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Abdel Naser Abdel Atty Gad Allah
Internal Medicine department, Faculty of Medicine, Menoufia University, Shibin elkom, Egypt

Abdallah Abdel Aziz Bahnacy
Internal Medicine department, Faculty of Medicine, Menoufia University, Shibin elkom, Egypt

Tary Salman
Hepato-Gastroenterology department, National liver institute, Menoufia University, Shibin elkom, Egypt

Ahlam Rabea Mahmoud Kanner
Internal medicine department, Sheben El-kom fever hospital, Menoufia, Egypt,
genasamir2013@gmail.com

Aliaa Sabry Abdel Wahed
Hepato-Gastroenterology department, National liver institute, Menoufia University, Shibin elkom, Egypt

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ORIGINAL STUDY

Prevalence and Predictors of Hepatitis C Virus Relapse in Egyptian Patients After Direct-Acting Antiviral Drugs

Abd elnasser A. Gad Allah [a], Abdallah A. Bahnacy [a], Tary Salman [b], Ahlam R.M. Kanner [c,*], Aliaa S. AbdelWahed [b]

[a] Department of Internal Medicine, Faculty of Medicine, Egypt
[b] Department of Hepato-Gastroenterology, National Liver Institute, Menoufia University, Shibin El-Kom, Egypt
[c] Department of Internal Medicine, Sheben El-Kom Fever Hospital, Menoufia, Egypt

Abstract

Objectives: **To assess the prevalence and factors that predict hepatitis C virus (HCV) relapse after direct-acting antiviral drugs.**

Background: **Egypt is known to be one of the countries with a heavy burden of HCV infections. The introduction of direct-acting antivirals has represented a paradigm shift in HCV management.**

Patients and methods: **The current study was a retrospective study done on 422 consecutive patients with HCV, who were selected from those attending the viral hepatitis C unit at Shebin El-Kom Teaching Hospital, Egypt from March 2019 to March 2020. All cases were subjected to thorough history taking, full clinical examination, and laboratory tests such as liver function profiles, renal function tests, complete blood count, serum alpha-fetoprotein, viral markers, and imaging data (abdominal ultrasonography and triphasic computed tomography).**

Results: **Alanine aminotransferase, aspartate transferase, creatinine, fibrosis 4 (FIB-4), direct bilirubin, albumin, PCR, and international normalized ratio showed significant increases in nonresponders when compared with responders. Platelets showed significant increase in responders when compared with nonresponders. Treatment experience, high viral load, and appearance of liver cirrhosis (ultrasound) and FIB-4 were independent RF for relapse between the studied cases with odds ratio of 26.36 (6.4−108.6), 2.42 (1.16−9.03), 12.14 (3.0−49.16), and 2.01 (1.3−9.91), respectively. FIB-4 showed area under curve of 0.744 and at a cutoff point of 0.996had a sensitivity of 75%, specificity of 61%, positive predictive value of 10.2%, and negative predictive value of 98.2%. Regarding viral load, area under curve was 0.729, and at a cutoff point of 860 063.0, sensitivity was 70%, specificity 65.5%, positive predictive value 9.0%, and negative predictive value 97.7%.**

Conclusion: **Simple basic investigations (complete blood count, liver function tests, renal function tests, and ultrasound) and case characteristics (age, sex, diabetes mellitus, hypertension, and smoking) are predictors of unresponsiveness and selection of more potent regimens aiming at possible eradication.**

Keywords: Direct-acting antiviral drugs, Egypt, Hepatitis C virus Relapse

1. Introduction

Hepatitis C virus (HCV) is a major health problem worldwide. WHO reported that 71 million people have chronic hepatitis C infection and 399 000 people die each year from hepatitis C complications, including liver cirrhosis and hepatocellular carcinoma globally [1]. Despite the decline in HCV prevalence from 14.7 to 10.0% among the adult population aged 15−59 years in the Egyptian Demographic and Health Surveys, which measured antibody prevalence, Egypt is still considered to be one of the most HCV-affected countries globally [2]. Approximately 1−5% of

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* Corresponding author. Department of Internal Medicine, Sheben El-Kom Fever Hospital, Menoufia 32511, Egypt
E-mail address: genasamir2013@gmail.com (A.R.M. Kanner).

