ASSESSMENT OF CORRELATION BETWEEN ACUTE VIRAL HEPATITIS AND SERUM LIPID LEVELS

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BACKGROUND

As liver is an essential organ in lipid metabolism, several stages of lipid synthesis and transportation, it is reasonable to expect an abnormal lipid profile in those with severe liver dysfunction. There is prominent decline in plasma cholesterol and triglyceride (TG) in patients with severe hepatitis and hepatic failure because of reduction of lipoprotein biosynthesis. For reduced liver biosynthesis capacity, low levels of TG and cholesterol is usually observed in chronic liver diseases. This study was conducted to assess the correlation between acute viral hepatitis with serum cholesterol and serum triglyceride values.

METHODS

This case control study was, conducted among 30 presumptive cases of acute viral hepatitis, who were admitted under the department of general medicine, KIMS, Karad, during the period of October 2015 to March 2017. Probable cases of acute viral hepatitis having clinical symptoms suggestive of hepatitis or liver, consistent with Acute Viral Hepatitis, and those cases that were sero-positive for either Hepatitis-A, -B, -C or -E were included in the present study. Similar number of controls (n=30) was selected in the present study. All the controls were matched for non-modifiable risk factors such as age and gender.

RESULTS

In this study, in patients with acute viral hepatitis in the acute phase, the mean total cholesterol was 169.700 ± 33.225 , which was lower in cases than controls. Mean triglyceride was 151.066 ± 53.677 , which was higher in cases than controls. The mean total cholesterol in cases was $32.730 (\pm 37.863)$ mg/dl and mean value of triglyceride was $+ 29.933 \pm 75.019$ mg/dl.

CONCLUSIONS

There is a significant decrease in mean total cholesterol in acute phase, while the mean triglyceride value was statistically significantly higher during acute phase of viral hepatitis compared to controls.

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BACKGROUND

Liver is the most important organ for the metabolism of lipids, lipoproteins and apolipoproteins. Under normal circumstances, most plasma endogenous lipids & lipoproteins are synthesized in liver and then are secreted into the blood circulation.^{[1,2],[3]} According to previous researches, chronic liver disease with dysfunction interfere with lipid metabolism and it may alter plasma lipid and lipoprotein levels.^[4]

Acute hepatitis may be defined by an inflammatory process of the liver persisting for less than six months. Hepatitis 'C' virus (HCV) belonged to genus Hepacivirus, hepatitis B virus (HBV) or HCV accounts approximately 78 % of hepatocellular carcinoma (HCC).^{[1],[2]} As liver plays an important role in lipid metabolism, several stages of lipid synthesis and transportation. Therefore, it is reasonable to expect an abnormal lipid profile in those with severe liver dysfunction.

'Financial or Other Competing Interest': None. Submission 01-01-2019, Peer Review 10-04-2019, Acceptance 16-04-2019, Published 22-04-2019. Corresponding Author: Dr. Pavan D. Patel, Department of Medicine, Krishna Institute of Medical Sciences, Karad, Satara-415110. Maharashtra, India. E-mail: researchexpert3@gmail.com DOI: 10.14260/jemds/2019/296 There is prominent decline in plasma cholesterol and triglyceride (TG) levels in patients with severe hepatitis and hepatic failure because of reduction of lipoprotein biosynthesis. For reduced liver biosynthesis capacity, low levels of TG and cholesterol is usually observed in chronic liver diseases.

In clinical, the course of acute hepatitis may vary from mild symptom that does not require treatment to the fulminant hepatic failure that needs emergency liver transplantation. Acute viral hepatitis is more common to be asymptomatic in younger people. In addition, acute hepatitis may occur less commonly with infections such as Epstein-Barr virus, cytomegalovirus, adenovirus, herpes simplex and Coxsackie virus or with other non-infectious reasons. It is been demonstrated that in the acute and/or chronic liver diseases, hepatic function could be altered, and the lipids & lipoproteins are not only present in abnormal amounts but they frequently also have abnormal composition including electrophoretic mobility and appearance.

Some researchers also found relationships between Hepatitis C and serum lipid levels. According to them, Lower serum cholesterol and LDL levels are found in patients infected with hepatitis C when compared with patients with hepatitis B or without infection). Recent studies have shown that chronic hepatitis C infection is associated with decrease in cholesterol and LDL when compared with matched control subjects. The present study was conducted to assess the correlation between acute viral hepatitis with serum cholesterol level and serum triglyceride values.

METHODS

It was a case control study, conducted among 30 presumptive cases of acute viral hepatitis, who were admitted under medicine department, KIMS, Karad during the period of October 2015 to March 2017. The study was conducted after the clearance from institutional ethical committee.

