Original Article

Effectiveness of generic sofosbuvir in the treatment of chronic hepatitis C virus infection in Saudi patients

Hamdan S. AlGhamdi, MBBS, MRCP, *Ali A. AlHabobi,* MBBS, *Rakan S. AlQahtani,* MBBS, *Firas A. Ghomraoui,* MBBS, *Khalefa M. AlThiab,* PharmB, *Abdulrahman A. AlOun,* MBBS, *Abduljaleel M. AlAlwan,* MBBS, *Mutaz B. Abdelmahmoud,* MBBS, MRCP, *Ibrahim H. AlTraif,* MBBS, FRCP, *Abdulrahman A. Aljumah,* MD, FRCP (I).

ABSTRACT

الأهداف: تقييم فعالية سوفوسبوفير العام (SOF) والداكلاتاسفير (DCV) ذو العلامة التجارية لعلاج المرضى المصابين بفيروس التهاب الكبد الوبائي المزمن (HCV).

المنهجية: في هذه الدراسة المرجعية التي تم إجراؤها في مركز واحد في المملكة العربية السعودية بين أغسطس 2017م ويوليو 2022م، قمنا بتسجيل 140 مريضًا متتاليًا مصابين بفيروس HCV الذين تلقوا SOF عام وDCV ذو العلامة التجارية. وكانت النتيجة الأولية الاستجابة الفيروسية المستدامة في الأسبوع 12 (SVR12).

النتائج: كانت غالبية المرضى من الإناث (62.1%)، المصابين بالنمط الجيني 4 (57.9%)، و 120 لم يخضعوا لأي علاج بالأدوية (85.7%) 55 من المرضى يعانون من تليف الكبد الأساسي (39.3%). كان متوسط عمر المرضى 61±13.6 سنة. في تحليل النية للعلاج حققَ 131 مريضًا (93.6%) SVR12. إضافةً لذلك، 85.7%، 100%، 100%، 88.9%، و 96.3% من الأنماط الجينية 1أ، 1ب، 2، 3، و 4، على التوالي، حققت SVR 12. في التحليل لكل بروتوكول حقق 131 (96.3%) مريضًا SVR قدره 12. بالإضافة إلى ذلك، 92.3%، 100%، 100%، 88.9%، و98.7% من المرضى الذين لديهم أنماط وراثية 1أ، 1ب، 2، 3، و 4، على التوالي، حققوا SVR12. ولم تحدث أي اختراقات فيروسية لفيروس HCV. في تحليل المجموعة الفرعية، كانت معدلات SVR12 قابلة للمقارنة بغض النظر عن الخصائص الأساسية، مثل تاريخ العلاج، وتليف الكبد، وسرطان الكبد. أظهر المرضى الذين حققوا SVR12 تحسنًا ملحوظًا في إنزيم الكبد، وفي مصل الدم بعد العلاج، ومستويات البيليروبين الإجمالية.

الخلاصة: تؤكد نتائج دراستنا فعالية دواء سوفوسبوفير كخيار علاجي لعدوى فيروس HCV.

Objectives: To assess the effectiveness of generic sofosbuvir (SOF) and branded daclatasvir (DCV) for the treatment of chronic hepatitis C virus (HCV)infected patients.

Methods: This retrospective study, performed in a single center in Saudi Arabia between August 2017 and July 2022, we enrolled 140 consecutive patients with HCV who received generic SOF and branded DCV. The primary outcome was sustained virologic response at week 12 (SVR12).

Results: The majority of the patients were female (62.1%), infected with genotype 4 (57.9%), and treatment-naïve in 120 (85.7%) patients with baseline cirrhosis in 55 (39.3%). The mean patient age was 61±13.6 years. In the intention-to-treat analysis, 131 (93.6%) patients achieved SVR12. Moreover, 85.7%, 100%, 100%, 88.9%, and 96.3% of genotypes 1a, 1b, 2, 3, and 4, respectively, achieved SVR12. In the per-protocol analysis, 131 (96.3%) patients achieved an SVR of 12. Additionally, 92.3%, 100%, 100%, 88.9%, and 98.7% of the patients with genotypes 1a, 1b, 2, 3, and 4, respectively, achieved SVR12. No HCV virologic breakthroughs occurred. In the subgroup analysis, SVR12 rates were comparable regardless of baseline characteristics, such as treatment history, cirrhosis, and hepatocellular carcinoma. Patients achieving SVR12 showed a significant improvement in post-treatment serum liver enzyme and total bilirubin levels.

