

Original article:

Assessment of lipid profile changes with respect to severity of liver dysfunction in cirrhosis of liver

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Abstract:

Objectives: Cirrhosis of Liver is the end stage result of many etiologies affecting Liver. It is important to assess severity since management varies accordingly. Liver plays a central role in lipid metabolism, lipids are known to be altered. Our aim was to assess severity of Cirrhosis by Child Pugh scoring and correlating with Lipid levels. We attempted to know the pattern of lipid abnormalities and assessed its role in prognostication.

Methods: This was a Cross sectional study done at Bapuji hospital, a tertiary care center at Davangere. 100 cirrhosis patients fulfilling inclusion criteria, were included in the study.

Results: Levels of cholesterol, LDL, HDL and VLDL in cases were significantly reduced when compared to control group ($P < 0.000$). Levels of TGL were marginally reduced in cases ($P < 0.05$). Total Cholesterol ($P < 0.001$), TGL ($P < 0.02$), HDL ($P < 0.05$) and LDL ($P < 0.000$) showed a significant negative correlation with Severity of Cirrhosis. VLDL had no correlation with the severity of Cirrhosis.

Conclusion: From this study, it was found that cholesterol, LDL, HDL and VLDL were significantly lower. The hypolipidemia may be due to decreased synthesis of Apolipoproteins in studies. Reduced HDLc could be attributed to decrease production of LCAT, apolipoprotein I and II. Hypolipidemia (except VLDL) was correlating to the severity of Cirrhosis. This is comparable to the earlier studies. In conclusion, dyslipidemia exists in patients with cirrhosis. Thus serum Lipid profile may serve as a sensitive indicator of Liver Dysfunction in Cirrhosis.

Key words : LDL;LipidProfile , VLDL;Cirrhosis

Introduction:

Chronic liver disease affects people in their most productive years of life and has a significant impact on the economy as a result of premature death, illness, and disability.¹ Derangement of serum lipid profile is a common observation in cirrhotics. Very little was known earlier about the alterations of lipids and lipoproteins in patients with cirrhosis.

The liver plays an important role in the synthesis, metabolism and degradation of these lipids and lipoproteins. Hence in cirrhosis the concentrations of these lipids and lipoproteins are altered. There are very few studies on dyslipidemia in cirrhosis in India, but this subject has been dealt in detail worldwide. Although there are vast array of biochemical tests available for diagnosing and assessing severity of liver cell damage, desired sensitivity and specificity are lacking. The

routine liver function tests, i.e. serum bilirubin; SGPT used in the assessment of liver function may give abnormal results in various kinds of liver disorders. Furthermore these tests reflect the extent of hepatic cell damage, rather than hepatic function assessment which is more important to evaluate the patient's condition and prognosis.

Data regarding lipid levels in cirrhosis was available in 1862 when Austin Flint had suggested that the blood cholesterol level was affected by the liver diseases.²

It was in 1978 that Neil McIntyre studied the levels of plasma lipoproteins patterns in liver diseases.³ Here we tried to evaluate the different lipid parameters such as Triglycerides, Total cholesterol, HDL, VLDL and LDL, as the important lipoproteins estimated in this study of 100 patients of cirrhosis and compared with controls in our hospital.

Objectives:

1. To Know the pattern of lipid of lipoprotein anomalies in cirrhosis of Liver.
2. To know whether it's possible to assess the severity of hepatic damage by knowing the quantum of lipid and lipoprotein anomalies in acute cirrhosis.
3. Do the lipid anomalies help in prognostication.

Methodology

Study Design: Cross sectional Study.

Study period: December 2012 to January 2014

Inclusion Criteria: Diagnosed cases of cirrhosis established by history, general examination of the patient, bio-chemical parameters and Ultrasound of Liver.

Exclusion Criteria: Patients with Diabetes mellitus, nephrotic syndrome, thyroid dysfunction, HIV patients, chronic smokers and those patients taking drugs which might affect blood lipids and lipoproteins.

The Ethical committee approval was obtained.

Method:

Cirrhosis patients admitted to Bapuji and Chigeteri Hospital, Davangere were studied. One hundred healthy controls who had come for blood donation were selected.

10 ml of Venous blood samples were drawn from all the patients after a minimum of 12 hours of complete fasting from the cubital fossa. Levels of lipids and lipoproteins obtained from the controls and subjects (patients) are tabulated and compared with each other and the results discussed.

Serum was separated within two hours of collection to prevent artifactual changes in concentration of HDL. The serum was transferred to centrifuge tube and centrifuged at 5000 rpm for 10 minutes. The supernatant clear serum was then pipetted out using dry piston pipettes with disposable tips and stored in dry thin walled vials at 4°C.

