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**ORIGINAL ARTICLE**

# Combine treatment of Sofosbuvir and Velpatasvir in Patients of Chronic Hapatitis C

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## ABSTRACT

**Objective:** The purpose of this research is to evaluate how well individuals with chronic hepatitis C respond to a combination treatment consisting of sofosbuvir and velpatasvir.
**Study Design:** Observational/ Prospective study
**Place of Study:** King Salman Armed Forces Hospital Tabuk KSA and Dow University of Health Sciences Karachi Pakistan.
**Duration of Study:** Jan, 2021 to Dec, 2021
**Methods:** This research included 42 participants of both sexes. Patients ranged in age from 20 to 78. After obtaining written permission, we collected demographic data about the patient, including age, gender, and height and weight. Patients with known genotypes of hepatitis C were presented. Patients were treated for 15 weeks with a SOF/VLP regimen that included sofosbuvir and velpatasvir. SPSS 24.0 version was used to analyse all of the data.
**Results:** There were majority males in this study. The mean age of the cases was 33.8±7.43 years with mean BMI 23.18±7.31 kg/m$^2$. Comorbidities were HTN, DM and obesity among all cases. There were 12 (28.6%) patients had treatment experienced. Frequency of effectiveness was found among 40 (95.2%) cases and 2 (4.8%) patients were died. Post-treatment, we found significantly improvement in aspartate aminotransferase (AST) 36.11 ± 9.13, alanine aminotransferase (ALT) 27.23 ± 11.45 and hemoglobin level 13.8 ± 4.19.
**Conclusion:** The results of this trial led us to the conclusion that the combination therapy of hepatitis C patients with sofosbuvir and velpatasvir was successful, safe, and well tolerated by the patients.
**Keywords:**, Sofosbuvir, Hepatitis C, Velpatasvir, Comorbidities

## INTRODUCTION

HCV is a single-stranded RNA virus from the Flaviviridae family with six main genotypes (GTs) that has infected 150 million individuals globally [1, 2]. HCV has six major genotypes (GTs). Cirrhosis, hepatic decompensation, and hepatocellular cancer may all develop as a result of persistent HCV infection, which also causes progressive liver fibrosis. A yearly death rate of half a million persons is attributed to chronic HCV infection-related liver disease [3].

While most of the real-world data on DAA treatment for chronic hepatitis C come from western nations [4-6], there are little Asian data on DAAs [7,8]. This disease is difficult to control in Asian nations for a number of reasons. In Asia, the availability and approvals of DAAs are much lower than in Europe and North America. [9] The HCV genotypes in this area are quite different. As a result, there is a pressing need to better understand how all-oral DAAs are used in Asian nations, especially Thailand, to treat HCV. Clinical efficacy and safety data are vital for patients and doctors to make treatment regimen choices and for health care policy to determine treatment coverage. These data are crucial

For years, conventional interferon-based therapy regimens with or without ribavirin have been used to treat chronic hepatitis C; however, the modality failed owing to low effectiveness, inadequate dosing schedule, poor compliance and the associated unpleasant effects. Directly acting antivirals (DAAs) for chronic hepatitis C therapy were a major breakthrough. By eliminating all the drawbacks of traditional therapy, this approach is now the one most often used [10,11].

Nonstructural protein 5B polymerase (NS5B) polymerase is a nonstructural protein 5B (NS5B) polymerase inhibitor that functions as a pangenotypic antiviral. Because of this, it's less likely to cause problems and is less likely to encounter opposition.[12,13] Velpatasvir is an HCV NS5A protein inhibitor. In addition, it is effective against all HCV genotypes. Sofosbuvir (NS5B inhibitor) and velpatasvir (NS5A inhibitor) for the treatment of chronic hepatitis C have showed an effectiveness of 98%–100% (SVR12) in non-cirrhotic treatment-nave patients. [14].

