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A COMPARATIVE STUDY ON BIOCHEMICAL PROFILE AMONG PRE AND POST-SOFOSBUVIR-TREATED IN HCV PATIENTS, PAKISTAN

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Abstract

The viral infection known as hepatitis C (HCV) is a significant threat to health in Pakistan. Although powerful antiviral therapies are readily available, the disease load in the general population as a whole continues to rise. This may be because the infection is non-symptomatic, and delaying diagnosis until the disease has progressed significantly. **Objectives:** The study aims to contrast the biochemical profiles of patients with HCV before and after treatment with Sofosbuvir. **Material and Methods:** This was a cohort type of study with a sample size of 106. Patients with hepatitis C who went to the Medical Unit at the District Head Quarters Hospital in Rawalpindi between May 2019 and January 2020 were enrolled. To learn more about the patients' personal and medical histories, a questionnaire was created. Venipuncture was used to draw blood, and the Beckman Coulter AU480 chemistry analyzer was used to calculate serum uric acid levels, total cholesterol levels, triglycerides levels, ALT levels, and TSH levels. Performa was used to log data, which was then transferred to SPSS for analysis. **Results:** In total 106 patients were studied, 75% were from Rawalpindi and 25% were from other areas of Pakistan. The mean age of patients enrolled in this study was 43.5 ± 12.3 years, 66.04% of the HCV patients have a negative family history, and the highest percentage (94.34%) of the patients are married. Patients were divided into two groups based on the duration of anti-HCV therapy Sofosbuvir as Pre- therapy and Post therapy. The Pre and Post Sofosbuvir therapy found non-significant results of uric acid levels Mean ± S.D of (4.79 ± 1.57) v/s (5.22 ± 1.51) with p-value (>0.05), total cholesterol levels Mean ± S.D of (164.2 ± 37.22) v/s (174.1 ± 43.27) with p-value (>0.05), triglycerides levels Mean ± S.D of (136.7 ± 37.9) v/s (110 ± 20.3) with p-value (>0.05) and TSH levels Mean ± SD (2.10 ± 1.97) v/s (2.93 ± 1.82) with p-value (>0.05). But the significant result was found for ALT levels (90.3 ± 104.1) v/s (43.6 ± 33.8) with p-value (<0.05). **Conclusion:** This study's findings support the use of Sofosbuvir in the treatment of chronic HCV due to its low risk and impressive effectiveness. Related to decreased alanine transaminase (ALT) levels and the suppression of viral replication.

Keywords: Thyroid Stimulating Hormone, Alanine Amino Transferase, Hepatitis C Virus.

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INTRODUCTION

Chronic inflammation of the liver, known medically as hepatitis, can be caused by several virus species, including types A, B, C, D, and E. Chronic hepatitis C virus infection affects an estimated 71 million persons worldwide. (Birajdar, S. V. et al., 2017). About 10 million persons are infected with HCV in Pakistan and this burden is growing day by day. (Butt et al., 2019) HCV prevalence is 5.46% in Punjab, 2.55 percent in Sindh, 6.07 % in Khyber Pakhtunkhwa, 25.77 % in Baluchistan, and 3.37 % within federally administered tribal territories. (Raja & Janjua, 2008) Hepatitis C virus (HCV) is responsible for both acute and chronic hepatitis, with symptoms ranging from a short, moderate disease to a severe, lifelong one. One of the leading causes of malignancies of the liver is the infection known as hepatitis C. Blood is the vector for the hepatitis C virus. Small amounts of blood from an HCV-positive individual are among the most common routes of transmission. Injecting drugs, transfusing unscreened blood and blood products, receiving subpar medical treatment, and engaging in risky sexual practices that expose one to blood can all result in hepatitis C infection. (Ashraf-Uz-Zaman, M.et al., 2010) Many people who are persistently infected will eventually be diagnosed with cirrhosis or cancer of the liver. According to the World Health Organization, cirrhosis and hepatocellular cancer accounted for over 399 thousand deaths from hepatitis C in 2016. More than 95% of people with hepatitis C infection can be cured with antiviral drugs, reducing the risk of mortality from cirrhosis and liver cancer; but, diagnosis and treatment are not widely available.

