Original Research Article

A cross-sectional observational study of lipid profile of cirrhosis of liver patients in a teaching hospital in North Odisha, India

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ABSTRACT

Background: Lipids are essential component of biological membranes: also a part of free molecules and metabolic regulators which control cellular function and homeostasis in the body. Liver plays a central role in lipid metabolism. Cardiovascular disease (CVD) risk stratification includes serum lipid profile. In the general population; global prevalence of cirrhosis from autopsy studies ranges from 4.5% to 9.5%. Deaths from cirrhosis have been estimated to increase and would make it as the 12th leading cause of death in 2020. Although several studies have been conducted on dyslipidemia in cirrhotics in developed countries, there is a paucity of data in this regard in India.

Methods: This observational study was carried out amongst 60 cirrhosis patients that fulfils the inclusion and exclusion criteria and attended the medicine OPD and admitted in medicine ward of Pandit Raghunath Murmu Medical College and Hospital, Baripada, Dist. Mayurbhanj, Odisha, India from June 2018 to Jan 2019.

Results: In our study we had 52 were male and 8 were female. The average age of the patients in the study was 49.62±13.59 yrs. 91.67 % of the patients were alcoholic. Abdominal distension (93.33%) and ascites (81.67%) were most common presenting complaints. Pallor was present in 65.00% cases. Splenomegaly was present in 29 (48.33%) patients of cirrhosis of liver. Renal dysfunction was present in 22 (36.67%) cases. We found decreased HDLC (<40 mg/ Dl) in 34 (56.67%) cases. Hypolipidemia, in particular decreased HDLC level is also an important risk factor for cardiovascular disease and vascular events.

Conclusions: From this study we can conclude that lipid abnormalities are commonly seen in patients with liver cirrhosis and screening for the same is important for intervention with appropriate therapy to prevent cardiovascular events. Further studies on lipid abnormalities in these patients and the need for treatment are recommended.

Keywords: Cholesterol, Cirrhosis, High-density lipoproteins, Low density lipoproteins, Lipid profile, Triglyceride

INTRODUCTION

Lipids are vital constituent of biological membranes and it is a part of free molecules and metabolic regulators. This controls cellular function and homeostasis in the body. Liver acts as a central character in lipid metabolism. It contributes both in endogenous and exogenous cycles of lipid metabolism and transport of lipids through plasma. The apolipoproteins are essential for assembling and structuring of lipoproteins. Lipoproteins take part in a vital role in the absorption of dietary cholesterol, long chain fatty acids and fat soluble vitamins. The transport of triglycerides, cholesterol and fat soluble vitamins from the liver to transport of cholesterol from peripheral tissue to liver is by lipoproteins. Apolipoproteins stimulate enzymes which are important in lipoprotein metabolism and to mediate the binding of lipoproteins to cell surface receptors. Liver
is the primary site of formation and clearance of lipoproteins. Hence, liver is involved in various steps of lipid metabolism and lipid transport. Thus, lipid metabolism is greatly disturbed in severe liver disease which is affected in an array of ways. Dyslipidemia found in chronic liver disease differs from secondary dyslipidemia associated with other etiologies, because circulating lipoproteins are not only present in abnormal amount; but they also often have abnormal composition, appearance and electrophoretic mobility.2

Hence, it is not astounding that plasma lipid levels can be affected in liver diseases in an array of ways. Chronic liver diseases due to different causes are frequently associated with remarkable reductions in plasma triglyceride and cholesterol level due to decreased lipoprotein biosynthetic capacity. Cholestasis, associated with hypercholesterolemia as the key excretory pathway of cholesterol, is blocked in this disorder. Aside from the different complications seen in cirrhotic patients, chronic dyslipoprotenemia is one which can initiate alterations in cellular membrane lipids that give rise to formation of abnormal RBCs, such as echinocytes and alterations in membrane function with potential pathophysiologic consequences.

