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Original Research Article

Comparison of Lipid Profile between Patients with Liver Cirrhosis & Matched healthy controls at SMS Medical College & Hospital, Jaipur

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Abstract

Background: Cirrhosis is considered as generalized involvement of liver by concurrent parenchymal necrosis, regeneration and diffuse fibrosis resulting in disorganization of the lobular architecture. Liver cirrhosis is defined as the diffuse process characterized by fibrosis and conversion of the normal liver architecture into structurally abnormal nodules. Cirrhosis in anatomical point of view is a diffuse process with fibrosis and nodule formation. Aims & **Objectives**: The aim of this study was to assess the serum lipid profile in liver cirrhosis patients and Comparable control groups and to find out association of serum levels of lipids (TG, Cholesterol, HDL, LDL, VLDL) with severity of liver cirrhosis based on Child Pugh Classification. Methods: This study was a cross sectional study in which clinically diagnosed cases of liver cirrhosis from OPD/IPD of Gastroenterology department of S.M.S. Medical College and Hospital, Jaipur were taken as cases. Results: 45 cases of liver cirrhosis and matched controls between age group of 35-65 years were analyzed in this study. In this study Mean age in cases group was 49.58 + 5.63 years while that of controls group was $48.82 \pm$ 9.23 years. The mean cholesterol for cases was 144.51 + 28.21 mg/dl and for Controls was 170.20 + 23.12 mg/dl, mean HDL for cases was 36.11 + 4.88 mg/dl and for Controls was 44.44 + 5.01 mg/dl and mean LDL for cases was 85.72 + 26.58 mg/dl and for Controls was 104.45 + 22.43 mg/dl which was statistically significant (p value < 0.001). However, the mean TG and mean VLDL were statistically non- significant. Mean Cholesterol and HDL levels were significant when compared with Child Pugh Grades. Conclusion: Dyslipidemia exists in patients with liver cirrhosis and screening for the same is important for intervention with appropriate therapy to prevent cardiovascular events so it would be recommendable to provide laboratory analysis of Lipid profile as a routine.. The total cholesterol, HDL and LDL cholesterol levels decrease gradually with progression of cirrhosis that can help in understanding disease prognosis.

Keywords: Cirrhosis, Cholesterol, HDL, LDL, Child Pugh Classification.

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Introduction

Cirrhosis is considered as generalized involvement of liver by concurrent parenchymal necrosis, regeneration and diffuse fibrosis resulting in disorganization of the lobular architecture. The article "Diseases of the liver and biliary tract" sponsored by the Fogarty International Center, states the definition given by WHO as Liver cirrhosis is defined as the diffuse process characterized by fibrosis and conversion of the normal liver architecture into structurally abnormal nodules. Cirrhosis in anatomical point of view is a diffuse process with fibrosis and nodule formation. It is the end result of all etiologies.[1]

Cirrhosis is the eleventh leading cause of death by disease in the United States. About 25,000 people die from cirrhosis each year. In India, cirrhosis is 2.74% of all the causes of death.[2,3] The leading cause of liver cirrhosis in India is excess alcohol consumption. There is also a great toll in terms of human suffering, hospital costs, and the loss of work by people with cirrhosis.

The most common causes of cirrhosis worldwide are chronic alcoholism and chronic hepatitis B and C, followed by biliary diseases and hemochromatosis.[4,5] Regardless of the cause of cirrhosis, the pathologic features consist development of fibrosis to the point that there is architectural distortion with the formation of regenerative nodules. This results in a decrease in hepatocellular mass and thus function, and an alteration of blood flow. The induction of fibrosis occurs with activation of hepatic stellate cells, resulting in the formation of increased amounts of collagen and other components of the extracellular matrix.[6,7]

Liver plays an essential role in lipid metabolism, synthesis, secretion, catabolism, and storage of lipids and lipoproteins. As majority of endogenous cholesterol is synthesized in the hepatic microsomes, synthesis and metabolism of cholesterol is impaired in chronic liver disease resulting in a decrease in plasma levels.[8]

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Hence, this study was aimed at studying the lipid profile changes in Cirrhosis and its progression (using Child Pugh Criteria), thereby reassessing the need for lipid profile in all the patients as a prognostic tool.

