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Efficacy of Direct-Acting Antiviral in Treatment-Naive Chronic HCV Patients and in Those Previously Treated with Interferon and Ribavirin

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This manuscript is part of PhD research work of SY, carried out under direct supervision of AS. SY developed the concept and designed the research methodology, carried out research work and wrote the manuscript. QM and NH helped in statistical analysis. MUK provided critical revisions and approved the final version for publication.

Key words
HCV, Genotype, Sofosbuvir, Daclatasvir, SVR, Ribavirin

ABSTRACT

Pakistan has been ranked second highest in prevalence of hepatits C virus (HCV), all over the world. HCV genome depicts huge genetic variability resulting in seven different HCV genotypes (GTs) including around 90 sub types. Direct acting antivirals had revolutionized HCV treatment with less side effects and higher sustained virological response rate (SVR). For achievement of better SVR, Pakistan National HCV treatment guidelines include the use of DAAs, sofosbuvir (SOF) and daclatasvir (DCV). Current study was designed to analyze treatment efficacy of two different DAA-based regimens in chronic HCV infected people among most recurrent genotypes (GT) of HCV in the patients employing DAAs for the first time (HCV treatment-naive) and in the patients those already experienced interferon (INF) plus ribavirin (RBV) combined treatment (HCV treatment-experienced).For this purpose blood samples were collected from patients positive for anti-HCV antibodies, processed for RNA isolation, detection and quantification of HCV RNA, followed by GT determination. Treatment response rate was determined in terms of end treatment response rate (ETR) and sustained virological response rate (SVR) at end of treatment and 12 weeks after completion of treatment respectively. 88.8% patients were found detected for HCV RNA, with 53.1% males, mean age 44.86 ± 13.19, and mean viral load of 6.68 ±1.8. HCV GT-3a was found to be most common as 87.3, while GT-1a was found as 9.9%, GT-3a/3b as 2.80%, and 7.8% were typable. For SOF+RBV, overall ETR against studied GTs was 88.9%, SVR was 85.4%, while for SOF+DCV ETR recorded was 92% and SVR was 88.8%.

INTRODUCTION

Hepatitis C virus (HCV) is responsible for both acute as well as chronic liver disease, also cause serious public health problems worldwide. An estimation showed about 58 million people have been infected by HCV world widely, and around 1.5 million HCV cases reported each year (Brunner and Bruggmann, 2021). Pakistan has been ranked second highest in prevalence of HCV all over the world. In accord with the National Hepatitis Elimination Profile of Pakistan which was refurbish by the Coalition for Global Hepatitis Elimination on June 8, 2022, stated that about 9.8 million HCV infected people are living in Pakistan (Babigumira *et al*., 2023). HCV prevalence in 2018 in distinct provinces of Pakistan was 4.8% in Punjab, 3.8 % in Sindh, 3.1 % in Balochistan and 3.8 % in Khyber Pakhtunkhwa, separately. The wide spread presence of anti-HCV antibodies in patients using intravenous drugs was 62 %, new HCV cases were 461,000 along with 17,644 deaths due to HCV, detailed in 2019 in Pakistan (Babigumira *et al*., 2023).

Genome of HCV depicts huge genetic variability resulting in seven varying HCV genotypes (GTs) including around 90 sub types. These GTs depict variability percentage from 31-33% nucleotide sequence with one another, while subtypes differ by 20-25% (Zhang *et al*., 2020). Worldwide distribution of HCV GTs shows, GT-1 as the most frequent i.e 49.1%, GT-3 as 17.9%, GT-4 as

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16.8% and GT-2 as 11.%. GT-5 and constitute remaining 5% of distribution (Petruzziello *et al*., 2019). In Pakistan HCV GT-3 is most common GT with a prevalence ranging from 75-90% (Haqqi *et al*., 2019).

