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# Effect of gender difference on psychiatric outcomes for hepatitis C virus patients receiving direct-acting antivirals in Egyptian population: a cohort study

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## Abstract

**Background:** Chronic liver disease is primarily caused by hepatitis C virus (HCV). HCV produces extrahepatic psychiatric problems. So, patients with CHC who received sofosbuvir-based direct-acting antiviral agents (DAAs) were evaluated for psychiatric manifestations, specifically depression and anxiety symptoms. Additionally, evaluate the impact of gender on psychiatric manifestations of sofosbuvir-based DAAs and identify their potential risk factors for psychiatric manifestations. In this prospective study, 170 CHC patients without prior treatment received DAA therapy who categorized into 2 groups, group 1 comprised male participants (Nb = 97), and group two comprised female participants (Nb = 73). All participants were evaluated with the five-factor model of personality (SIFFM), Hamilton Depression Rating Scale (HDS), and Hamilton Anxiety Rating Scale (HAS) at baseline and repeated follow up until 3 months after treatment end.

**Results:** Our findings indicated that, a progressive decline in the mean HADS-A and HADS-D scores between baseline (before treatment) and consequence follow-up (during and after treatment) measurements without significant difference regarding gender. No statistically significant difference between the groups regarding the mean values of SIFFM. High levels of extraversion were more likely to increase depression levels.

**Conclusions:** DAA treatment significantly improved anxiety and depression symptoms in CHC patients. Gender did not affect sofosbuvir-based DAA psychiatric symptoms. High extraversion increased depression risk.

**Keywords:** Anxiety, Chronic hepatitis C, Personality, Depression, Gender, Direct-acting antivirals

## Background

Hepatitis C virus (HCV) infection is a leading cause of chronic liver disease worldwide, which can progress to cirrhosis and hepatocellular carcinoma (HCC) [1]. Patients with chronic HCV infection exhibit higher rates of psychiatric issues than the general population, such

as substance abuse (36%) and mood disorders (28%) [2–4]. Extrahepatic manifestations of HCV in the central nervous system included stroke, cerebrovascular accidents, encephalopathy, myelitis, cognitive, fatigue, psychiatric disorders, myopathies, and peripheral neuropathy [5]. HCV infection causes psychiatric symptoms through inflammatory pathways, direct brain damage, metabolic and neurotransmitter system disruption, and immune-mediated responses [6]. Since October 2014, the National Committee for Control of Viral Hepatitis (NCCVH) in Egypt has launched a mass treatment

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program using sofosbuvir-based drug combinations, with annual updates in the regimens employed [7–9]. Significant improvements in patient-reported outcomes are associated with the treatment hepatitis with direct-acting antiviral agents (DAAs) that persist long after a sustained viral response (SVR) is achieved [10–12].

Because of their lack of neuropsychiatric side effects, DAAs might be prescribed to patients with severe mental disease and drug addiction. Additionally, DAAs had no effect on anxiety or depression symptoms during or after the course of treatment. Furthermore, controlled interactions were observed between DAAs and antipsychotics, and antidepressants. Therefore, it was suggested that DAAs be used safely and effectively in patients who had or were currently experiencing psychiatric problems [4, 13]. Moreover, there were notable gender distinctions in the morbidity, data collected. In Egypt, the incidence of HCV increased with age and male sex [14]. In contrast, anxiety and major depressive disorder are more prevalent among women than men in the general population [15–19]. However, no research has examined how DAAs may influence gender differences in psychiatric comorbidity in HCV.

In addition, HCV Patients with personality disorders are less likely to be treated for chronic HCV infection [20], and when therapy is initiated, both adherence and response to treatment are expected to be lower [21]. However, there is conflicting research on this topic [22].

So, in this study, patients with chronic hepatitis C infection who received sofosbuvir-based DAAs were evaluated for personality problems and psychiatric manifestations, specifically depression and anxiety symptoms. Additionally, participants were evaluated in order to determine the impact of gender on personality problems and psychiatric manifestations of sofosbuvir-based DAAs and identify potential risk factors for psychiatric manifestations of sofosbuvir-based DAAs.

