ORIGINAL ARTICLE

Serum lipid profile in alcoholic cirrhosis: A study in a teaching hospital of north-eastern India

Jyoti Prakash Phukan, Anuradha Sinha, Jatindra Prasad Deka[1]

Department of Pathology, Bankura Sammilani Medical College, Bankura, West Bengal, [1]Gauhati Medical College, Guwahati, Assam, India

ABSTRACT

Background: Alcoholic cirrhosis is often associated with impaired lipid metabolism. However, there are only a few studies regarding lipid profile in alcoholic cirrhosis that have been undertaken in India. The aim of the study is to assess the degree of alteration of serum lipid profile in alcoholic cirrhotic patients and also to detect its relationship with the age of the patients and the alcohol consumption pattern. **Patients and Methods:** This cross-sectional study was conducted in a teaching hospital of north-eastern India for 1 year with 100 patients with alcoholic cirrhosis (cases) and 50 healthy individuals (controls) without history of alcohol consumption. A questionnaire of personal characteristics including history of alcoholism was completed for each patient. Serum lipid profile (total, low-density lipoprotein (LDL), high-density lipoprotein (HDL) cholesterol and triglyceride) was recorded for each case and control. *t* test of significance was applied for statistical analysis. **Results:** Majority of the cases were in the 41-50 years age group. There was no relationship of cirrhosis with the type of alcoholic beverage, but a definite relationship was observed with the quantity and the duration of alcohol consumption. In patients with cirrhosis, the total serum cholesterol level was decreased. There was a significant decrease in serum HDL and LDL cholesterol compared with the control group ($P < 0.001$). However, the serum triglyceride levels were significantly increased in alcoholic cirrhotic patients compared with the control group ($P < 0.001$). **Conclusion:** In this study, we found that there was marked alteration of serum lipid profile values in patients with alcoholic cirrhosis compared with normal, non-cirrhotic individuals. Therefore, a search for lipid profile abnormality should be performed in every cirrhotic patient.

Key words: Alcohol consumption, alcoholic cirrhosis, serum lipid profile

Address for correspondence:
Dr. Anuradha Sinha, Department of Pathology, Bankura Sammilani Medical College, P. O. Kenduadihi, Bankura - 722 102, West Bengal, India.
E-mail: doctor_anuradha@yahoo.co.in

INTRODUCTION

In an effort to solve the major health problems of developing countries, the importance of liver has been well recognized since a long time. The liver plays an essential role in lipid metabolism, several stages of lipid synthesis and transportation.[1-3] Alcohol consumption cause fatty liver, alcoholic hepatitis and ultimately, alcoholic cirrhosis in some patients.[4-6] In Western countries, alcohol is the major cause of liver cirrhosis, and it is gradually increasing in countries like Japan and India.[6,7] Alcohol-related liver deaths account for up to 48% of cirrhosis-associated deaths in the United States, and are also major contributors to liver disease-related mortality in other countries.[6]

Access this article online	
Quick Response Code:	Website: www.nigeriamedj.com
	DOI: 10.4103/0300-1652.108886

Alcoholic cirrhosis is the end spectrum of alcoholic liver disease (ALD), which includes fatty liver or simple steatosis, alcoholic hepatitis, fibrosis, cirrhosis and superimposed hepatocellular carcinoma.[6] Fatty liver is the most common form of ALD, which develops in more than 90% of heavy drinkers. But, only about 30% of heavy drinkers develop a more severe form of ALD, such as fibrosis and cirrhosis.[6] Cirrhosis is the final result of chronic liver damage, which is characterized by parenchymal injury leading to extensive fibrosis and nodular regeneration. As about 30% of the heavy drinkers develop cirrhosis, there are many other factors that are involved in the development of alcoholic cirrhosis, which include sex, obesity, drinking patterns, dietary factors, non-sex-linked genetic factors and cigarette smoking.[8,9]

