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TO DETERMINE THE REVERSIBILITY IN PATIENTS OF COMPENSATED CIRRHOSIS OF CHRONIC HEPATITIS C BY APRI AND TRANSIENT ELASTOGRAPHY (FIBRO SCAN) AFTER THE COMPLETION OF ANTI-HCV THERAPY

Gastroenterology

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ABSTRACT

Introduction: Hepatitis C virus (HCV) affects 122-185 million globally, with a 0.9%-1.9% prevalence in India. Patients with chronic HCV infection and fibrosis have a risk of hepatic and extrahepatic complications, including liver decompensation and hepatocellular carcinoma (HCC). Although DAAs can efficiently eliminate HCV in most cases, viral elimination is not an indicator of cure of the liver disease, particularly in patients with hepatic fibrosis. To know the effect of DAA treatment on the liver-related complications is crucial for prognosis and future management. **Objective** - To determine the reversibility of Compensated cirrhosis of HCV patients by changes found in APRI score and Transient elastography after the completion of DAA. **Methods:** This longitudinal observational study involved 122 patients with compensated cirrhosis of HCV conducted at S.N. Medical College and Hospital, Agra, from January 2023 to June 2024. Inclusion criteria included All Compensated cirrhosis patient of Chronic hepatitis C, positive anti-HCV antibodies, and detectable HCV RNA viral load. Exclusion criteria involved patients with liver diseases from other etiologies, low viral loads undetectable before treatment. DAA therapy sofosbuvir (SOF) and velpatasvir (VEL) given to all patients included in our study for 12 weeks. Data were analyzed using SPSS version 25.0, employing descriptive and inferential statistics with a p-value <0.05 considered significant. **Results:** Among 122 patients, the largest age group was 31-40 years (41.4%), with a mean age of 39.41±7.7 years. Males constituted 67.3%. After the completion of 12 weeks, 95.1 % patients achieved SVR with marked changes in their APRI score and LSM reported. APRI score reduced from 2.201 +- 0.952 to 0.758+- 0.328 and LSM (FIBROSCAN) decreased from 27.5+-10.68 to 10.8+-6.52. these changes denotes that there is marked reduction in the hepatic fibrosis and its complications which significantly improves the life span of these patients. **Conclusion:** The study found that patients with chronic hepatitis C show a significant response when achieving SVR. This study shows the effectiveness of DAA in reducing hepatic fibrosis and further complications of decompensated liver disease. DAA therapy is much more effective in early stages of liver disease as compared to later decompensated stage. Therefore, the most important thing is to screen or diagnose HCV infection in early stage and start the treatment effectively to achieve maximum results and improve prognosis.

KEYWORDS

Hepatitis C virus; sustained virologic response; direct-acting antivirals; Fibroscan; LSM (liver stiffness measurement); reversibility of fibrosis.

INTRODUCTION

Hepatitis C virus (HCV) represents a substantial global health challenge, with considerable morbidity and mortality affecting an estimated approximately 150 million individuals all over the world with chronic infection.

According to WHO estimates, about 242,000 people died from hepatitis C in 2022, with most deaths caused by cirrhosis and hepatocellular carcinoma (HCC) [2]

The introduction of DAA has been transformative, offering cure Rates above 95% (3). The world health organisation (WHO) set forth the goal of eliminating viral hepatitis by 2030(4). Daclatasvir (DCV), ledipasvir (LDV), velpatasvir (VEL), and sofosbuvir (SOF) are the only four DAAs accessible in India. The development of pangenotypic drugs has eliminated the need for genotype testing. In accordance to the availability of these pangenotypic drugs, we assess the SVR in our study irrespective of genotype. Although direct-acting antivirals (DAA) can cure most of the hepatitis C cases, the availability of diagnosis and treatment is inadequate. Efforts to improve healthcare infrastructure, raise public awareness, and expand access to treatment are crucial in combating the global impact of HCV. Continued advocacy and international collaboration are key to achieving widespread elimination goals and improving outcomes for those affected by this persistent viral infection (3,4). Acute HCV infections are usually asymptomatic and most do not lead to a life-threatening disease. Around 30% (15–45%) of infected persons spontaneously clear the virus within 6 months of infection without any treatment. The remaining 70% (55–85%) of persons will develop chronic HCV infection. Of those with chronic HCV infection, the risk of cirrhosis ranges from 15% to 30% within 20 years.

The stage of liver fibrosis plays a critical role in determining the prognosis of chronic hepatitis C (CHC) infection after the DAA therapy. Early detection and management of liver fibrosis are crucial to prevent progression to advanced stages and reduce associated mortality and morbidity rates among affected individuals (6).

