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ORIGINAL ARTICLE

Association of lipid profile with severity of hepatitis B virus related chronic liver disease in adult

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Abstract

Background: *Chronic liver disease (CLD) is a major health problem and contributes to a common cause of hepatocellular carcinoma, disability and death worldwide. Hepatitis B virus (HBV) is the leading cause of CLD in our country. Abnormal lipid profile is expected in those with severe liver dysfunction.*

Objective: *The objective of the study was to determine the alteration of lipid profile (total cholesterol, triglyceride, LDL-C and HDL-C) in HBV positive adult CLD patients and to correlate with severity of liver damage.*

Methods: *This case control study was conducted for one year between January 2018 to December 2018. One hundred and three patients, >18 years old, admitted with HBV positive CLD in Dhaka Medical College Hospital were recorded as case and 103 age and sex matched, healthy population, were recorded as control. A standard case record form including demographics, histories, clinical examinations and different investigations were completed for each group. Then lipid profile values of cases were compared to controls and different Child-Pugh and MELD scores, were used to see severity of liver damage in CLD patients.*

Results: *In patients with HBV positive adult CLD, there were a significant decrease in serum total cholesterol. LDL-C and HDL-C levels compared to the control group (mean 131.4 vs 179.3, 72.5 vs 109.6, and 31.0 vs 40.4 mg/dl, respectively; p<0.001). Comparison of lipid profile with pathologic progression of CLD revealed that these values were diminished gradually with progression of liver damage. Overall triglyceride level was decreased marginally in cases when compared to controls (mean 139.2 vs 146.6 and p=0.047) and this reduction was observed in only advanced stage.*

Conclusion: *Serum total cholesterol, LDL-C and HDL-C level in HBV positive CLD patients were low and diminished gradually with severity of liver damage. Triglyceride level was marginally significant and diminished in advanced CLD.*

Keywords*: HBV positive CLD, Lipid profile, Child-pugh, MELD score*

Introduction

Hepatitis B Virus (HBV) is an enveloped member of the Hepadnaviridae family genus Orthohepadnavirus.[1] HBV infection with serious long-term morbidity and mortality, is one of the most important infectious diseases in the world. More than 2 billion people have been infected with HBV, and 360 million have chronically infected with HBV worldwide. Approximately 600,000 people died from acute or chronic HBV every year.[2] Chronic HBV infection is a major cause of cirrhosis along with important risk factor to develop Hepatocellular Carcinoma.[3] Bangladesh is in the intermediate prevalence zone of HBV with the estimated prevalence of 5.4% in general population.[4] HBV is responsible for approximately 30% cases of acute hepatitis, 75% cases of chronic hepatitis, 60% cases of liver cirrhosis and 65% cases of hepatocellular carcinoma in Bangladesh.[5-7]

Lipids are one of the necessary components which control cellular functions and homeostasis. Liver plays an essential role in lipid synthesis, metabolism and transportation. Therefore, it is reasonable to expect an abnormal lipid profile in those with severe liver dysfunction. For reduced liver biosynthesis capacity, low levels of TG and cholesterol is

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usually observed in chronic liver diseases (CLD).7 CLD patients need frequent visits and multiple hospitalization for management of its complications. However, choice of proper treatment plan depends on the severity, type of liver damage and possibility of assessing its extent. To evaluate severity of CLD, Child-Pugh criteria can be used.8 In addition, MELD criteria are used to choose liver transplantation candidates which are substituted by PELD criteria for children under 12 years. Although, several studies have been performed on lipid profile alteration in those with liver disease worldwide, contributions from Bangladesh are scarce.

Despite diverse results, some outcomes have observed to be common. Due to the high prevalence of chronic liver disease in our country, this study was conducted to determine lipid profile in patients with HBV positive adult CLD and to assess its correlation with the severity of liver damage.

Materials and Methods

During the study period from January 2018 to December 2018, all patients aged >18 years, admitted in the Department of Medicine, DMCH were under gone through a complete history review and physical examination according to structured case record form. Patients, both male and female, with clinical features of CLD, confirmed hepatitis B virus related by HBsAg or HBeAg or anti- HBc or HBV-DNA or combination of two or more positive. If clinical feature of CLD was present and ultra-sonographic changes were present (liver is small, shrunken, coarse and of high echogenic texture with or without splenomegaly or ascites or dilated portal vein), it was considered as CLD. If clinical feature of CLD was absent but feature of decompensation was present and ultra-sonographic changes were present, it was considered as CLD. If clinical feature of CLD and feature of decompensation was absent but ultra-sonographic changes were present/liver biopsy confirmed, were also considered as CLD.

