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Lipid Staus in Patients with Chronic Hepatitis C Before & After Interferon Based Therapy

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Conflicts of Interest: Nil

Abstract

Objective: To determine the lipid status in patients with chronic Hepatitis C before and after interferon based treatment.

Method: ***Type of Study:-*** Descriptive case series.

Place of Study:- Out patients department of hepatitis control program medical unit III at Liaquat University Hospital Jamshoro.

Duration of Study:- 1st Feburary 2015 to 31st Jannuary 2016.

Total 90 patients with chronic hepatitis C were included in this study through descriptive purposive sampling. The lipid profile was assessed pre and post treatment.

Results: Of 90, 46 (51.1%) were males and 44(48.8%) were females. Pre-treatment 76 (84.4%) of patients have dyslipidemia from which, male were 44(57.8%) and female were 32(42.1%). Post treatment normal lipids were observed in 52/76 (68.4%) and the remainder 24/76 (31.5%) had insistent lipid. The pre-treatment laboratory values of cholesterol, LDL, HDL and triglycerides represented as mean±SD were 272.75±21.83, 160.44±37.93, 62.82±9.09 and 273.4±53.14 while post treatment values were 227.74±10.72, 107.62±8.53, 42.85±6.72 and 172.76±9.84 respectively. The major pre-treatment dyslipidemia was decrease in components of lipid profile such as 70% have <200mg/dl cholesterol, while ↓LDL, ↓HDL and ↓triglycerides were observed in 71.4%, 66.6% and 80% whereas significant improvement in these values were observed post treatment.

Conclusion: The lipid profile can play a vital role as a treatment monitoring tool because the pre treatment laboratory values shows a significant improvement post treatment.

Keywords: Chronic HCV, Interferon, Lipid profile

Introduction

Hepatitis C, particularly its genotype 3 imparted a significant health burden on our country Pakistan. The strong association has been seen between between hepatitis C and lipid metabolism. [1,2] Lipids play crucial role in viral entry in patient's liver cells. Few viral particles are attached to triglycerol rich lipoprotein called lipoviral particles. [3] Those particles enter liver cell through LDL receptor and their level signifies high infectivity rate. [4]

Besides, HCV replication in hepatocyte also depends on its interaction with lipids of host. Newly formed viron has to bind to the endoplasmic reticulum, cell membrane or to the membranous web associated with endoplasmic reticulum.[5] Replication of HCV can potentially decreased cholesterol synthesis through two different mechanisms. First it shunts Geranyl pyrophosphate out of Mevalonate pathway so decreasing an important substrate

for cholesterol synthesis. Second it consumes cholesterol for production of membrane necessary for HCV replication. so the net effect is decreased intracellular cholesterol resulting in increased LDL receptor and decreased serum LDL, decreased peripheral delivery of cholesterol via VLDL. [6] HCV replication also decreases serum triglyceride level [7,8] So HCV viral clearance can potentially raise or normalize serum lipids.

The purpose of this study is to prove this association and prove interferon based therapy have a as positive influence of lipid profile which will help in the assessment of prognosis.

Material & Methods

This was a descriptive case series study conducted at Liaquat University Hospital Jamshoro and Hyderabad from 1st February 2015 to 31st January 2016. Using nonprobability consecutive sampling technique a sample size of 90 were selected using RAOSOFT software with 95% CI and 5% error margin.

Patients with chronic Hepatitis C of either gender seeking treatment for the first time were enrolled after written informed consent while patients with cirrhosis of liver, liver cancer, co infections such as B and D and with comorbidities such as diabetes mellitus, obesity were placed in the list of exclusions.

After brief history regarding sociodemographic data, disease, examination and BMI calculation, patient's blood samples were taken for the overnight fasting lipid profile before treatment. The lipid profile was also repeated after treatment with interferon based therapy. Structured proformas were utilized to maintain and assemble the recordings and data. Data were analyzed using SPSS, Mean±SD computed for descriptive variables while frequency and percentage for categorical variables. P values were also calculated to compute the statistical significance in pre treatment group.

Results

A total of **90** subjects were included in the study from which**, 46 (51.15%)** were males and **44(48.8%)** were females. The age is divided into different groups which were stratified according to gender and frequency/ percentages of age groups were calculated. The age group between 20-29 years includes the **43(84.9%)** patients which is major portion of sample. **Table 1**.

Among pre-treatment group dyslipidemia was detected only in **76 (84.4%)** of 90 patients from which **44 (57.8%)** male and **32 (42.1%)** female with most common abnormality was noted in cholesterol level. The mean ± standard deviation of cholesterol, LDL-C, HDL-C and TG levels were **272.75±21.83, 160.44±37.93, 62.82±9.09, 273.4±53.14** respectively. The major pre-treatment dyslipidemia was decrease in components of lipid profile such as 70% have <200mg/dl cholesterol, while ↓LDL, ↓HDL and ↓triglycerides were observed in 71.4%, 66.6% and 80% and p values were calculated which were statistically significant. **Table 2**.

