Original Article

COMPARISON OF LIPID PROFILE IN CHRONIC HEPATITIS "C" PATIENTS BEFORE AND AFTER ANTIVIRAL TREATMENT

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ABSTRACT

Objective: To evaluate the lipid profile: cholesterol, triglycerides (TG), Low density lipoprotein (LDL), High density lipoprotein (HDL) in Chronic HCV infected patients before and after antiviral therapy.

Material and Methods: This study was conducted in Department of Chemical Pathology at King Edward Medica University, Lahore. Fasting blood samples were collected from 84 HCV infected patients before and after 6 months of treatment from Out Patient department (OPD) Mayo Hospital Lahore for lipid profile and were processed at Chemical Pathology Department of KEMU, Lahore. The blood samples were analyzed for lipid profile by standard enzymatic methods.

Results: The study was conducted on 84 patients including 30 males and 54 females with a mean age of 38±10 years. According to Body Mass Index (BMI) only 12 patients were overweight while rest of the patients having normal BMI. We analyzed lipid profile before and after treatment. There was a significant increase in post treatment cholesterol level 179±27mg/dl as compare to pre- treatment 151±19 mg/dl with a P-value <0.001. Mean Triglyceride (TG) levels also increased significantly after treatment 87±18 mg/dl v/s 119±26 mg/dl with a P-value <0.001. Low Density Lipoprotein (LDL) was also increased significantly after treatment 89.8±15.1 mg/dl v/s 112.8±24.1mg/dl with a P-value <0.001. But the mean High-Density Lipoprotein (HDL) was not changed significantly after treatment 43±7mg/dl as compared to before treatment 42±6 mg/dl with a p-value 0.399.

Conclusion: Hepatitis C infection was associated with deranged (lowering) of lipid profile that was rearranged (normal) after the resolution of infection in successfully treated patients. Lipid profile monitoring may help in the prognosis of hepatic infection severity and may also act as a good predictive sign. This may help the clinicians in better counseling and timely anticipation and intervention regarding chronic HCV to decrease the risk of coronary heart disease (CHD) in future.

Key Words: Chronic hepatitis C, Cholesterol, Coronary heart diseases, HDL-c, Lipid profile.

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INTRODUCTION

Hepatitis C is caused mainly by Hepatitis C virus (HCV), according to world Health Organization (WHO) about 170 million people are infected worldwide [1]. Egypt has the highest prevalence of HCV about 15% while in Pakistan HCV is endemic and about 10 million remains a major heath concern [2,3]. Morbidity rate of this disease is also increasing due to unawareness of the general population of the transmission routes, low socio-economic status and poor health facilities [4,5].

HCV infection can be considered not only as viral disease but as a metabolic disease with high propensity to develop persistent infection, liver fibrosis, cirrhosis and hepatocellular carcinoma (HCC) [6]. Genetic heterogeneity is an essential decision criterion for HCV treatment plan, duration of treatment and dosage selection while in Pakistan genotype 3 contributes 78.96% of infection with subtype of 3a as 58.01% [7].

Liver is a vital organ of human body and plays a central role in lipid production, metabolism, storage and transportation. HCV infection produces a remarkable decrease in serum cholesterol, triglyceride (TG), low density lipoprotein (LDL) and high-density lipoprotein (HDL) [8]. Lipids provide a medium to HCV for its circulation and entry into hepatocytes. A circulating HCV particle makes a complex with host triacylglycerol rich lipoproteins known as Lipoviro particle (LVP) and it uses LDL receptors (LDL-r) for their entry in the hepatocytes [9]. HCV could lower the intrahepatic cholesterol synthesis as it shunts the geranyl pyrophosphate and also utilize the cholesterol for the production of membranous web, the net effect of these two steps, would cause the decrease in intracellular cholesterol which leads to increase in LDL-r, causing in LDL uptake and resulting in low LDL level [10].

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The low levels of triglycerides are dependent on VLDL (which exports triglyceride and cholesterol to the plasma) assembly in two stages. In 1st stage, microsomal triglyceride transfer protein (MTP) transfers TG from cytosolic lipid droplet to a nascent Apo lipoprotein (Apo) B-100 (gives structural integrity to LDL). In the 2nd stage Apo B containing VLDL particle fuse with TG droplet in endoplasmic reticulum (ER). TG is transferred as VLDL by MTP to luminal compartment. After assembly into lipid droplet (LD) LVP is secreted from the hepatocyte after budding. The LD using VLDL secretary pathway by blocking the VLDL secretion causes decreased production of LDL and enhances LVP secretion [11].

