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Changes in Serum Lipid Profile among Patients Suffering from Chronic Liver Disease Secondary to Hepatitis C

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Abstract

Objective: To find out the changes in lipid metabolism among patients suffering from chronic liver disease secondary to hepatitis C. **Study Design:** Hospital based observational study. **Setting:** Medical Unit-I, Ward-5, Jinnah Postgraduate Medical Centre, Karachi. **Duration:** July 2013 to December 2013. **Patients and Methods:** About 110 patients admitted in Medical Unit-I with a diagnosis of chronic liver disease were included in the study. Patients suffering from DM, HTN, CKD were excluded from the study. Fasting lipid profile was done in all cases. **Results and Observations:** There were 44 (40%) male and 66 (60%) female patients. Mean age of the patients was 50.18 (± 11.7) years. Total cholesterol was decreased in 76 (69.09%) patients. Normal range was present in 34 (30.91%) patients. None of the patient had hypercholesterolemia. Serum triglyceride levels were low in 14 (12.72%) patients, normal in 82 (74.54%), borderline high in 7 (6.36%) and hypertriglyceridemia was seen in 7 (6.36%). HDL-c was below normal in 26 (23.63%) cases, normal in 78 (70.91%), and high in 6 (5.45%). LDL was near optimal/above optimal in only 5 (4.5%) patients. Mean TC/HDL ratio was 2.53 (± 1.02). Mean LDL/HDL ratio was 1.23 (± 0.73). Mean TC of HCV +ve patients was 130.5 mg/dl as compared to that of HCV -ve patients which was 82.85 mg/dl (P-value: 0.011). Mean TGs of HCV +ve group was 151.5 mg/dl while that of HCV -ve was 79.9 mg/dl (P-value: 0.025). Mean HDL & LDL levels were 43.67 mg/dl and 39.78 mg/dl in HCV group while 34.83 mg/dl & 64.67 mg/dl in the other group with P-value of 0.026 and 0.081 respectively. **Conclusion:** When it comes to its relationship with lipid metabolism, HCV is a remarkable virus. Its interaction with lipoproteins and its ability to induce massive steatosis are quite unique and idiosyncratic. Despite of causing hepatic steatosis,

chronic HCV infection is associated with a paradoxically favorable lipid profile, although its reason cannot be enlightened precisely. There is a need for very well settled molecular and genetic studies to well understand HCV infection and lipid metabolism.

Keywords

Dyslipidemia, Hepatitis C, Chronic Liver Disease

1. Introduction

Hepatitis C is a worldwide problem. The hepatitis C virus is a major cause of both acute and chronic hepatitis. An estimated population of more than 185 million worldwide was infected with hepatitis C virus in 2005, making a prevalence of 2.8% [1] [2]. Hepatitis C is divided into six distinct genotypes throughout the world with multiple subtypes in each genotype class. Among them, genotypes 1, 2, and 3 appear to have a worldwide distribution and their relative prevalence varies from one geographic area to another. HCV subtypes 1a and 1b are the most common genotypes in the United States [3]. These subtypes also are predominant in Europe. The predominant HCV genotype in Pakistan is type 3a followed by 3b and 1a [4].

Many authors had made efforts to find out the interaction between chronic hepatitis C virus and lipid metabolism [5] [6]. Several important interactions were noticed. First, host serum lipid has a role in the entry of hepatitis C virion in liver cells and its circulation in blood. A fraction of circulating hepatitis C viral particles makes lipovirions on assimilation with host lipoproteins [7], and uses LDL receptors to get entered in hepatocytes [8]. After entering into the hepatocytes, the replication of HCV virion is again dependent on host lipid interactions. New hepatitis C virion formation requires viral binding to either an endoplasmic reticulum phospholipid membrane or an endoplasmic reticulum-associated membranous web [9].