Cardiovascular disease (CVD) risk stratification includes serum lipid profile. It is infrequently considered a useful screening tool for the assessment of liver diseases; however there is reason to think otherwise.3 Many previous studies concluded an inverse association of lipid parameters such as total cholesterol (TC), triglyceride (TG), high density lipoprotein (HDL) and low density lipoprotein (LDL) with severity of liver disease. However, some other studies did not find such correlation especially for the TG and HDL levels.4,5 Further, Sen et al showed that TC, HDL and TG were higher in grade 3 fatty liver.6

In the clinical perspective, chronic liver disease is a disease process of the liver that involves progressive destruction and regeneration of the liver parenchyma leading to fibrosis and cirrhosis.7 In the general population; global prevalence of cirrhosis from autopsy studies ranges from 4.5% to 9.5%,8-10 Hence, taking the adult population into count, we estimate that more than fifty million people in the world would be affected with chronic liver disease. Globally, the most common causative factors are alcohol, NASH and viral hepatitis. Prevalence of cirrhosis is possibly to be underestimated as almost one third of the patients remain asymptomatic. The estimated worldwide mortality from cirrhosis was 771,000 people during 2001; it was ranked 14th and 10th as the leading cause of mortality in the world and in developed countries, respectively.11 Deaths from cirrhosis have been anticipated to rise and would make it as the 12th important cause of death in 2020.12 Even though, several studies have been conducted on dyslipidemia in cirrhotics in developed countries, there is a paucity of data in this regard in the developing country like India.

**METHODS**

This observational study was carried out amongst 60 cirrhosis patients that fulfils the inclusion and exclusion criteria and attended the medicine OPD and admitted in medicine ward of Pandit Raghunath Murmu Medical College and Hospital, Baripada, Dist. Mayurbhanj, Odisha, India from June 2018 to Jan 2019.

**Inclusion criteria**

All cirrhosis of liver patients irrespective of etiology is above 15 years of age. Cirrhosis was diagnosed on the basis of combination of clinical features, hematological profile and radiological imaging. Clinical signs and symptoms were those of portal hypertension, i.e. ascites and/or gastrointestinal varices. Hematological profile included evidence of anemia and thrombocytopenia. Radiological features, with transabdominal ultrasound, had to demonstrate a small shrunken liver with or without splenomegaly and intra-abdominal varices.13,14

**Exclusion criteria**

Patients suffering from concomitant diseases, which can alter the lipid profiles, like diabetes mellitus, malignancy, chronic renal disease, acute pancreatitis, recent parenteral nutrition, history of hyperlipidemia, patients who were on glucose or lipid lowering drugs, patient on immunsuppressive drug were excluded.

The results were compared with a group of 50 healthy persons, served as controls in Mandal SK et al, study done in Kolkata.4 After due consideration into inclusion and exclusion criteria, detailed history and clinical examination was undertaken in all subjects. Patients were subjected to routine investigation and fasting lipid profile test. Routine test included complete blood count (CBC) (Sysmex XS-800i), renal function test, liver function test, HBsAg, HCV antibody, Ultrasoundography of whole abdomen. A fasting serum lipid profile included serum cholesterol, triglyceride, HDL and LDL cholesterol on Fully Automated analyzer (Erba EM360).

In the present study, anemia was defined using the World Health Organization definition hemoglobin (Hb) concentration <12g/dl (females), <13g/dl (males).The severity of anemia was classified as mild anemia (Hb concentration between 11-12.9g/dl for males and 11-11.9g/dl for females); moderate anemia (Hb concentration between 8-10.9g/dl), and severe anemia (Hb concentration <8g/dl).10 Thrombocytopenia was defined with a value <150x103/μl.

**Statistical analysis**

All the data were entered on excel spreadsheet, and statistical analyses were made using SPSS version 21.0 software. Results were expressed in average ± SD, frequencies and percentages. Continuous data were...
compared using Student’s t-test. A p-value <0.05 was considered as statistically significant for all tests conducted.

RESULTS

During the study period, 60 patients with cirrhosis of liver admitted in medicine ward of P.R.M.M.C.H., Baripada, fulfill inclusion and exclusion criteria. All the cases were studied for the clinical presentation, risk factors and laboratory parameters.

