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Effectiveness of Direct-Acting Antivirals in Treatment of Elderly Egyptian Chronic Hepatitis C Patients

Shimaa Kamel [1], Hagar Elessawy [2], Ossama Ashraf [2], Ahmed Elbaz [1,*], Hany Dabbous [1], Manal El-Sayed [3], Safaa Ali [4] and Heba Kamel [4]

1 Department of Tropical Medicine, Ain Shams University, Cairo 11566, Egypt; shimaayoussif81@gmail.com (S.K.); drhdabbous@med.asu.edu.eg (H.D.)
2 Department of Internal Medicine, Hepatology, and Gastroenterology, Ain Shams University, Cairo 11566, Egypt; hagarahmed@med.asu.edu.eg (H.E.); Ossama_ashraf@med.asu.edu.eg (O.A.)
3 Department of Pediatrics and Clinical Research Center (MASRI-CRC), Ain Shams University, Cairo 11566, Egypt; manalhelsayed@yahoo.co.uk
4 Department of Geriatrics and Gerontology, Ain Shams University, Cairo 11566, Egypt; sfaa.ali@med.asu.edu.eg (S.A.); heba_youssif@yahoo.com (H.K.)
* Correspondence: ahmedelbaz75@gmail.com or drahmed_elbaz@med.asu.edu.eg

Abstract: Background: Hepatitis C virus treatment has dramatically improved by direct-acting antiviral (DAA) therapy. The aim of this study was to assess the efficacy and safety of DAA in elderly Egyptian chronic hepatitis C (CHC) patients. Methods: The study was carried out on 327 CHC elderly patients >60 years; patients were divided into 3 age subgroups (<65, 65–75 and >75 years) on DAA therapy for 12 weeks. Ninety-one patients (27.8%) were treated with dual therapy, 234 patients (71.6%) with triple therapy and 2 patients (0.6%) with quadrable therapy. Results: All patients achieved end-of-treatment virological response (100%). ALT levels normalized during therapy. The follow-up rate of sustained virological response at 12 weeks after the end of treatment (SVR12) was 100%. One hundred and two patients had missed SVR12 data due to being lost tofollow-up. Two hundred twenty-two adverse events were reported (67.8%), including anemia in 30 patients (9.1%), leucopenia in 129 patients (39.4%) and thrombocytopenia in 63 patients (19.2%). No serious side effects led to discontinuation of therapy. No hepatic decompensation was observed, and no patients died. Conclusion: Age does not influence the success of DAA treatment and all DAA regimens are well tolerated, safe and highly efficacious, even in those aged 75 years or older.

Keywords: direct-acting antiviral therapy; hepatitis C; lost to follow-up; sofosbuvir; ribavirin; sustained virological response

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1. Introduction

Hepatitis C virus (HCV) is a worldwide problem affecting 2.8% of the population, as estimated by the presence of HCV antibodies [1]. It causes acute and chronic hepatitis that progressively leads to cirrhosis in about 20–30% of patients [2]. Egypt is considered one of the countries with a high prevalence of HCV infection [3]. The Egyptian Health Issues Survey (EHIS) found that, in 2015, 10% of their study population were positive for HCV antibodies and 7% were positive for HCV Ribonucleic acid (RNA) [4].

Combined pegylated interferon and ribavirin therapy has been considered an effective treatment for chronic hepatitis C (CHC) for several years. Since 2014, a number of HCV direct-acting antiviral (DAA) agents have been approved for the treatment of HCV infection [5].

Recent studies show that HCV genotypes consist of 7 genotypes and 67 subtypes. GT4 accounts for 13% of all HCV infections, mainly in the Middle East and Africa. This Genotype represents 93% of HCV-infected Egyptian patients [6,7]. In comparison to other genotypes, GT4 was reported less often in different clinical studies [6] with difficulty in its

treatment and lower rates of sustained virological response [8]. In the DAA era, GT4 HCV treatment was highly concerned in different clinical trials; however, further continuous and high-paced clinical research is needed [9].