The samples were analysed the same day or within 48 hours. Care was taken to exclude the hemolysed serum.

The lipid and lipoprotein assay was done using the Dr. Lange LP 700 equipment.

1. Estimation of Serum Total Cholesterol by Carr and Drecker Method⁴:
2. Determination of Serum HDL Cholesterol by Carr and Drecker Method⁵:

3. Determination of Triglyceride by Enzymatic end Point Peroxidase Coupled Method:
4. Determination of LDL - Cholesterol using Fried Wald's Formula⁶ :

Results:

Lipid profiles of the cases and controls were computed and analysed. Data was tabulated in Microsoft excel and later SPSS software was used. Student Unpaired t test and ANOVA test were used for statistical analysis.

TABLE-1 GRADING OF ASCITES AND ENCEPHALOPATHY

Parameters	Grades	No of patients
Ascities	1	15
	2	43
	3	34
	4	8
Encephalopathy	1	39
	2	17
	3	24
	4	20

In the study 77% of the patients were of grade 2 and 3. While encephalopathy was maximum of 39% in grade 1

TABLE-2 LIVER FUNCTION TEST

Parameters	Cases N=100		Controls N=100		Statistical Analysis Unpaired t test
	Mean	Std Deviation	Mean	Std Deviation	
Total bilirubin	4.44	2.86	0.59	0.33	13.36, p<0.000
SGPT	74.58	28.21	26.85	8.38	16.21, p<0.000

In the study, 42% cases had Jaundice and Mean SGPT was 74.58 U/dl.

TABLE-3 LIPID PROFILE AND SUBJECTS

Parameters	Cases N=100		Controls N=100		Statistical Analysis Unpaired t test
	Mean	Std Deviation	Mean	Std Deviation	
Total cholesterol	131.60	27.92	168.48	19.32	10.86, p<0.000
Triglyceride	81.94	26.35	88.80	18.04	2.15, p<0.05
HDL	32.48	8.18	41.77	5.45	9.45, p<0.000
LDL	78.48	24.24	103.36	10.44	9.24, p<0.000
VLDL	16.38	5.86	32.39	2.66	24.88, p<0.000
TSH	2.71	0.81	2.74	0.76	0.24, NS

The results of this study showed that all the five studied variables (total cholesterol, LDL, VLDL, HDL & TGL) were significantly low in the study population than in the control group (p value <0.05)

TABLE-4 LIPID PROFILE AND CHILD PUGH CLASS

Parameters	Child PUGH score						One way Analysis of Variance (ANOVA)
	A N=18		B N=33		C N=49		
	Mean	Std Deviation	Mea n	Std Deviation	Mean	Std Deviation	F Value & Sig
Total cholesterol	146.50	22.31	138.95	33.11	121.17	21.66	8.13, p<0.001
Triglyceride	88.87	24.85	88.68	30.24	74.85	22.42	3.66, p<0.02
HDL	34.83	6.27	34.15	6.87	30.48	9.20	3.01, p<0.05
LDL	89.67	8.81	87.79	29.48	68.09	19.70	10.56, p<0.000
VLDL	16.66	5.99	17.46	6.32	15.54	5.47	1.08, NS
TSH	2.96	0.74	2.88	0.94	2.50	0.69	3.43, p<0.03

The levels of lipid (TGL, LDL, HDL, Total Cholesterol) in cases were significantly reduced in Child Score C compared to B and B compared to A i.e. decrease in Lipids was proportional to Child class. There was no significant variation in the VLDL levels in all the Child Classes.

Discussion

In our study, Cirrhosis was seen predominantly in older age group with 87% of patients >40 years of which 68 % were in between 41 and 60 years of age. This may attribute to the delayed presentation of cirrhosis of liver of various etiologies due to their complications. The most affected age group was 40 to 50 years and 90% of cirrhotic patients were over 40 years of age. This is supported by the epidemiological studies done Clark et al and Poynard T et al.^{7,8} Poynard et al extend their discussion to quote that three independent factors were associated with an increased rate of fibrosis: age at infection older than 40 years, daily alcohol consumption of 50 g or more and male sex.