With the advances of pan-genotypic direct-acting antivirals (DAAs), HCV cure and control had a paradigm shift (Tayyab *et al*., 2021). Pakistan Government has launched its National Hepatitis Control Framework to assist World Health Organization (WHO) to achieve global targets of hepatitis elimination. A commitment of providing free of cost hepatitis diagnosis and treatment to patients has been made through development of provincial Hepatitis Prevention and Control Program. For achievement of better sustained virological response rate (SVR) with fewer side effects, Pakistan HCV treatment guidelines include the use of DAAs, sofosbuvir (SOF) and daclatasvir (DCV) (Tayyab *et al*., 2021). SOF is an NS5B (RNA dependent RNA polymerase) inhibitor while DCV is NS5A replication complex inhibitors. Current study was designed to analyze treatment efficacy of two different DAA-based regimens in chronic HCV infected people. Treatment response rate was compared against the most recurrent GT of HCV in the patients employing DAAs for the first time (HCV treatment-naive) and in the patients those already experienced interferon (INF) plus ribavirin (RBV) combined treatment (HCV treatment-experienced) and relapsed HCV infection.

MATERIALS AND METHODS

Study design and sample collection

Patients, male and female, 18 or more than 18 years of age, positive for anti-HCV antibodies, and with no record of HCV treatment and other who have been treated with INF/RBV previously, were included in this study. Patients co-infected with HBV or HIV, or having severe renal infection and other active malignancy were not included in the study. Patient's data was collected on prescribed questionnaire including information regarding age, sex, family history of HCV, any surgical intervention or dental procedures, previous HCV treatment history. Informed consent was taken from each patient before blood with drawl. Plasma separated from the blood samples collected from patients were stored at -20°C.

HCV RNA genotype determination

QIAamp DSP virus kit (Qiagen, Germany) was used for extraction of viral RNA from the patient plasma, while amplification and quantification was performed with Artus HCV RG RT-PCR kit (Qiagen, Germany), by following protocol of manufacturer.

Genotypes of HCV positive samples were determined by using type-specific primers following the slightly modified method developed by Ohno *et al*. (1997). Firstly, HCV1R primer was used to synthesize cDNA, followed by amplification of core gene with following primer

HCV1F:5`GGGAGGTCTCGTAGACCGTGCACCATG3`
R: 5`AGACGGGTATAGTACCCCATGAGAGTCGGC3`

in the first round of PCR. In the second round of PCR type-specific primers were used to determine HCV GTs. Primer sequences are:

HCV 2F: 5`AGACCGTGCACCATGAGCAC3`
HCV2G1a: 5`GGATAGGCTGACGTCTACCTC3`
HCV2G1b: 5`CCTGCCCTCGGGTTGGCTAC3`
HCV2G2a: 5`CACGTGGCTGGGATCGCTCCC3`
HCV2G3b: 5`CGCTCGGAAGTCTTACGTACC3`
HCV2G3a: 5`GCCCAGGACCGGCCTTCGCTCCGG3`
HCV2G4: 5`CCCGGGAACTTAACGTCCATC3`
HCV2G5a: 5`GAACCTCGGGGGGAGAGCAAG3`
HCV2G6a: 5`GGTCATTGGGGCCCCAATGT3`

Gel electrophoresis was used to visualize the amplified PCR products.

Assessment of treatment response rate

DAAs in two different combinations were used to evaluate their effectiveness. SOF and RBV for 24 weeks were given to patients in first combination and SOF+DCV±RBV for 12 weeks were given to patients in second combination (as prescribed by their physicians). HCV RNA was quantified by Real Time PCR before start of treatment, end of treatment, 12 weeks after completion of treatment. Those patients with negative PCR for HCV RNA at end of treatment were labeled to have end-treatment response rate (ETR), those who were negative 12 weeks after treatment completion were termed to have sustained virological response rate (SVR), While the patients those did not respond to treatment i.e., lack ETR or SVR after employing DAAs were and categorized as non-responders to therapy.