SVR may be lower in real-world clinical settings, despite clinical studies showing SOF/VEL to be very effective [13, 14], because to variations in patient demographics, resources, and compliance with optimal procedures. According to our knowledge, there are only a few major published studies that have investigated SOF/VEL in real-world settings utilising conservative intention-to-treat (ITT) techniques in real-world settings [15]. (ie, included all treated individuals within a jurisdiction). To fully grasp the real-world aspects that contribute to poor SVR, conservative analytic methods must be used [9, 15]. These methods do not exclude persons who have been lost to follow-up. Studying effectiveness in populations that often have poorer treatment outcomes due to biological and/or social reasons, such as those with cirrhosis or decompensated disease or GT3 infection, as well as those with a prior history of HCV treatment or those who inject drugs, requires more conservative, real-world studies. In addition, real-world evidence on the efficiency of SOF/VEL against different genotypes is few, and it is not obvious if the addition of ribavirin (RBV) to SOF/VEL increases SVR [15]. Finally, the absence of population-based analysis restricts the generalizability of research findings to all real-world activity within a jurisdiction. As a result, further research is required to assess SOF/VEL efficacy outside of controlled clinical trial settings in order to guide clinician, programming, and policy choices.

We did this study to examine the effectiveness of sofosbuvir and velpatasvir combined therapy in hepatitis C patients.

## MATERIAL AND METHODS

This prospective/observational study was conducted at King Salman Armed Forces Hospital Tabuk KSA and Dow University of Health Sciences Karachi Pakistan. From Jan, 2021 to Dec, 2021 and comprised of 42 patients. After receiving the patients' informed written permission, detailed demographic information was collected. Patients with serious medical conditions and those who did not give any kind of written agreement were not allowed to participate in this research.

The patients ranged in age from 20 to 78. Both male and female hepatitis C patients aged 20 to 60 years old were included.

During the 15-week course of treatment, all patients received oral doses of 400 mg sofosbuvir and 100 mg velpatasvir per day as fixed-dose combination tablets. Ribavirin was also given to the combination of sofosbuvir and velpatasvir if the patient had liver cirrhosis. After optimising haemoglobin in cirrhotic patients with supplements and starting them on ribavirin at 600 mg per day, the drug was utilised to treat those who still had low haemoglobin after starting it. The identification of HCV RNA fragments by RT-PCR (reverse transcription-polymerase chain reaction) in the hospital laboratory provided the basis for the diagnosis of chronic hepatitis C. RT-PCR detected chronic HCV infection when the HCV RNA level remained over 50 copies for more than six months. When it comes to determining someone's liver health, the following criteria were used: (1) physical examination for signs of chronic liver disease such as palmar erythema and jaundice; (2) laboratory tests such as abnormally low albumin levels or an INR greater than 1.2; and (3) imaging techniques such as ultraxial computed tomography.

For the first 12 weeks, the patients had weekly physical examinations and regular blood tests to keep track of their progress. SVR12, or the sustained virologic response 12 weeks after therapy, was used to gauge the success of the medication. If the HCV viral load was undetectable or less than 50 IU/ml at 12 weeks after therapy, individuals were regarded to have achieved SVR12 or responders. Treating failures/non-responders were referred to as SVR12 failures. No complaints, mild, moderate, and severe adverse occurrences were the four levels of severity that were assigned to the adverse events. Whenever an adverse event was brief and didn't need hospitalisation or a change in therapy, we classified it as moderate. Anorexia, headaches, and epigastric discomfort were all classified as "minor side effects," according to the manufacturer. Child-Pugh score, MELD score, liver function tests, and renal profile derangement were among the moderate adverse events that occurred. When all other possible causes of death had been ruled out, the death was classified as a severe adverse response. SVR12, adverse events and demographics were examined using SPSS 24.0 after the collection of data.

## RESULTS

There were majority males 29 (69.05%) and 13 (30.95%) females in this study.(fig 1)