The value of serum total cholesterol was significantly lower in patients with cirrhosis when compared to controls in our study. This observation supports the earlier reports. The probable explanation for the reduced serum total cholesterol due to the decline in synthetic function and altered metabolism. This was confirmed in the study conducted by Phillips et al in 1960.^{9,10,11}

Miller et al found that in cirrhosis without cholestasis, cholesterol and apo B levels was reduced. LCAT activity and the proportion of plasma cholesterol esterified was also be markedly reduced.¹² D'Arienzo A et al said in their study that a low serum cholesterol level is associated with a higher mortality rate in patients with liver cirrhosis.¹⁹

Further comparison of the total cholesterol values in different Child Pugh Classes

showed a direct relation between the severity of Liver damage and reduction in the cholesterol level. This was supported by study conducted by Jarikre AE et al, Ahenaku et al, Spósito et al. They suggested that Cholesterol fall as the disease advances. The most frequent disorder of serum lipids in liver diseases is an increase of the ratio of free to total cholesterol.^{17,18,20,26}

The serum triglyceride levels were significantly lower in cases of cirrhosis than in control ($p < .05$) in our study group. This observation is in full agreement with the study conducted by Ahenaku et al¹⁸

The mechanism responsible for reduction of triglyceride level in patient with cirrhosis could be that the metabolism of free fatty acids might be reduced in cirrhotics due to decreased reserve of liver parenchyma as suggested by Neil McINTYRE.⁴ Mandal et al found that Triglyceride values showed a decline in CLD patients but it was not statistically significant.²⁶ The poor nutrition, altered metabolism and abstinence from alcohol of cirrhosis patients may explain the lower TGL in cirrhosis in them.

In our study we found that the level of reduction of the TGL was proportionate to the severity of the parenchymal liver disease ($p < 0.001$). This was supported by the studies done by Ahenaku et al, Jarikre AE et al, Mandal et al and Varghese et al.^{18,20,21,26}

The level of serum HDL in our study was significantly decreased in cases of Cirrhosis when compared to control ($p < .0000$), are consistent with a large volume of publications on this subject.

Subhan et al observed that in patients with chronic liver parenchymal disease without cholestasis, HDL levels decline and become worse as the disease progresses.²⁵ Thus HDL estimation in patients with cirrhosis is an important marker of hepatic function. The decrease in HDL in patients with cirrhosis can be attributed to decreased hepatic synthesis of HDL. This could be due to LCAT deficiency. Liver is the only source of this enzyme (LCAT) and serum levels of this enzyme are decreased in liver disorders.^{13,14,15}

The decreased LCAT results in impairment of conversion of nascent HDL to mature HDL resulting in an increase in immature HDL in blood which is more prone for degradation, resulting in decreased levels of HDL as suggested by Vergani G. Trovati.¹⁶

Neil McIntyre in 1978 also observed that HDL was decreased in patients with liver parenchymal disease and attributed this decrease in HDL to decreased production of enzyme LCAT.⁴ We also found that the levels of HDL reduction was proportional to the severity of liver damage in cirrhosis. This HDL reduction is also suggested by Jarikre AE et al, Ahenaku et al, Mandal et al, Varghese et al, Subhan et al, and many others studies around the world.^{18,20,21,25,26}

There was a significant decrease in levels of serum LDL in patients with cirrhosis, when compared to controls ($p < 0.000$) in our study. This is in accordance with previous study by Ahenaku et al, Varghese et al, Breier C et al and Mandal et al.^{18,21,23,26} But studies by McIntyre in 1978 observed that the LDL concentration was

decreased in patients with chronic liver disease. As these patient had a very low VLDL which is thought to be the precursor of LDL, it seems likely that their LDL metabolism was greatly altered resulting in reduced level of LDL.⁴ We found that the reduction in the LDL level was proportionate to the Severity of Liver damage in Cirrhotics as detected by the Child Pugh scoring system. This was supported by Subhan et al. Their study showed that patients with liver diseases had lower lipid levels, i.e. Lower LDL in cirrhotic patients than in the comparison group. Besides, the amount of decrement in the serum LDL was significant with increasing severity of liver damage.²⁵

In our study, we found that the reduction in VLDL levels did not correlate with the severity of liver disease though the levels were significantly low. This could be probably due to the increased in metabolism of the lipoproteins by lipases which are inactivated by liver.²⁷ A study conducted by Neil McINTYRE et al suggested that the VLDL levels were strikingly depressed in patients with parenchymal liver disease and low LCAT and were much lower than in either of the other two conditions mentioned. Presumably these low levels were due to failure of VLDL synthesis and release, either because of malnutrition or because of damage to the parenchymal cells responsible for the manufacture of VLDL.⁴

In our study, a significant difference was observed between patients and the comparison group in all lipid profile values studied ($p < 0.05$) This

finding is in keeping with our observations that in severe liver disease as the liver function deteriorates, more decline is observed in LDL, HDL, total cholesterol levels and TGL levels. Our study is comparable in results with other studies like Mandal et al, Subhan et al, Varghese et al, Chrostek et al and others,

where they showed a progressive decline in the lipid levels with progression of liver disease.^{21,25,26,27}

Conclusion:

In conclusion estimation of serum Lipid Profile allows better assessment of hepatic function and evaluation of prognosis of patients with Cirrhosis of Liver.

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