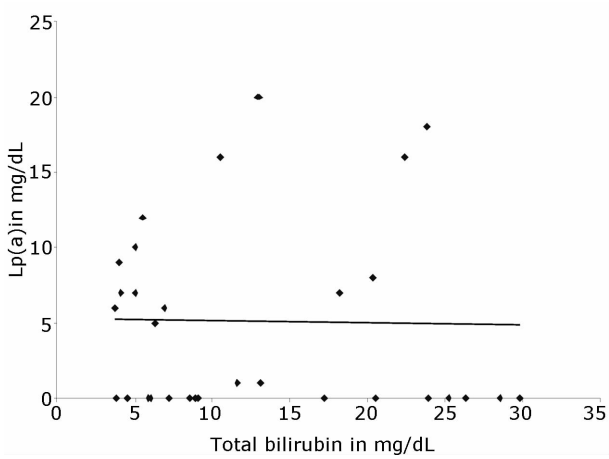

Figure 1 Patient's serum Lp (a) levels decreased with increase in serum bilirubin

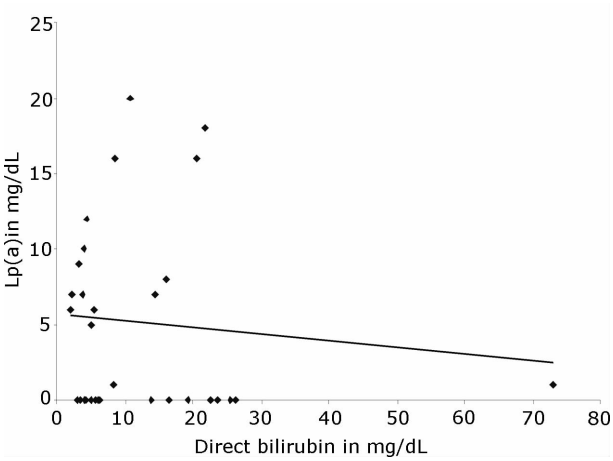

Figure 2 Patient's serum Lp (a) levels decreased with increase in serum direct bilirubin

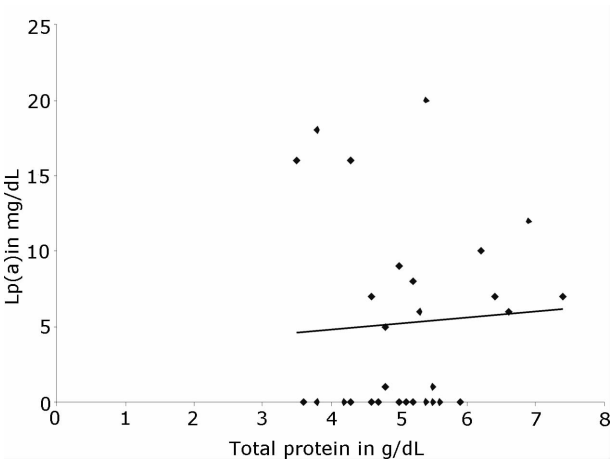

Figure 3 Patient's serum Lp (a) levels decreased with decreased serum total protein

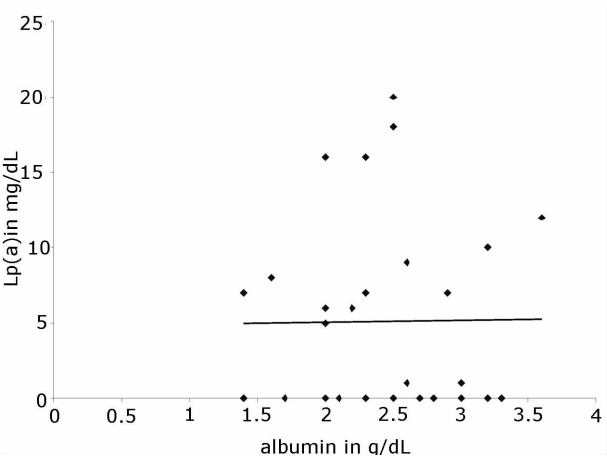

Figure 4 Patient's serum Lp (a) levels decreased with serum albumin

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