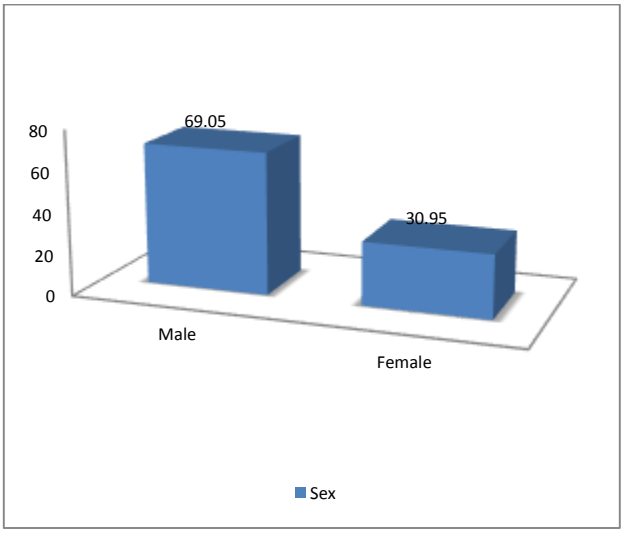


Figure-1: Distribution of gender among all cases

The mean age of the cases was 33.8±7.43 years with mean BMI 23.18±7.31 kg/m$^2$. Comorbidities were HTN, DM and obesity among all cases. There were 12 (28.6%) patients had treatment experienced. (table 1)

Table 1: Details of patients that have been enrolled

| Variables | Frequency | %age |
|---|---|---|
| Mean age (years) | 33.8±7.43 | |
| Mean BMI (kg/m$^2$) | 23.18±7.31 | |
| Other Diseases | | |
| HTN | 21 | 50 |
| Diabetes | 15 | 35.7 |
| Obesity | 6 | 14.3 |
| Patients type | | |
| Experienced | 12 | 28.6 |
| Naive | 30 | 71.4 |

Frequency of effectiveness was found among 40 (95.2%) cases and during follow up 2 (4.8%) patients were died.(fig 2)

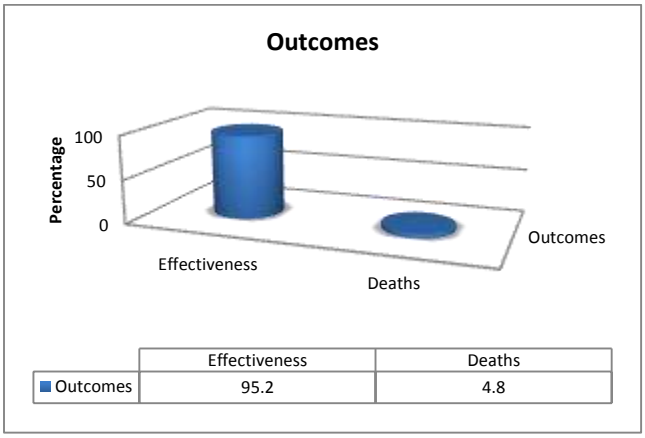


Figure-2: Frequency of efficacy and died patients

Post-treatment, we found significantly improvement in aspartate aminotransferase (AST) 36.11 ± 9.13, alanine aminotransferase (ALT) 27.23 ± 11.45 and hemoglobin level 13.8 ± 4.19. Adverse events among all cases were headache, fatigue and nausea. (table 2)

Table 2: Post-treatment effectiveness among enrolled cases

| Favorable Outcomes | Frequency | %age |
|---|---|---|
| Lab Findings | | |
| AST (U/L) | 36.11 ± 9.13 | |
| ALT (U/L) | 27.23 ± 11.45 | |
| Hemoglobin, g/dl | 13.8 ± 4.19 | |
| bilirubin (mg/dl) | 0.9±1.27 | |
| Adverse Outcomes | | |
| headache | 23 | 54.8 |
| fatigue | 14 | 33.3 |
| nausea | 5 | 11.9 |

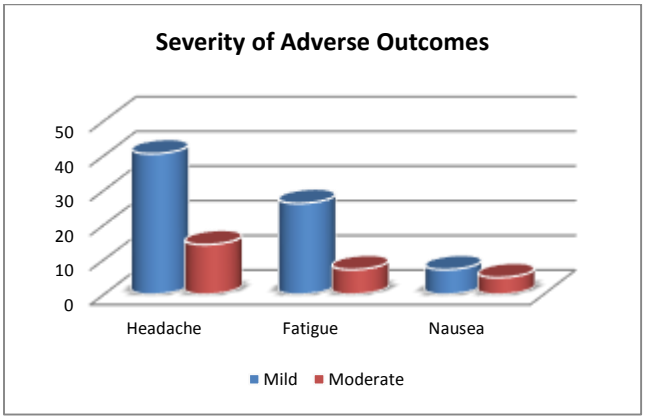


Figure-3: Association of adverse outcomes with severity

Among 23 cases of headache, 17 cases had mild headache and 6 cases had moderate. In 14 cases of fatigue 11 cases had mild and 3 cases had moderate. We found 3 cases of nausea had mild and 2 cases had moderate adverse events. No any severe case of adverse event found among all cases.(fig 3)