Historically, HCV has been difficult to treat in elderly patients due to its association with rapid progressive fibrosis and cirrhosis, along with a higher incidence of liver cancer compared to younger patients [10,11]. Additionally, there is an increased exposure risk of drug interactions between multiple concomitant medications for different common comorbidities in the elderly [12]. With the recent approval of DAAs, few clinical trials have expanded their study of these medications on this special elderly population [13–18].

Our aim was to assess the efficacy and safety of different DAA regimens for the treatment of elderly Egyptian chronic hepatitis C patients.

2. Materials and Methods

2.1. Study Population

We conducted a retrospective observational cohort study on three age subgroups of elderly patients above 60 years (<65 years, 65–75 years and >75 years) with CHC who were referred to our hepatological center of Ain Shams University between 2015 and 2018 and started therapy with DAA.

The hepatological centre of Ain Shams University is a large referral tertiary centre that provides surveillance, counselling, investigation, and treatment for HCV patients.

We identified 804 patients using a database search. We included 327 patients in our study for DAA therapy for 12 weeks.

2.2. Inclusion Criteria

Eligible patients were diagnosed with CHC infection based on anti-HCV antibody levels and detectable serum HCV RNA [19].

The patients included in the study were either non-cirrhotic or compensated cirrhotic. Cirrhosis was determined by either liver biopsy with a METAVIR score $\geq$F3, Ishak fibrosis score $\geq$5, or transient elastography (TE, FibroScan, Echosens, Paris, France) with a liver stiffness $\geq$14.6 kPa [19].

2.3. Exclusion Criteria

We excluded all patients who had decompensated liver diseases, present or past evidence of Child–Pugh–Turcotte (CPT) score C, hepatocellular carcinoma, extra-hepatic malignancy, uncontrolled diabetes mellitus (HbA1c > 8%), HIV co-infection, or severe chronic kidney disease defined by the estimated GFR (eGFR) calculated using the Modification of Diet in Renal Disease (MDRD) equation (<30 mL/min/1.73 m^2).

2.4. Pre-Treatment Assessment

Patients were clinically evaluated and laboratory investigations were done that included complete blood picture, liver function tests, renal function tests, and international normalized ratio. All patients were evaluated using abdominal ultrasound. HCV RNA was assessed in all patients before therapy using an artus HCV polymerase chain reaction (PCR) kit. For quantitative detection of HCV-specific RNA, we used real-time reverse transcription (RT) PCR with Rotor-Gene Q Instruments (QIAGEN, Hilden, Germany) with a low detection limit of 21 IU/mL and a linear amplification range of HCV RNA from approximately 35 to 1.77 $\times$ 10^7 IU/mL.

2.5. Protocol of Management

Antiviral therapy was administered for 12 weeks to each patient according to the severity of liver disease based on the protocol provided by the National Committee for Control of Viral Hepatitis in Egypt (NCCHC guidelines for the management of adult patients with HCV infection) available at the time of enrolment.

All patients received one of the following 8 predefined regimens: Ombitasvir/Paritaprevir/ritonavir ± Ribavirin (OBV/PTV/r ± RBV), Sofosbuvir/Daclatasvir ± Ribavirin (SOF/DCV ± RBV), Sofosbuvir/Ledipasvir ± Ribavirin (SOF/LDV ± RBV), Sofosbuvir/Simeprevir ± Daclatasvir/Ribavirin (SOF/SIM ± DCV/RBV). Weight-based ribavirin was administered according to the discretion of the physician. Type of assigned drug was based on type of included patient as naive or treatment experienced with different previous regimens, CPT classification, hemoglobin level, platelet count and associated comorbidities.

2.6. Follow-Up

Patients were monitored during antiviral therapy for 12 weeks. Adverse effects of DAA were reported. Virological response at the end of treatment (EoT), and 12 weeks after the end of treatment (SVR12), were defined by the HCV RNA PCR test. Patients without follow-up serological test of viral RNA 12 weeks after EoT were defined as lost to follow-up (LTFU).