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patients with liver cirrhosis develop liver cancer and 3–6% progress to liver decompensation. The risk of death after a decompensation episode is between 15 and 20% within the following year [3].

Recently, Egypt has implemented a mass screening and treatment program and is considered one of the few countries in the world that has moved efficiently forward toward the WHO's goal of HCV elimination by 2030 [4].

Many challenges face HCV-elimination programs. One of the main challenges that face HCV-elimination programs is the noncompliance of patients to assess the virological response or to receive a more potent treatment course after confirming viral nonresponse or relapse, making them a nidus for more HCV spread. This makes it very important to identify predictors of treatment failure to establish strategies that can improve virological response rates [5].

HCV management by mixture of different types of direct-acting antiviral (DAA) drugs increases the rate of sustained virological response (SVR), up to 90–95% and even more. On the contrary, there are a low number of unresponsiveness chronic cases [6].

New DAAs for HCV treatment are profoundly successful in providing levels of SVR that exceed 95%. Such regimens are often very secure and convenient, requiring oral drug administration once or twice every day for few weeks [7]. These characteristics encouraged policymakers to put plans to achieve HCV elimination by 2030. Egypt, which has the highest prevalence of HCV, is one of the few countries in the world that is actively and effectively reaching toward this goal through mass treatment of HCV-infected persons [4].

Although DAAs achieve high SVR, the remaining percentages of nonresponse and viral relapse can affect HCV-eradication strategies in the real world when these strategies are implemented on a larger scale [7]. This issue is very important, especially as the compliance of a large number of treated persons to follow-up for assessment of virologic response cannot be guaranteed. This issue should be put into consideration in planning for cost-effective HCV eradication strategies [1].

The aim of this study was to assess the prevalence and factors that predict HCV relapse after DAAs drugs.

2. Patients and methods

This was retrospective study done on 422 consecutive cases with HCV selected from Shebin El-Kom Teaching Hospital, Egypt, during the period from March 2019 to March 2020. Approval from the ethics committee of the Faculty of Medicine, Menoufia University, was taken. Eligibility of each case for therapy of hepatitis C with DAAs was assessed according to the guidelines of the NCCVH, which categorized cases into two groups: easy-to-manage cases (cases that were management naïve and did not have cirrhosis or had adequate hepatic function tests – they were managed with Sofosbuvir (SOF)-daclatasvir (DCV) for 3 months without ribavirin prothrombin time (PT) (RBV)) and difficult-to-treat patients [cases that in the past failed interferon or SOF-based management, cases with cirrhosis, and cases having serum albumin <3.5 g/dl, bilirubin >1.2 mg/dl, international normalized ratio (INR) > 1.2, and/or platelet count <150 000/cmm – they were managed with SOF-DCV-RBV for 3 months]. Cases aged 18–70 years old and diagnosed with HCV + ve, as well as cases were either naïve or had previously treated with DAA were included in the present study. We excluded cases with complicated cirrhosis, hepatic encephalopathy, pregnant females, patients unwilling to comply with contraceptive methods, renal impairment, INR more than 1.7, serum albumin less than 2.8 g/dl, TB more than 3 mg/dl, platelet count less than 50 000/mm^3, previous history of hepatocellular carcinoma, and viral infection other than HCV (HBV, HIV, and HDV).

History taking, full examination, and biochemical data such as liver function profiles [serum albumin, serum bilirubin, aspartate transferase (AST), alanine aminotransferase (ALT), PT, and INR], Renal Function Tests (RFTs) (blood urea and serum creatinine), complete blood count (CBC), serum alpha-fetoprotein (AFP), and viral markers (anti-HCV antibody-HCV-RNA in serum or plasma-HBsAg) were done for all cases. Imaging data included abdominal ultrasonography and triphasic computed tomography (if there is suspicious focal lesion in ultrasound to exclude HCC). Stage of hepatic fibrosis was determined by the fibrosis 4 (FIB-4) score. The anti-HCV medications were used following the guidelines of NCCVH regarding doses, routes of usage, and duration of treatment. Treatment regimens that had been used in our study were sofosbuvir 400 mg + daclatasvir 60 mg once a day per oral, or sofosbuvir 400 mg + daclatasvir 60 mg once a day + ribavirin per oral. Naïve cases without cirrhosis were managed with sofosbuvir and daclatasvir for 1 month and half. Weight-based ribavirin was used plus this regimen when managing difficult to treat or experienced cases. Management regimens that were used in our study in cases with virological relapse were sofosbuvir 400+velpatasvir + voxilaprevir in a single pill once a day for 3 months or sofosbuvir 400+