Conclusion: The findings of our study confirm the effectiveness of generic sofosbuvir as a treatment option for HCV infection.

Keywords: hepatitis C, generic, antiviral agents, sofosbuvir, treatment outcome

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From the Hepatobiliary Sciences & Organs Transplant Department (AlGhamdi, AlAlwan, Alqahtani, Aloun, Abdelmahmoud, ATraif), Hepatology Section and From the Department of Internal Medicine (AlHabobi), King Abdulaziz Medical City of National Guard; from King Saud Bin Abdulaziz University for health sciences (AlGhamdi, AlAlwan, AlThiab); from King Abdullah International Research Centre (AlGhamdi, AlAlwan, AlThiab), Ministry of National Guard Health Affairs; From the Department of Pharmaceutical Care Services (AlThiab), King Abdulaziz Medical City of National Guard; Form the College of Medicine (AlJumah), Dar Al-Uloom University, Riyadh, Kingdom of Saudi Arabia; and From the Department of Internal Medicine (Ghomraoui), Sisters of Charity Hospital, Buffalo, New York, United States of America.

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Address correspondence and reprint request to: Dr. Hamdan S. AlGhamdi, King Saud Bin Abdulaziz University for Health Sciences, Department of Hepatobiliary Sciences and Organs Transplant Centre, King Abdulaziz Medical City of National Guard, Riyadh, Kingdom of Saudi Arabia, Email: alghamdiha@mngha.med.sa
ORCID ID: https://orcid.org/0000-0003-0584-4694

The prevalence of hepatitis C virus (HCV) infection in Saudi Arabia is estimated to be less than 2%.[1] Chronic HCV infection is one of the commonest causes of liver failure, hepatocellular carcinoma (HCC), and transplantation.[2,3] Since the approval of sofosbuvir as the first pan-genotypic direct-acting antiviral agent (DAA) by the United States Food and Drug Administration (FDA) in 2013, considerable progress has been made in the management of HCV infection. Indeed, more than 95% of HCV-infected patients achieve a sustained virologic response (SVR) or cure at various stages of hepatic fibrosis.[4]

Sofosbuvir is a nucleotide inhibitor of the HCV NS5B polymerase, and daclatasvir, on the other hand, is an inhibitor of the HCV NS5A replication complex.[5,6] The combination of sofosbuvir and daclatasvir is indicated as a pan-genotypic regimen for the treatment of patients with HCV.[7] In 2016, the World Health Organization (WHO) endorsed a set of global health sector strategies to eliminate viral hepatitis as a public health threat by 2030.[8] However, the cost of treatment with branded sofosbuvir-based regimens compared with generic versions is extremely high in many countries.[9] By including sofosbuvir in the WHO's list of essential medicines, it enabled generic versions of sofosbuvir to be accessible in many countries at an affordable price, including in Saudi Arabia.[10] Thus, the availability of a generic, low-cost version of sofosbuvir has attracted attention for its use in HCV elimination programs enabling the treatment of a larger pool of HCV-infected patients.[11,12]

A locally produced generic version of sofosbuvir (Sovira®) was made available in Saudi Arabia in June 2016. Despite the widespread use of generic sofosbuvir across many hospitals in Saudi Arabia, there is still insufficient local data on the effectiveness of generic sofosbuvir across all HCV genotypes. Therefore, we retrospectively studied the effectiveness of generic sofosbuvir in combination with the branded drug daclatasvir in patients with various HCV genotypes and clinical features who presented to our outpatient hepatology clinic.