Table 1 shows out of 60 patients, 52 (86.67%) were male and 8 (13.33%) were female with M: F of 6.5:1. The age range was from 16 to 76. The average age of the patients in the study was 49.62±13.59 yrs. Table 2 shows 35.00% of the patients were between 40 and 50 years of age.

| Table 1: Gender distribution. |
|-----------------------------|
| N | Male | Female | Total |
|---|------|--------|-------|
| f | 86.67% | 13.33% | 100% |

| Mean age±SD | 49.69±13.43 | 49.13±16.38 | 49.62±13.59 |
|-------------|-------------|-------------|-------------|
| Youngest patient | 17 | 16 | 16 |
| Eldest patient | 76 | 70 | 76 |

Table 2: Age distribution.

| Age group | Male | Female | Total | % |
|-----------|------|--------|-------|---|
| <20       | 1    | 1      | 2     | 3.33% |
| 21-30     | 5    | 0      | 5     | 8.33% |
| 31-40     | 7    | 0      | 7     | 11.67% |
| 41-50     | 18   | 3      | 21    | 35.00% |
| 51-60     | 9    | 2      | 11    | 18.33% |
| 61-70     | 10   | 2      | 12    | 20.00% |
| 71-80     | 2    | 0      | 2     | 3.33% |
| Total     | 52   | 8      | 60    | 100 |

Table 3: Etiology of cirrhosis.

| Etiology | f | % |
|----------|---|---|
| Alcoholic | 55 | 91.67% |
| Non-alcoholic | 5 | 8.33% |
| Hepatitis B | 0 | 0.00% |
| Hepatitis C | 0 | 0.00% |
| Total | 60 | 100% |

Table 3 shows 91.67% of the patients were alcoholic. Out of 8 female, seven gave alcohol history and out of 52 male 48 were alcoholic. Abdominal distension (93.33%) and ascites (81.67%) were most common presenting complaints. Pallor was present in 39 (65.00%) cases. Splenomegaly was present in 29 (48.33%) patients of cirrhosis of liver. Renal dysfunction was present in 22 (36.67%) cases. Icterus was present in 14 (23.33%) cases. Six (10.00%) patients presented with hematemesis and/or melena with all of them having platelet count <1.5 lakhs/ml. The findings on clinical examination are listed in Table 4.

| Symptoms/ signs | f | % |
|-----------------|---|---|
| Pallor          | 39 | 65.00% |
| Icterus         | 14 | 23.33% |
| Edema           | 20 | 33.33% |
| Asteriaxis      | 1  | 1.67% |
| Ascites         | 49 | 81.67% |
| Encephalopathy  | 0  | 0.00% |
| Breathlessness  | 3  | 5.00% |
| Hematemesis     | 3  | 5.00% |
| Malena          | 5  | 8.33% |
| Splenomegaly    | 29 | 48.33% |
| Renal dysfunction/decreased GFR | 22 | 36.67% |
| Abdominal distension | 56 | 93.33% |

Figure 1: Severity of anemia in cirrhosis of liver patients.
Figure 2: Types of anemia in cirrhosis of liver patients.

Figure 1 shows hematological profile of cirrhosis of liver patients with mean hemoglobin of 7.99±2.18 gm/dl of which 62 (89.85%) patients had hemoglobin <11 gm/dl among which 37 (53.62%) had hemoglobin ≤8 gm/dl. Statistically 58 (96.67%) of the patients had anemia. Only 2 patients had hemoglobin within normal range.

Table 5: Platelet levels in cirrhosis of liver patients.

| Platelet count (lakh per ml) | f  | %   |
|-----------------------------|----|-----|
| ≤1.5 (Thrombocytopenia)     | 39 | 65.00% |
| 1.5-4.5                     | 20 | 33.33% |
| >4.5                        | 1  | 1.67%  |
| Total                       | 60 | 100%  |

Table 6: Laboratory parameters of cirrhosis of liver patients.