(ombitasvir 12.5 mg + paritaprevir 75 mg + ritonavir 50 mg)+ribavirin for 3 months, or sofosbuvir 400 mg once a day + daclatasvir 60 mg once a day plus ribavirin for 6 months. The effect of sofosbuvir and daclatasvir combination with or without ribavirin was assessed by the number of cases that were completely cured, known by maintained virologic response 3 months after the termination of therapy (SVR12). SVR12 was known as HCV-RNA less than 15 IU/ml, 3 months after treatment. All cases were followed up during treatment at the 4th week by CBC, AST, ALT, bilirubin, and RFTs and at the 12th week (at end of treatment) by CBC, AST, ALT, bilirubin, RFTs, and PCR. After the end of treatment, virological response was checked 3 months after the termination of therapy to determine the SVR using PCR for HCV-RNA.

2.1. Statistical analysis

The data were taken, put into tables, and analyzed by SPSS, version 17.0 on IBM compatible computer (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics included percentage, mean, and SD. Analytic statistics included χ^2 test to study the link between two qualitative variables, Fisher's exact test for the analysis of 2 × 2 contingency tables when at least 25% of cells had expected number less than 5, t test for comparison among two groups normally distributed having quantitative variables, Mann–Whitney U test for comparison between two groups not normally distributed having quantitative variables, and regression analysis to assess the relationships between variables.

3. Results

In the current study, age of our patients ranged from 18 to 70 years, with mean ± SD of 42.80 ± 11.94. A total of 226 (53.6%) patients were males, whereas 196 (46.4%) were females. In our study, 395 (93.6%) patients did not receive any previous antiviral treatment for their HCV infection. However, HCV treatment was previously administered in 27 (6.4%) patients in the form of different treatment regimens. Diabetes mellitus (DM) was diagnosed in 58 (13.7%) patients, whereas hypertension (HTN) was diagnosed in 75 (17.8%) patients. Approximately 75 (17.8%) patients had history of cigarette smoking (Table 1).

Insignificant differences were found among responder and nonresponder groups regarding hemoglobin, total bilirubin, and AFP. However, ALT, AST, creatinine, FIB-4, direct bilirubin, albumin, PCR, and INR showed a significant increase in nonresponders when compared with responders.

Table 1. Descriptive statistics of the studied patients regarding age, sex, and comorbidities.

Sociodemographic criteria	The studied group (N = 422) [n (%)]
Age (years)	
Mean ± SD	42.80 ± 11.94
Range	18–70
Sex	
Male	226 (53.6)
Female	196 (46.4)
Comorbidities	
Treatment experience	
Naïve	395 (93.6)
Experienced	27 (6.4)
Smoking	
Yes	75 (17.8)
No	347 (82.2)
Diabetes mellitus	
Yes	58 (13.7)
No	364 (86.3)
Hypertension	
Yes	75 (17.8)
No	347 (82.2)

Platelets showed a significant increase in responders when compared with nonresponders. Nonresponders were more likely to gain liver cirrhosis when compared with responders (60 vs. 8%) (Table 2). Treatment experience and treatment regimens among the studied patients in relation to SVR showed that there was a significant increase in naïve patients in the responder group when compared with nonresponders. Retreatment of relapsed patients was done. SVR was achieved in 83.3% (10 patients) in naïve patients who failed first regimen of DAAs and were retreated. However, only 25% (two patients) who had history of previous HCV treatment could achieve SVR (third course of HCV treatment). The difference was statistically significant (Table 3).