RESULTS

Epidemiological and biochemical characteristics of the study group

Real-time PCR was used for accurate detection and quantification of viral RNA. Results were interpreted according to instructions of provided with HCV RG RT-PCR kit (Qiagen, Germany). In real time PCR assay a positive reaction was detected by accumulation of a fluorescent signal. The Ct (cycle threshold) value is defined as the number of cycles required for the fluorescent signal to cross the threshold (i.e., exceeds background level). Ct levels are inversely proportional to the amount

of target nucleic acid in the sample (i.e., the lower the Ct level the greater the amount of target nucleic acid in the sample. Ct <29 was strong positive reactions indicative of abundant target nucleic acid in the sample, Ct 30-35 were positive reactions indication of moderate amounts of target nucleic acid and Ct 36-40 were weak reactions indicative of minimal amounts of target nucleic acid which could represent an infection state or could be due to environmental contamination. 928 (88.8%) patients were found positive for HCV RNA and 117 (11.2%) patients were not detected for HCV.

Mean age calculated for HCV RNA positive patients was 44.86±13.19 (Fig. 1A), number of males (i.e., 53.1%) was higher than the females (46.9%). The average viral load of HCV-RNA positive patients was 6.68±1.8Log10IU/ml before treatment. The viral load of HCV RNA in different age groups is illustrated in Figure 1B.

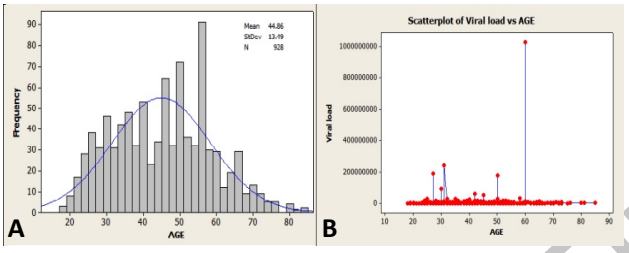

Fig. 1. Age distribution (A) and viral load (B) among different ages of HCV positive patients.

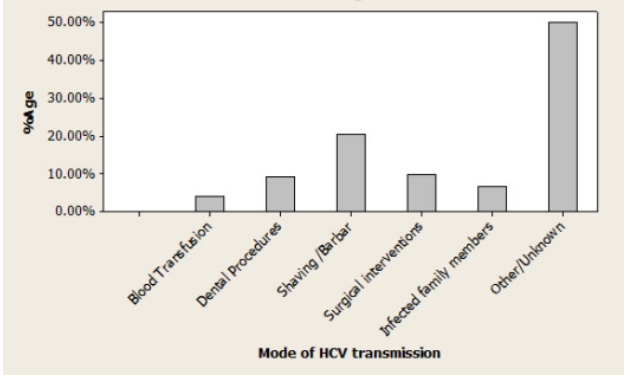

Fig. 2. Possible routes of HCV transmission in the study group.

To check HCV prevalence in different ages, HCV positive patients were divided into various age groups and age wise prevalence was calculated by Chi-square test.

More patients (27.1%) were observed in age group 50-59, (Fig. 2), indicating HCV to be more prevalent in this age group, while patients in the 60-69 years age group were found to have the highest mean viral load, i.e., 7.37±2.0 (Fig. 1B), compared to other groups. No significant difference was observed among different age groups in HCV RNA levels. According to the male-to-female ratio of HCV-positive patients, HCV is more prevalent in males than females, as males were more numerous in all age groups except in the last two groups i.e., 60-69 and >70 years of age (Table I).

Table I. Age distribution of HCV positive patients.

Age (years)	Average age ± SD	Gender (M/F)	HCV RNA detected (% age)	Average viral load Log10 IU/ml ± SD
18-29	24.9±2.8	82/60	142(15.4%)	6.74±1.3
30-39	34.0±2.7	116/77	193(20.7%)	6.80±2.1
40-49	44±2.8	106/103	209(22.6%)	6.4±1.8
50-59	53.6±2.6	133/118	251(27.1%)	6.52±1.9
60-69	63.4±2.6	39/57	96(10.4%)	7.37±2.0
>70	74.1±4.4	17/20	37(3.8%)	6.28±1.7
Total	44.86±13.19	493/435	928(100%)	6.68±1.8

Common modes for HCV transmission identified were blood transfusion in 4.03% subjects, 9.3% underwent dental procedures, 20.37% had history of using contaminated shaving blades (through barbers), 9.80% had surgical interventions, infected family members as 6.70%, while remaining 49.8% remained unconfirmed (may be accidental injuries, intravenous drug intake or others) (Fig. 2).