The molecular pathogenesis of ALD involves alcohol metabolism and secondary mechanisms such as oxidative stress, endotoxin, cytokines, and immune regulators.[10] The final and irreversible form of ALD is alcoholic cirrhosis, which usually develops slowly and insidiously. Fibrosis that occurs in alcoholic cirrhosis is a wound-healing response that occurs virtually in all forms of chronic liver

injury, and is characterized by excessive accumulation of collagen and other extracellular matrix proteins.[6] Activated hepatic stellate cells are the major source of the increased production of extracellular matrix proteins, along with portal fibroblasts and bone marrow-derived myofibroblasts.[6]

Clinical features of alcoholic cirrhosis are similar to those of other forms of cirrhosis. Commonly, the patients present with jaundice, ascites and peripheral oedem. Complications such as portal hypertension with life-threatening variceal hemorrhage may occur in some patients. The ultimate causes of cirrhotic death are progressive liver failure, complications due to portal hypertension and development of hepatocellular carcinoma.

The liver plays a key role in the metabolism of plasma lipids and lipoproteins.[11] 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.[12] Severe metabolic impairment in cirrhosis can produce a worsening of the serum lipoprotein pattern. High-density lipoprotein (HDL) cholesterol and its major apolipoproteins have been shown to be reduced in cirrhosis, as also the serum levels of low-density lipoprotein (LDL) cholesterol.[12]

It is also known that long-term ingestion of alcohol causes serum lipid profile abnormality.[13] In India, there is rarely any study on lipid profile abnormality in cases of alcoholic cirrhosis. Viewed from this angle, the present study was undertaken with the following aims and objectives:

I. To assess the degree of alteration of serum lipid levels in alcoholic cirrhosis, and
II. To detect its relationship to age of the patients, type, amount and duration of alcohol consumed.

PATIENTS AND METHODS

This cross-sectional study was conducted in a teaching hospital of the north-eastern state of Assam in India for a duration of 1 year. A total of 100 patients of alcoholic cirrhosis (cases) and 50 healthy individuals (controls) without history of alcohol consumption were included in the study. The age of the patients ranged from 27 years to 78 years. This teaching hospital gets patients referred from the surrounding areas, including the neighboring states of Arunachal Pradesh and Nagaland. Controls were selected in different age groups as the cases. All participants gave written consent to participate in the study.

The criteria for inclusion of cases were history of alcoholism with clinical, biochemical and ultrasonographic evidence of cirrhosis. Detailed history of alcohol intake was taken in every patient.

Clinical signs of cirrhosis include hard and nodular consistency of liver, splenomegaly, ascites, varices and related hemorrhage, spider angiomata, palmar erythema, signs of hepatic encephalopathy, etc.

Biochemical tests including liver function tests were performed, which assisted in the diagnosis of alcoholic cirrhosis. These included serum levels of the enzyme aspartate aminotranferase (AST), alanine aminotransferase (ALT) and gamma glutamyltransferase (GGT). If the ratio of AST to ALT was greater than two in cirrhotic patients, the cause was most likely attributed to alcohol. Elevated GGT levels in blood also indicate heavy alcohol use and liver injury.

All cases were subjected to ultrasonographic examination. Typical imaging findings of alcoholic cirrhosis include hepatomegaly, bluntness of liver edges, irregular liver surface and coarse liver texture.[14] Caudate lobe hypertrophy is also a characteristic morphologic feature of cirrhosis. Computed tomography scan and magnetic resonance imaging were performed only in few cases.

Cases of cirrhosis arising due to reasons other than alcohol were excluded from the study.