Multivariate regression analysis for factors affecting relapse among patient demonstrated that treatment experience, high viral load, and having liver cirrhosis (ultrasound) and FIB-4 were independent risk factors for relapse in the studied cases, with odds ratio of 26.36 (6.4–108.6), 2.42 (1.16–9.03), 12.14 (3.0–49.16), and 2.01 (1.3–9.91), respectively (Table 4).

Regarding, receiver operating characteristic curve analysis demonstrated the accuracy of FIB-4 and viral load for prediction of nonresponsiveness among patients, FIB-4 showed area under curve (AUC) of 0.744, and at a cutoff point of 0.996, the sensitivity was 75%, specificity 61%, positive predictive value (10.2%), and negative predictive value (98.2%). Regarding viral load, AUC was 0.729, and at a cutoff point of 860 063.0, the sensitivity was 70%,

Table 2. Laboratory investigations before treatment and cirrhosis by ultrasound among the studied patients in relation to sustained virological response results.

Variables	SVR among the studied group ($N = 422$)		Test	P value
	Responding ($N = 402$)	Nonresponding ($N = 20$)		
HB (g/dl)				
Mean ± SD	13.07 ± 1.37	13.67 ± 1.43	t test	0.06
Range	10.2–17	10.2–17	1.89	
Platelets ($\times 10^3/mm^3$)				
Mean ± SD	259.59 ± 72.57	186.6 ± 57.62	t test	<0.001[a]
Range	83–532	80–295	4.42	
AST (IU/ml)				
Mean ± SD	34.02 ± 13.87	43.60 ± 21.26	$U = 2.12$	0.03[a]
Range	12–105	19–105		
ALT (IU/ml)				
Mean ± SD	35.62 ± 13.70	44.7 ± 17.34	$U = 2.31$	0.02[a]
Range	13–95	23–89		
PCR ($\times 10^6$ IU/l)				
Mean ± D	2.44 ± 8.85	7.8 ± 15.98	$U = 3.47$	0.001[a]
Range	0.004–87.21	0.01–68.29		
Creatinine (mg/dl)				
Mean ± SD	0.88 ± 0.14	1.03 ± 0.15	t test	
Range	0.5–1.3	0.7–1.2	4.75	<0.001[a]
Albumin (g/dl)				
Mean ± SD	4.22 ± 0.28	4.35 ± 0.36	t test	0.04[a]
Range	3.4–5	3.5–5	2.09	
Total bilirubin (mg/dl)				
Mean ± SD	0.75 ± 0.17	0.81 ± 0.43	$U = 1.27$	0.21
Range	0.2–1.3	0.3–1.4		
Direct bilirubin (mg/dl)				
Mean ± SD	0.20 ± 0.07	0.26 ± 0.17	$U = 2.22$	0.03[a]
Range	0.03–0.5	0.1–0.9		
AFP (ng/dl)				
Mean ± SD	5.31 ± 1.85	5.8 ± 2.33	$U = 0.83$	0.41
Range	2.1–9.3	2–9.8		
INR				
Mean ± SD	1.04 ± 0.06	1.05 ± 0.05	$U = 2.45$	0.01[a]
Range	1–1.4	1–1.2		
FIB-4				
Mean ± SD	1.11 ± 0.78	2.33 ± 1.39	$U = 4.34$	<0.001[a]
Range	0–4.14	0–5.88		
US (cirrhosis)				
Cirrhotic	32 (8.0)	12 (60.0)	FE = 55.24	<0.001[a]
Noncirrhotic	370 (92.0)	8 (40.0)		

AFP, alpha-fetoprotein; ALT, alanine aminotransferase; AST, aspartate transferase; FIB-4, fibrosis 4; HB, hemoglobin; INR, international normalized ratio; SVR, sustained virological response; US, ultrasound.
U = Mann–Whitney U test, FE=Fisher's exact test.
[a] Significant.

specificity 65.5%, positive predictive value 9.0%, and negative predictive value 97.7% (Table 5 and Fig. 1).