Methods. We retrospectively studied all patients infected with HCV who presented to the hepatology clinic of King Abdulaziz Medical City of National Guard Hospital, Riyadh, between August 2017 and July 2022 and met our inclusion criteria. The study was carried out in accordance with the guidelines set forth in the Helsinki Declaration and was approved by the Institutional Review Board of the King Abdullah International Medical Research Center. Informed consent was waived due to the retrospective nature of the study.

We searched the electronic medical records of hepatology outpatient clinics using the International Classification of Diseases, Ninth Revision, using the term HCV. We included patients who were treated with generic sofosbuvir in combination with the original formulation of daclatasvir with or without ribavirin (RBV) if they were ≥18 years of age, had a positive HCV antibody result, and had a pretreatment HCV ribonucleic acid (RNA) level of >1000 IU/mL for at least 6 months before starting the DAA treatment regimen. We excluded patients with decompensated cirrhosis (child's-Pugh ≥7), pregnant or breastfeeding women, human immunodeficiency virus or hepatitis B virus co-infection, and patients previously treated with daclatasvir, ledipasvir, or other NS5A inhibitors.

Demographics and patient outcome data were collected in a specified case report form, which was later transferred to an Excel spreadsheet for final analysis. These data included age, gender, weight, HCV RNA levels at baseline and 12 weeks post-treatment, HCV genotype, previous treatment history, liver fibrosis stage, presence or prior history of HCC, diabetes mellitus, use of RBV, pre- and post-treatment liver biochemistry, baseline serum chemistry, and pre- and post-treatment HbA1c levels.

The FibroScan (Echosens, Paris, France) score was used to categorize liver fibrosis stages: Metavir F0 ≤5 kPa, F1=5.1–7 kPa, F2=7.1–9 kPa, F3=9.1–12.49 kPa, and F4 ≥12.5 kPa. The diagnosis of cirrhosis was established either on liver stiffness measurements or based on liver imaging showing typical morphological changes of cirrhosis. The diagnosis of HCC was based on liver radiological findings (computed tomography [CT] or magnetic resonance imaging) of cirrhosis with a ≥1 cm lesion within the liver exhibiting contrast hyperenhancement in the arterial phase (wash-in) and washout in the portal venous or delayed phase, with or without elevation of the alpha-fetoprotein level.[13]

Treatment protocol. Prescriptions of 400 mg of generic sofosbuvir (Sovira®, Saudi Pharmaceutical Industries, and Medical Appliances Corporation [SPIMACO], Riyadh, Saudi Arabia) and 60 mg of branded daclatasvir (Daklinza®, Bristol-Myers

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Squibb, Dublin, Ireland) were obtained from our outpatient pharmacy electronic records. The number of prescriptions per patient was reviewed by our clinical pharmacist to ascertain whether 84 tablets were dispensed per drug per patient during the 12-week study period. The treatment regimen consisted of a combination of generic sofosbuvir and daclatasvir for 12 weeks, with or without RBV. The addition of RBV was desirable for patients infected with HCV genotype 3, according to our unit protocol. For patients with other HCV genotypes or cirrhosis, RBV was administered according to physician discretion. The initial RBV dose was 1000-1200 mg/day. There was no predefined protocol for adjusting RBV doses. Modification of the RBV dose was according to clinical and hematological tolerance, once again at the discretion of the treating physician. Drug-drug interactions between the DAA regimen and the patient's current medications were assessed using the University of Liverpool application on smartphones (Liverpool HEP iChart). Drugs contraindicated for sofosbuvir or daclatasvir were discontinued or changed, if possible. All patients were followed up until the SVR report.

End point analysis. The primary efficacy endpoint of the study was the percentage of SVR12 achieved in the study, defined as undetectable HCV RNA levels 12 weeks after treatment discontinuation. Quantitative HCV RNA was measured by AmpliPrep/COBAS® TaqMan® V2.0 HCV RNA assay (Roche Diagnostics, Pleasanton, California, USA), with a lower limit of detection of 15 IU/ml. Qualitative HCV RNA was performed using the Abbott Real Time HCV Kit (Abbott m2000rt) with a lower limit of detection of 12 IU/ml. The qualitative HCV RNA was used to confirm SVR status at week 12 after treatment discontinuation.