The baseline biochemical parameters including complete blood count, liver function tests of HCV positive patients was as follows: haemoglobin 12.21+1.88 mg/dL, mean corpuscular volume 83.2+10.11 fL, alanin aminotransferase (ALT) 67.23+87.22 U/L, aspartate aminotransferase (AST) 46.13+31.11 U/L, gamma-glutamyl transpeptidase 43.69±631.37 U/L, urea 33.1+13.39 mg/dl, creatinine 0.81+0.59 mg/dl.

Genotyping of the HCV RNA

The genotyping of HCV is a crucial factor in determining therapy strategies for patients. To determine GT distribution in the current research group, 928 HCV RNA-positive individuals were processed for HCV genotyping. Most samples (856 or 92.2%) were successfully genotyped. However, 72 (7.80%) were not; despite being run through the lab twice, they did not provide a GT result.

Mean age of patients and mean viral load of HCV in different GTs, is given in Table II.

Table II. Mean age and mean viral load in different genotypes of study group.

Genotype	Age group	Mean age	N (%age)	Mean viral load log10 ± SD
1a	22-73	43±12.97	85(9.9%)	6.67±2.1
3a	18-85	45±13.49	748(87.3%)	6.23±1.8
3a/3b	19-67	41±13.71	23(2.8%)	5.70±1.2
UT	21-72	42±13.81	72(7.80%)	4.73±1.7

Efficiency of direct-acting antiviral drugs (DAA) against various HCV genotypes

DAAs are now used as the first line of defense against persistent HCV infection in Pakistan, since 2014.

Effectiveness of SOF+RBV's

The response rate to SOF/RBV was statistically significant among the GTs tested according to the clinical guidelines of Pakistan, and this treatment was given to a total of 572 HCV-infected individuals. 538 GT-3a patients received SOF+RBV therapy 503 (93.4%) patients achieved ETR after 24 weeks of treatment, whereas 35 (6.6%) patients had treatment failure. The SVR rate for GT-3a was 91.2%, whereas 12.2% of patients had recurrent HCV infections. Collectively, 35 (6.6%) patients who experienced a failed ETR and 12 (2.2%) relapsed cases accounted for 47 (8.8%) percent of the study population and were classified as non-responders (NR).

Twenty four people with GT-1a who obtained SOF/RBV therapy got ETR, but only four (16.6%) failed to respond to the therapy. The SVR for this GT was 75% because two patients (8.4%) had relapsed, and four (16.6%) had failed treatment.

Of the ten patients with mixed GT 3a/3b who followed this therapy, 9 (90%) obtained ETR, whereas one was unable to proceed; that is why not included in the trial. The SVR was not changed for this GT. ETR of this therapy against the various GTs examined was 88.9%, with an SVR of 85.4%.

Two-way ANOVA found that the overall treatment response rate to the tested GTs was significant (i.e., 0.01).

Effectiveness of SOF+ DCV±RBV

In 2018, DCV was launched in Pakistan and added to treatment protocols to improve the effectiveness of HCV therapy. The effectiveness of combination SOF/DCV±RBV treatment was assessed in 284 HCV patients with varying GTs. There were 210 GT-3a patients, 61 GT-1a patients, and 13 of GTs 3a/3b. 193 GT-3a patients (91.9%) obtained ETR, whereas 190 (90.4%) achieved SVR among 210 patients. After therapy, 17 (8.10%) GT-3a patients were still positive, whereas three (1.5%) patients relapsed after 12 weeks.

There were 61 patients in all undergoing SOF/DCV combination treatment for GT-1a. 56 (91.8%) of these patients reached ETR, while 5 (8.2%) did not achieve ETR. The SVR rate in this GT was 90.1%, with just one patient experiencing a relapse (1.7%).