4. Discussion

DAA has revolutionized the management of HCV infection. Patients receive oral medications for a shorter period and without significant adverse effects. Moreover, drug–drug interactions are less common. The findings of our study indicated that DAAs for the management of HCV infection is much more effective and failure rate is low in clinical practice. Additionally, successful eradication of HCV infection gives a multitude of health benefits, which include reduction or decrease in progression of hepatic fibrosis, decreased risk of occurrence hepatic failure and HCC, control of some extrahepatic complications of HCV infection and overall, and improvement of patient's survival [8]. Therefore, we aimed to assess factors that could predict SVR12 after end of treatment in cases managed with sofosbuvir-based regimens with or without RBV, especially the combination of sofosbuvir and daclatasvir. In Egypt, this combined therapy is usually used. Daclatasvir is a broad-spectrum and safe antiviral treatment. Combination of daclatasvir

Table 3. Treatment experience and treatment regimens as well as retreatment of relapse patients among the studied patients in relation to sustained virological response.

Treatment experience and regimens	SVR among the studied group ($N = 422$) [n (%)]		Test of significance	P value
	Responders ($N = 402$)	Nonresponders ($N = 20$)		
Treatment experience				
Naïve	383 (95.3)	12 (60.0)	FE = 39.58	<0.001[a]
Experienced	19 (4.7)	8 (40.0)		
Treatment experience				
Naïve	383 (95.3)	12 (60.0)		
Experienced dual (SOF/DAC)	13 (3.2)	6 (30.0)	40.12	<0.001[a]
Experienced triple (sof/DAC/RBV)	6 (1.5)	2 (10.0)		
Retreatment	Treatment experience Naïve ($N = 12$)	Experienced ($N = 8$)	Test	P value
SVR				
Responding	10 (83.3)	2(25.0)	$\chi^2 = 6.81$	0.009[a]
Nonresponding	2 (16.7)	6 (75.0)		

χ^2, χ^2 test; FE, Fisher's exact test; SVR, sustained virological response.
[a] Significant.

and sofosbuvir has elevated SVR rates in unresponsiveness cases [9].

In our study, 422 Egyptian cases with chronic HCV infection who finished their antiviral therapy were included and followed up for 3 months after stoppage of therapy to assess their SVR. These cases were retrospectively enrolled for HCV therapy with DAAs from viral hepatitis C unit. The age of our cases ranged from 18 to 70 years, with mean ± SD of 42.80 ± 11.94 years. Approximately 226 (53.6%) patients were males, whereas 196 (46.4%) were females. DM was diagnosed in 58 (13.7%) patients, whereas HTN was diagnosed in 75 (17.8%) patients. Approximately 75 (17.8%) patients had history of cigarette smoking. SVR at posttreatment week 12 was 95.3%, whereas the failure rate was 4.7%.

Table 4. Multivariate regression analysis for factors affecting relapse among the studied patients.

Parameters	Wald χ^2	P value	Odds ratio	95% CI (lower −upper)	
Age (years)	0.12	0.73	0.98	0.89	1.08
Smoking	2.84	0.09	2.84	0.84	9.64
Treatment experience	20.5	<0.001[a]	26.36	6.40	108.6
DM	1.73	0.19	2.42	0.65	9.03
PCR>1 million (IU/l)	6.58	0.01[a]	1.04	1.01	1.08
Bilirubin (mg/dl)	1.24	0.27	16.7	0.12	2355
Platelets ($\times 10^3/mm^3$)	3.6	0.06	1.02	1.0	1.06
Creatinine (mg/dl)	2.69	0.10	80.98	0.43	354.3
Ultrasound (cirrhosis)	12.23	<0.001[a]	12.14	3.0	49.16
FIB-4	3.88	0.04[a]	2.01	1.3	9.91
Albumin (g/dl)	3.64	0.06	17.49	0.93	330.37
AST (mg/dl)	2.16	0.14	0.10	0.004	2.17
ALT (mg/dl)	1.82	0.18	1.05	0.98	1.13

χ^2, χ^2 test; ALT, alanine aminotransferase; AST, aspartate transferase; CI, confidence interval; DM, diabetes mellitus; FIB-4, fibrosis 4.
[a] Significant.