HCV reproduction may produce effects similar to those observed with HMGCR inhibitors. Intrahepatic cholesterol synthesis is affected by HCV through two possible pathways; first, it may shunt geranylpyrophosphate, out of the mevalonate pathway, decreasing the quantity of this necessary intermediate available for cholesterol synthesis. Second, it may divert cholesterol to the synthesis of intracellular membranes that are necessary for the viral replication complex. The net effect of these diversions is the decrease of available cholesterol for physiologic intracellular processes and for peripheral delivery via VLDL, ultimately resulting in decreased serum cholesterol levels. The decrease in available intracellular cholesterol may also lead to an increase in LDL receptors and intrahepatic LDL. This increase in LDL uptake may account for the decreased serum LDL levels in HCV infection [9]. Also the metabolic processes which are associated with viral replication may be associated with a drop in triglycerides levels [10] [11].

2. Materials and Methods

This study was carried out in the Department of Medicine, Medical Unit-I, Ward-5, Jinnah Postgraduate Medical Centre, which is a tertiary care public sector hospital in Karachi, Pakistan with four medical units where around 4000 patients are admitted annually in each unit. About 110 patients were consecutively enrolled from July 2013 to December 2013. The patients included were suffering from chronic liver disease. Most of the patients belong to class B and C of Child Pugh's Classification. **Table 1** refers the child Pugh's classification. Study was approved by research ethics committee (REC) of the institute and all patients gave informed written consent.

2.1. Exclusion Criteria

1. Patients with hepatitis B infection or any other chronic liver disease..
2. Patients consuming alcohol or on lipid lowering medications.
3. The body mass index of $>30 \text{ kg/m}^2$.
4. The patients suffering from concomitant illnesses like diabetes mellitus, hypertension, chronic kidney disease or thyroid problem.

All patients in this study were subjected to:

1. Full medical history and examination.
2. Liver function tests (total plasma proteins, serum albumins, SGOT, SGPT, total and direct serum bilirubin, alkaline phosphatase and prothrombin time).
3. Lipid profile: Fasting cholesterol, low density lipoproteins (LDL), high density lipoproteins (HDL), and triglycerides.
4. Kidney functions tests (serum urea and creatinine).
5. Random blood glucose level and electrolytes.
6. Complete blood count.
7. Anti HCV antibody.
8. Thyroid function test.

Table 1. Child Pugh's classification.

Clinical and Lab criteria	Points		
	1	2	3
Encephalopathy	None	Mild to moderate (Grade 1 or 2)	Severe (Grade 3 or 4)
Ascites	None	Mild to moderate (Diuretic responsive)	Severe (Diuretic refractory)
Bilirubin (mg/dl)	<2	2 - 3	>3
Albumin	>3.5	2.8 - 3.5	<2.8
Coagulation			
PT (seconds prolonged)	<4	4 - 6	>6
Or			
INR	<1.7	1.7 - 2.3	>2.3

Child Turcotte-Pugh class (obtained by adding score of each parameter) [12] [13]. Child A (5 - 6): Mild disease; Child B (7 - 9): Moderate disease; Child C (10 - 15): Severe disease.

9. Abdominal ultrasound.
10. Body mass index (BMI) (weight in kilogram/height in cubic meter).

2.2. Operational Definitions

Levels of triglycerides and total, LDL & HDL cholestrols were defined according to ATP III classification as shown in **Table 2**.

2.3. Data Management

Statistical analysis was done using SPSS statistical package version 19 and results were got as mean \pm standard deviation (mean \pm SD). For statistical analysis, independent sample t test was used and the relation between variables was examined with Pearson correlation. $P < 0.05$ value was accepted meaningful statistically.

3. Results

There were 44 (40%) male and 66 (60%) female patients. Mean age of the patients was 50.18 (\pm 11.70) years. Most of the cases belonged to middle age group. Age and gender distribution of the 110 patients included in the study is shown in **Figure 1** & **Figure 2**, while **Figure 3** shows prevalence of HCV among study patients. **Table 3** summarizes the laboratory parameter of patients included in study along with their child and MELD scores which were comparable in the two groups.

In our group of study, total cholesterol was decreased in 76 (69.09%) patients while

Table 2. ATP III classification of triglycerides and total, LDL & HDL cholestrols (mg/dl) [14] [15] [16].