Materials and Methods

This study was a hospital based comparative analysis in the Department of Biochemistry and Central Lab S.M.S. Medical College and Hospital, Jaipur. The Study Design was a Cross sectional study done from Nov. 2015 to Nov. 2016.

diagnosed cases of Clinically liver cirrhosis from OPD/IPD ofGastroenterology department of S.M.S. Medical College and Hospital, Jaipur was taken as cases. Known and established cases of Cirrhosis of liver between age group of 35-65 years willing to participate were included in this study. Compilation of complete clinical records was done along with informed consent. Age and gender matched healthy subjects were taken as control groups. Patients who use Insulin or other Oral Hypoglycaemic drugs, anti-hyperlipidemic drugs, chronic smokers and having other diseases like Diabetes Mellitus, Hypertension, nephrotic syndrome or thyroid problem were excluded.

Statistical Analyses:

Sample size was calculated to be 42 of either sex for each of the two groups (cases and controls) at α -error 0.05 and power of study 80% assuming difference of mean to be detected as mean in total cholesterol in liver cirrhosis and healthy controls 0.50 \pm 0.80 (as per seed article). At the precision of 10% (Absolute allowable error) for the

study purpose, 45 liver cirrhosis patients and 45 matched healthy controls were taken. Quantitative data expressed in the form of Mean \pm SD and inference was drawn with the use Student's t test. Samples were analyzed on fully automated analyzer Beckman Coulter AU-680.

Results

The characteristics of the studied population including age and lipid profile values are shown in Table 1.

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Table 1: The characteristics of the studied population including age and lipid profile values

values							
	Group	N	Mean	Std. Deviation	'p' Value*		
Age (years)	Cases	45	49.58	5.63	0.638(NS)		
	Controls	45	48.82	9.23			
TG (mg/dl)	Cases	45	113.42	22.07	0.136 (NS)		
	Controls	45	106.53	21.41			
Total Cholesterol (mg/dl)	Cases	45	144.51	28.21	0.000		
	Controls	45	170.20	23.12			
HDL (mg/dl)	Cases	45	36.11	4.88	0.000		
	Controls	45	44.44	5.01			
LDL (mg/dl)	Cases	45	85.72	26.58	0.000		
	Controls	45	104.45	22.43			
VLDL (mg/dl)	Cases	45	22.68	4.40	0.138(NS)		
	Controls	45	21.31	4.28			

^{*}Unpaired t-test

The mean age in cases group 49.58 + 5.63 years was slightly more than controls group $(48.82 \pm 9.23 \text{ years})$. The mean total cholesterol for cases was 144.51 ± 28.21 mg/dl and for Controls was 170.20 ± 23.12 mg/dl, mean HDL for cases was 36.11 + 4.88 mg/dl and for Controls was 44.44 + 5.01 mg/dl and mean LDL for cases was 85.72 + 26.58 mg/dl and for Controls was 104.45 + 22.43 mg/dl which was

statistically significant (p value < 0.001). The mean TG for cases was 113.42 + 22.07 mg/dl and for Controls was 106.53 + 21.41 mg/dl which was statistically nonsignificant (p value =0.136). The mean VLDL for cases was 22.68 + 4.40 mg/dl and for Controls was 21.31 + 4.28 mg/dl which was statistically non-significant (p value =0.138). (Table 1, Figure 1)