Our data were comparable with the reported results by Merat et al. [10], who showed that the overall 12-week SVR rate was 98% in overall treated patients by using SOF plus DCV with ribavirin regimen. Moreover, a previous study noted that mixture of sofosbuvir and daclatasvir had elevated the effect of antiviral therapy, with more than 90% SVR rate in cases with chronic infection with HCV [11]. The SVR12 rate achieved was also similar to Abdel-Moneim et al. [12], where the overall SVR12 reached up to 95% in patients treated with SOF/DCV and about 92% in patients treated with SOF/DCV/RBV.

In our study, old age had lower SVR rates. In agreement with our results, Reid and colleagues noted that older cases with chronic HCV infection had lower SVR rates comparable to younger patients, this might be attributed to an elevated risk of HCV-linked hepatic disease caused by HCV infection for a long time or aging-related factors [13]. On the contrary, the study performed by Conti et al. [14] demonstrated that age did not affect the success of interferon-free therapy in old aged cases with

Table 5. Validity of fibrosis 4 and viral load for prediction of non-responsiveness among the studied patients.

ROC analysis	PCR	FIB-4
AUC	0.729	0.744
P value	0.001	<0.001
95% CI	0.62−0.84	0.66−0.83
Cutoff point	860 063.0	0.996
Sensitivity	70.0%	75.0%
Specificity	65.5%	61%
PPV	9.0%	10.2%
NPV	97.7%	98.2%

AUC, area under curve; CI, confidence interval; FIB-4, fibrosis 4; NPV, negative predicted value; PPV, positive predicted value; ROC, receiver operating characteristic curve.