## DISCUSSION

Chronic HCV infection has been treated with interferon-based therapy for many years. In addition to its ineffectiveness, the regimen was complicated and posed several safety risks. DAAs were a game-changer in the fight against chronic HCV. Sofosbuvir (NS5B inhibitor) and velpatasvir (NS5A inhibitor) are two of the second-generation DAAs that have solved all of the shortcomings of earlier chronic HCV therapy options [16,17].

In current 42 patients of hepatitis C was presented. There were majority males 29 (69.05%) and 13 (30.95%) females. The mean age of the cases was 33.8±7.43 years with mean BMI 23.18±7.31 kg/m$^2$. Comorbidities were HTN, DM and obesity among all cases. There were 12 (28.6%) patients had treatment experienced. Findings of current research showed comparable outcomes to the previous studies.[18,19] Efficacy of sofosbuvir and velpatasvir with or without ribavirin in patients with chronic hepatitis C was investigated at 99.5 percent by Wong et al. in Asia, but only 88 percent by patients with decompensated cirrhosis, according to the research. SVR patterns were found to be comparable to those seen in our research [20]. Sofosbuvir and velpatasvir were used in a trial of 1,388 patients with chronic HCV in Pakistan, where 30 percent of the patients got the treatment, and the overall SVR rate was 94.7 percent, while in patients with cirrhosis, the rate was 88 percent. A similar conclusion may be drawn from this research [21]. Patients with cirrhosis had an SVR rate of just 89.7 percent, compared to 98.3 percent in non-cirrhotic chronic hepatitis C patients, according to our previous research. Research from previous years has shown that this pattern is common [20,21].

In current research, frequency of effectiveness was found among 40 (95.2%) cases and during follow up 2 (4.8%) patients were died. Sofosbuvir and velpatasvir had comparable effectiveness in individuals with decompensated cirrhosis as described in the ASTRAL trial, which found 89 percent to 100 percent efficacy in such patients [22]. Patients without cirrhosis had an effectiveness rate of 92,5 percent in a research done at another Pakistani facility [23]. Phase three research on genotype 3 chronic HCV with cirrhosis found a 95 percent SVR12 in individuals without cirrhosis, which is similar to our study's findings [24]. In patients with chronic HCV infection treated with a sofosbuvir and velpatasvir combination regimen, regardless of HCV genotype or cirrhosis status, Buggisch et al. reported a 99 percent SVR12 rate [25].

Post-treatment, we found significantly improvement in aspartate aminotransferase (AST) 36.11 ± 9.13, alanine aminotransferase (ALT) 27.23 ± 11.45 and hemoglobin level 13.8 ± 4.19. Adverse events among all cases were headache, fatigue and nausea. Among 23 cases of headache, 17 cases had mild headache and 6 cases had moderate. In 14 cases of fatigue 11 cases had mild and 3 cases had moderate. We found 3 cases of nausea had mild and 2 cases had moderate adverse events. No any severe case of adverse event found among all cases. These results were comparable to the previous researches.[26,27] Dasabuvir is the only NNI medication that has been licenced and is commonly used in conjunction with ritonavir/paritaprevir and ombitasvir. Against HCV genotype 1, dasabuvir had the most impact. In patients with HCV-1-compensated cirrhosis, these three medications demonstrated good SVR rates at 12 weeks when administered in combination. Nausea, tiredness, pruritus, and headache were the most common mild adverse events (AEs) reported in approximately 80% of patients, particularly those receiving RVR. There was a little reduction in haemoglobin levels, occasionally reaching the lower end of the normal range.[28,29] Serious adverse events (AEs) were very infrequent. Post-marketing observation, on the other hand, revealed that many cirrhotic patients had developed liver decompensation or failed completely. According to the FDA's warning, this therapy might cause significant liver damage in individuals with cirrhosis[30].

## CONCLUSION

The results of this trial led us to the conclusion that the combination therapy of hepatitis C patients with sofosbuvir and velpatasvir was successful, safe, and well tolerated by the patients.

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