2.7. Statistical Analysis

Data were analyzed by Statistical Package for Social Science (IBM SPSS) version 23. Number and percentages represented the qualitative data. Mean, standard deviations and ranges represented parametric quantitative data, while median with inter-quartile range (IQR) represented quantitative nonparametric ones. Qualitative data were compared between groups by Chi-square test. Quantitative data with parametric distribution were compared between groups by one-way ANOVA, while data with nonparametric distribution were compared by Kruskal–Wallis test. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant if p-value < 0.05.

3. Results

3.1. Patient Demographics

A total of 327 elderly patients (above 60 years) with CHC were included in the study. These patients were treated with different DAA regimens during the study period. In terms of age, 98 patients (30%) were <65 years old, 123 patients (37.6%) were 65–75 years old and 106 patients (32.4%) were >75 years old. No gender difference was found between patients in these groups. Baseline clinical characteristics of included patients are shown in Table 1.

Prevalence of comorbidities, such as hypertension, diabetes mellitus, and cardiovascular disease, were the same among the three age groups.

Liver cirrhosis was found in 95 elderly patients (23.5% of <65 years old, 26.8% of 65–75 years old and 36.8% of >75 years old) (p = 0.088), and pretreatment CPT score classification was not significantly comparable between different patient age groups. Three hundred seven patients (93.8%) had a CPT-A class score. Baseline serum liver function tests aspartate aminotransferase (AST), total bilirubin, alpha-fetoprotein (AFP), eGFR and pre-treatment serum HCV-RNA levels were found to be significantly higher in the >75-years-old age group.

3.2. DAA Therapy

HCV treatment-naïve (98.7%) patients were included in our study. Ninety-one patients (27.8%) were treated with dual therapy, two hundred thirty-four patients (71.6%) with triple therapy and 2 patients (0.6%) with quadrable therapy.

The distribution of DAA therapy was not statistically different between the three age groups. Sofosbuvir-based regimens were used in 238 patients (72.7%), while ribavirin was administered to 237 patients (72.4%) with a median dose of 600 mg.

All patients were compliant with DAA regimens. The baseline characteristics of patients treated with different DAA regimens are shown in Table 2.

Table 1. Baseline demographics, clinical and laboratory parameters of patients treated with DAAs regimens in different age groups.

Parameter	<65 Years (n = 98)	65–75 Years (n = 123)	>75 Years (n = 106)	*p*-Value
Gender (female/male)	57/41	79/44	59/47	0.394
BMI (kg/m^2, mean ± SD)	29.94 ± 6.06	28.63 ± 5.23	29.78 ± 3.28	0.096
Comorbidities				
Diabetes mellitus (n (%))	64 (65.3%)	87 (70.7%)	76 (71.7%)	0.566
Hypertension (n (%))	51 (52.0%)	73 (59.3%)	67 (63.2%)	0.261
Cardiovascular disease (n (%))	2 (2.0%)	4 (3.3%)	1 (0.9%)	0.483
Cirrhosis (n (%))	23 (23.5)	33 (26.8)	39 (36.8)	0.088
Child Pugh score (n (%))				0.702
A	92 (93.9%)	117 (95.1%)	98 (92.5%)	
B	6 (6.1%)	6 (4.9%)	8 (7.5%)	
Laboratory investigations				
ALT (IU/L, median (IQR))	44 (28–60)	40 (23–53)	45 (36–52)	0.084
AST (IU/L, median (IQR))	44.5 (33–66)	45 (27–57)	50 (45–55)	0.049
Albumin (g/dL, mean ± SD)	3.89 ± 0.48	3.86 ± 1	4.02 ± 1.33	0.442
Total bilirubin (mg/dL, median (IQR))	0.8 (0.6–1.1)	0.8 (0.5–1.1)	1.25 (1–2)	0.000
INR (median (IQR))	1.12 (1.04–1.22)	1.1 (1.02–1.2)	1.1 (1–1.2)	0.775
AFP (IU/mL, median (IQR))	4.9 (2.4–8.3)	4.9 (2.8–9.8)	8 (5–12)	0.000
TSH (mIU/L, mean ± SD)	2.61 ± 1.78	2.44 ± 1.13	2.58 ± 1.17	0.597
White blood cells (10^3/uL, mean ± SD)	6.37 ± 2.33	6.27 ± 2.12	6.24 ± 2.04	0.906
Hemoglobin (g/dL, mean ± SD)	13.05 ± 2.68	13.22 ± 1.81	12.75 ± 1.39	0.200
Platelets (10^3/uL, median (IQR))	192.5 (140–233)	201 (154–242)	198.5 (175–230)	0.515
eGFR (mL/min/1.73 m^2, median (IQR))	113.67 (97.53–146.26)	106.85 (85–141.62)	68.87 (63.3–75.43)	0.001
Log10 HCV RNA (IU/mL, median (IQR))	3.78 (2.9–5.85)	4.68 (3.3–5.88)	5.27 (5.25–5.28)	0.002
Type of patient				
Naïve	96 (98.0%)	121 (98.4%)	106 (100.0%)	0.364
IFN experienced (n (%))	1 (1.0%)	2 (1.6%)	0 (0.0%)	0.433