A questionnaire of personal characteristics including history of alcoholism, type, quantity and duration of alcohol intake and demographic variables was completed for each patient. The amount of alcohol consumed in grams was calculated using the following formula:

Volume of alcohol (in ml) × Density (0.794) = Weight in grams

Fasting blood samples were sent for lipid profile, both in cases and in controls. Lipid profile estimation was performed using a semi-automated biochemistry analyzer (Model: CHEM-7; ERBA diagnostic Mannheim GmbH-Transasia, Bio-Medicals Ltd. Transasia House, 8 Chandivali Studio Road, Mumbai - 400 072, India. Total cholesterol was estimated by an enzymatic method (Cholesterol oxidase-Peroxidase), end point, and triglyceride by an enzymatic method (Glycerol phosphate oxidase-Peroxidase), end point. HDL cholesterol was estimated by the phosphotungstic acid precipitation method. LDL cholesterol was determined by Friedewald's equation.[15] Total serum cholesterol, HDL cholesterol, LDL cholesterol, and triglyceride levels were recorded for cases and controls.

Statistical analysis

T test of significance was applied to determine whether the differences observed in the two groups of cases and controls were significant or not. A $P < 0.05$ was considered statistically significant.

RESULTS

In our study, a total number of 100 patients (cases) and

50 non-cirrhotic, non-alcoholic, individuals (controls) were included. The most common age group affected was 41-50 years (41%) [Table 1]. All cases were male, except one. We observed that majority of the cases (51%) had consumed alcohol regularly for a period of 5-10 years, followed by 22% cases having consumed alcohol for 10-15 years. Majority of the cases (53%) consumed a daily amount of 75-100 g of alcohol, followed by 43% cases consuming 50-75 g of alcohol. Cases in our study consumed different types of alcoholic beverages like molasses preparation, rice beer, brandy, whisky, etc., We have noted that all types of alcoholic beverages were more or less equally associated with the development of alcoholic cirrhosis.

In patients with cirrhosis, total serum cholesterol level, although decreased, was significant compared with the control group in the 31-40 years and 41-50 years age group (P = 0.002 and 0.005, respectively) [Table 2]. There was a significant decrease in serum HDL and LDL cholesterol compared with the control group in all age groups (P < 0.001) [Table 3]. However, the serum triglyceride levels were significantly increased in alcoholic cirrhotic patients compared with the control group (P < 0.001) [Table 4].

Table 1: The age distribution of cases

Age in years	No. of cases	Percentage
<30	16	16
31-40	24	24
41-50	41	41
51 and above	19	19

n=100

Table 2: The alteration in serum total cholesterol levels in cases and controls of different age groups

Age group (in years)	Serum total cholesterol (mmol/L)				*P* value
	Cases		Controls		
	No.	Mean±SD	No.	Mean±SD	
<30	16	5.18±0.75	9	5.56±0.61	0.208
31-40	24	5.16±0.63	12	5.89±0.57	0.002
41-50	41	5.41±0.48	14	6.05±0.76	0.005
>51	19	5.36±0.58	15	5.73±0.80	0.128

SD – Standard deviation

DISCUSSION

The history of alcohol consumption is as old as the history of civilization. In India, the evolution of alcohol use can be traced back to the Vedic era (ca. 1500-700 Before the Commom Era).[16] Now-a-days, ALD is a major cause of morbidity and mortality throughout the world. ALD represents a spectrum of clinical illness and morphological changes that includes steatosis, alcoholic hepatitis and cirrhosis.[6,17] There is a relationship between amount of alcohol consumption and extent of hepatic damage, but no clear cut set amount is present.[5,18,19] The severity of ALD not only depends on the amount of alcohol consumption but also on genetic and environmental factors.[20] In fact, the majority of long-term heavy drinkers develop fatty liver, but only 10-35% develop hepatitis and only 8-20% will progress to cirrhosis.[18,21-23]

In our study, we found that the most common age group involved by alcoholic 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.[24] We found that 99% of cirrhotics were men. The Dionysos study group found a male: Female ratio of 9:1 in alcoholic cirrhosis.[18]

The safe limit of alcohol intakes is controversial.[7] Guidelines recommended by the Royal College of Physician advice a weekly limit of alcohol intake of 210 g for men and 140 g for women. Most previous retrospective studies have shown that the risk of developing irreversible liver damage increases with the amount of alcohol consumed above a level of 40-80 g/day.[25,26] A western study has concluded that 30 g of alcohol per day is the minimal quantity of alcohol compatible with a measurable risk of developing cirrhosis in both sexes.[18] In our study, majority of the cases (53%) consumed a daily amount of 75-100 g of alcohol, followed by 43% cases consuming 50-75 g of alcohol per day. This finding is similar to the findings of the above-mentioned studies.