Among post-treatment group, the mean ± standard deviation of cholesterol, LDL-C, HDL-C and TG levels were **227.74±10.72, 107.62±8.53, 42.85±6.72, 172.76±9.84** respectively. The frequency and percentages of patients in each lipid abnormality were calculated which shows clear improvement after treatment especially cholesterol level. **Table 3.**

The frequency of dyslipidemia in relation to age and gender in both pretreatment and post treatment group were summarized in **Figures 1-2**. Both figures clearly demarcate the declining frequency in post treatment group. Among pretreatment group, highest frequency of dyslipidemia was seen in 20-29 years of age group that was **41(56.9%)** while lowest in 15-19 years of age group that was **5(6.9%).** Pretreatment dyslipidemia is more

common among male **(41[56.9%])** as compared to female patients **(31[43.05%])**.

Table 01: The Stratification for Age and Gender

		GENDER		Total
		Male	Female	
AGE (GROUPS)	15-19	5 (10.4%)	3 (7.5%)	**8 (9.1%)**
	20-29	27 (56.3%)	16 (40%)	**43 (48.9%)**
	30-39	11 (22.9%)	17 (42.5%)	**28 (31.8%)**
	40-50	5 (10.4%)	4 (10%)	**9 (10.2%)**
Total		**48**	**40**	**88**

Table: 02: Pattern of Dyslipidemia in Patients with Chronic HCV Infection (Pre-Treatment)

Lipid Profile	Mean ±SD	*n* = 76	Total	P Value
(1)**Cholesterol** (mg/dL)				
< 200	272.75±21.83	19 (70%)		
> 200		08(30%)		
			27(37.5%)	**0.02**
(2) **LDL-C** (mg/dL)				
< 100	160.44±37.93	10 (71.4%)		
> 100		04 (28.5%)		
			14(19.4%)	**<0.01**
(3) **HDL- C** (mg/dL)				
< 40	62.82±9.09	08 (66.6%)		
> 40		04 (33.3%)		
			12(16.6%)	**0.05**
(4) **TG** (mg/ dL)				
< 150	273.4±53.14	12 (80%)		
> 150		03 (20%)		
			15(20.8%)	**0.04**
(5)**Mixed Dyslipidemia**		04 (5.5%)	04(5.5%)	
TOTAL			**72(100%)**	

Table: 03: Pattern of Dyslipidemia in Patients with Chronic HCV Infection (Post-Treatment)

Lipid Profile	*n* = 76	Mean ±SD	Total
(1) **Cholesterol** (mg/dL)			
<200	23 (85.1%)		
>200	04 (14.8%)	227.74±10.72	27(37.5%)
(2) **LDL-C** (mg/dL)			
<100	09 (64.1%)		
>100	05 (35.7%)	107.62±8.53	14(19.4%)
(3) **HDL- C** (mg/dL)			
<40	10 (83.2%)		
>40	02 (16.6%)	42.85±6.72	12(16.6%)
(4) **TG** (mg/ dL)			
<150	12 (79.9%)		
>150	03 (20%)	172.76±9.84	15(20.8%)
(5) **Mixed Dyslipidemia**			
No	03 (75%)		04(5.5%)
Yes	01 (25%)		

Figure 1: The Age in Context to Lipid Profile (Pre & Post-Treatment)

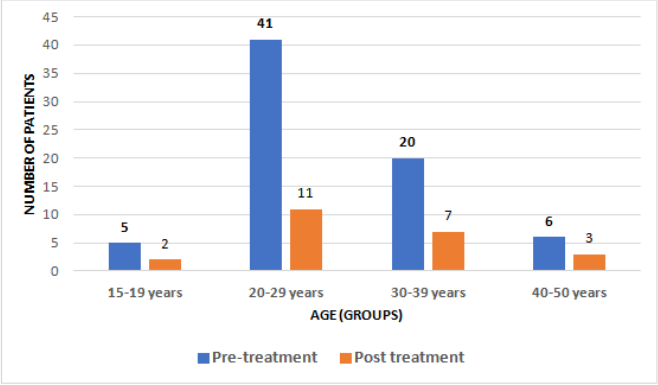
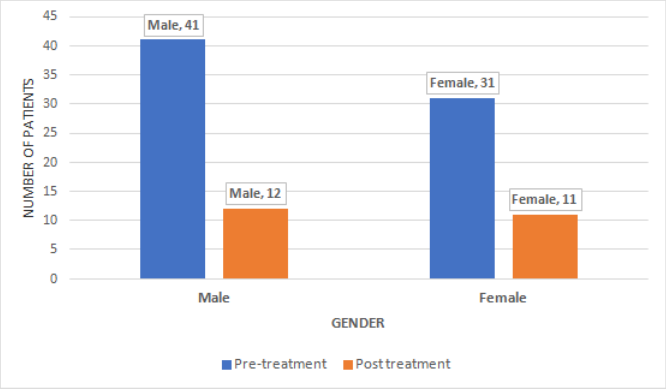