## Methods

Between December 2019 and December 2020, 170 Chronic hepatitis C (CHC) patients without prior treatment participated in this prospective study. They were recruited from the Outpatients Virology Clinic of the Al-Rajhi Liver Hospital Patients were prescribed a 3-month course of sofosbuvir/daclatasvir for treating HCV. In this study, group 1 comprised male participants (Nb=97), and group 2 comprised female participants (Nb=73).

CHC was defined as sustained or intermittent elevations in blood transaminase levels for at least six months in conjunction with detectable anti-HCV antibodies and serum HCV-RNA [23]. Co-infection with HIV or hepatitis B, extreme ages (< 18 and > 60), cirrhosis of the liver, pregnancy, and patients with liver cancer were excluded

from the study. Before being diagnosed with HCV infection, the patient had a history of neurological disease, substance abuse, treatment with pegylated interferon or DAAs, as well as previous or current psychiatric disorders, diabetes, and hypertension were excluded.

In accordance with the NCCVH in Egypt's protocol and the National Community College Hispanic Council's (NCCHC) guidelines for managing adult patients with HCV infection, the non-cirrhotic group received DAA therapy for 12 weeks consisting of a once-daily oral dose of sofosbuvir (400 mg) and daclatasvir (60 mg) based on body weight (for non-cirrhotic). According to the 2016 EASL Recommendations for the Treatment of Hepatitis C, the combination of sofosbuvir and daclatasvir is still a viable option [24–26].

All participants were evaluated at the beginning of the study, at the 1st, 2nd, and 3rd months of treatment, and three months after the end of therapy. At the beginning of the study, each participant underwent a comprehensive psychiatric and medical evaluation. Additionally, participants were administered a structured interview for the five-factor model of personality at the beginning of the study. Additionally, abdominal ultrasound was used to rule out liver cirrhosis. Researchers evaluated participants using the Hamilton depression (HDS), and Hamilton anxiety (HAS) scales during treatment. At the conclusion of therapy, SVR was determined by quantitative PCR analysis of HCV-RNA.

The EPI info statistical package version 7 was used to calculate the sample size. The parameters used for determining the sample size were a proportion of 0.5, a confidence level of 95%, and a margin of error of 5%; thus, we calculated that a sample size of 35 was required according to previous studies [13, 27]. Meanwhile, this study relied on regular follow-up, which could lead to an increase in dropouts. As a result, we employed a conventional sample. The mental history and physical examination are evaluated using the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria by psychiatrist. The measures were used as following.

*Demographic data:* Age, gender, body mass index (BMI) (body weight/height<sup>2</sup> (meter), occupation, residence, education level, marital status, and other comorbidities (diabetes mellitus and hypertension).

*The laboratory assessment:* The complete blood count was computed using the automated hematology analyzer KX-21 N (Sysmex, Japan). Total bilirubin, alanine transaminase (ALT), aspartate transaminase (AST), urea, and creatinine levels were measured using the AU480 Clinical System (Beckman Coulter, Japan).

*Structured interview for the five-factor model of personality (SIFFM) (Arabic version) [28]:* This model proposes five fundamental dimensions commonly used to define

human personality. Five characteristics were denoted by the acronyms OCEAN or CANOE: receptivity to experience, conscientiousness, extraversion, agreeableness, and neuroticism. Total sum of each domain was classified into low level (0–12), moderate level (13–35), high level (36–48).

**Hamilton depression scale assessment** [29, 30]: Clinically, this scale is used to evaluate the severity of depression. The total score is determined by adding the scores for each item, which range between 0 and 4. The 17-item variant's scores could range from 0 to 54.

**Hamilton anxiety rating scale** [31]: The Hamilton rating scale is typically clinician-reported and is intended to measure the level of anxiety; The 14-item scale and each question are scored from 0 (not present) to 4 (severe), with a score range of 0–56 overall.

### Statistical analysis

Statistical analysis was executed by SPSS (Statistical Package for the Social Science, version 20, IBM, and Armonk, New York). Continuous data were represented by the mean  $\pm$  SD, while nominal data were represented by frequency (percentage). Repetitive ANOVA measures were done to measure difference of mean HADS-D and HADS-A in subsequently measures among studied groups. The potential risk factors for psychiatric

comorbidity were evaluated using univariate linear regression for difference between pre-post treatment scores of depressions and anxiety. The confidence level was set at 95%; therefore, the *P* value was considered significant if *P* < 0.05.