The major achievement for HCV therapy is to attain sustained viral response (SVR), as up till now no vaccine is available against HCV infection. The only treatment plan for majority of HCV infected patients is a combination of conventional Interferon (IFN-α) and Ribavirin [13]. The Standard of Care (SOC) for the chronic HCV patients is peg-IFN in combination with Ribavirin [12]. Due to prohibitive cost of Direct Acting Antiviral Agents (DAAs) conventional IFN is still used as a predominant form of therapy for HCV infected patients in developing countries like Pakistan. Moreover, conventional IFN is no more considered to be as SOC as per International guidelines and achieves less viral clearance as compared to Peg-IFN [13].

The purpose of this study was to evaluate the lipid profile (cholesterol, TG, LDL and HDL) in Chronic HCV infected patients before and after antiviral treatment.

MATERIAL AND METHODS

Total of 84 subjects of both genders presenting in outpatient department of Mayo Hospital Lahore were offered enrollment in the study. Detailed history of the patients of chronic HCV subjects was taken on a specially designed questionnaire. After obtaining informed consent, demographic information such as name, age, and gender were collected. Subjects were interviewed for absence of hypertension, diabetes. Body weight in kilograms and height in centimeters was measured to calculate BMI.

Inclusion criteria:

- HCV infected patients (n=84) not receiving any treatment.
- Patients having genotype 3a
- Patients having age 18 years or above
- Both genders were included.

Exclusion Criteria: Patients suffering from hepatitis B infection, cirrhosis, diabetes mellitus. Patients taking cholesterol lowering treatment. Lipid profile was analyzed in Pathology Department of King Edward Medical University, Lahore in accordance with the reagent manufacturer's instruction, using specific enzymatic kit for cholesterol, TG, LDL and HDL.

Data entry and analysis was done by using SPSS Version 20. Quantitative variables, like age was presented in the form of mean and Standard Deviation (SD), while qualitative variables like gender were presented in the form of frequency and percentage. The comparison of lipid profile before and after treatment was assessed by using paired sample t-test p-value < 0.05 is taken as significant.

RESULTS

This study included 84 patients suffering from chronic HCV infection. Data regarding their age, gender, height, weight and BMI were collected before starting treatment. Out of total 84 patients, 30 (35.7%) patients were male and 54 (64.3%) were females (Table-1). In our study both the male and females have a minimum age of 19 years while the maximum age for males were 60 year and 56 years for females, the mean was 37.98±9.91 years (Table-1). Body mass index (BMI) was calculated with the help of height and weight, their mean was 21.95±3.08 (Table-1).

The four parameters of lipid profile (cholesterol, TG, LDL, and HDL) were analyzed before treatment and after the completion of treatment and t-test were applied to compare the change in lipid profile after treatment. The mean cholesterol level increased significantly after treatment 179±27 mg/dl than before treatment 151±19 mg/dl with a P-value <0.001 (Figure-1). The mean TG level before treatment was 87±18mg/dl and after treatment it was raised to 119±26 mg/dl, this increase in TG was significant after treatment with a P-value < 0.001 (Figure-2). LDL level was increased significantly after treatment 112±24.1 mg/dl as compared to before treatment 89.8±15.1 with P-value <0.001 (Figure-3). The mean HDL level was not changed significantly after treatment. The mean HDL level before treatment was 43±7 mg/dl while after treatment it was 44±6 mg/dl (Figure-4).

Table-1: General characteristics of study population.

Characteristics	Mean
Age (years)	37.98±9.91
BMI (kg/m^2)	21.95±3.08

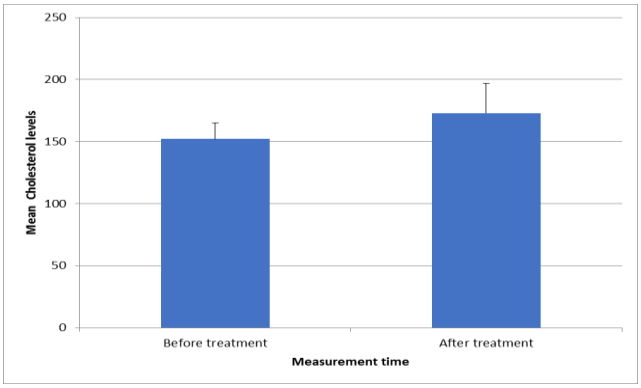

Figure-1: Comparison of cholesterol levels measured before and after treatment.