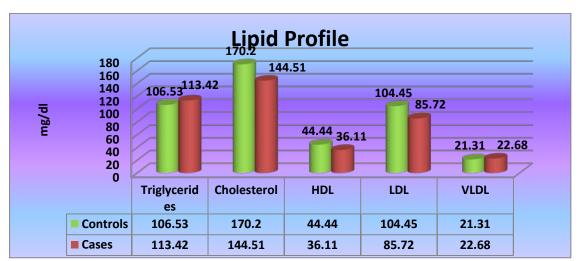


Figure 1: Mean Lipid Profile Comparison between Cases and Controls

The Child-Pugh score is calculated by adding the scores of the five factors and can range from 5 to 15. Child-Pugh class can be A (a score of 5-6), B (7-9), or C (10 or above). Decompensation indicates cirrhosis with a Child-Pugh score of >7 (class B). (Table 2)

Table 2: Child Pugh Classification of Cirrhosis

Factor	Units	1	2	3
Serum bilirubin	mol/L	<34	34-51	>51
	mg/dL	<2.0	2.0-3.0	>3.0
Serum albumin	g/L	>35	30-35	<30
	g/dL	>3.5	3.0-3.5	<3.0
Prothrombin time	seconds	0-4	4-6	>6
	prolonged INR	<1.7	1.7-2.3	>2.3
Ascites		None	Easily	Poorly
			controlled	controlled
Hepatic encephalopathy		None	Minimal	Advanced

When assessed using Child Pugh grading, the mean Triglycerides and the mean total Cholesterol level difference was not significant between the three grades. However, the mean HDL level in CP Grade A, Grade B, Grade C was 39.50 ± 3.21 mg/dl, 36.33 ± 5.82 mg/dl, and 33.13 ± 2.47 mg/dl respectively. There was significant fall in HDL levels with severity and it was statically significant (p value <0.001). (Table 3, Figure 2)

Table 3: HDL variations with CP Grading

		N	Mean	Std. Deviation	One way ANOVA 'p' Value*	
	Controls	45	44.44	5.01		
HDL (mg/dl)	A- grade	12	39.50	3.21	< 0.001	
	B- grade	18	36.33	5.82		
	C- grade	15	33.13	2.47		

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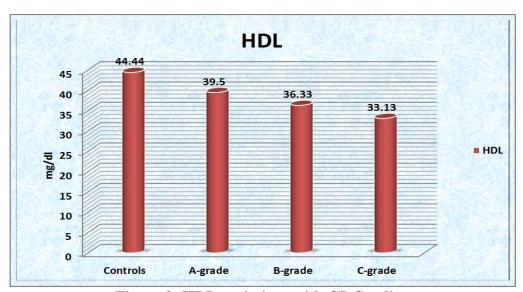


Figure 2: HDL variations with CP Grading

Discussion

Cirrhosis of liver is a common medical problem in India. Cirrhosis is defined anatomically as a diffuse process of fibrosis and nodule formation due to different causes. Cirrhosis is elucidated histopathologically and has a variety of clinical manifestations and complications, some of which can be life threatening. Lipids are one of the necessary components which control cellular functions and homeostasis. Liver plays an essential role in lipid metabolism, several stages of lipid synthesis and transportation.

Age range of this study is between 35-65 years. In our study Mean age in cases group 49.58 + 5.63 years was slightly more than controls group (48.82 ± 9.23) years). This difference was statically not significant (p value =0.638). The mean age of patients from other studies are as follows; 57.9 years by Andreu et al from Spain 1993[9], 54.1 years by Toledo et al in 1913 from Barcelona[10], 58.5 years by Guarner et al 1999 from Spain[11], Aparna Agarwal from North India noted mean age of 50.7 years in 2001.[12] In our study, we found that the most common age group involved by cirrhosis is 41-50 years. This result corroborates with previous studies, which show that the mean age for alcoholic cirrhosis is 44 years in South Asian males.[13]

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In our study mean TG for cases was 113.42 + 22.07 mg/dl and for Controls was 21.41 mg/dl which 106.53 + non-significant statistically (p =0.136). This study shows the same trend as the study results of Phukan et al in 2013, the serum triglyceride levels were significantly increased in alcoholic cirrhotic patients compared with the control group (p < 0.001).[14] This finding is similar to the results of a study done in India by Singh B et al in 2011.[15] In contrast in another study, different results were obtained by Mehboob, et al, in 2007, who studied 160 patients with chronic liver diseases. There were significant declines in the serum TG levels of patients.[16]