### Results

**Demographic data:** We observed a significant difference between the BMI, occupation, and hypertension of males and females in the studied group. Females had a higher mean BMI ( $26.50 \pm 4.28$ ) compared to males ( $24.69 \pm 3.74$ ) (Table 1).

Females had a greater proportion of non-workers (91.8%), whereas all males were employed (manual and official workers). Regarding the male population, manual laborers comprised a greater proportion (64.9%) than office workers (35.1%). Males were significantly more likely to be affected by hypertension (8.2%) than females (1.4%).

**The structured interview for the five-factor model of personality (SIFFM):** As shown in Table 2, there was no statistically significant difference between the groups regarding the mean values of the structured interview for the five-factor model of personality (SIFFM) subscales and total. Neuroticism, extraversion, and agreeableness were exhibited by a greater proportion

**Table 1** Demographic features of the studied groups

	Total participants (n = 170)	Male group (n = 97)	Female group (n = 73)	Chi <sup>2</sup> / t	P value
Age (years)	41.11 $\pm$ 9.22	40.7 $\pm$ 9.76	41.66 $\pm$ 8.48	0.668	0.505
BMI (kg/m <sup>2</sup> )	25.46 $\pm$ 4.07	24.69 $\pm$ 3.74	26.50 $\pm$ 4.28	2.94	0.004*
Occupation					
None	67 (39.4%)	0(0%)	67 (91.8%)	149.18	< 0.001*
Manual work	63 (37.1%)	63 (64.9%)	0(0%)		
Office work	40 (23.6%)	34 (35.1%)	6 (8.2%)		
Residence					
Rural	42 (24.7%)	21 (21.6%)	21 (28.8%)	1.134	0.287
Urban	128 (75.3%)	76 (78.4%)	52 (71.2%)		
Marital status					
Single	63 (37.1%)	29 (29.9%)	34 (46.6%)	4.96	0.026*
Married	107 (62.9%)	68 (70.1%)	39 (53.4%)		
Education level					
Illiterate	22 (12.9%)	11 (11.3%)	11 (15.1%)	7.31	0.063
Read and write	30 (17.6%)	17 (17.5%)	13 (17.8%)		
Primary level	92 (54.1%)	48 (49.5%)	44 (60.3%)		
Secondary level	26 (15.3%)	21 (21.6%)	5 (6.8%)		
Comorbid diseases					
Hypertension	9 (5.3%)	8 (8.2%)	1 (1.4%)	3.93	0.047*
Diabetes mellitus	32 (18.8%)	20 (20.6%)	12 (16.4%)	0.476	0.49

Data expressed as frequency (percentage), mean (SD). BMI body mass index

\* is significant *P* value

**Table 2** The structured interview for the five-factor model of personality (SIFFM) among studied groups

	Total participants (n = 170)	Male group (n = 97)	Female group (n = 73)	t/ Chi <sup>2</sup>	P value
Neuroticism (mean ± SD)	14.74 ± 2.98	14.67 ± 2.768	14.82 ± 3.272	0.327	0.327
Low	46 (27.1%)	26 (26.8%)	20 (27.4%)	0.007	0.931
Moderate	124 (72.9%)	71 (73.2%)	53 (72.6%)		
Extraversion (mean ± SD)	20.42 ± 4.27	20.42 ± 4.61	20.42 ± 3.819	0.003	0.109
Low	46 (27.1%)	26 (26.8%)	20 (27.4%)	0.007	0.931
Moderate	124 (72.9%)	71 (73.2%)	53 (72.6%)		
Openness to experience (mean ± SD)	11.16 ± 5.13	11.74 ± 5.08	10.38 ± 5.12	1.719	0.791
Low	106 (62.4%)	57 (58.8%)	49 (67.1%)	1.24	0.265
Moderate	64 (37.6%)	40 (41.2%)	24 (32.9%)		
Agreeableness (mean ± SD)	19.31 ± 4.07	19.68 ± 4.01	18.81 ± 4.132	1.386	0.964
Low	10 (5.9%)	5 (5.2%)	5 (6.8%)	0.216	0.642
Moderate	160 (94.1%)	92 (94.8%)	68 (93.2%)		
Conscientiousness (mean ± SD)	9.79 ± 5.23	9.19 ± 5.49	10.59 ± 4.775	1.743	0.266
Low	124 (72.9%)	75 (77.3%)	49 (67.1%)	0.219	0.139
Moderate	46 (27.1%)	22 (22.7%)	24 (32.9%)		