Probable cases of acute viral hepatitis having clinical symptoms suggestive of hepatitis or liver consistent with Acute Viral Hepatitis, AND those cases that were seropositive for either Hepatitis-A, B, C or E admitted under department of medicine were included in the present study. Similar number of controls (n=30) were selected in the present study. All the controls were matched for non-modifiable risk factors such as age, gender.

With reference to the study conducted by Shweta et al, among cases of hepatitis, they observed mean SGOT values among cases as 495±115, and among controls 578±90. Using above reference values, at 95% confidence interval, and 90 power the sample size of 27 was calculated. Hence, we took 30 cases and 30 controls for the given study. All the study subjects were included after taking their consents.

Inclusion Criteria

Cases

30 Probable cases of acute viral hepatitis with clinical symptoms suggestive of hepatitis or liver consistent with Acute Viral Hepatitis, and those cases that were sero-positive for either Hepatitis-A, B, C or E, admitted under department of medicine, in a hospital were selected randomly (simple random sampling) and included in the present study.

• Probable Case of Acute Viral Hepatitis

Symptoms (Anorexia, Nausea, Vomiting, Alteration of taste, Arthralgia, Malaise in Prodromal phase. Dark urine, Pale colour stool, Prostration, Yellow eyes, Abdominal pain and Pruritus in Icteric phase) and Liver consistent with Acute Viral Hepatitis.

• Recovering Phase of Acute Viral Hepatitis

Absence of constitutional symptoms like anorexia, nausea, vomiting, fatigue, malaise and arthralgia. All the patients were enrolled after written and informed consent. Detailed history was taken. Thorough general and systemic examination was carried out. All findings were recorded in the Patient's Proforma. Investigations, as mentioned in the Patient's Proforma, were carried out on admission and during recovering phase of acute viral hepatitis. Fasting serum lipid profile levels of study group were compared with controls two times, once during the acute phase and then in the recovering phase of viral hepatitis.

Controls

30 healthy controls, without any clinical symptoms or liver function suggestive of acute viral hepatitis and sero-negative for hepatitis A, B, C, or E, were selected in the present study. All the controls were matched for non-modifiable risk factors such as age, gender. All the controls were selected randomly from the outpatient department under the department of medicine.

Statistical Methods

Statistical Methods Results on continuous measurements are presented on Mean± standard deviation and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. Student t test has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. SPSS 15.0 was used for the analysis of the data and Microsoft word and Excel have been used to generate tables, graphs etc.

RESULTS

The present study is conducted among 30 probable cases of acute viral hepatitis admitted under the department of general medicine, KIMS, Karad. In this study, age of patients was ranging from 21-70 years. The maximum incidence of acute viral hepatitis was in 3rd decade (50%). Age group distribution was almost equal in both groups. Average age of the patients was 35.5(±13.89) years in this study. Out of 30 both among cases and controls, 22 (73.3%) were male and 08 (26.6%) were female. Sex distributions in case and control groups were comparable. (Table 1) (Figure 1)

In this study, HEV infection in 73.3% (22) cases was found to be the most common viral infection followed by 13.3 % (04) HAV infection, 6.66 % (02) HBV infection, and 6.66 % (02) HCV infection (Table 2). In this study, the majority of the cases presented with nausea/vomiting and dark yellow urine 86.6% (26) cases, followed by anorexia and icterus were in 83.3% (25) cases, abdomen pain was in 60% (18) cases, fever was in 53.3% (16) cases, hepatomegaly was in 36.6% (11) cases and pruritus was in 23.3.% cases. There was no splenomegaly in any cases. P-value \leq 0.05 was considered significant.

In this study in patients with acute viral hepatitis at time of acute phase, the value of Mean total cholesterol was 169.700 (\pm 33.225), which was lower in cases than controls. While mean triglyceride was 151.066 \pm 53.677, which was higher in cases compared to controls. The mean values of total cholesterol in cases was 32.730 \pm 37.863 mg/dl and mean value of triglyceride was + 29.933 \pm 75.019 mg/dl.

In our study, among the cases, mean total cholesterol was lower in acute phase than recovering phase. The mean difference in total cholesterol was 27.266 mg/dl, it was not found to be significant. Similarly, the mean triglyceride level was higher during acute phase of disease than recovering phase of disease. The difference in mean triglyceride was 10.200 ± 42.966 , and it was also found to be non-significant.

In this study, out of 30 patients of acute viral hepatitis, 13.3% (4) were developed bleeding from gums or bleeding per rectum which was the most common complication of acute viral hepatitis, followed by hepatic encephalopathy in 6.6% (2), fulminant hepatic failure in 6.6% (2), and hepatorenal syndrome in 3.3%% (1) cases. In this study, Total cholesterol was lower among the complicated cases than uncomplicated cases of acute viral hepatitis. Mean triglyceride was increased in complicated cases while compared to uncomplicated cases.