The secondary efficacy endpoints of the study were as follows: viral breakthrough, defined as an increase of at least one log10 above the nadir during the treatment period; post-treatment relapse, defined as detectable HCV RNA after week 12 in those who had an undetectable level at the end of treatment; assessment of improvement in liver biochemistry; and differences in SVR12 with respect to end-of-treatment virologic response, RBV addition, fibrosis stage, age, gender, HCC, and post-treatment glycemic control among patients with DM.

Statistical analysis. All analyses were performed using the Statistical Package for the Social Sciences software for Windows, version 21.0 (IBM Corp., Armonk, N.Y., USA). Data were presented as means ± standard deviations for continuous variables and frequencies with percentages for categorical variables. Chi-square or Fisher's exact tests were used to analyze the correlations between categorical variables. The relation between continuous variables before and after therapy was studied by student's t-test. The primary efficacy endpoint (SVR12) was analyzed using intention-to-treat (ITT) and per-protocol (PP) analyses. All statistical analyses were based on 2-sided hypothesis tests with a significance level of $p<0.05$.

Results. *Patients baseline clinical and laboratory characteristics.* In total, 140 consecutive patients were treated with generic sofosbuvir and daclatasvir, with or without RBV. Demographic and laboratory characteristics of the patients are presented in Table 1. There were significant variations in the treatment experience and stage of liver fibrosis. Patients in the sofosbuvir/daclatasvir (SOF-DCV) without RBV group were treatment-naïve ($p=0.001$) and had a lower stage of liver fibrosis ($p=0.019$) than those in the SOF-DCV with RBV group.

The mean patient age was 61±13.6 years, with a majority being female (62.1%) and infected with genotype 4 (57.9%). The mean pre-treatment HCV RNA level was 1253598 ± 276512 IU/ml. Additionally, 55 (39.3%) and 85 (60.7%) of the patients had cirrhosis and a pretreatment fibrosis stage of F3 or lower, respectively. While a minority of patients (5.7%) were diagnosed with HCC before treatment, 120 (85.7%) patients were treatment-naïve, aand 20 patients had previously received other HCV treatments, including 9 patients treated with pegylated interferon-α2a with ribavirin , 7 patients treated with pegylated interferon-α2a with sofosbuvir and RBV , and 4 patients treated with sofosbuvir combined with simeprevir.

The pretreatment biochemical values for the patients receiving SOF-DCV with or without RBV were found to be similar. In general, the baseline liver biochemistry showed elevation of liver biochemistry with mean serum ALT 59.7±48.8, AST 57.0±41.6, total bilirubin 21.49±20.7 µmol/l, and albumin 36.16±5.6 g/L. The mean platelet count was 203.3 ± 96.3 103/mm.

Effectiveness of SOF-DCV. Treatment effectiveness data are presented in Table 2. Of the 140 patients enrolled in the study, we could not determine SVR12 status in 4 patients. One patient completed 12 weeks of treatment but died before SVR12 status could be confirmed because of multiorgan failure. Two patients were administered only a 4-week supply of the study regimen, which was later changed to different DAA regimens due to the unavailability of generic sofosbuvir, and one patient was lost to follow-up before completing the week 8 treatment.

Table 1 - Baseline demographic and laboratory characteristics of 140 patients.