| Laboratory parameters          | Cirrhosis patients (Mean±SD) (N=60) | Sanjay Mandal et al study controls (Mean±SD) (N=50) | p-value |
|--------------------------------|--------------------------------------|-----------------------------------------------------|---------|
| Haemoglobin                    | 7.95±2.21                           | 9.00±1.5                                           | <0.0001 |
| RBC (M=4.7-6.1 and F= 4.2-5.4) | 3.15±0.94                           | 4.00±0.8                                          | <0.0008 |
| MCV (80-100)                   | 76.5±12.29                          | 80.0±10.0                                         | <0.005  |
| PCV (M=40.7-50.3 and F=36.1-44.3) | 23.90±7.05                    | 27.0±5.0                                          | <0.0001 |
| MCHC (33.4-35.5)               | 33.1±6.24                           | 35.0±5.0                                          |         |
| Total bilirubin direct         | 1.97±2.79                           | 2.00±0.5                                          |         |
| SGPT                           | 68.1±45.22                          | 70.0±10.0                                         |         |
| SGOT                           | 84.6±60.29                          | 90.0±10.0                                         |         |
| ALP                            | 132.7±85.69                         | 150.0±20.0                                        |         |
| Blood urea (10-40 mg/dL)       | 44.7±5.08                           | 45.0±5.0                                          |         |
| Serum creatinine (0.5-1.3 mg/dL) | 1.58±1.59                    | 1.20±0.5                                          |         |

Figure 2 shows Microcytic hypochromic anemia was predominant in cirrhosis patients. Macrocytic anemia was more common in males.

Table 5 shows 39 (65.00%) of the patients had decreased platelet count. Table 6 shows different laboratory parameters of cirrhosis of liver patients. Table 7 shows the comparisons between lipid profile of cirrhosis patients and healthy controls which is significant (p <0.05).

Table 7: Comparisons between lipid profile of cirrhosis patients and controls.

| Indices         | Cirrhosis patients (MEAN±SD) (N=60) | Sanjay Mandal et al study controls (MEAN±SD) (N=50) | p-value |
|-----------------|-------------------------------------|-----------------------------------------------------|---------|
| Serum cholesterol| 123.94±37.15                       | 192±21.34                                          | <0.0001 |
| Serum triglyceride | 111.71±51.25                     | 137.6±14.36                                        | <0.0008 |
| HDL             | 35.91±13.91                        | 41.78±5.04                                         | <0.005  |
| LDL             | 71.50±26.30                        | 122.8±19.29                                        | <0.0001 |

DISCUSSION

Study group consisted of 68 patients of cirrhosis of liver, out of which 52 (86.67%) were male and 8 (13.33%) were female with the age range from 16 to 76. In our study, the average age of male patients was 49.62±13.59 years and female patients were 49.13±16.38 years. The average age of the patients in the study was 49.8±13.19 years, which is comparable with study by Suthar et al (41 years), Sarin et al (43±8.7 years).15,16 In our study, M:F ratio was 6.5:1, which be due to the cultural and traditional influences in our country. 35.00% of the patients were between 40 and 50 years of age, which shows a high prevalence of this disease among the productive age group. In our study we found, 91.67% of the patients were alcoholic. Out of 8 female, seven gave alcohol history and out of 52 male 44 were alcoholic.

In the study, abdominal distension (93.33%) and ascites (81.67%) were most common presenting complaints.

In previous studies also ascites was common finding Suthar et al (60%), Pathak et al (57.5%), Mendenhall et al (29.52%).
Splenomegaly was present in 29 (48.33%) patients of cirrhosis of liver in our study.

In study by Suthar et al, Splenomegaly was seen in 60% cases. In our study, the blood urea was raised (>40 mg/dl) in 35.00% (21 cases) of the patients indicating indirectly towards acute renal injury (49.1% in study by Pathak et al, 37% in study by Hegde et al. The creatinine was raised in 19 patients (i.e. 31.67% of the study group) which was comparable with 39.4% in study by Pathak et al, 20% in study by Hegde et al. It was observed that 23 patients had GFR <60 ml/min, thus 38.33% of the patients had significantly reduced GFR. Hegde et al, study that 30% of the patients had significantly reduced GFR.