	Range	Interpretation
Triglycerides	<150	Normal
	150 - 199	Borderline high
	200 - 499	High
	>500	Very high
Total Cholestrol	<200	Desirable
	200 - 239	Borderline high
	>240	High
LDL Cholestrol	<100	Optimal
	100 - 129	Near optimal
	130 - 159	Borderline high
	160 - 189	High
	>190	Very high
HDL Cholestrol	<40	Low
	40 - 60	Optimal
	>60	High

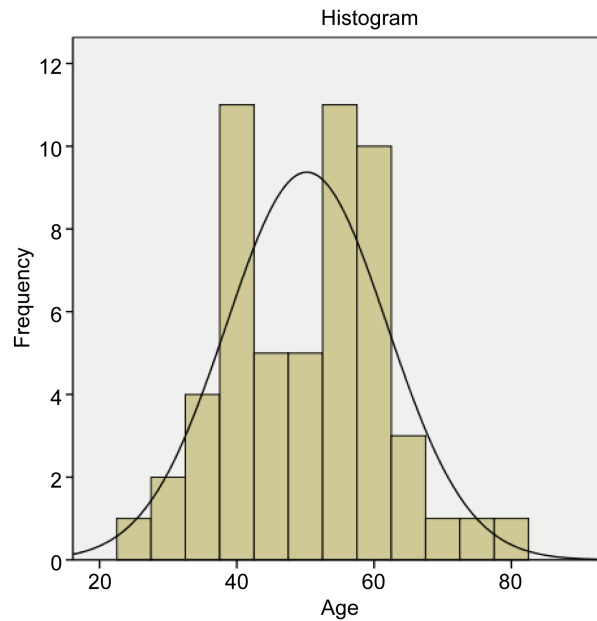


Figure 1. Histogram showing age frequency of patients included in study.

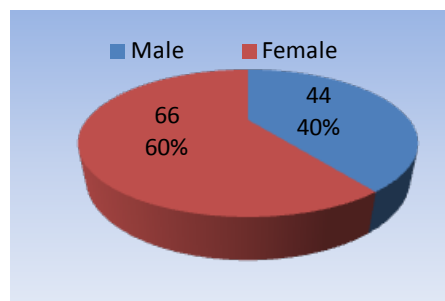


Figure 2. Gender distribution of patients included in study.

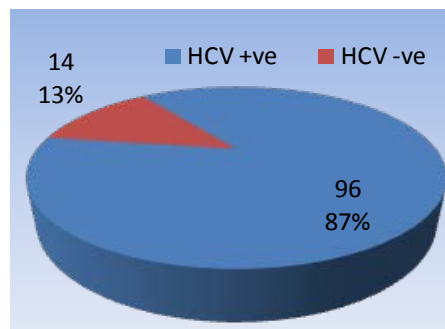


Figure 3. Prevalence of hepatitis C among study group.

normal range was present in 34 (30.91%) patients. None of the patient had hypercholesterolemia.

Serum triglyceride levels were low in 14 (12.72%) patients, normal in 82 (74.54%), borderline high in 7 (6.36%) and hypertriglyceridemia was seen in 7 (6.36%). HDL-c

Table 3. Laboratory parameters of patients enrolled in study.

	<i>HCV -ve</i>	<i>HCV +ve</i>	<i>P-value</i>
Gender (Male)	14 (50%)	32 (39%)	NA
Age	40.00 (\pm 11.40)	51.46 (\pm 11.34)	0.057
Hemoglobin (mg/dl)	8.88 (\pm 2.36)	8.11 (\pm 2.25)	0.477
Platelets	144.67 (\pm 90.09)	90.49 (\pm 50.50)	0.204
Creatinine (mg/dl)	2.08 (\pm 1.89)	1.15 (\pm 0.63)	0.284
Total Bilirubin (mg/dl)	3.5 (\pm 5.74)	3.7 (\pm 4.13)	0.963
Serum Albumin (mg/dl)	2.4 (\pm 0.73)	3.67 (\pm 4.67)	0.124
INR	1.33 (\pm 0.20)	1.64 (\pm 0.64)	0.025*
CTP score	8.6 (\pm 1.67)	9.04 (\pm 2.13)	0.606
MELD	17.80 (\pm 8.075)	16.18 (\pm 6.725)	0.685

NA: Not applicable; *Significant P-value.

was below normal in 26 (23.63%) cases, normal in 78 (70.91%), and high in 6 (5.45%).