Hepatitis C vaccine development is still in progress, although there is presently no effective vaccine available. Hepatitis C virus replicates in the cytoplasm of hepatocytes but does not directly cause cytopathy. Jaundice development is a hallmark of liver illness. Although other factors, such as excessive alcohol consumption, use of certain hepatotoxic drugs, and other infectious and dietary agents, can contribute to the development of viral liver disease, hepatotoxic viruses are the leading cause of this condition. Liver damage from infectious hepatitis can be evaluated according to biochemical criteria. Therefore, the severity of various hepatitis viruses can be estimated by measuring the biochemical parameters. (Ashraf-Uz-Zaman, M.et al., 2010). A significant decrease in HCV RNA levels during treatment with Sofosbuvir coupled with peg-interferon and ribavirin led to a sustained virologic response at 24 weeks post-treatment in 92 percent of individuals with HCV genotype 2 or 3 infections, according to studies worldwide Eighty-nine percent of patients with HCV genotype 1 infection who were treated with the same combination of Sofosbuvir, peg interferon, and ribavirin for 12 weeks achieved a durable virologic response 24 weeks following treatment. These numbers, however, are based on the response rates of Western people, where the genotype distribution differs from that of a population like Pakistan's. (SIDDIQUI, M. S. et al., (2017) More extensive research into the link between elevated serum uric acid and liver disease has been conducted among individuals with NAFLD and/or NASH, although the results have been inconsistent. Significantly less is understood regarding serum uric acid presentation in CHC patients than in the majority of the population. Its relationship to the severity of liver damage in CHC patients is also unclear. (Jang et al., 2018) Serum

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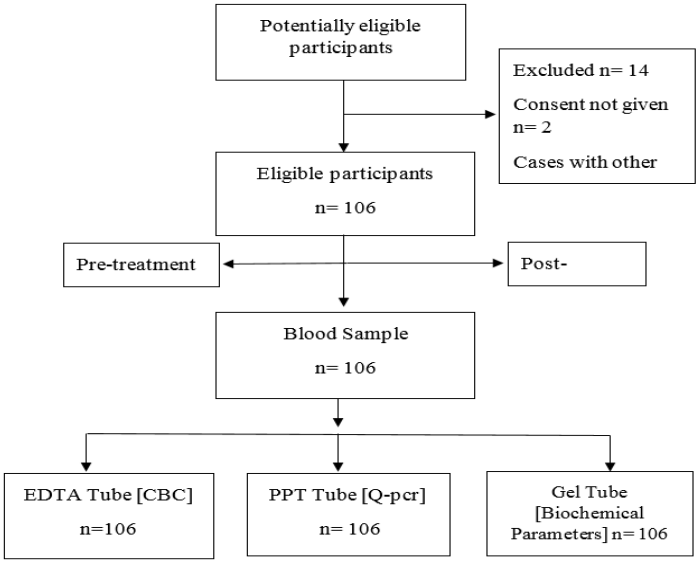
levels of both lipoproteins and cholesterol might shift as an outcome of damage to cells in the liver, altering liver functioning. Damage to the liver caused by HCV is associated with lipid metabolic abnormalities. Cholesterol and fatty acids (FA) both contribute significantly to HCV development. (Ibrahim, H. et al., 2016) There is mounting evidence from research on people with HCV infection that interferon therapy raises the danger of thyroid problems. Thyroid antibodies and the proliferation of memory T cells, natural killer cells, and dendritic cells are produced as part of an innate immune response to HCV, and this reaction has been researched extensively. While several research studies have focused on the role that interferon therapy can have in exacerbating thyroid diseases, none have looked at the correlation between thyroid dysfunctions and individuals who were given interferon-free regimens. (Wahid, B. et al., 2018).

MATERIALS AND METHODS

106 HCV patients who needed biochemical evaluations were referred to the pathology department at District Headquarters Hospital from May 2019 to January 2020. The instances were chosen from a pool over six months. Chronic active HCV infection, as evidenced by a positive Anti-HCV (ELISA) test and a qualitative polymerase chain reaction (PCR) analysis, was a requirement for case selection. And received Sofosbuvir for their illness. Patients with active persistent Hepatitis B Virus (HBV) infection or other acute viral hepatitis (HBV carriers were eligible for induction), those who were immune-deficient, alcohol users, or those with renal or liver disorders were excluded from the case selection process. To learn more about the patients' personal and medical histories, a questionnaire was created. Venipuncture was used to draw blood, and the Beckman Coulter AU480 chemistry analyzer was used to calculate serum uric acid levels, total cholesterol levels, triglycerides levels, ALT levels, and TSH levels. Performa was used to log data, which was then transferred to SPSS for analysis. Mean and standard deviation were used for continuous variables, whereas frequency and percentage were used to represent categorical ones.