Patients of CLD who had diabetes mellitus, nephrotic syndrome, thyroid dysfunction, hepatitis C virus positive, malabsorption, malignancy, HIV, chronic smokers, familial hyperlipidemia and those patients taking drugs which might affect Fasting Lipid Profile were excluded from the study. For exclusion of nephrotic syndrome, diabetes mellitus, thyroid dysfunction, hepatitis C virus infection- Urine R/M/E, FBS/RBS/2hr ABF, thyroid function test and Anti-HCV were done. Each hepatitis B virus positive CLD patient were assessed -S. Bilirubin, S. Albumin, PT with INR, S. Creatinine for Child-Pugh and MELD scoring.

First 103 patients of hepatitis B virus related CLD who were given an informed written consent and fulfilled the diagnostic criteria used for the diagnosis of CLD, were included in the study as case. Age and sex matched same number of healthy populations, might be patient's attendant or outside the hospital, who were HBsAg (ELISA) negative, were selected in the study as control. In both case and control, Fasting Lipid Profile was done for compare. Both groups were thoroughly informed about the aims, objectives and detail procedure of the study before included in the study. He/she was encouraged for voluntary participation and allowed freedom to withdraw from the study whenever like even after participation. Data was analyzed by SPSS-21. Statistical significance was determined at $p<0.05$.

Results

One hundred and three patients with hepatitis B virus positive CLD and 103 age and sex matched healthy controls were studied. In this study, 85.4% of patients were >40 years and 67% were in between 40-59 years, 76.7% were from Muslim ethnic back ground. Most of the patients were male (78.6%) and married (83.5%). Driver and business man (49.5%) & urban people (53.4%) were more affected. Most predominant clinical findings were anaemia (94.2%), leukonychia (79.6%), ascites (79.6%), scanty hair (75.7%) and splenomegaly (68.9%).

Table I

Biochemical parameters in study cases

Investigations	Mean	SD	Range
Serum Bilirubin (mg/dl)	2.7	1.9	0.8-9.9
Serum Albumin (gm/dl)	3.1	1.2	1.4-7.6
PT prolonged (seconds)	7.8	5.7	0-26
INR	1.7	0.5	1.0-3.4
Serum Creatinine (mg/dl)	1.6	0.6	0.7-3.9

PT=Prothrombin Time, INR=International Normalized Ratio; SD-Standard Deviation.

Mean+SD of Serum Bilirubin, Albumin, Creatinine Prothrombin time and INR were shown in Table I. The INR was calculated by the ratio of a patient's prothrombin time to a normal (control) sample, raised to the power of the ISI value. In this study, 103 HBV positive CLD patients were divided into Child-pugh A, Child-pugh B and Child-pugh C. Values of Serum Bilirubin, Albumin and Prothrom

bin time were gradually deteriorating according to the severity of liver damage (Table II).

Table II

Biochemical parameters in study cases according to Child-Pugh score

Score	n	%	Serum Bilirubin (mg/dl)	Serum Albumin (gm/dl)	PT prolonged (seconds)
Child A	16	15.5	1.3+0.4	5.0+1.7	1.9+1.2
Child B	36	35.0	1.6+0.4	3.1+0.3	4.7+1.3
Child C	51	49.5	3.8+2.1	2.4+0.5	11.7+5.6

Total 103 HBV positive CLD patients were also divided into MELD scores; MELD <10, 11< MELD<18, 19<MELD<24 and MELD>25. Values of Serum Bilirubin, INR and Serum Creatinine were gradually deteriorating according to the progression of MELD score (Table III).

Table III

Biochemical parameters in study cases according to MELD score

Score	n	%	Serum Bilirubin (mg/dl)	INR	Serum Creatinine (mg/dl)
MELD <10	14	13.6	1.3+0.4	1.2+0.1	0.9+0.1
11<MELD<18	35	34.0	1.6+0.4	1.5+0.1	1.3+0.2
19<MELD<24	43	41.7	2.9+0.8	1.9+0.4	1.6+0.4
MELD>25	11	10.7	6.8+2.7	2.5+0.6	2.9+0.8

MELD-Model for End-Stage Liver Disease.

Table IV

Comparison of lipid profile values in hepatitis B virus positive adult CLD patients (cases) with control group

Lipid profile (mg/dl)	Case N=103	Control N=103	Statistical Analysis Unpaired t test & Sig
TC	131.4+23.5	179.3+23.5	14.6, p<0.001
TG	139.2+23.8	146.6+28.9	2.0, p=0.047
LDL-C	72.5+17.7	109.6+19.1	14.5, p<0.001
HDL-C	31.0+8.2	40.4+6.2	9.3, p<0.001

TC=Total Cholesterol; TG-Triglyceride; LDL-C=Low Density Lipoprotein Cholesterol; HDL- C-High Density Lipoprotein Cholesterol.

All components of lipid profile were significantly decreased in case compared with control (Table IV).