Majority of our patients had a history of regular alcohol consumption for a minimum of 5-10 years (51%) and 10-15 years (22%). Becker *et al*. found that when compared for 0-6 years and 6-12 years periods, the relative risk of developing alcoholic cirrhosis was almost equal.[5] However,

Table 3: The alteration in serum high- and low-density lipoprotein cholesterol levels in cases and controls of different age groups

Age group (in years)	Serum HDL cholesterol (mmol/L)			Serum LDL cholesterol (mmol/L)		
	Cases	Controls	*P* value	Cases	Controls	*P* value
	Mean±SD			Mean±SD		
<30	0.35±0.17	1.22±0.26	<0.001	1.12±0.50	3.12±1.09	<0.001
31-40	0.46±0.21	1.25±0.29	<0.001	1.54±0.67	3.21±0.90	<0.001
41-50	0.43±0.21	1.27±0.38	<0.001	1.36±0.60	3.62±0.11	<0.001
>51	0.37±0.20	1.20±0.34	<0.001	1.16±0.57	3.80±1.00	<0.001

SD – Standard deviation; HDL – High-density lipoprotein; LDL – Low-density lipoprotein

Table 4: The alteration in serum triglyceride levels in controls and cases of different age groups

Age group (in years)	Serum triglycerides (mmol/L)				*P* value
	Cases		Controls		
	No.	Mean±SD	No.	Mean±SD	
<30	16	4.69±0.61	9	2.11±0.21	<0.001
31-40	24	4.72±0.74	12	2.11±0.29	<0.001
41-50	41	4.79±0.69	14	1.98±0.32	<0.001
>51	19	4.49±0.70	15	2.15±0.31	<0.001

SD – Standard deviation

in another study, it was found that the mean duration of alcohol intake was 21 years and 20 years for men and women, respectively, for developing alcoholic cirrhosis.[18]

Previous studies have found that there is no relation between the type of drink and risk of alcoholic cirrhosis.[27,28] These findings are similar to our study. Rice beer and molasses preparation drinking is common in this part of the country. We have noted no relationship between the types of alcoholic beverage consumption with the development of alcoholic cirrhosis.

We have found that serum total cholesterol values are lowered in alcoholic cirrhotic patients compared with the normal, healthy individuals. The serum HDL cholesterol and LDL cholesterol levels are also significantly decreased compared with the normal controls. Dyslipidemia is seen in ALD, which progressively increases from steatosis to hepatitis to alcoholic cirrhosis.[29] Kackar *et al*. found that the serum cholesterol levels decreases progressively with the progress of alcoholic cirrhosis.[30] Few studies on cirrhosis of liver showed that serum HDL cholesterol, LDL cholesterol and total cholesterol values were significantly diminished.[3,31] In a Nigerian study, the median total cholesterol and HDL cholesterol levels were significantly higher in controls compared with cirrhotic patients; however, LDL cholesterol levels were higher in controls compared with cirrhotic patients and the difference was not statistically significant.[32] The serum LDL cholesterol level is inversely proportional to the severity of liver damage and therefore, it is expected that the serum LDL cholesterol would be low in cirrhotic patients.[31] However, alcoholic cirrhosis may be associated with increased total cholesterol and LDL cholesterol levels, as found by Varghese *et al*.[33]

Serum triglyceride level was significantly higher in cases than in controls in our study. This finding is similar to the results of a study done in India.[34] However, in contrast to this, some other studies revealed that serum triglyceride levels decreased in cirrhosis.[3,32]

The total cholesterol, HDL and LDL cholesterol levels decrease gradually with progression of cirrhosis. This is reasonably expected as liver biosynthesis has been reduced. But, we cannot comment on this as our study was a cross-sectional hospital-based study. Therefore, there was no scope of follow-up.