Treatment efficacy, or the effectiveness of antiviral therapy in eliminating viral infection, is measured by the percentage of individuals who achieve a sustained virologic response (SVR). SVR in CHC refers to the outcome of antiviral treatment, where HCV RNA in the in the bloodstream becomes undetectable or falls below the minimum quantifiable level. Although DAAs can efficiently eliminate HCV in most cases, viral elimination is not an indicator of cure of the liver disease, particularly in patients with hepatic fibrosis. To know the effect of DAA treatment on the liver-related complications is crucial for prognosis and future management. The prime objective of our study is not only to see the effectiveness of DAA therapy in eliminating HCV virus but also to see the reversibility of liver fibrosis and related complications.

MATERIALS AND METHODS

A longitudinal observational study was conducted on 122 naïve hepatitis C patients from January 2022 to June 2024 at a tertiary care hospital. The study included patients aged 16 and older with Hepatitis C infection, who tested positive for anti-HCV antibodies and had a detectable HCV RNA viral load with considerable cirrhosis on ultrasound but without any sign or symptoms of decompensation of liver like hepatic encephalopathy, varices, ascites, jaundice, malena, coagulopathy. these patients fall in to the category of 'compensated cirrhosis'. Patients with chronic liver disease (CLD) attributable to non-Hepatitis C etiologies (e.g., alcoholic liver disease, hepatitis B, NASH, autoimmune hepatitis or other causes) and those with alternative liver pathologies (e.g., hepatocellular carcinoma, metastatic disease, or infectious etiologies) were excluded from

participation in this study and those with coexisting Hepatitis B or HIV infection were also excluded from the study.

Patient who came positive for anti HCV , a thorough past history and examination was taken for any prior episode of decompensation of liver, any other complications or prior hospitalisation and ruling out any other cause for chronic liver disease for exclusion .After diagnosing or screening out, a baseline battery of investigation was done of all the enrolled patients for record or comparison like complete blood picture, liver function test, kidney function test, viral marker (hiv, hbsag, antihcv), HCV RNA viral load. For assessment of liver fibrosis we performed transient elastography (TE) and ultrasound abdomen. we also calculated a marker for fibrosis that is APRI which was calculated using Aspartate Aminotransferase (AST) level measured in IU/L and the platelet count taken per liter of blood. The value of AST was taken as times above the upper limit of normal value. All the subjects included in the study were initiated on a DAA regimen comprising 400mg of Sofosbuvir and 100mg of Velpatasvir. Then post treatment patient were assessed for changes in their hepatic fibrosis with the help of changes in the values of AST, platelet count, APRI, LSM (TE) values.

The data were processed using SPSS software (version 19.0, SPSS Inc., Chicago, IL, USA). The results of the measurements are expressed as the average value (mean) accompanied by the standard error of the mean, providing a clear representation of the data's central tendency and variability. T-tests and Chi-square tests were used for analysis. P values <0.05 were considered highly significan.

RESULTS AND OBSERVATIONS

Among the total 122 study participants, 25-35 age range accounts for 33.6% making it the largest group, followed by 36-45 age group comprises 28.7% making it the second largest and 46-55 age group includes 26.2% and rest 7.5% individuals were the age group 56 and above. The mean age of the study was 39.41±7.7 years. The study comprises 72 males and 52 females participants. In our study, we included compensated cirrhotic patients without any history of UGIE bleeding, hepatic encephalopathy, coagulopathy, ascites, malena, hematemesis etc. In our study after DAA therapy for 12 weeks 95.1% patients achieved SVR (that is HCV RNA load become undetectable).This substantial decrease in HCV RNA load presence highlights the effectiveness of the antiviral therapy administered. The mean AST level was found to be 54.4+- 19.3 which after treatment become 29.8+- 10.2 which was a significant reduction. The mean platelet level was119+-33.8 which after treatment increase to 194+-32. the mean value of APRI score reduced from 2.201 +- 0.952 to 0.758+- 0.328and the mean of LSM (Fibroscan) decreased from 27.5+-10.68 to 10.8+- 6.52. These changes indicate significant improvement in liver fibrosis and related complications, leading to improved patient outcomes and increased life expectancy.