Table 1. *Cont.*

Parameter	<65 Years (n = 98)	65–75 Years (n = 123)	>75 Years (n = 106)	*p*-Value
DAA experienced (n (%))	1 (1.0%)	0 (0.0%)	0 (0.0%)	0.309
DAA treatment (n (%))				
OBV/PTV/r	1 (1.0%)	4 (3.3%)	3 (2.8%)	
OBV/PTV/r/RBV	22 (22.4%)	33 (26.8%)	26 (24.5%)	
SOF/DCV	24 (24.5%)	25 (20.3%)	30 (28.3%)	
SOF/DCV/RBV	50 (51.0%)	56 (45.5%)	46 (43.4%)	0.727
SOF/LDV	1 (1.0%)	1 (0.8%)	1 (0.9%)	
SOF/LDV/RBV	0 (0.0%)	1 (0.8%)	0 (0.0%)	
SOF/SIM	0 (0.0%)	1 (0.8%)	0 (0.0%)	
SOF/SIM/DCV/RBV	0 (0.0%)	2 (1.6%)	0 (0.0%)	
Ribavirin				
RBV usage [n (%)]	72 (73.5%)	93 (75.6%)	72 (67.9%)	0.416
RBV dosage (mg, median (IQR))	600 (500–600)	600 (200–600)	600 (600–600)	0.716
RBV dosage increase (n (%))	8 (11.3%)	13 (14.3%)	8 (11.8%)	0.953
RBV dosage decrease (n (%))	2 (2.8%)	2 (2.2%)	1 (1.5%)	
Adverse events (n (%))				
Anaemia	8 (12.1%)	14 (14.9%)	8 (11.3%)	0.766
Leucopenia	40 (60.6%)	49 (52.1%)	40 (55.6%)	0.569
Thrombocytopenia	17 (25.8%)	29 (30.9%)	17 (23.6%)	0.557

AFP, alphafetoprotein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; DAA, direct-acting antiviral; DCV, daclatasvir; eGFR, estimated glomerular filtration rate; HCV, hepatitis C virus; IFN, interferon; INR, international normalized ratio; IQR, interquartile range; LDV, ledipasvir; OBV, ombitasvir; PTV, paritaprevir; RBV, ribavirin; RNA, Ribonucleic acid; r, ritonavir; SD, standard deviation; SIM, simeprevir; SOF, sofosbuvir; TSH, Thyroid stimulating hormone.

Table 2. Comparison between demographic, clinical and laboratory characteristics of patients treated with different DAA regimens.