Parameter	Patients (n=140)	SOF-DCV with ribavirin (n=42)	SOF-DCV without ribavirin (n=98)	*P*-value
Age (y), mean (SD)	61.5±13.6	63.8±12.5	60.6±14.0	0.221
Female, n (%)	87 (62.1)	28 (66.7)	59 (60.2)	0.470
Weight (kg), mean±SD	71.7±15.9	68.6±13.4	73.0±16.8	0.136
Diabetes mellitus, n (%)	45 (32.1)	10 (23.8)	35 (35.7)	0.167
Treatment naive, n (%)	120 (85.7)	29 (69.0)	91 (92.9)	0.001
Organ transplant, n (%)	9 (6.4)	4 (9.5)	5 (5.1)	0.452
Hepatocellular carcinoma, n (%)	8 (5.7)	2 (4.8)	6 (6.1)	0.751
HCV genotypes, n (%)				0.951
G1a	14 (10.0)	5 (11.9)	9 (9.2)	
G1b	16 (11.4)	4 (9.5)	12 (12.2)	
G2	8 (5.7)	2 (4.8)	6 (6.1)	
G3	9 (6.4)	3 (7.1)	6 (6.1)	
G4	81 (57.9)	23 (54.8)	58 (59.2)	
Mixed genotype	4 (2.9)	2 (4.8)	2 (2.0)	
Indeterminant genotype	8 (5.7)	3 (7.1)	5 (5.1)	
Fibrosis stage, n (%)				0.019
F0	34 (24.3)	7 (16.7)	27 (27.6)	
F1	22 (15.7)	6 (14.3)	16 (16.3)	
F2	13 (9.3)	1 (2.4)	12 (12.2)	
F3	16 (11.4)	3 (7.1)	13 (13.3)	
F4	55 (39.3)	25 (59.5)	30 (30.6)	
MELD, mean±SD	9.3±2.7	9.0±2.8	9.5±2.7	0.458
Bilirubin total (µmol/l), mean±SD	21.49±20.7	19.0±16.2	22.5±22.4	0.359
ALT (IU/L) mean±SD	59.7±48.8	68.1±62.2	56.1±41.7	0.182
AST (IU/L), mean±SD	57.0±41.6	66.4±57.1	52.9±32.3	0.079
Albumin (g/L), mean±SD	36.16±5.6	36.1±4.6	36.2±6.0	0.899
WBC (10^3/mm^3), mean±SD	6.3±2.4	5.8±2.2	6.5±2.4	0.101
Hemoglobin (g/L), mean±SD	133.3±19.6	130.4±21.5	134.5±18.7	0.260
Platelets (10^3/mm^3), mean±SD	203.3±96.3	182.0±90.7	212.5±97.6	0.086
eGFR (ml/min), mean±D	86.3±27.7	82.7±32.4	87.8±25.5	0.329
HCV RNA (IU/ml), mean±SD	1253598±276512	1801326.7±420948	1018857.0±1811329	0.125
HbA1 C (%), mean±SD	7.9±1.8	7.8±1.5	8.0±1.8	0.806

SOF-DCV: Sofosbuvir-Daclatasvir, SD: standard deviation, MELD: model of end-stage liver diseases, ALT: alanine aminotransferase, AST: aspartate aminotransferase, WBC: white blood cells, GFR: glomerular filtration rate, HCV: hepatitis C virus, G1a, b,2,3,4: Genotype 1a, b,3,4, HCV: Hepatitis C virus, RNA: ribonucleic acid

Table 2 - Assessment of treatment effectiveness in patients with SVR 12.

Treatment response	Overall N=140	SOF-DCV with ribavirin (n=42)	SOF-DCV without ribavirin (n=98)	*P*-value
Intention to treat (ITT) analysis (n=140)				
Undetectable HCV RNA at EOT*	130 (92.9)	37 (88.1)	93 (94.9)	0.1520
Detectable HCV RNA at EOT	10 (7.1)	5 (11.9)	5 (5.1)	
SVR12	131 (93.6)	38 (91.0)	93 (94.9)	0.666
Failed	9 (6.4)	3 (7.2)	6 (6.1)	
Per protocol (PP) analysis (n=136)				
Undetectable HCV RNA at EOT*	129 (95.6)	36 (94.7)	93 (95.9)	0.937
Detectable HCV RNA at EOT	5 (3.7)	2 (5.3)	3 (3.1)	
SVR12	131 (96.3)	35 (92.1)	96 (98.0)	0.133
Failed	5 (3.7)	3 (7.9)	2 (2.0)	