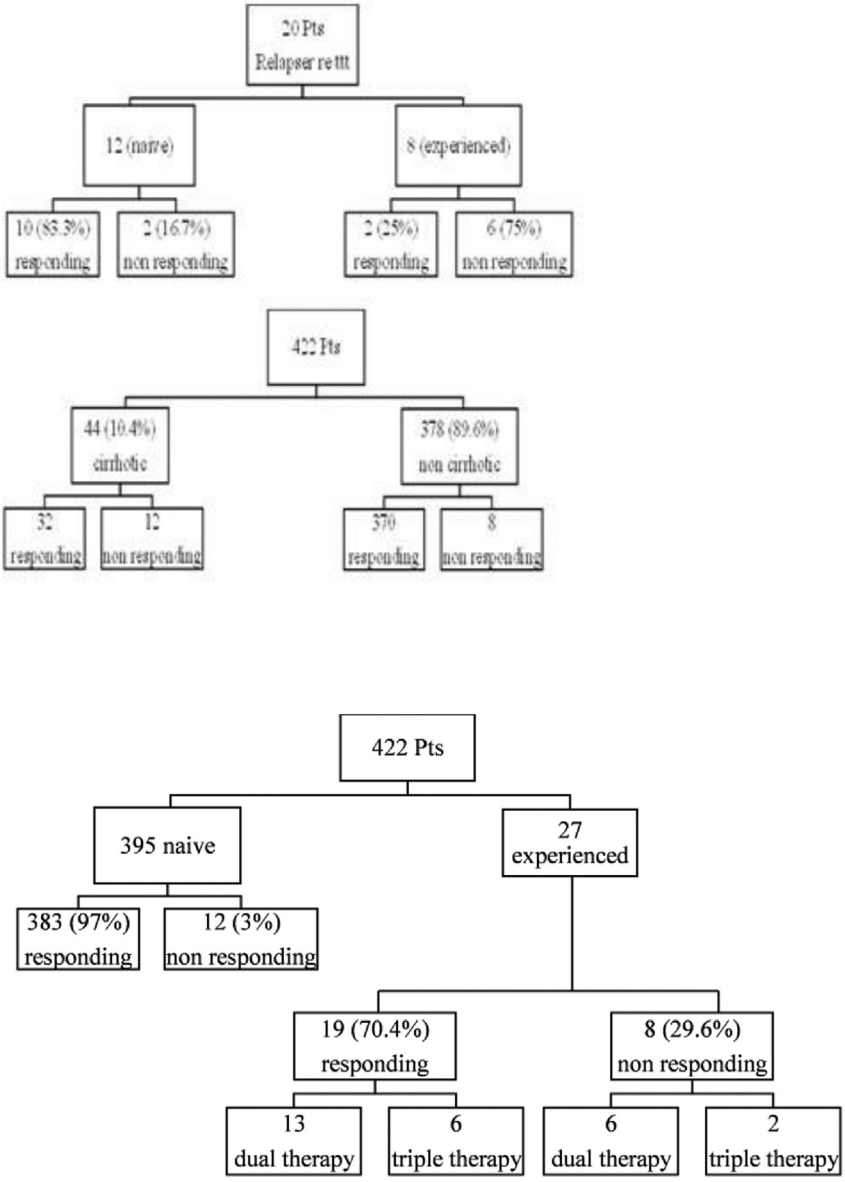

Fig. 1 Flow chart of the studied participants.

chronic hepatitis C and that all DAA protocols are safe in patients with severe hepatic disease and in those more than 75 years.

In our study, sex did not affect the response of DAA therapy. Similarly, Belci et al. [15] reported that SVR was nonsignificant higher in females than males; however, the difference became important after stratification by age, especially in the group aged below 50 years old. On the contrary, in study done by Shousha et al. [16], sex was significantly linked with SVR12.

In our study, 395 (93.6%) of our patients were naive. However, HCV treatment was previously administered in 27 (6.4%) patients in the form of different treatment regimens (SOF/DAC or SOF/DAC/RBV). In our work, SVR12 was higher in naïve patients than experienced. On the contrary, Sulkowski and colleagues noted that SVR12 rates were the same after subanalysis of many items, such as history of therapy failure with first-generation protease inhibitors (telaprevir and boceprevir), subgenotypes, IL28 phenotype, race, or RBV use [17]. Moreover, the overall response rate did not differ between therapy-naïve cases and those with previous history of INF-based treatment in a study done over 205 patients with CHC (195 naïve and 15 experienced) [18].

In our study, thrombocytopenia had a negative effect on SVR. Similarly, Werner et al. [19] found

that sign of portal HTN, especially pretreatment platelets less than 100 × 10^3/nl was associated with decreased response to oral antiviral drugs. In our study, a higher viral load was associated with lower rates of SVR. In line with our finding, Foster et al. [20] documented in their study done on 800 chronic HCV cases that received sofosbuvir plus RBV that viral load more than 800 000 IU/ml had a negative effect on response to oral DAAs.

In our study, elevation of transaminases affects SVR as AST ranged from 12 to 105 IU/ml with mean ± SD of 34.02 ± 13.87 in patients who achieved SVR, whereas it ranged from 19 to 105 IU/ml with mean ± SD of 43.60 ± 21.26 in patients who did not achieve SVR ($P = 0.03$). In our study, patients with higher ALT level had lower SVR than those with lower ALT level. In a study done on patients with CHC who were candidates for antiviral therapy, higher AST and ALT were predictors of nonresponse among other pretreatment factors [16].

The FIB-4 index is a cheap and specific marker to detect fibrosis and has an important role in the diagnosis of advanced fibrosis stages. Patients who scored less than 3.25 were classified as nonfibrotic, and patients who scored greater than 3.25 were scored as fibrotic patients [21]. However, Backus et al. [22] reported that FIB-4 cutoff value of more than 3.25 was an important predictor of SVR in genotype 1 HCV cases.

Regarding cirrhosis in our study, cirrhosis was diagnosed in 44 (10.4%) patients, whereas 378 (89.6%) of the studied patients had no signs of cirrhosis in their abdominal ultrasound. Lower SVR rates occurred in cirrhotic cases. These data are in line with the previous results by Ferenci et al. [23], who noted that massive liver dysfunction alters the response to DAA, with elevated SVR in cases with CH or Child A than in cases with Child B or C. However, Boglione et al. [24] reported that cirrhosis had no effect on the viral response and the SVR did not differ in cases with hepatic cirrhosis versus those without.