Parameter	OBV/PTV/r (n = 8)	OBV/PTV/r/RBV (n = 81)	SOF/DCV (n = 79)	SOF/DCV/RBV (n = 152)	SOF/LDV (n = 3)	SOF/LDV/RBV (n = 1)	SOF/SIM (n = 1)	SOF/SIM/DCV/RBV (n = 2)	*p*-Value
Gender (female/male)	4/4	46/35	55/24	88/64	1/2	0/1	1/0	0/2	0.188
BMI (kg/m^2, mean ± SD)	30.45 ± 4.84	28.68 ± 4.35	29.90 ± 4.57	29.48 ± 5.48	29.10 ± 4.93	39.11 ± 0.00	30.12 ± 0.00	23.18 ± 1.38	0.202
Comorbidities									
Diabetes mellitus (n (%))	7 (87.5%)	54 (66.7%)	52 (65.8%)	110 (72.4%)	2 (66.7%)	1 (100.0%)	0 (0.0%)	1 (50.0%)	0.575
Hypertension [n (%)]	6 (75.0%)	44 (54.3%)	51 (64.6%)	84 (55.3%)	3 (100.0%)	1 (100.0%)	1 (100.0%)	1 (50.0%)	0.436
Cardiovascular disease (n (%))	0 (0.0%)	0 (0.0%)	4 (5.1%)	3 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.618
Cirrhosis (n (%))	2 (25.0%)	21 (25.9%)	17 (21.5%)	53 (34.9%)	1 (33.3%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	0.266
Child–Pugh score (n (%))									
A	7 (87.5%)	75 (92.6%)	74 (93.7%)	145 (95.4%)	3 (100.0%)	0 (0.0%)	1 (100.0%)	2 (100.0%)	0.16
B	1 (12.5%)	6 (7.4%)	5 (6.3%)	7 (4.6%)	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	
Type of patient									
Naïve	8 (100%)	81 (100%)	79 (100%)	148 (97.3%)	3 (100%)	1 (100%)	1 (100%)	2 (100%)	0.701
IFN-experienced (n (%))	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.837
DAA-experienced (n (%))	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.992
RBV dosage change (n (%))									
RBV dosage increase	0 (0.0%)	15 (19.0%)	0 (0.0%)	14 (9.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.756
RBV dosage decrease	0 (0.0%)	2 (2.5%)	0 (0.0%)	3 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Adverse events (n (%))									
Anaemia	1 (20.0%)	8 (11.1%)	3 (7.3%)	18 (17.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.762
Leucopenia	2 (40.0%)	47 (65.3%)	19 (46.3%)	61 (57.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.061
Thrombocytopenia	0 (0.0%)	6 (8.3%)	8 (19.5%)	46 (43.0%)	0 (0.0%)	0 (0.0%)	1 (100.0%)	2 (100.0%)	0.000

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; DAA, direct-acting antiviral; DCV, daclatasvir; IFN, interferon; INR, international normalized ratio; IQR, interquartile range; LDV, ledipasvir; OBV, ombitasvir; PTV, paritaprevir; RBV, ribavirin; r, ritonavir; SD, standard deviation; SIM, simeprevir; SOF, sofosbuvir.

3.3. Follow-Up Investigations

In all patients treated with DAA therapy, ALT levels normalized during therapy (Median (IQR): 43 (31–55) IU/mL at baseline vs. 18.5 (12.85–27) IU/mL at week 12; $p < 0.01$). Also, AST levels normalized during therapy (Median (IQR): 48 (36–57) IU/mL at baseline vs. 22 (17–30) IU/mL at week 12; $p < 0.01$). However, the eGFR decreased significantly after therapy (Mean ± SD: 102.73 ± 48.82 mL/min/1.73 m^2 at baseline vs. 46.74 ± 45.88 mL/min/1.73 m^2 at week 12; $p < 0.01$).

3.4. Sustained Virological Response

All patients achieved virological response at EoT (100%). The SVR12 rate was 100% for patients who presented for follow-up at 12 weeks after EoT (N = 225/327; 68.8%). One hundred and two patients had missed SVR12 data due to LTFU. Most of these patients were from the Cairo government where our tertiary hospital is located (N = 71/102; 69.6%), less than 75 years (78/102; 76.5%) with governmental support (N = 84/102; 82.4%).