In GT 3a/3b, the ETR was 92.3%, and only one patient (7.7%) did not respond to treatment. With one recurrence (7.7%), the SVR against 3a/3b was 84.6%. In this investigation, the overall ETR for SOF/DCV for various GTs stayed at 92%, SVR as 88.3%, with a p-value of 0.02 computed through ANOVA. Table III shows the therapeutic response of this regimen against various GTs.

Table III. The effectiveness of SOF+RBV and SOF+DCV for different genotypes of HCV.

Genotype	NR	ETR	SVR	p-value
SOF+RBV				
GT-3a	8.8%	93.4%	91.2%	0.02
GT-1a	25%	83.4%	75.0%	0.011
GT 3a/3b	-	90.0%	90.0%	0.05
Overall	14.6%	88.9%	85.4%	0.01
SOF+DCV				
GT -3a	9.6%	91.9%	90.4%	O.02
GT-1a	9.9%	91.8%	90.1%	0.011
GT- 3a/3b	15.4%	92.3%	84.6%	0.05
Overall	11.6%	92.0%	88.3%	0.02

NR, non-responder; ETR, end treatment response rate; SVR, sustained virological response.

Efficacy of the SOF+RBV in treatment-naive and INF/RBV-treated patients

Patients positive for HCV RNA, with previous history of INF/RBV treatment were also examined for the effectiveness of the above regimens. Five hundred seventy-two patients received SOF/RBV treatment for 24 weeks, while 163 of these had also previously underwent INF/RBV therapy. Out of 409 treatment-naive patients, 378 (92.4%) had achieved ETR, 31 (7.6%) did not respond to treatment and remained positive for HCV RNA, 369 (90.2%) had attained SVR. The total number of NRs in the treatment-naive group was 40 (9.8%) (Table IV).

Among patients previously treated with INF/RBV, 152 (93.3%) reached ETR, and 11 (6.7%) did not responded to this therapy, while 92.0% achieved SVR. 1.3% patient had relapsed and 8.0% overall NR. The treatment response was found to be non-significant, determined by two-way ANOVA, suggesting no significant difference in treatment

response rate between the two analyzed groups (Table IV).

Table IV. SOF/RBV and SOF+DCV+RBV treatment rate among HCV non-treated and INF/RBV-treated patients.

Patient group	NR	ETR	SVR	p value
SOF/RBV treatment				
Non-treated	9.8 % (40)	92.4 % (369/409)	90.2 % (369/409)	0.30
INF/RBV treated	8. % (13)	93.3 % (150)	92 % (150)	
SOF+DCV+RBV treatment				
Non-Treatments	9.6% (20)	91.9% (193)	90.4% (190)	0.5
INF/RBV treatments	11.9% (8)	93.2% (69)	89.1% (66)	

Efficacy of SOF+DCV±RBV in treatment-naive and INF/RBV-treated patients.

Seventy-four patients in the SOF+DCV group had previous treatment experience, whereas the other 210 patients were treatment-naive. In addition to SOF+DCV, weight-based RBV was added to treat INF/RBV-treatment experienced patients. We found 193 (91.9%) of 210 non-treated patients achieved ETR, and 17 (8.1%) did not, 190 (90.4%), with three relapsed patients (1.5%), obtained SVR, and 9.6% patient remained non-responders (NR) (Table IV)

Among 74 INF/RBV-treatment experienced patients, ETR was achieved by 69 (93.2%) and 5 (6.7%) could not attain ETR, and 66 (89.1%) achieved SVR, with 3 (4.2%) relapsing. The response rate to SOF+DCV therapy was the same for patients who had never been treated and those treated with INF/RBV (P-value = 0.5).