LDL was near optimal/above optimal in only 5 (4.5%) patients. Mean TC/HDL ratio was 2.53 (\pm 1.02). Mean LDL/HDL ratio was 1.23 (\pm 0.73). When compared, there was significant difference among patients who were HCV positive vs HCV negative patients in terms of total cholesterol [82.85 mg/dl vs 130.5 mg/dl (p-value 0.011)], triglycerides [79.09 mg/dl vs 151.5 mg/dl (p-value 0.025)], HDL cholesterol [43.67 mg/dl vs 34.83 mg/dl (p-value 0.026)], TC/HDL ratio [2.23 vs 3.89 (p-value 0.030)], however difference between LDL cholesterol and LDL/HDL ratio between the two groups was not significant as shown in **Figure 4**.

4. Discussion

Dyslipidemia is a frequent finding in chronic liver disease and HCV. Internationally this subject has been dealt in detail. But to the best of our knowledge no study was done for dyslipidemia in chronic liver disease secondary to HCV in Pakistan. So it was aimed to contribute to the literature through this study.

When it comes to its relationship with lipid metabolism, HCV is a remarkable virus. Its interaction with lipoproteins and its ability to induce massive steatosis are quite unique and idiosyncratic. In addition, HCV infection is generally associated with glucose tolerance disorder or diabetes and both these two situations are closely related with steatosis. Due to these two situations, HCV infection can be related with lipid metabolism indirectly.

Although changed serum lipid is commonly found in patients with chronic liver disease of any etiology, the relationship between HCV and lipid metabolism seems to be more specific.

Fernandez-Rodriguez *et al.* [17] documented in their study that Hepatitis C genotype 3 chronic liver diseases is associated with serum lipid changes and these changes are