Sex	Cases No (%)	Controls No. (%)			
Male	22 (73.3%)	22 (73.3%)			
Female	08 (26.7%)	08 (26.7%)			
Total	30(100%)	30(100%)			

Table 1. Sex Distribution of Cases and Controls

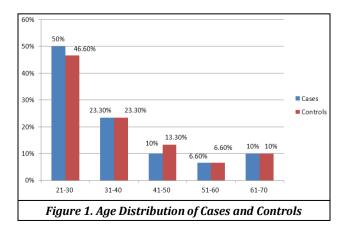
Clinical Presentation	No. of Cases	Percentage (%)	
Anorexia	25	83.3 %	
Nausea/Vomiting	26	86.6 %	
Fever	16	53.3 %	
Icterus	25	83.3 %	
Yellow Urine	26	86.6 %	
Abdominal Pain	18	60.0 %	
Pruritus	07	23.3 %	
Hepatomegaly	11	36.6 %	
Splenomegaly	00	00 %	

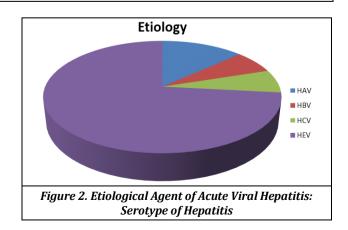
Table 2. Clinical Manifestations of Patients with Acute Viral Hepatitis

Variables		Mean Total Cholesterol (mg/dl)	Mean Triglycerides (mg/dl)	p Value
Comparison of Serum lipid levels in acute phase of hepatitis with controls	Cases-acute phase	169.70 ± 33.22	151.06± 53.67	0.001
	Controls	202.43 ± 31.31	121.13 ± 42.26	0.024
	Differences(mean of lipid in case - lipid in control group)	-32.73 ± 37.86	29.93± 75.01	0.004
	Acute phases	169.70 ± 3.22	151.06 ± 53.67	0.001
Serum lipid levels in cases acute	Recovering phases	196.96 ± 48.85	140.86 ± 29.23	0.018
phase of hepatitis	Differences	-27.26 ± 52.17	10.20 ± 42.96	0.016
Complicated Vs Uncomplicated viral hepatitis	Complicated viral hepatitis	160.25±10.21	160.25 ± 8.71	0.017
	Uncomplicated viral hepatitis	171.15 ±35.37	149.65 ±56.09	0.022
Aetiology	HAV	166.5 ± 38.55	154.5 ± 61.59	0.014
	HBV	155.5 ± 38.02	135.0 ± 84.12	0.001
	HCV	196.5 ± 36.81	128.5 ± 13.94	0.004
	HEV	169.13 ± 33.22	153.95 ± 53.67	0.012
Hospital stay	Patients who required hospital stay ≤7 days	174.20 ± 35.37	152.16 ± 56.09	0.023
	Patients who required hospital stay >7 days	151.66 ± 28.56	146.66 ± 27.69	0.004

Table 3. Comparison of Various Clinical Parameters with Triglycerides and Cholesterol Mean Values

Lipid Present Study		Bhattacharya et al ^[128]		Abbas al-Tamimi et al [127]		p Value	
Parameter	Cases	Controls	Cases	Controls	Cases	Controls	
Mean total cholesterol (mg/dl)	169.700 ± 33.225	202.430 ± 31.313	228.84 ± 31.34	90.68 ± 24.19	148.36 ± 42.26	215.34 ± 75.85	0.024
Mean triglycerides (mg/dl)	151.066 ± 53.677	121.133 ± 42.266	164.6 ± 70.82	111.18 ± 24.15	254.86 ± 120.8	247.04 ± 135.3	0.014
Table 4. Correlation of Complications of Acute Viral Hepatitis with Lipid Parameters							





DISCUSSION

The present study is conducted among probable cases of acute viral hepatitis, with an objective to study clinical presentations of various acute viral hepatitis (viz. Hepatitis A, B, C, D and E), and hence to correlate the diagnosis with liver profile levels. In this study we enrolled total 30 cases and 30 controls, who were matched for age, gender and risk factors. Mean age for these cases was 35.50 ± 13.89 years and in controls it was 35.86 ± 13.66 years. The mean ages are comparable between the cases and control groups. In a study by Abbas al-Tamimi et al,^[5] total number of cases were 63 and the mean age in cases was 30.3 years and in controls it was 36.16 years which can be compared to our study. In the Bhattacharya et al^[6] study, total 100 subjects were studied (50 cases, 50 controls). The mean age in cases was 25.68 vears while in controls it was 24.2 years (Table 5). In our study, out of 30 cases, 73% cases were male, while 27% were female, while in Bhattacharya^[6] study 48% cases were male, and 52% cases were female.