3.5. Adverse Events

There were 222 adverse events (AE) reported in our study population, with a percentage of AEs (67.8%) including anaemia in 30 patients (9.1%), leucopenia in 129 patients (39.4%) and thrombocytopenia in 63 patients (19.2%), with similar frequency among the three age groups. Twelve patients (3.6%) had pancytopenia, 5 patients (1.5%) had combined leucopenia and anemia, while 2 patients (0.6%) had combined leucopenia and thrombocytopenia. No serious side effects led to discontinuation of therapy among studied patients.

Significant anaemia was determined by decline in hemoglobin levels <12 g/dL or decline more than 3 g/dL. Anaemia was reported in 26 patients (11%) who received ribavirin-based regimens. Only 5 patients required ribavirin dose reduction without statistical significance among the three studied age groups and erythropoietin was never used.

Higher prevalence of thrombocytopenia was observed among patients on Sofosbuvir/Daclatasvir-based regimens (Table 2).

No hepatic decompensation was observed, and no patient died in our study.

4. Discussion

CHC in the elderly is expected to increase in the upcoming years due to the acquisition of HCV during middle age [20,21].

Pegylated interferon and ribavirin are commonly used for the treatment of HCV infection with a SVR rate of 55% [22]. This rate dramatically increases to >95% with the introduction of DAA therapy for all HCV genotypes with shortened treatment duration [8,23].

Several reports suggest that HCV treatment in elderly patients improves life expectancy and health-related quality of life in addition to the elimination of HCV infection with its complications [24,25].

Multiple clinical studies in different countries were conducted to assess the efficacy and safety of DAA regimens in elderly patients with CHC. Rodriguez-Osorio et al. reported a SVR12 rate of 88.3% in 120 patients [26]; Conti et al. observed a 94.7% SVR12 rate in HCV older patients recruited in northern Italy centres [21]. A large real-world Spanish National Registry (Hepa-C) of >1200 elderly patients reported a SVR12 rate of 94% [27]. Likewise, in a real-world analysis of >4500 elderly patients treated with different DAA regimens in the US Veterans Affairs Healthcare System, there was a high SVR achievement in elderly patients compared to younger patients [28].

Egypt is considered one of the pioneers in the treatment of CHC infection. A national mass treatment program was established by the Egyptian National Committee for the Control of Viral Hepatitis for the eradication of HCV in Egypt after the development of highly effective DAA therapy. Few clinical studies have examined different DAA regimens in elderly patients in Egypt. Thus, the aim of this study was to assess this treatment in elderly Egyptian CHC patients.

In our eligibility inclusion criteria, we did not specify an age limit in order to represent a wide spectrum of elderly patients.

Our study shows that DAA produces high SVR even in the oldest age (>75 years) and that advanced age is not an independent negative predictor of SVR, as was concluded by one previous study [28]. Also, our results were similar to a report by Villani et al. (2018), which showed a rate of SVR12 99.3% in elderly vs. 98.3% in younger patients [29], and Foster et al. (2019), which showed a SVR12 rate of 97.9% in elderly patients vs. 97.3% in non-elderly patients [19]. Thus, our results should reassure providers that DAA therapy in older individuals offers a similar likelihood of HCV clearance as in younger individuals.

To date, studies conducted as clinical trials or field-practice show promising curing rates up to 100% for DAA therapy given for 12 weeks, even in cirrhotic or treatment-experienced GT4 patients [30].

In our current study, all patients who received DAA regimens with or without ribavirin achieved SVR, suggesting that ribavirin-free regimens do not negatively impact SVR, which aligns with results from different previous studies [29,31].

Regarding OBV/PTV/r efficacy, several studies report results similar to ours. In the PEARL-I study, 135 CHC GT4 patients treated with OBV/PTV/r achieved SVR 100% in treatment with RBV and 91% in those treated without RBV [32]. Also, Welzel et al. reported the achievement of SVR12 in all 53 GT4 patients treated with OBV/PTV/r ± RBV [33].