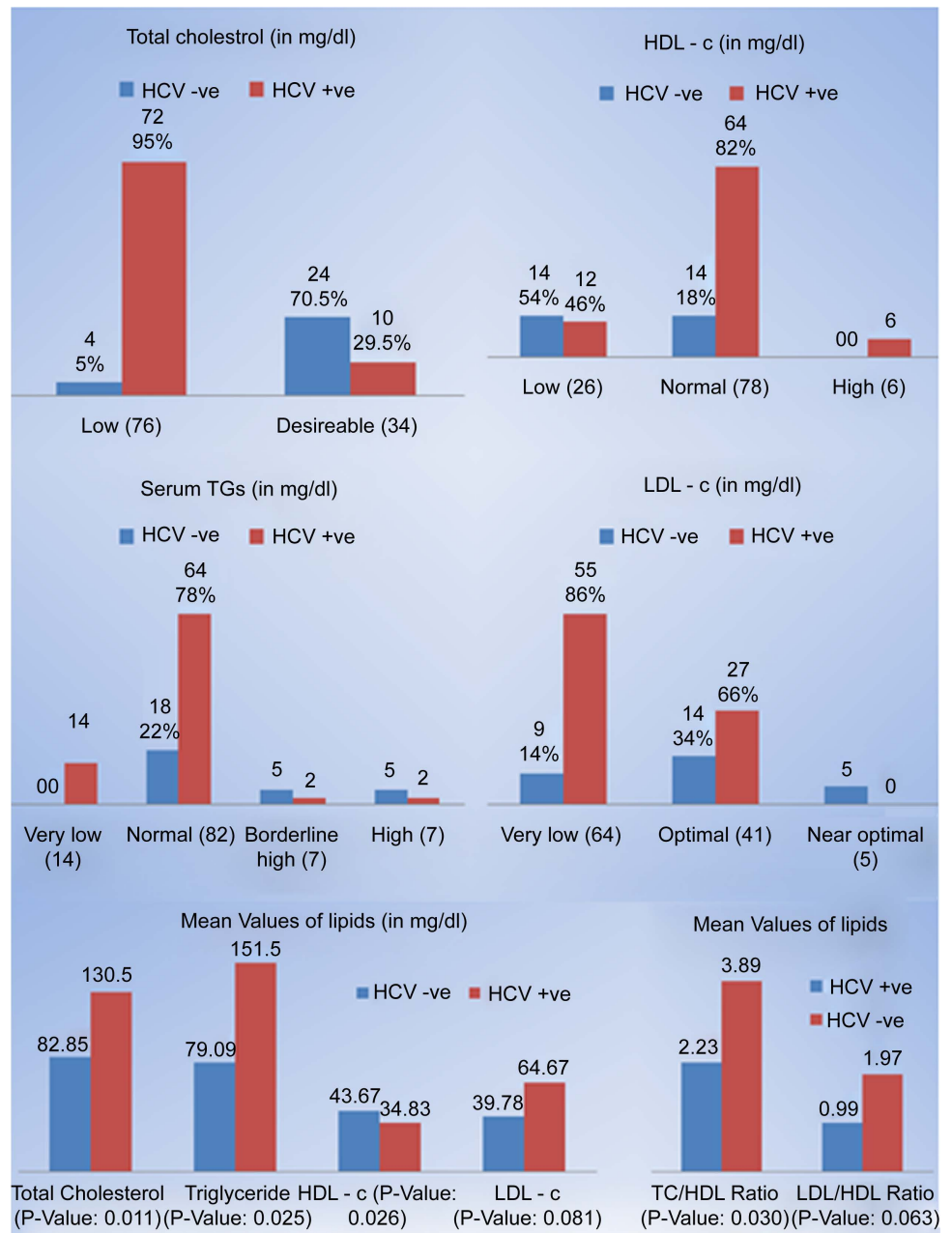


Figure 4. Comparison of lipids among patients with hepatitis C Vs non hepatitis C CLD.

reversible with sustained viral response. This interference with lipid pathway is related to viral load.

Patients in the HCV Group had significantly lower total cholesterol and LDL-c levels than the HCV negative control group, (P: 0.011 and 0.081 respectively). These results agree with Fabris *et al.* [5], Serfaty *et al.* [6], Marzouk *et al.* [11], Floris-Moore *et al.* [18], Corey *et al.* [19], Ehab H Nashaat [20], Mustafa Güçlü [21], and Mahmoud A. Khattab, 2012 [22], who observed that frequency of hypocholesterolemia in noncirrhotic HCV-infected patients was five times higher than in their reference population.

Also patients in the HCV group had significantly lower triglycerides levels when compared to the uninfected control group ($p = 0.025$). These results agree with Perlemuter *et al.* [10], Marzouk *et al.* [11], Ehab H Nashaat [20], and Mahmoud A. Khattab [22], which refers this drop to the metabolic processes associated with viral replication. But these results disagree with Corey *et al.* [19] and Mustafa Güçlü [21], who did not found significant difference as regard triglycerides between patients and controls.

HDL levels were also statistically significant between the HCV group and uninfected controls ($p = 0.026$). These results agree with Mahmoud A. Khattab *et al.* [22], but disagree with Corey *et al.* [19], Ehab H. Nashaat [20], and Mustafa Güçlü *et al.* [21].

Smaller sample size and unequal number of patients in the two groups due to consecutive sampling seems to be potential limitation of our study which actually reflects the commonest cause of CLD in our population. A larger study with good number of Non HCV CLD patients may overcome this limitation.

5. Conclusion

When it comes to its relationship with lipid metabolism, HCV is a remarkable virus. Its interaction with lipoproteins and its ability to induce massive steatosis are quite unique and idiosyncratic. Despite of causing hepatic steatosis, chronic HCV infection is associated with a paradoxically favorable lipid profile, although its reason cannot be enlightened precisely. There is a need for very well settled molecular and genetic studies to well understand HCV infection and lipid metabolism.

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