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RESULTS

Baseline characteristics and clinical presentation of patients. In total 106 patients were included, 75% of the patients were from Rawalpindi and 25% were from other areas of Punjab. Patients were divided into 4 groups according to their age. The mean age of patients enrolled in this study was 43.5 ± 12.3 years. 66.04% of HCV patients are having negative family history while 33.96% have positive family history. The highest percentage (94.34%) of the patients are married and 90.57% of the HCV patients are non-smokers.

Patients were divided into two groups based on the duration of anti-HCV therapy Sofosbuvir as Pre- therapy and Post therapy. 52.84% of the patients are female and 47.16% are male. The highest percentage of the patients fall into the fatigue (36.79%) and normal (19.82%) category. Patients had four categories according to the duration of HCV diagnosis. 78.30% had 1-5 years, 10.38% had 6-10 years, 4.72% had 11-15years and 6.60% had 16-20 years of duration. Patients were divided into two groups according to their previous treatment 2.83% were taking Interferon previously and 97.17% were treatment naive. The frequency of different Gastrointestinal and CVS complications was fatty liver, splenomegaly, cholelithiasis, cardiomegaly, and coarse liver. 37.5% of the cases are normal, 30.8% have fatty liver, 15.0% have coarse liver, 3.3% have splenomegaly, 0.8% have cardiomegaly, and 0.8% have cholelithiasis.

The Pre and Post uric acid levels among Sofosbuvir-treated HCV patients have mean ± S.D of (4.79 ± 1.57) v/s (5.22 ± 1.51) with p-value (0.18) and it is a non-significant value. Among Sofosbuvir-treated patients Pre and Post total cholesterol levels have mean ± S.D of (164.2 ± 37.22) v/s (174.1 ± 43.27) with p-value (0.07) and it is also a non-significant value while Pre and Post Triglycerides levels have mean ± S.D of (136.7 ± 37.9) v/s (110 ± 20.3) with p-value (0.65) and it is highly non-significant value. TSH levels have Mean ± SD (2.10 ± 1.97) v/s (2.93 ± 1.82) with p-value (0.21). So the Sofosbuvir have no effect on serum uric acid, total cholesterol, triglycerides and TSH levels.

The Pre and Post ALT levels among studied patients Mean ± SD (90.3 ± 104.1) v/s (43.6 ± 33.8) with a p-value (0.04) and this value is statically significant. That shows ALT levels were improved after taking the sofosbuvir.

Table 1: Mean and Standard Deviation of ALT, Uric acid, Total Cholesterol, and Triglycerides

Measurement	Pre-therapy results	Post-therapy results	p-value
ALT Levels	90.3 ± 104.1	43.6 ± 33.8	0.04
Uric Acid Levels	4.79 ± 1.57	5.22 ± 1.51	0.18
Total Cholesterol Levels	164.2 ± 37.22	174.1±43.27	0.07
Triglycerides Levels	136.7 ± 37.9	110 ± 20.3	0.65
TSH Levels	2.10 ± 1.97	2.93 ± 1.82	0.21

If $p<0.05$ = Significance and if $p>0.05$ = No Significance

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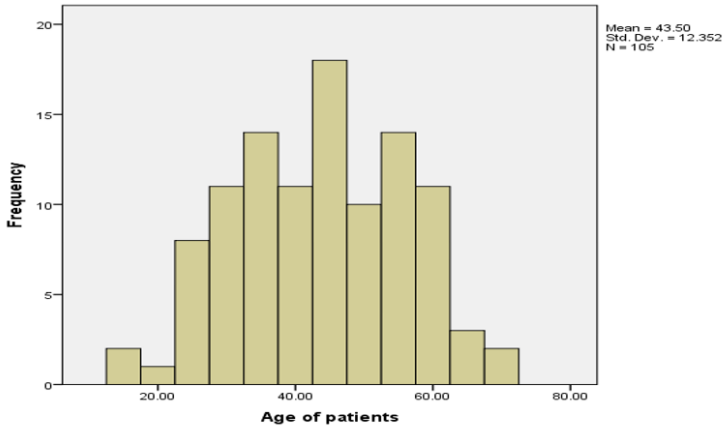