Table V

Lipid profile variation in hepatitis B virus positive adult CLD patients according to Child-Pugh score

Lipid profile (mg/dl)	Child A N=16 15.5%	Child B N=36 35.0%	Child C N=51 49.5%	One way ANOVA F & p
TC	155.8+20.3	139.1+20.4	118.3+17.5	28.5, p<0.001
TG	144.9+20.1	146.7+25.5	132.1+21.9	4.8 p=0.009
LDL-C	88.3+13.7	78.7+11.9	63.3+17.0	21.6, p<0.001
HDL-C	38.6+27.4	31.1+19.3	28.6+6.0	10.8, p<0.001

ANOVA-Analysis of Variance

All components of lipid profile were significantly decreased with the deterioration of Child-pugh score (Table V). Here Triglyceride level was decreased only in advanced stage. All components of lipid profile were significantly decreased with the deterioration of MELD score (Table VI). Here Triglyceride level was also significantly decreased only in advanced stage.

Table VI

Lipid profile variation in hepatitis B virus positive adult CLD patients according to MELD score

Lipid profile (mg/dl)	MELD <10 N=14 13.6%	11<MELD<18 N=35 34.0%	19<MELD<24 N=43 41.7%	MELD>25 N=11 10.7%	One way ANOVA F & P
TC	159.2+19.3	140.4+19.5	120.8+17.8	109.0+11.8	24.5, p<0.001
TG	147.4+20.2	146.6+24.7	132.7+23.6	130.5+17.7	3.5, p=0.019
LDL-C	90.1+13.7	79.5+11.5	65.3+17.2	56.5+11.9	17.6, p<0.001
HDL-C	39.7+7.2	31.5+9.0	29.0+6.0	26.5+6.5	9.1, p<0.001

Discussion

In this study, CLD was seen predominantly in older age group with 85.4% of patients >40 years and 67% were in between 40 and 59 years of age. This may attribute to the delayed presentation of CLD due to their complications. The most affected age group was 50 to 59 years. It was discussed to quote

that few independent factors were associated with an increased rate of fibrosis eg. age at infection, older than 40 years, male sex etc.[10]

The value of serum total cholesterol was significantly lower in patients with CLD when compared to controls in this study. This observation was supported by some reports.[10-14] The probable explanation for the reduced serum total cholesterol was due to the decline in synthetic function and altered metabolism.[12]

Further comparison of the total cholesterol values in different Child Pugh and MELD scores showed a direct relation between the severity of liver damage and reduction in the cholesterol level and this was supported by few previous studies.[10.12-13] They suggested that Cholesterol fall as the disease advances. There was a significant decrease in levels of serum LDL in patients with CLD, when compared to controls ($p<0.001$) in this study. This was in accordance with many previous studies.[10,12-15] In a study, it was suggested that the LDL concentration was decreased in patients with chronic liver disease. As these patients 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.[15]

In this study, it was found that the reduction in the LDL level was proportionate to the severity of liver damage in CLD patients as detected by the Child Pugh and MELD scoring system. This was supported by many previous studies and in their studies, they showed that the amount of decrement in the serum LDL was significant with increasing severity of liver damage.[10,12,13,15] The level of serum HDL in this study, was significantly decreased in cases of CLD when compared to control ($p<0.001$) and inversely co-related with severity of liver damage, were consistent with some of publications on this subject.[12,15]

The serum triglyceride levels were significantly lower in cases of CLD than in control group ($p= 0.047$). This observation is in full agreement with some previous studies.[10,12] In a previous study, it was found that Triglyceride values showed a decline in CLD patients but it was not statistically significant. The poor nutrition, altered metabolism and abstinence from alcohol of CLD patients may explain the lower serum triglyceride in CLD patients.15 In some previous study, it was found that the level of reduction of the serum triglyceride was proportionate to the severity of the parenchymal liver disease.[12,13,15]

An interesting observation found in this study was overall Triglyceride level decrease marginally in CLD patients when compared to controls ($p=0.047$) and reduction observed in only advanced stage. This was also supported by a previous study. In this study, a significant difference was observed between patients and the comparison group in total cholesterol, LDL-C, HDL-C ($p<0.001$). This finding was consistent with observation that in severe liver disease as the liver function deteriorates, more decline was observed in total cholesterol, LDL-C, HDL-C. This finding was comparable in results with many studies, where they showed a progressive decline in the lipid levels with progression of liver disease.[10, 12-16]

This study is limited by several factors: it was conducted in a single tertiary care center, only HBV related CLD was included in this study and liver biopsy for histopathological severity was not done.

Conclusion

Low level of different lipid profile values exists in HBV positive CLD patients. Patients suffering from the disease should be investigated with fasting lipid profile especially with total cholesterol, LDL-C, HDL-C for diagnostic purpose and to see the severity of liver damage. New scoring system should be developed including fasting lipid profile values by further study.

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