Values are presented as number and precentages (%). *Two patients had no HCV RNA performed at EOT. EOT: end of treatment, SVR: sustained virologic response, HCV: hepatitis C virus, SOF-DCV: sofosbuvir-daclatasvir

In the ITT analysis, of the 140 patients analyzed, 131 (93.6%) achieved SVR12. Moreover, 85.7% of genotype 1a, 100%of genotype 1b, 100% of genotype 2, 88.9% of genotype 3, and 96.3% of genotype 4 infected patients achieved SVR12. In the PP analysis of 136 patients, 131 (96.3%) achieved SVR12. Additionally, 92.3% of genotype 1a, 100% of genotype 1b , 100% of genotype 2, 88.9% of genotype 3 , and 98.7% of genotype 4 infected patients achieved SVR12. The PP analysis for SVR12 results according to treatment with or without RBV and patient characteristics is presented in Figures 1 and 2.

The variation in SVR12 results, as shown in Figure 1, was notable among the different HCV genotypes treated with SOF-DCV without RBV versus (vs.) SOF-DCV with RBV (p=0.001). Of the 3 patients treated with SOF-DCV and RBV who had genotype 3, 2 achieved SVR12, compared to 33 patients with non-G3 genotypes (66.7% vs. 94.3%); however, the SVR12 was not significant (p=0.224). On the other hand, similarly high SVR12 was obtained in SOF-DCV without RBV in HCV genotype 3 (100%) vs. other genotypes (97.8%), p=0.715. The overall SVR12 in HCV genotype 3 (n=8/9) irrespective of RBV was 88.9% vs. 96.9% in non-G3 genotypes (n=123/127, p=0 .294).

No HCV virologic breakthrough occurred during the treatment period. Five (3.7%) patients experienced relapse 12 weeks after treatment discontinuation. Patients with and without HCC achieved similar

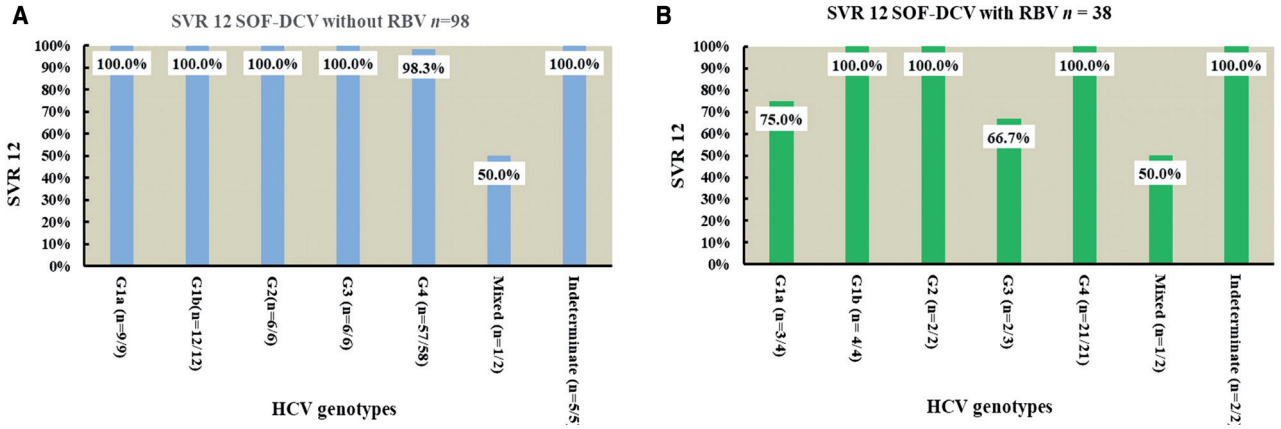

Figure 1 - Per protocol sustained virologic response 12 (SVR 12) across various hepatitis C virus genotypes. (**A**) SVR 12 SOF-DCV without RBV, (**B**) SVR12 sofosbuvir/daclatasvir (SOF-DCV) with ribavirin (RBV).