DISCUSSION

HCV has infected 4.8%–8.2% of Pakistan's population with GT-3a found to be the most prevalent genotype (Haqqi *et al*., 2019). DAAs introduction in HCV treatment, proved to be game changer because of their high SVR and less severe side effects, with short treatment duration and enhanced tolerance (Spengler, 2018). The current research examines the effectiveness of two DAA regimens in HCV isolates from Lahore, Pakistan. HCV isolates, mainly from Lahore. 88.8% of patients with HCV RNA measured by real-time PCR were positive, compared to 11.2% of negative patients with anti-HCV antibody positivity. There are two possible explanations for a negative HCV PCR with positive anti-HCV antibodies: A past HCV infection, cleared by the host's immune system, as in 20–37% of instances of acute infection (Aisyah *et al*., 2018), or a false positive antibody screening test (Khan *et al*., 2020). Multiple studies have shown false-positive antibody testing; hence, it cannot be regarded as accurate. Nevertheless, real-time PCR is recommended to detect and quantify HCV RNA (Khan *et al*., 2020; Moorman *et al*., 2017). The average viral load and age of HCV RNA-positive patients were 6.68±1.8 and 44.86±13.19 for males and females, respectively, with 46.9% females and 53.1% males, indicating a male majority in HCV patients. Several studies have shown a male majority in HCV patients (Inamullah *et al*., 2011), but some studies also show a greater frequency of HCV in females (Qamar *et al*., 2021) than in males. As a result, both genders are equally susceptible to HCV.

In context of age distribution of HCV patients, HCV was found to be more common in 50 to 59 years old people. In contrast to other age groups, the 60–69 years patient group was shown to have the considerably high viral load. Khan *et al*. (2020) also reported higher prevalence of HCV among age groups ranging from 41 to 60 years.

Because the antiviral therapy response rate varies across HCV GTs, determining HCV RNA GT is a significant predictor of successful treatment regimens (Kumar *et al*., 2018). HCV GT-3a was found to be most frequent as identified in 87.3%, followed by GT-1a, i.e., 9.9%, and the 3a/3b mixed genotype with 2.80%, while 7.8% of samples remained untypeable. According to research conducted in 2021, GT-3a was the most frequent HCV genotype in Punjab (Yousaf *et al*., 2021). Khan *et al*. (2020) projected an 83.5% prevalence of HCV GT-3a in Lahore in 2020, with GT-1a accounting for 5.1 %. In the current research, 7.8% of HCV-positive individuals remained untypable. Haqqi *et al*. (2019) found an increase in untypable HCV patients while lowering the number of other GTs such as 2a, 2b, 1a, and 3b. Between 2000 and 2009, another large-scale study found that 17% of HCV patients remained untypable (Butt *et al*., 2010). The absence of a proofreading function in HCV RNA polymerase causes mutations at a rate of 10^{-3} nucleotides per replication cycle, resulting in the development of variants. Genotyping tests depend on conserved regions, However, mutations in these regions make the assays untypable. It is challenging to identify treatment regimens for untypable GT. Hence, improved genotyping tests must be created to address the issue (Afzal *et al*., 2014).

Since 2014, DAAs have been used as the first line of treatment for HCV in Pakistan. SOF and RBV regiments are registered and extensively accessible in Pakistan (Khaliq and Raza, 2018). Several types of research on the

effectiveness of DAAs against various GTs, notably GT-3a, have been reported in Pakistan. SOF/RBV effectiveness was tested in various GTs. Patients were administered SOF+RBV, and response rate was determined as ETR and SVR. For GT-3a, ETR calculated was 93.4%, and SVR as 91.2% indicating a solid response for SOF+RBV treatment, 8.8% of patients remained NR. However, the ETR and SVR of GT-1a are 83.4% and 75%, respectively, with an NR rate of 25%. For GT-3a and 3b, the ETR and SVR were the same, i.e., 90% with no NR and one patient who did not continue medication. The VALENCE clinical study on HCV GT-3 patients with 24-week SOF+RBV treatment obtained a high SVR of 85%. Zeuzem *et al*. (2014) and Majid *et al*. (2022) found that this treatment regimen was effective against GT-3a, with an ETR of 95.69%, 4.12% relapsed, and 4.90% failure. However, for GT-1a, ETR was 89.36%, with 9.52% relapsed, and 10.63% failure (Majid *et al*., 2022; Zeuzem *et al*., 2014). Akhter *et al*. (2016) reported a similar response rate for SOF/RBV therapy for GT-3a (i.e., ETR as 96.5% and SVR as 85% (Mushtaq *et al*., 2020). The total response rate to this medication was 88.9% for ETR and 85.4% for SVR, similar to studies reported in previous research (Dalgard *et al*., 2017; Mushtaq *et al*., 2020). The effectiveness of SOF+RBV in treating HCV in the present research may be summarized as "SOF being pan-genotypic is beneficial.