In our study, AFP did not affect SVR. On the contrary, another Egyptian study done by Werner et al. [19] found that the nonresponder cases had significantly elevated frequency of cases with increased AFP. In our study, at posttherapy week 12, old age; previous antiviral managed cases; cirrhotic texture on ultrasound; elevated AST, ALT, and bilirubin; decreased serum albumin, creatinine, and platelet count; and high viral load FIB-4 were the significant factors linked to nonresponse but treatment experience, elevated viral load, FIB-4, and existence of cirrhosis (ultrasound) were independent RF for relapse by a multivariate regression model. In line with our finding, Omar et al. [25], noted that SVR12 in genotype 4 cases may be affected by sex, bilirubin, serum albumin, INR, and platelet count. Young aged female patients with decreased DM prevalence; decreased baseline SGOT, SGPT, bilirubin, and FIB-4; and elevated serum albumin, hemoglobin, white blood cells, and platelet count achieved SVR12. These results are also in accordance with Buti et al. [26], who noted that SVR rates were higher in various DAA protocol. Decreased response rates happened more likely in therapy-experienced cases, those with massive hepatic cirrhosis, HCV genotypes 3 or 1a infections, high serum HCV-RNA, decreased drug adherence, or earlier drug stoppage.

In our study, 20 relapse cases received retreatment. Overall, 65% of relapsed patients (13 patients) received sofosbuvir + velpatasivir + voxilaprevir in one pill once a day for 12 weeks, 25% of patients (five patients) received sofosbuvir 400+Qurevo (ombitasvir 12.5 mg + paritaprevir 75 mg + ritonavir 50 mg)+ribavirin for 12 weeks, and 10% (two cases) had sofosbuvir + daclatasvir 60 mg + ribavirin once every day for 24 weeks, and the overall SVR was 60% in relapsers. Treatment of relapse patients was done by Naguib et al. [27] for all patients who were prescribed the PAR/OMB/SOF/RBV protocol, 98.1% in patients who were prescribed SOF/DAC/SIM/RBV, and 71.4% in patients who were prescribed the SOF/DAC/RBV protocol. Moreover, Bourlière et al. [28] showed that the incidence of SVR was 96% in patients receiving 'sofosbuvir−velpatasvir−voxilaprevir' when compared with no person in the placebo group. In POLARIS-4, the response rate was 98% with sofosbuvir−velpatasvir−voxilaprevir and 90% with sofosbuvir−velpatasvir.

In our study, receiver operating characteristic curve analysis demonstrated the accuracy of FIB-4 and viral load for prediction of nonresponsiveness among patients. FIB-4 showed AUC of 0.744, and at a cutoff point of 0.996, its sensitivity was 75%, specificity 61%, positive predictive value (10.2%), and negative predictive value (98.2%). Regarding viral load, AUC was 0.729, and at a cutoff point of 860 063.0, its sensitivity was 70%, specificity 65.5%, positive predictive value 9.0%, and negative predictive value 97.7%. Moreover, Shereen and colleagues documented that SVR12 after therapy was 91.4%. Pretherapy transient elastography values and FIB-4 were reduced in sustained responders when compared with relapse cases. The best cutoff values for liver stiffness by transient elastography and FIB-4 score to assess failure to therapy response were 16.7 kPa and 2.4, respectively. Between multiple treatment strategies, cases with FIB-4 more than

2.4 and transient elastography levels more than 16.7 kPa are usually associated with failed therapy except if they had SOF/SIM therapy protocols in their study on 7256 patients with chronic HCV [29].

In conclusion, basic investigations and case characteristics can be used for prediction of nonresponse and to choose more potent protocols in the future aiming at possible eradication. DAAs have improved the landscape of HCV treatment with SVR more than 95%. Proper choice of therapy protocols depend on pretherapy data, which could help improve the response rate. Thus, if we can achieve response in all cases by accurate choice of therapy protocols, it could decrease the spread of infection, as nonresponders represent only 4.7% of the study population. Further related studies with a large number of nonresponders may conclude an equation that could predict nonresponders.

5. Conclusion

Treatment experience, high viral load, and presence of cirrhosis by ultrasound and FIB-4 were independent risk factors for relapse among the studied patients. Polymerase chain and FIB-4 showed significant AUC that can predict responsiveness among studied cases. Furthermore, relapse occurs more in dual therapy.

Conflict of interest

There are no conflicts of interest.

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