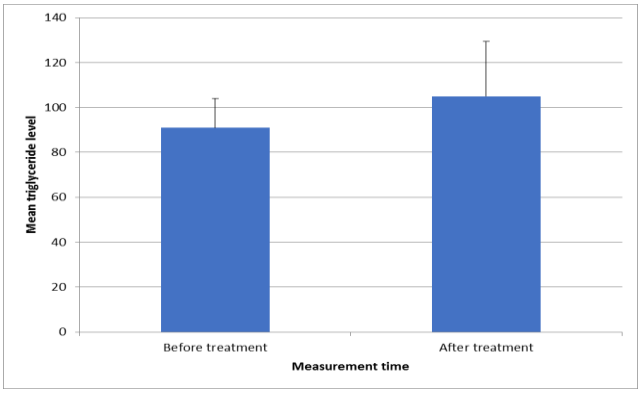

Figure-2: Comparison of triglyceride levels measured before and after treatment.

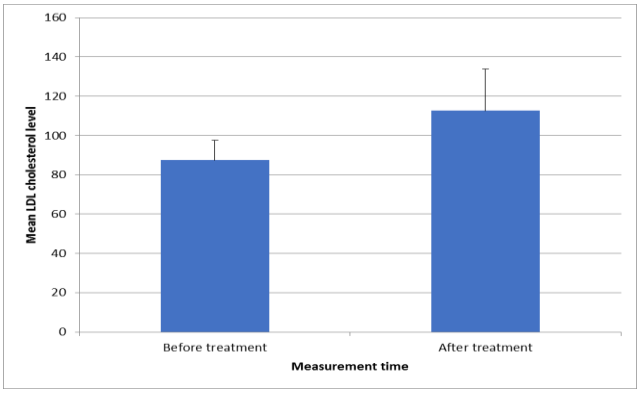

Figure-3: Comparison of LDL levels measured before and after treatment.

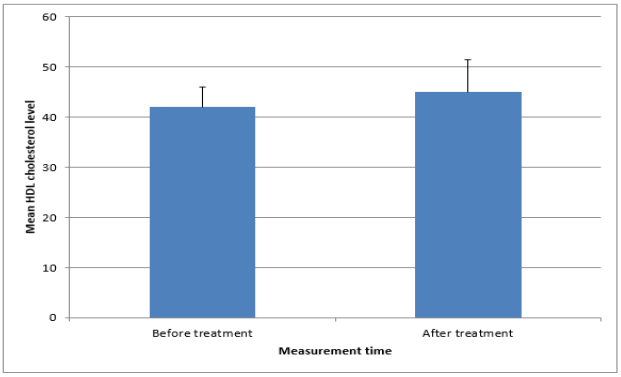

Figure-4: Comparison of HDL levels measured before and after treatment.

DISCUSSION

HCV infection is one of the major public health problem. Worldwide >185 million people are affected while in Pakistan rate of HCV infection is becoming higher as approximetly 10 million people are suffering with HCV infection due to increasing socioeconomic burden of infectious diseases [14,15]. Approximately 80% of acute HCV infection persist and 20% of those may develop complications like fibrosis, steatosis and HCC etc. making HCV one of the major serious cause of high morbidity and mortality worldwide [16].

HCV infected patients have low lipid levels that increase and rebound to normal levels after the resolution of infection. The treatment with IFN will suppress HCV replication and hepatocytes may normalize their function because HCV has direct effect on hepatocytes and lipid metabolic functions [17,18].

This study was conducted on patients suffering from HCV infection confirmed by ELISA and PCR who did not receive any antiviral treatment. We excluded the patients having diabetes mellitus (DM), liver cirrhosis, heaptitis B infected patients and patients on lipid lowering medications.

In our study, out of 84 HCV patients 30 (35.7%) were males and 54 (64.3%) were females like in a study conducted by Ishiguro H, *et al*. in 2013 having more females than male patients as in our study [19]. Another study conducted in Tiawan 2011 also had more females in their study [20]. Mustafa *et al*. observed in 2012 and few other had more males than females [10,21].

In our study we have more females than males but it does not represent the actual gender distribution of this disease, as HCV is more prevalent in males than females. It was totally by chance that we have more females because we do a random sampling, so it’s a chance oriented sampling to get patients of either gender to complete the sample size [22].

Patients in our study have a mean±SD age of 38±10 with minimum age of 19 years in both gender while the maximum age for males were 60 years and 56 years in females. The age distribution of our study was almost similar with the study of Arain SQ *et al* [23]. The study conducted in Tiawan in 2011 was also were in our agreement [20]. The study done by Ehab H Nashaat in 2010 had almost the similar mean age as our study [10]. In our study we have maximum patients older than 20 years of age, as HCV appears to be less prevelent in youngers. So the chronicity of this disease increases 76% for those older than 20 years [24].