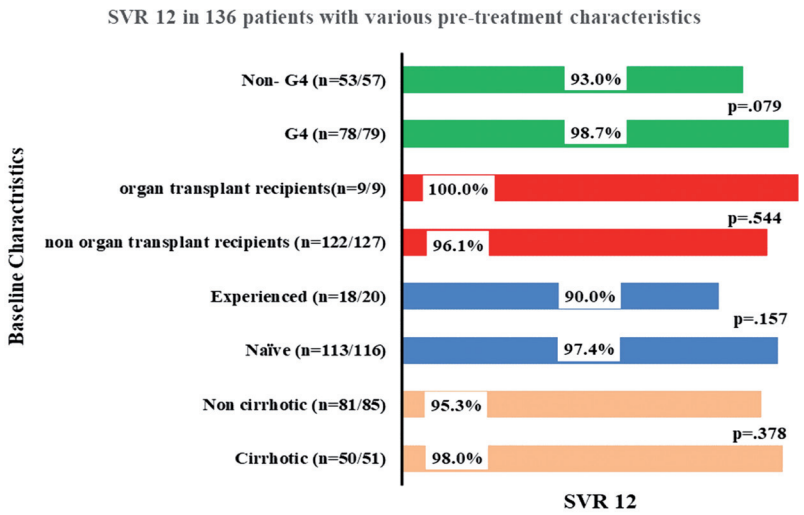

Figure 2 - Per protocol sustained virologic response 12 (SVR 12) with various baseline characteristics.

SVR12 (100% vs. 96.1%, p=0.569) as those with and without cirrhosis (98.0% vs. 95.3%, p=0.410). The rates of SVR12 between HCV treatment-naïve and treatment-experienced patients were similar (97.4% vs. 90.0%; p=0.104).

Serum liver biochemistry improved significantly in patients who achieved SVR12, including alanine aminotransferase (ALT) levels (59.7 U/L vs. 23.4 U/L, p<0.0001), aspartate aminotransferase (AST) levels (56.9 U/L vs. 24.8 U/L, p<0.0001), and serum bilirubin (21.5 µmol/L vs. 18.2 µmol/L, p=0.020).

In total, 45 patients (32.1%) were diagnosed with type 2 diabetes mellitus at baseline. Of these, 32 had available data on pre- and post-treatment HbA1c levels. HbA1c levels decreased from 8.1% to 7.1% in patients who achieved SVR12 (p=0.001).

Discussion. In this study, we assessed the effectiveness of a locally produced generic version of sofosbuvir in combination with a branded formulation of daclatasvir across different HCV genotypes. Overall, a high SVR12 rate was achieved (96.3%) in our study, similar to the reported rates in early registration trials of branded drugs.[14,15]

Perazzo et al[16] reported on the effectiveness of generic DAAs for HCV treatment. In their review of 19 studies , the pooled overall SVR12 result was 98%. Our high SVR12 rate across all HCV genotypes was similar to what Perazzo et al[17] found in their systematic review, which shows that locally made generic sofosbuvir is efficacious. In Saudi Arabia, genotype 4 constitutes 60% of the HCV-infected population. In our study, we reported a 98.7% SVR12 rate in patients with genotype 4 infection. In a local study utilizing generic sofosbuvir and branded daclatasvir, as reported by Johrji et al,[18] SVR12 was 99.1% among 102 HCV genotype 4-infected patients.

Also, our results showed that different genotypes had different SVR12 rates. Those with genotype 3 had a lower overall SVR12 rate (88.9%) than those with other genotypes, but this did not reach statistical significance. Currently, the SOF-DCV treatment regimen is considered a suboptimal first-line option for HCV genotype 3 with cirrhosis.[4]