Our study had some limitations. Our study was a hospital-based study, which caused some bias in patient selection. The study period was also short. Number of cases and controls were limited. Histological diagnosis of cirrhosis was not performed. Therefore, severity of liver damage could not be assessed with certainty. We relied upon history, clinical findings and ultrasonographic and biochemical evidence, which may not be accurate in every case.

However, the result of this study serves as a baseline for further studies on lipid abnormalities in alcoholic cirrhosis.

CONCLUSION

Dyslipidemia is seen commonly in alcoholic cirrhosis. Therefore, alcoholic cirrhotic patients should be routinely screened for lipid profile abnormality. Further research in this field is justified. This may, in the future, provide a valid relationship between progression of alcoholic cirrhosis and severity of dyslipidemia. Thus, studies of lipid profile may guide us in the prognosis and treatment of alcoholic cirrhosis in the near future.

REFERENCES

1. McIntyre N. Plasma lipids and lipoproteins in liver disease. Gut 1978;19:526-30.
2. Kroon PA, Powell EE. Liver, lipoproteins and disease: I. Biochemistry of lipoprotein metabolism. J Gastroenterol Hepatol 1992;7:214-24.
3. Ghadir MR, Riahin AA, Havaspour A, Nooranipour M, Habibinejad AA. The relationship between lipid profile and severity of liver damage in cirrhotic patients. Hepat Mon 2010;10:285-8.
4. Lelbach WK. Cirrhosis in the alcoholic and its relation to the volume of alcohol abuse. Ann N Y Acad Sci 1975;252:85-105.
5. Becker U, Deis A, Sorensen TI, Gronbaek M, Borch-Johnsen K, Muller CF, *et al*. Prediction of risk of liver disease by alcohol intake, sex, and age: A prospective population study. Hepatology 1996;23:1025-9.
6. Gao B, Bataller R. Alcoholic liver disease: Pathogenesis and new therapeutic targets. Gastroenterology 2011;141:1572-85.
7. Walsh K, Alexander G. Alcoholic liver disease. Postgrad Med J 2000;76:280-6.
8. O'Shea RS, Dasarathy S, McCullough AJ. Alcoholic liver disease. Hepatology 2010;51:307-28.
9. Wilfred de Alwis NM, Day CP. Genetics of alcoholic liver disease and nonalcoholic fatty liver disease. Semin Liver Dis 2007;27:44-54.
10. Seth D, Haber PS, Syn WK, Diehl AM, Day CP. Pathogenesis of alcohol-induced liver disease: Classical concepts and recent advances. J Gastroenterol Hepatol 2011;26:1089-105.
11. Canbay A, Bechmann L, Gerken G. Lipid metabolism in the liver. Z Gasteroenterol 2007;45:35-41.
12. Jarike AE, Momoh JA. Plasma total cholesterol, high density lipoprotein cholesterol and low density lipoprotein cholesterol levels in liver cirrhosis in Nigerians. Nig Qt J Hosp Med 1996;6:157-9.
13. Vaswani M, Hemraj P, Desai NG, Tripathi BM. Lipid profile in alcohol dependence. Indian J Psychiatry 1997;39:24-8.
14. Huang YW, Yang SS, Kao JH. Pathogenesis and management of alcoholic cirrhosis: A review. Hepat Med 2011;3:1-11.
15. Friedewald WT, Levy RI, Fredrickson DS. Estimation of