In our study mean total cholesterol for Cases was 144.51 + 28.21 mg/dl and for Controls was 170.20 + 23.12 mg/dl which was statistically significant (p value < 0.001). In a study by Ghadir et al 2010 it was found that lower lipid levels are found in patients with liver diseases, and all four studied variables (HDL, LDL, total cholesterol and TG) were significantly lower in cirrhotic patients than in the comparison group.[17] The results of our study also correlate with study conducted

in Greece by Siagris D et al in 2006 on 155 patients infected with HCV and 138 healthy people who served as the comparison group, where the serum total cholesterol level was lower in patients than the comparison group.[18]

In our study HDL shows significant difference between the cases and control groups. It was observed from the results of our study that the mean HDL for cases was 36.11 + 4.88 mg/dl and for Controls was 44.44 ± 5.01 mg/dl, mean LDL for cases was 85.72 + 26.58 mg/dl and for Controls was 104.45 + 22.43 mg/dl which was statistically significant (p value < 0.001). The mean value of HDL and LDL was lower for Cases when compared to controls. The mean VLDL values when compared between cases Controls statistically non-significant (p value =0.138).

Selimoglu and colleagues, in their study in 2002, showed that with the exception of serum triglyceride levels, other variables like serum HDL, LDL level decreased in cirrhotics. This finding shows hypolipidemia is expected in severe liver disease due to decline in synthetic function.[19] In a similar study by Varghese et al, 2007, Decreased levels of VLDL, total cholesterol, HDL was found in the patients.[20] Similar studies conducted by Edith N. Okeke[21] and Mohammad Reza Ghadir, in 2010, showed significant derangement of lipid level in cirrhotics and a negative relation to extent of liver damage.[17]

Dyslipidemia is a frequent finding in chronic liver disease. The plasma lipids and lipoproteins tend to decrease with parenchymal liver disease, and the level and composition of the lipoproteins depends on the activity of enzymes involved in lipid metabolism. These include lipoprotein lipase (LPL), lecithin-cholesterol acyltransferase (LCAT), and hepatic triglyceride lipase (HTGL).[22,23] The results of this study confirm that the

concentrations of lipids and lipoproteins in the liver diseases are changed.

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When assessed using Child Pugh grading, the mean Triglycerides and the mean total Cholesterol level difference was not significant between the three grades. However, there was significant fall in HDL levels with severity and it was statically significant (p value <0.001). Selimoglu et al in their study in 2002 found that HDL level is lower in Child-Pugh B than Child-Pugh A and apo-A level is the most affected factor in those with liver damage.[19] In this study, the change in HDL level was higher in Child A than B, and higher in Child B than C which shows that that is the severity of liver function that causes HDL level to decline. This is exactly in accordance to the results of our study. Some have found out low HDL in the study population and compared with severity such as A.C. Spósitol et al in 1997.[24]

Conclusion

The purpose of this study was to see the lipid metabolism derangement in patients suffering from chronic liver disease. The number of decrements measured in the levels of total cholesterol, LDL and HDL in cirrhotic patients are related to the progress in cirrhosis. It is recommended that lipid profile should be done in all cases suffering from chronic liver disease. In chronic liver disease due to decreased biosynthetic capacity of liver unusually low levels of cholesterol and other lipid profile parameters are found. Seeing the results of our study, this can be said that the correction of serum Lipid Profile may have prognostic effect and give better insight for treatment, complications and progression of the diseases, so it would be recommendable to provide laboratory analysis of Lipid profile as a routine.

Further research in this field is justified. This may, in the future, provide a valid relationship between progression of cirrhosis and severity of dyslipidemia.

Thus, studies of lipid profile may guide us in the prognosis and treatment of cirrhosis in the near future.

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