Figure 1: Age of Patients of the Studied Patients

Table 2: Demographic Characteristics of Studied Patients

Characteristic	Frequency	Percentage
1-Gender (n =106)		
Male	50	47.16%
Female	56	52.84%
2-Marital Status (n =106)		
Married	100	94.34%
Un-married	6	5.66%
3-Smoking Status (n =106)		
Yes	10	9.43%
No	96	90.57%
4-Family History (n =106)		
Positive	36	33.96%
Negative	70	66.04%

Table 3: Hepatitis History of the Studied Patients

Hepatitis history	n (106)	Percent %
1-5 years	83	78.30
6-10 years	11	10.38
11-15 years	5	4.72
16-20 years	7	6.60

Table 4: Clinical Findings of the Studied Patients

Clinical Findings	n (106)	Percent %
Fatigue	39	36.79
abdominal pain	16	15.09
Fever	15	14.15
Hyperemia	1	0.94
Diarrhea	6	5.66
Legs Pain	6	5.66
Cough	2	1.89
Normal	21	19.82

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Table 5: Descriptive Analysis of Pre-biochemical Profile of Studied Patients

Measurements	n(106)	P Value
Pre ALT Levels	90.3 ± 104.1	0.001
Pre Uric Acid Levels	4.79 ± 1.57	0.003
Pre-Total Cholesterol Levels	164.2 ± 37.22	0.02
Pre Triglyceride Levels	136.7 ± 87.9	0.02
Pre TSH Levels	2.10 ± 1.97	0.05

Table 6: Descriptive Analysis of Post-Biochemical Profile of the Studied Patients

Measurements	n (106)	P Value
Post ALT	43.6 ± 33.8	0.04
Post Uric Acid	5.22 ± 1.51	0.05
Post Total Cholesterol	174.1 ± 43.27	0.06
Post Triglycerides	138.6 ± 83.6	0.05
Post TSH	2.93 ± 1.82	0.06

Table 7: Ultrasound Findings of the Studied Patients

Ultrasound findings	n (106)	Percent%
Normal	45	42.46
Fatty Liver	37	34.91
Cholelithiasis	1	0.94
Splenomegaly	4	3.77
Cardiomegaly	1	0.94
Coarse Liver	18	16.98