The mean ± SD BMI of HCV patients in our study was 21.95±3.08 kg/m^2, the result of our study was similar with Ishiguro H, *et al*. who reported, the mean ± SD BMI 23.2±2.1 kg/m^2 [19]. But the results of our study were not as consistent with the study conducted by Nashaat EH in 2010 that had a mean ± SD BMI 29.8±2.43 kg/m^2 [10]. The result of another study conducted by Hee Jae *et al*. in Korea (2014) was almost consistent with our study that had a mean ± SD BMI 24±2.8 kg/m^2 [18]. Likewise, the results of the study conducted in Taiwan (2011) were also consistent with our study had a mean ± SD BMI 24.6±3.6 kg/m^2 [20]. In our study we have majority of patient’s normal in accordance with their BMI because obesity correlates with the degree of steatosis in HCV patients and may affect the antiviral therapy response [10]. The mean cholesterol level before and after antiviral treatment was 151±19 mg/dl v/s 179±27 mg/dl respectively so the cholesterol level increased significantly after treatment with a P-value < 0.001. The results of our study were consistent with a study conducted by Arain SQ *et al*. in which cholesterol mean ± SD before treatment was 149.9±49.0 mg/dl which was raised after treatment to the level of 169±18.8 mg/dl [25]. The results of a study conducted in United States 2016 were also similar with our study as the mean Cholesterol level were also increased after antiviral treatment as before treatment it was 161.4 ±35.5 mg/dl while after treatment it was raised to 181.5±23.5 mg/dl with a p-value 0.001 [26].

The TG levels before treatment in our study was 87±18 mg/dl and after treatment was increased to 119±26 mg/dl the increase in TG level was found significant with a P-value < 0.001. The results of the study conducted by Arain SQ *et al*. were not consistent with our study in which no significant change was seen in TG levels before and after treatment 113.1±54.1 mg/dl v/s 123±19.7 mg/dl [25]. The results of the study conducted in United States in 2016 were not consistent with our results because the TG level was not increased after treatment as before treatment it was 119.0±58.6 mg/dl while after treatment it fell to 112.6±47.1 mg/dl with a p –value 0.36 [26].

In our study the mean LDL level was 89.8±15.1 mg/dl before treatment and 112.8±24.1 mg/dl after antiviral treatment. This increase in LDL level after treatment was significantly high with a P-value <0.001. The results of our study are in agreement with a study conducted by Arain SQ *et al*. in which mean LDL before treatment was 74.3±35.9 mg/dl while after treatment elevated to 97.5±2.9 mg/dl [25]. The results of our study were similar with study conducted in United States 2016 in which mean LDL level before treatment was 92.5±26.1 mg/dl which was increased to 110.4±21.4 mg/dl after treatment with a P-value 0.003 [26].

In our study mean HDL levels were was compared before and after antiviral treatment, irrespective of the success of the treatment and the change in mean HDL level observed was not significant as mean HDL before treatment was 42±6 mg/dl while after treatment it was 43±7 mg/dl. The results of our study were not consistent with a study conducted by Arain SQ *et al*. in which HDL mean level before treatment was 37.1±11.2 mg/dl which was raised to mean HDL 45.7±8.9 mg/dl after treatment [25]. The results of another study conducted in United States 2016 were consistent with our study as HDL level before treatment was 49.3±14.0 mg/dl which was raised after treatment to 53.2±14.3 mg/dl with a P –value 0.37 [26].

Hepatitis C infection was associated with derangement (lowering) of lipid profile that was normalized after the resolution of infection in successfully treated patients. Lipid profile monitoring may help in the prognosis of hepatic infection severity and may also act as a good predictive sign. This may help the clinicians in better counseling and timely anticipation and intervention regarding chronic HCV to decrease the risk of coronary heart disease (CHD) in future.

CONCLUSION

It is concluded that increased levels of lipid after 24 weeks of therapy, end of treatment, in responders is proposed as a predictive marker as patients with sustained viral response have a rebound in levels of lipid profile parameters. But in contrast to those who did not achieved end-of-treatment response at end of treatment still have low lipid levels as non- sustained viral response. It is recommended to review another aspect of HCV patient and to pay attention to those who achieve end treatment response and sustained viral response.

As the lipid level changed after viral clearance and achieving reference interval levels or even higher than this, would involve the patients in heart related complications like coronary heart disease, which could be life threatening if left ignored or unmanaged.

RECOMMENDATIONS

Sustanined Viral Response (SVR) should be calculated. Comparison of conventional IFN with peg-IFN to check the efficacy.Comparison of peg-IFN with IFN free regimen (sovaldi) to check the efficacy.

AUTHOR CONTRIBUTION

Shafaq Dastgir Sheikh: Main researcher
Rafiq Ahmad Shahid: Suprevised the whole reasarch
Sheikh Sadaf Dastgir: Helped in analysing data
Amna Rizvi: Helped in collection the clinical data

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