Figure 02: The Gender In Context To Dyslipidemia (Pre & Post Treatment)



Discussion

The incidence of viral hepatitis is increasing in developing nations because of poor hygiene, overcrowding, usage of unsterilized instruments poor quality of blood screening and sexual promiscuity while in developed countries the most common mode of transmission is sexual promiscuity. [9-11] The present study was concerned with lipid alterations on patients with chronic viral hepatitis before and after the interferon therapy, the mean age ±SD of overall population of present study was 34.84±7.83 with male predominance (46 males and 44 females while the study by Pal N, et al [12] also showed male predominance with mean age ±SD of 37.87±10.63 respectively. The first data regarding alteration of lipids in viral hepatitis is available in 1862 from Austin Flint who suggested cholesterol level is altered by liver and found dyslipidemia in cases with liver disease. Hence liver play a crucial role in lipid metabolism. Triglycerides and total cholesterol were the important lipid factors and HDL, VLDL and LDL were the important lipoproteins estimated in this study. [9]

Our study showed that total cholesterol was significantly reduced in seventy persent of cases with viral hepatitis which is also supported by earlier reports, an study done nu Pal N, et al [12] states that total cholesterol was low in 49 % of cases in viral hepatitis while Neil McIntyre, et al [10] and Vergani C, et al [11] and Goel VK, et al [13] states that cholesterol remain unchanged in viral hepatitis. [10,11,13] possible explanation of decreased cholesterol is reduced activity of Lecithin cholesterol acyltransferase and intrahepatic biliary obstruction in infective hepatitis.

Our study proved that serum triglyceride were low in 80% of patients which has also been proved from study conducted by Neil McIntyre in 1978 and Goel VK, et al in 1993. On contrary Papadopoulos NM et al [14] conducted study found triglyceride were in broad normal range in patients with infective hepatitis which is against our study findings. Possible mechanism of altered triglycerides is that fatty acids that are mobilized from bodily fat are reeastrfied again to triglyceride in hepatocyte and are transported back to peripheral tissue as evident in Goel VK [13] besides there in decrease in hepatic lipase activity and increase in lipoprotein lipase activity of non hepatic origin which can decrease triglyceride level.

Our study demonstrates that serum HDL was reduced in 66.6% of case, so is evident in former studies which showed it was low in 58.7 % of chronic viral hepatitis [15] besides HDLc has been shown to be reduced in patients who died as compared to those who recovered hence it could have a prognostic significance. follow up studies showed HDLc increases following recovery in patients on INF therapy. HDLc decreases possibly because of decreased activity of LCAT so its level comes to normal once patient fully recovered and hepatic function normalizes. while liver enzyme like ALT level normalizes once damage halts at start of recovery, so HDLc reflects hepatic functional recovery. [14]

LCAT is only produced in liver and its level decreases in liver disease. Mechanism leading to its deficiency in viral hepatitis is unknown, it could be because of bile salt interaction with apoprotein activator or may be minor derangements in lipoprotein metabolism, It looks like

LCAT imparts a significant role in conversion of Nascent HDL to mature HDL which results in increase in immature HDLc which is suitable to degradation so its level decreases as proposed by Vergani G.Trovati. [15] reduced production of apo lipoprotein I and II can also play a role for reduced HDLc production.Same effect is seen by Mcintyre N who states that HDLc is reduced in cases with viral hepatitis because of decreased production of LCAT. [10]

As per Kundaje GN et al study serum HDL is reduced in 69% of patients of with viral hepatitis which becomes normal or even elevated at the time of recovery. [15] Kundaje GN et al and Gol VK et al [13] seen increased serum HDLc in improved patients with improved hepatic function so suggested HDLc role in prognosis of viral hepatitis. Irshad M, et al. [16] observed 50 patients with viral hepatitis and seen reduced HDLc level in 24% of patients irrespective of etiology. Our study also favors the previous study like decrease in pre treatment group and significant improvement post treatment in HDLc.

This study showed LDLc decreased by 71.4% which is coincides with Goel VK, et al.[13] but McIntyre states that LDLc concentration remained same in 53% of cases with viral hepatitis. [10] In our study VLDLc reduced by 28%. While Goel VK.et al has seen a drop of 32% in VLDL cholesterol in patients with viral hepatitis. [13]

So aforementioned facts clearly signify the importance of serum lipids both prognostic ally and in management of patients with chronic viral hepatitis.

Conclusion

The components of lipid profile including cholesterol, triglycerides, High density lipoproteins and Low density lipoproteins were low during infective or pre- treatment period and post treatment significant improvement were observed, so this study reaches the conclusion that interferon based treatment have a significant impact on lipid profile of patients with chronic hepatitis c and lipid profile can be used as a treatment monitoring tool in these patients.

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