In this present study, the more common clinical manifestations were nausea/vomiting and dark yellow urine which were present in 86.6% (26) cases, followed by anorexia and icterus were in 83.3% (25) cases, abdomen pain was in 60% (18) cases, fever was in 53.3% (16) cases, hepatomegaly was in 36.6% (11) cases and pruritus was in 23.3% cases. There was no splenomegaly in any cases. Most common symptoms in Bhattacharya et al^[6] were jaundice and yellow coloured urine –were present in all (100%) cases followed by anorexia in 90% cases, hepatomegaly in 72% cases, nausea/vomiting and fever in 70% cases, abdomen pain in 30% cases and pruritus in 20% cases (Table 4).

Mean total cholesterol level in our study during acute phase of viral hepatitis, was 169.700± 33.225 mg/dl, whereas it was 228.84 ± 31.34 mg/dl in the Bhattacharya [6] study and 148.36±42.26 mg/dl in the Abbas al-Tamimi^[5] study. Among the controls mean total cholesterol was 202.430 ± 31.313 mg/dl in our study whereas it was 90.68 ± 24.19 mg/dl in the Bhattacharya study^[6] and 215.34±75.85 mg/dl in the Abbas al-Tamimi^[5] study. In our study, mean total cholesterol was lower in acute phase of viral hepatitis, which was same as in Abbas al-Tamimi^[5] study. While in Bhattacharya^[6] study mean total cholesterol was higher in acute phase. Mean serum total cholesterol level in complicated cases was 160.25 ± 10.210 mg/dl which was lower than uncomplicated cases, contrary to the Bhattacharya et al^[6] study. Our study showed that there is no significant change in serum total cholesterol levels among acute phase and among controls.

Mean triglycerides level in this study among cases during acute phase of viral hepatitis, was $151.066 \pm 53.677 \text{ mg/dl}$, whereas it was $164.6 \pm 70.82 \text{ mg/dl}$ in the Bhattacharya ^[6] study and $254.86 \pm 120.8 \text{ mg/dl}$ in the Abbas al-Tamimi^[5] study. Among the controls, mean triglycerides was $121.133 \pm$ 42.266 mg/dl in this study whereas it was 111.18 ± 24.15 mg/dl in the Bhattacharya study^[6] and $247.04 \pm 135.3 \text{ mg/dl}$ in the Abbas al-Tamimi ^[5] study. Thus, in our study, triglycerides were higher in acute phase, which was same as Bhattacharya ^[8] study Abbas al-Tamimi ^[5] study. Mean serum triglyceride level in complicated cases was 160.25 ± 38.715 mg/dl which was higher than uncomplicated cases, same as the Bhattacharya et al^[6] study. Our study showed that there is no significant change in serum triglyceride levels among acute phase and among controls. The significant decline in the serum total cholesterol and TG levels in cirrhotic patients compared with healthy people has been confirmed earlier in other studies, which is reasonably expected since liver biosynthesis has been reduced. For instance, the same results were obtained in a study by Mehbob I, et al^[7], in 2007, who studied 160 patients with chronic liver diseases. There were significant declines in the serum total cholesterol and TG levels of patients. Another study in Greece was performed by Siagris^[8] 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.

In this study, out of 30 patients of acute viral hepatitis, 13.3% (4) developed gum bleeding or per rectum bleeding which was the most common complication of acute viral hepatitis, followed by hepatic encephalopathy in 6.6% (2), fulminant hepatic failure in 6.6% (2), and hepato-renal syndrome in 3.3%% (1); while Bhattacharya et al^[6] study, most common complication was hepatic encephalopathy present in 6% cases, followed by GI bleed and fulminant hepatic failure in 4% cases.

In our study, HEV infection in 73.3% (22) cases were found to be the most common viral infection followed by 13.3 % (04) HAV infection, 6.66 % (02) HBV infection, and 6.66 % (02) HCV infection; while in Bhattacharya study^[6] HEV infection in 30% cases were found to be most common viral infection followed by HAV in 25%, HBV in 14% and HCV in 4% cases.

There was no correlation found in any lipid profile parameters in the study during acute phase in relation to etiological agent of viral hepatitis.

CONCLUSIONS

In acute phase of viral hepatitis, there is a significant decrease in mean total cholesterol levels, while the mean triglyceride is higher in acute phase. Mean total cholesterol levels were lower in this study in the acute phase than recovering phase of viral hepatitis. Lipid parameters were deranged in acute viral hepatitis as compared to controls, more deranged in acute phases of acute viral hepatitis than recovering phases of viral hepatitis and in complicated cases, as compared to uncomplicated cases, so we can use serum lipid profile as a prognostic marker in acute viral hepatitis.

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