Since 2018, DCV has been included in Pakistan's national therapy guidelines for HCV, expanding the usage of DAAs in HCV treatment beyond SOF (Khaliq and Raza, 2018). Including this combination therapy in government policy has produced successful treatment outcomes. Umar *et al*. (2018) reported an SVR of 83% with SOF+DCV combined treatment, indicating that this combination therapy has a high SVR. The present research additionally assessed the efficacy of SOF+DCV±RBV against different GTS. The ETR of GT-3a against this treatment was 91.9%, and the SVR was 90.4%, with an NR of 9.6%. ETR for GT-1a was 91.8%, SVR was 90.0%, and NR was 9.9%. For GT-3a and GT-3b, the ETR was 92.3%, the SVR was 84.6%, and the NR was 15.4%. The overall results against the GTs analyzed showed an ETR of 92%, and SVR of 88.8%, and NR of 11.6%. Almost the same results were found in a trial of SOF+DCV+RBV for HCV patients conducted by Butt *et al*. (2021), which showed an ETR of 97.33% and an SVR of 88.3%. The SVR achieved in the current research was lower than the that reported by Abozeid *et al*. (2018). The decline in SVR after treatment may be because patients with advanced liver disease have a lower response rate to SOF regimens and are more likely to develop HCC and cirrhotic consequences (Morio *et al*., 2018). In this study, the response to treatment for 1a and GT-3a was almost the same, while the SVR for a mixed GT-3a and 3b infection was 84.6%. Multiple studies previously reported have evaluated treatment response against single GT, only Few studies have examined the effectiveness of DAAs in treating a mixed GT infection. Based on the results of the present investigation, the present study concluded that HCV genotypes 1a and 3a could be successfully treated with SOF plus DCV. However, further study is required to determine the effectiveness of this therapy strategy against mixed GTs infection.

Patients who were treatment naive and those who had already experienced INF/RBV treatment had no significant difference in treatment response rate of studied treatment regimens i.e., SVR and ETR for SOF/RBV, was 90.2% and 92%, respectively, and with SOF+DCV+RBV, it was 90.4% and 89.1%, respectively. Butt *et al*. (2019) study revealed that past HCV drug history did not affect treatment results.

CONCLUSION

In conclusion, Direct-Acting Antivirals (DAAs), specifically the combination of SOF (Sofosbuvir) and DCV (Daclatasvir), exhibit remarkable effectiveness in the treatment of Hepatitis C Virus (HCV) due to their pangenotypic nature. Importantly, the treatment outcomes remain consistently favorable, regardless of the patient's prior history of interferon (INF) treatment. Our findings support the recommendation of SOF and DCV for HCV treatment, given their consistent efficacy. Furthermore, our comparison of treatment responses among treatment-naive individuals and those previously treated with INF and ribavirin reveals no significant differences in outcomes with these two regimens. This observation highlights the equal effectiveness of DAAs in patients who were either initially treated with DAAs or had a history of INF-based regimens. In summary, DAAs, due to their pangenotypic efficacy, emerge as a highly effective option for combating different HCV genotypes. The clinical significance of our study lies in the fact that treatment outcomes remain robust, even in patients with a prior history of INF-based treatment. Therefore, we advocate the widespread use of SOF and DCV in HCV therapy for consistently positive results.

DECLARATIONS

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IRB approval

This study was performed after getting permission from the Advance Studies and Research Board, University of the Punjab, at the Centre for Applied Molecular Biology (CAMB), University of Punjab, Lahore.

Ethical statement

To ensure the ethical integrity of this research, informed consent was taken from the participant, the confidentiality of participant data was strictly maintained, and all collected data was stored securely in encrypted digital files, accessible only to the research team.

Statement of conflict of interests

The authors have declared no conflict of interest.

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