Similar to our findings, several studies showed that the SOF/DCV regimen is effective for the treatment of CHC. Babatin et al. reported SVR 100% in all studied GT4 patients treated for 12 weeks with either SOF/SIM ± RBV (group 1) or SOF/DCV ± RBV (group 2) [34]. Another study showed a SVR12 rate of 96.67% in treating non-cirrhotic GT4 patients with SOF/DCV [35]. In advanced stages of liver fibrosis, GT4 patients treated with SOF/DCV/RBV achieved a SVR12 rate of 97% in one French study [36], and a lower SVR rate of 68% in another multicentre study with Child B cirrhotic, treatment-experienced patients [30].

Consistent with our results, SOF/LDV ± RBV achieved a SVR12 rate of 98% in patients with CHC aged ≥65 years [14] and a 87.6% SVR12 rate in a large retrospective field-practice study by the Veterans Affairs National Health Care System [37].

Several studies have shown that the SOF/SIM regimen is effective at treating CHC, which is similar to the findings of our study. A multicentre cohort study in Egypt stated that the SVR12 rates in both naïve patients and those with previous interferon treatment were 94% to 99% for mild to moderate fibrosis (F1–F3) and 80% to 90% for advanced fibrosis (F4), respectively [38]. Another Egyptian cohort study of 6211 chronic HCV GT4 patients found that the SVR12 rates in easy- and difficult-to-treat patients (Fib 4 index >3.25 and METAVIR score F3–F4) were 96% and 93%, respectively [39]. All studied GT4 patients, either naïve or experienced to SOF/SIM therapy, achieved SVR12 in PLUTO and OSIRIS clinical trials [40,41].

In our cohort, treatment-naïve patients predominated, which could be explained by the availability of new safe and effective DAA medications implemented by the broad national HCV eradication program in our country.

In our study, liver enzymes improved significantly in patients treated with different DAA regimens. This agreed with different studies that reported improvement of liver function during DAA therapy, regardless of HCV genotype [42,43].

In terms of AE, there were 222 (67.8%) reported in our study. This result is consistent with the range (50–95%) of AEs reported in previous studies [26,40,44]. We should consider that our study was conducted in a tertiary referral centre for chronic viral hepatitis.

The AE number was similar across the different age groups in our study, which is in agreement with a previous study that showed that there was no statistically significant difference between elderly subgroups (30% in those aged 65–75 years versus 27% in those aged ≥75 years) [29]. Another study showed a similar frequency of AEs between old and very old patients [44].

The most commonly reported AEs in patients treated with DAA were leucopenia, anaemia and thrombocytopenia, without significant difference between regimens with or without ribavirin, which is consistent with several previous studies [38,42,45]. Our data agreed with Villani et al. in providing a rationale for the usage of ribavirin in elderly patients, given that all DAA combinations were effective and safe [45].

Regarding renal function, eGFR was decreased in our studied patients treated with DAA without influence on treatment outcome. There is scarce evidence in the literature about the effect of DAAs on renal function. The reduction in renal function in our study may therefore be attributable to age-related decline in GFR [46]. Thus, further longitudinal studies with untreated controls are needed to clarify these findings in elderly patients.

Our treatment DAA regimens were well tolerated and no patient discontinued treatment due to adverse events like other previous studies [34,42,47].

All studied patients had clinic appointments for follow-up 12 weeks after EoT. However, several patients were noncompliant with the high rate of LTFU patients despite easy access to our nearby institution and financial coverage of our healthcare services. This highlights the need for applying further stringent monitoring requirements as reported in a previous study [48], and to increase awareness of general practitioners of new case findings, especially the silent HCV-infected patients, and referring them for treatment and care as reported by a recent study [49].

This study has limitations due to its retrospective nature and the small numbers for some treatment regimens. Additionally, this clinical study was not designed to compare the efficacy and safety of DAA in elderly versus non-elderly patients. Therefore, in this regard, future larger studies are needed.

5. Conclusions

In conclusion, the results of our study demonstrate that age does not influence the success of DAA treatment and that all DAA regimens were well-tolerated, safe, and highly efficacious, even in those aged 75 years or older.

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