The mean hemoglobin level in our study was 7.95 + 2.21 g% whereas in other studies the findings were as Hegde et al (9.12 gm %). It was found that 38 (96.67%) of the patients had anemia, out of which 32 (53.33%) had hemoglobin ≤8 gm/dl, i.e. severe anemia. A study by Rosario Gonzale Z, et al, showed that anemia in CLD patients were 75%. Macrocytic anemia was more common in males than females. Microcytic hypochromic anemia was predominant in cirrhosis patients. This may be due to the low socioeconomic and poor nutritional status of most of the cases. According to interesting article by Tody L Kujovich MD – “Haemostatic defects in end stage liver disease”, critical care clinics 21 (2005), mild to moderate thrombocytopenia occurs in 49 to 64% of patients with decompensated chronic liver disease (DCLD). In our study 39 (65.00%) patients had thrombocytopenia (<1.5 lakhs /mm3).

Liver is one of the most vital organs for the metabolism of plasma apolipoproteins, endogenous lipids and lipoproteins; most of them are synthesized by the liver, which depends on the integrity of cellular functions of liver. Under normal physiological circumstances, liver plays vital role to control lipid and lipoprotein metabolisms. Liver synthesizes and secretes endogenous lipoprotein, synthesizes the key enzyme for the LDL metabolism, i.e., lecithin cholesterol acyltransferase (LCAT), hepatic lipase and apolipoproteins, and also regulates catabolism of various plasma lipoproteins through hepatic cellular surface lipoprotein receptors. It helps in maintaining levels of plasma lipids and lipoproteins in vivo. Hepatic cellular damage can impair these processes, which progresses to an alteration of plasma lipid and lipoprotein patterns; and synthesis of cholesterol, triglycerides, apo AI, apo B and Lp (a) could be altered and their plasma concentrations will be changed correspondingly. Therefore, serum lipid level decrease gradually with severity of liver disease; hence assessment of plasma lipid and lipoprotein levels will be useful to evaluate the extent of the hepatic damage.

Cirrhosis of the liver is a rising health problem in India and fatality from this disease is increasing rapidly among both men and women. In cirrhosis of liver disease, derangement of serum lipid profile is a common observation. To the best of our knowledge, this subject has been dealt in detail worldwide, but there are very few studies on dyslipidemia in cirrhosis in India. Our study was conducted to evaluate any derangement in lipid profile in cirrhosis of liver patients. The results of our study showed that all the four studied lipid profile parameters (Total Cholesterol, triglyceride, LDL and HDL) were significantly (p <0.05) decreased in cirrhosis of liver patients as compared to controls group. Similar results were observed in Muhammed et al study. Brier C et al study conducted on lipoproteins in the plasma of patients with post alcoholic liver cirrhosis, showed that in alcoholic cirrhosis of liver, total cholesterol, HDL, VLDL, HDL-cholesterol were all decreased. The study, conducted by Selimoglu and colleagues showed that variables like serum HDL, LDL level decreased in cirrhotics with the exception of serum triglyceride levels. This finding has some resemblance with our results and hypolipidemia is anticipated in severe liver disease due to decline in synthetic function. It is well recognized that NASH and alcoholic cirrhosis are associated with increase in serum triglyceride concentrations. Significant decrease triglyceride level was found in this study. This may be due to the low socioeconomic and poor nutritional status of most of the patients. However, most of the studies conducted elsewhere showed all the lipid parameters in cirrhosis of liver patients were lower than in control. Decreased HDLC (<40 mg/ Dl) in 34 (56.67%) cases was found. Hypolipidemia, in particular decreased HDLc level is also a key risk factor for cardiovascular disease and adverse vascular events.

CONCLUSION

Lipid abnormalities are commonly seen in patients with cirrhosis of liver and screening for the same is essential for intervention with appropriate treatment to prevent adverse cardiovascular events. The levels of serum total cholesterol, TG, LDL and HDL in patients with cirrhosis are related to the advancement in cirrhosis. It helps in diagnosis of severity of liver disease and also acts as a good prognostic sign. In all cases with advanced liver disease, lipid profile should be advised. This kind of study requires a large group of cases and controls for further study. Further studies on lipid abnormalities in these patients and the need for treatment are recommended.

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