the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972;18:499-502.
16. Sharma HK, Tripathi BM, Pelto PJ. The evolution of alcohol use in India. AIDS Behav 2010;14:S8-17.
17. Tome S, Lucey MR. Review article: Current management of alcoholic liver disease. Aliment Pharmacol Ther 2004;19:707-14.
18. Bellentani S, Saccoccio G, Costa G, Tiribelli C, Manenti F, Sodde M, *et al*. Drinking habits as cofactors of risk for alcohol induced liver damage. The Dionysos Study Group. Gut 1997;41:845-50.
19. Klatsky AL, Armstrong MA, Friedman GD. Alcohol and mortality. Ann Intern Med 1992;117:646-54.
20. Stewart S, Jones D, Day CP. Alcoholic liver disease: New insights into mechanisms and preventative strategies. Trends Mol Med 2001;7:408-13.
21. Sorensen TI, Orholm M, Bentsen KD, Hoybye G, Eghoje K, Christoffersen P. Prospective evaluation of alcohol abuse and alcoholic liver injury in men as predictors of development of cirrhosis. Lancet 1984;2:241-4.
22. Teli MR, Day CP, Burt AD, Bennett MK, James OF. Determinants of progression to cirrhosis or fibrosis in pure alcoholic fatty liver. Lancet 1995;346:987-90.
23. Gramenzi A, Caputo F, Biselli M, Kuria F, Loggi E, Andreone P, *et al*. Review article: Alcoholic liver disease – Pathophysiological aspects and risk factors. Aliment Pharmacol Ther 2006;24:1151-61.
24. Douds AC, Cox MA, Iqbal TH, Cooper BT. Ethnic differences in cirrhosis of the liver in a British city: Alcoholic cirrhosis in South Asian men. Alcohol Alcohol 2003;38:148-50.
25. Pequignot G, Tuyns AJ, Berta JL. Ascitic cirrhosis in relation to alcohol consumption. Int J Epidemiol 1978;7:113-20.
26. Norton R, Batey R, Dwyer T, MacMahon S. Alcohol consumption and the risk of alcohol related cirrhosis in women. Br Med J (Clin Res Ed) 1987;295:80-2.
27. Tuyns AJ, Esteve J, Pequignot G. Ethanol is cirrhogenic, whatever the beverage. Br J Addict 1984;79:389-93.
28. Pelletier S, Vaucher E, Aider R, Martin S, Perney P, Balmes JL, *et al*. Wine consumption is not associated with a decreased risk of alcoholic cirrhosis in heavy drinkers. Alcohol Alcohol 2002;37:618-21.
29. Whitfield JB. Alcohol-related biochemical changes in heavy drinkers. Aust N Z J Med 1981;11:132-9.
30. Kackar RR, Desai HG. Serum cholesterol in cirrhosis of liver. J Assoc Physicians India 2004;52:1007.
31. Cicognani C, Malavolti M, Morselli-Labate AM, Zamboni L, Sama C, Barbara L. Serum lipid and lipoprotein patterns in patients with liver cirrhosis and chronic active hepatitis. Arch Intern Med 1997;157:792-6.
32. Okeke EN, Daniyam CA, Akanbi M, Ugoya SO, Agaba EI. Lipid profile of patients with liver cirrhosis in Jos, Nigeria. J Med Trop 2010;12:56-9.
33. Varghese JS, Krishnaprasad K, Upadhuyay R, Revathy MS, Jayanthi V. Lipoprotein profile in cirrhosis of liver. Eur J Gastroenterol Hepatol 2007;19:521-2.
34. Singh B, Gupta AK, Vishwakarma PK, Bundela RS. Study of blood sugar profile and lipid profile in cases of cirrhosis of liver. J Med Sci Research 2011;2:34-9.

How to cite this article: Phukan JP, Sinha A, Deka JP. Serum lipid profile in alcoholic cirrhosis: A study in a teaching hospital of north-eastern India. Niger Med J 2013;54:5-9.

Source of Support: Nil, **Conflict of Interest:** None declared.