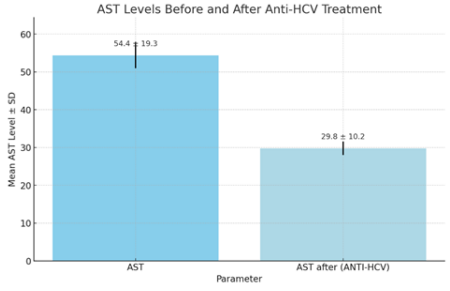

Figure 1: Descriptive statistics for AST and AST after (Anti-HCV therapy) study population

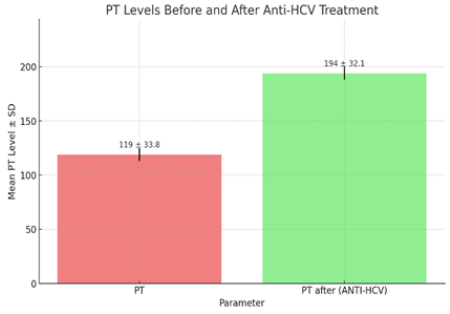

Figure 2: Descriptive statistics for PT and PT after (Anti-HCV therapy) study population

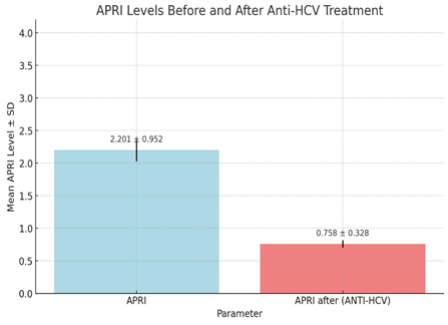

Figure 3: Descriptive statistics for APRI before and APRI after Anti-HCV therapy in study population

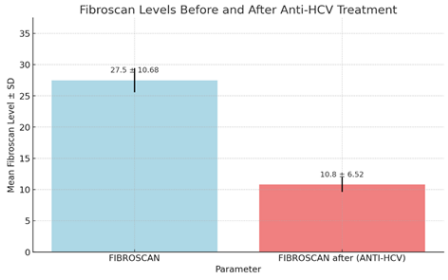

Figure 4: Descriptive statistics for Fibroscan(LSM) before and after Anti-HCV trreatment in study population

DISCUSSION

DAA (sofosbuvir + velpatasvir) therapy has been proven to be very effective not only in eradicating the HCV from body (achieving high SVR12) but also in reversing the hepatic fibrosis in long term in patients of compensated cirrhosis and has significant improvement in the values of platelet count , aspartate transaminase (AST) and also in index assessing fibrosis like APRI, transient elastography.

Furthermore, our study achieved a high rate of viral suppression, with 95.1% of patients showing undetectable HCV RNA levels post-treatment. This success rate is comparable or slightly better than those reported in similar studies. **Agrawal et al**. and **Kashani M et al.** found a similar success rate 96% and 94.3% respectively (7, 8) (p-value < 0.001), while **Jordan J. Feld et al.** reported slightly higher rates of 99% (9), possibly reflecting variations in patient management or treatment regimens (p-values < 0.001). The consistently high rates of undetectable HCV RNA across studies emphasize the significant impact of DAA therapy on viral load reduction.

In our study, a notable decrease in AST levels was observed, moving from an initial mean of 54.418 to 29.811 post-DAA therapy, with the change marked by highly significant p-values. **Cheng CH et al.** saw a decrease from 55 to 29, noted reduction(10). **Huynh T et al**, achieved similar results which closely align with our findings (11) i.e. normalisation of ast values. This highlight the consistent efficacy of the treatment. These comparative insights validate the effectiveness of DAA treatments in reducing AST levels.

In our study, notable improvement in the values of platelet count was observed moving from 119 to 194 after DAA therapy with highly significant p-values. Slightly lower results were obtained in few studies like **Saif-Al-Islam M et al.** from 112 to 146 and few others (12).

In our study, we noticed improvement in the parameters for hepatic fibrosis assessment like APRI and fibroscan (LSM) values after the DAA therapy like the mean value of APRI score reduced from 2.201 +- 0.952 to 0.758+- 0.328 and the mean of LSM (Fibroscan) decreased from 27.5+-10.68 to 10.8+-6.52. In a study, similar or lower results were seen like **Cheng CH et al.**, the APRI increased from 1.62 to 0.64 and LSM decreased from 26.3 to 20.9 (13) and **Bachofner JA et al.** the mean APRI score decreased from 1.10 to 0.43 and the LSM values decreased from 12.65 to 8.55. **Armandi et al.** LSM values decreased from the 19.3 to 11.6 (14) and **Alswat et al.** LSM decrease from 21.10 to 13.84 (15). these changes denotes the the significant improvement in

fibrois after the DAA therapy(14).

Finally , DAA not only helps in eradicating the virus from the body but also reversing the disease process i.e. fibrosis and improving the symptoms, complication and increasing the life span of the patient and plays as boon for hepatitis C.

CONCLUSION

Our study shows that sofosbuvir/velpatasvir treatment is highly effective in reversing liver fibrosis in HCV-infected cirrhotic patients. Additionally, HCV eradication improved liver steatosis in patients with higher levels of fatty liver disease. However, larger, longer-term studies with more precise liver histology assessments are needed to confirm these findings, address limitations, and identify factors contributing to liver fibrosis regression in HCV patients treated with direct-acting antivirals (DAAs).

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