Table 8: Previous Treatment Status of the Studied Patients

Previous Treatment	n (106)	Percent%
No	103	97.17
Yes	3	2.83

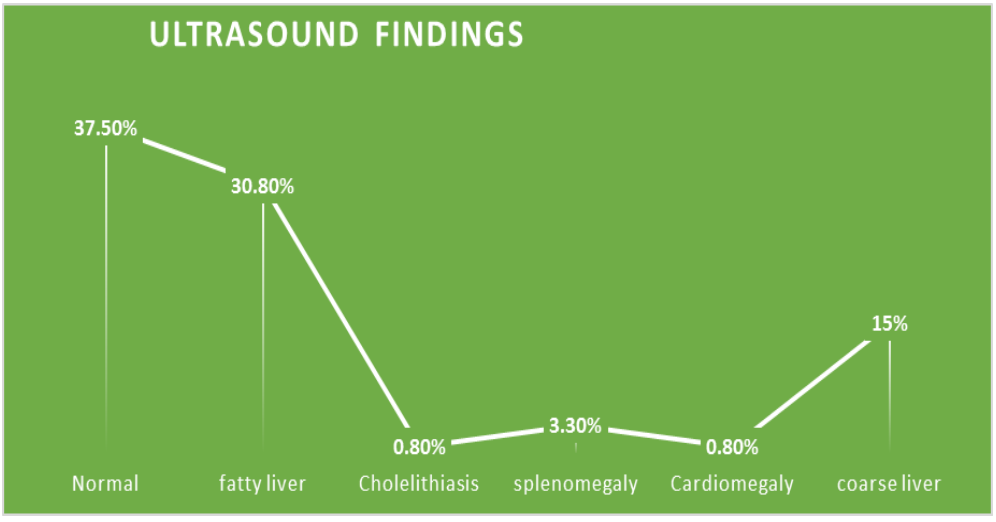

Figure 2: Ultrasound Findings of the Studied Patients

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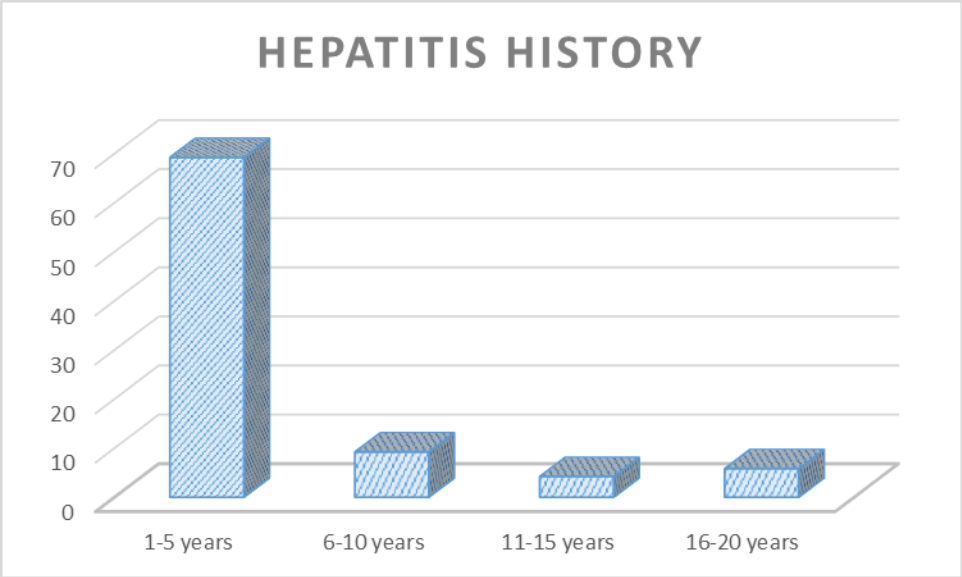

Figure 3: Hepatitis History of the Studied Patients

DISCUSSION

Hepatitis C is most common in the nation of Pakistan, where about 4.8% to 8.2% of the population is infected. The chronic Hepatitis C recovery ratio has skyrocketed following the release of the new oral medication Sofosbuvir. Pan-genotypic activity, a single dose per day, no meal restrictions, few adverse reactions, limited interactions between medications, the high hereditary barrier to resistance, good effectiveness and safety for individuals who have severe liver damage, and beneficial sustained virological response rates in patients with unfavorable baseline characteristics are just some of the many desirable characteristics of sofosbuvir.

Our follow-up analysis of 106 patients demonstrated very high response rates towards eradication of HCV by Sofosbuvir treatment. The current study found significant improvement in ALT levels (p=0.04) after the therapy and our results are in line with (Mohamed et al., 2017). After HCV eradication by Sofosbuvir LFT parameters were improved in chronic hepatitis C patients. This study found non-significant results in uric acid levels (p=0.18) after 3 months of Sofosbuvir therapy which means Sofosbuvir does not increase nor decrease uric acid levels in HCV patients. Our results are contrary to (Shujaullah et al., 2018) showing a significant decrease in uric acid levels after Sofosbuvir therapy.

Our study found non-significant results of triglycerides levels (p=0.65) post-sofosbuvir therapy which means there is no effect of Sofosbuvir on triglycerides levels and these results are in line with (Shujaullah et al., 2018) showing constant results in pre and post therapy of Sofosbuvir. However in contrast to the current study (Chang et al., 2014) showing a decrease in triglyceride levels. The current study shows non-significant results in total cholesterol levels (0.07) which means there is no increase nor decrease in total cholesterol levels and this result is consistent with (Bernuth et al., 2016). This result is

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contrary to (Shujaullah et al., 2018) showing an increase in total cholesterol after Sofosbuvir therapy.

The current study found non-significant results of TSH levels (p=021) which means there is no thyroid dysfunction occurring due to Sofosbuvir therapy. In contrast to our study (Wahid et al., 2018) showing a hyperthyroidism after Sofosbuvir and interferon therapy.

CONCLUSION

This study concluded that Sofosbuvir therapy is safe to treat HCV infection with no effect on biochemical parameters. In addition, ALT levels are improved through the Sofosbuvir drug and there is no effect of Sofosbuvir therapy on uric acid levels, triglycerides levels, TSH levels, and total cholesterol levels.

Limitation and Recommendations

The sample size of the current study is small we recommend further studies on the Sofosbuvir drug to find the consequences of Sofosbuvir therapy.

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