The detection of pretreatment mutations in NS5A region of HCV genotype 3 significantly impacts SVR12 results with some NS5A inhibitors, including daclatasvir.[19] The ALLY-3+ study reported a lower SVR12 in genotype 3 cirrhotics (63% vs. 96%) who were treated with SOF-DCV.[20] In another study, the administration of sofosbuvir and velpatasvir (another NS5A inhibitor) in Asian genotype 3b-infected patients also yielded low SVR12 results.[21] In countries with high prevalence rates of chronic HCV genotype 3 infection, the use of generic SOF-DCV was associated with an SVR 12 rate of over 95% in treatment-naïve genotype 3 patients, but lower SVR 12 results were observed in compensated cirrhotic patients. A study involving 300 patients by Butt et al,[22] of whom 83% were genotype 3, were treated with generic SOF-DCV. Of these, 43 patients had compensated cirrhosis, and 97.9% of treatment-naïve chronic HCV patients achieved SVR12. However, among compensated cirrhotic patients, 91.8% achieved SVR12. In another study by Mushtaq et al,[23] 993 patients were treated with generic SOF-DCV, with or without RBV. The study group was primarily composed of patients with genotype 3 (99.6%) and included only 32 (3.2%) patients with child A cirrhosis. The study found that SVR12 was achieved in 98.2% of patients with chronic HCV, compared to 93.8% in those with cirrhosis. While the SVR rates for this regimen in treatment naïve HCV genotype 3 with cirrhosis are relatively lower than those in non-cirrhotic patients, many are still considering it as a treatment option due to its affordability and availability. Despite the recent emergence of effective pan-genotypic regimens for treating genotype 3 cirrhotic patients, this regimen remains a viable option for many resource-constrained healthcare systems.[24-27]

Our study showed that the combination of generic sofosbuvir and daclatasvir was associated with high cure rates (≥90%) among HCV patients with different baseline characteristics, such as treatment experience, stage of fibrosis, cirrhosis, and HCC. Additionally, our study was strengthened by providing SVR12 results for all HCV genotypes with different patient characteristics.

A recent systematic review and meta-analysis showed low SVR12 among HCC patients treated with DAAs.[28] In this review, an overall SVR of 88.3% was achieved in patients with HCC, which was lower than that in patients without HCC, irrespective of the baseline fibrosis stage. In our study, the pretreatment prevalence of HCC was 5.7% of the study cohort. All HCC patients achieved similar SVR12 results to those without HCC. It is possible that we did not observe any differences because our analysis included only a small number of patients with HCC (n=8) and was not powered to examine the variation in SVRs between patients with and without HCC.

Hepatitis C virus infection is associated with an increased prevalence of diabetes mellitus. In a study from the western province of Saudi Arabia, diabetes mellitus was present in 21.2% of the 165 patients with chronic HCV infection.[29] In our study, we found a 32.1% prevalence of diabetes mellitus among patients

with chronic HCV infection. Delgado-Borrego et al[30] showed that among patients who achieved SVR12, there was significant improvement in insulin resistance independent of other factors such as age, fibrosis stage, or body mass index. In our study, there was a significant reduction (1%) in the mean HbA1c level among those who achieved SVR, indicating glycemic control. Our results are in line with those reported by Hum et al,[31] who confirmed the beneficial effects of SVR12 in patients with diabetes by improving glycemic control and reducing insulin doses in responders.

Study limitations. Our study has some limitations due to its observational and non-randomized design, highlighted by the lack of a control group. Our sample size was relatively small, and we were unable to obtain SVR12 data from 4 patients due to discontinuation, loss of follow-up, and death. Apart from one mortality during the study period, we could not report adverse events related to the study medications due to insufficient clinical record documentation. Nevertheless, we are confident that clinically significant severe adverse events will not be overlooked or omitted from reporting on the patient's record if they do occur. A prior local study discussed the safety profile of generic sofosbuvir.[18] In this study, there were no major serious adverse effects when compared to the reported side effects of branded sofosbuvir in the clinical trial by Sulkowski et al.[14]

In conclusion, pan-genotypic once-daily treatment with a combination regimen of generic sofosbuvir and daclatasvir showed high SVR12 rates and was effective in patients with different genotypes and patient profiles. The regimen achieved a high SVR12 among HCV genotype 4, which is the most common genotype in Saudi Arabia. Our study could aid in the appropriate selection of generic DAAs for national HCV elimination programs with locally produced, effective regimens. The results of this study will also enable a larger pool of HCV-infected patients to be treated in elimination programs.

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