Data expressed as frequency (percentage), mean (SD). SIFFM: structured interview for the five-factor mode, P value significant if < .05

of moderate-class individuals than those from lower-class backgrounds (72.9% vs. 27.1%, 72.9% vs. 27.1%, 94.1% vs. 5.9%). In contrast, the percentage of the low class that was open to experience and conscientiousness was greater than that of the moderate class (62.4% vs. 37.6%, 72.9% vs. 27.1%). In our analysis of gender,

males outnumbered females in the moderate class on all SIFFM subscales except for conscientiousness. Laboratory data and the sustained virological response of studied groups: There was no significant difference between the groups in laboratory data. (Table 3).

**Table 3** Laboratory data and sustained virological response of studied groups

	Total participants (n = 170)	Male group (n = 97)	Female group (n = 73)	t/ Chi <sup>2</sup>	P value
HCV RNA by PCR (10 <sup>6</sup> u/l)	5.56 ± 0.24	4.3 ± 0.15	7.17 ± 0.32	0.741	0.116
ALT (u/l)	42.99 ± 20.74	41.64 ± 18.69	44.79 ± 23.20	0.98	0.235
AST (u/l)	40.85 ± 30.37	38.48 ± 32.98	44 ± 26.43	1.173	0.574
Bilirubin (mg/dl)	0.91 ± 0.29	0.89 ± 0.27	0.93 ± 0.34	0.668	0.118
Albumin (g/dl)	3.99 ± 0.44	3.97 ± 0.46	4 ± 0.44	0.483	0.239
Hemoglobin (mg/dl)	13.28 ± 1.39	13.35 ± 1.43	13.19 ± 1.34	0.724	0.272
Leucocytes (10 <sup>3</sup> /ul)	6.39 ± 1.56	6.51 ± 1.62	6.21 ± 1.48	1.237	0.203
Platelets (10 <sup>3</sup> /ul)	231.41 ± 52.40	229.98 ± 52.65	233.30 ± 52.37	0.408	0.854
Creatinine (mg/dl)	1.57 ± 7.36	2.01 ± 9.7	0.98 ± 0.19	0.903	0.107
INR	1.06 ± 0.109	1.06 ± 0.11	1.06 ± 0.104	0.393	0.964
After treatment (12 weeks)					
SVR				2.41	0.12
Achieved	163 (95.9%)	95 (97.9%)	68 (93.2%)		
Not achieved	7 (4.1%)	2 (2.1%)	5 (6.8%)		

Data expressed as frequency (percentage), mean (SD). HCV RNA hepatitis C virus ribonucleic acid, PCR the polymerase chain reaction, ALT alanine transaminase, AST aspartate transaminase, INR international randomized ratio, SVR Sustained virological response

**Psychometric scales**

In the repetitive measures, there was a statistically significant difference in reaction time of depression at male group ( $F=364.105, P < 0.000$ ) and female group, ( $F=241.584, P < 0.000$ ) but there was not a statistically significant difference in the reaction time between the two groups ( $F=0.387, P=0.788$ ). Also, there was a statistically significant difference in reaction time of anxiety at male group ( $F=325.894, P < 0.000$ ) and female group, ( $F=252.94, P < 0.000$ ) but there was not a statistically significant difference in the reaction time between the two groups ( $F=0.117, P=0.912$ ) (See Table 4).

*Relation studies:* Linear regression: Table 5 displays univariate linear regression for difference between pre-post treatment scores of HAD-D and HAD-A with demographic data and SIFFM subscales. Our findings revealed that individuals with high levels of extraversion were also more susceptible to increased depression levels.

**Discussion**

In the current study we aimed to examine the effect of gender differences on personality problems and psychiatric symptoms among chronic HCV patients receiving DAAs with repeated follow up to 3 months after treatment. Our study included 170 participants, who were divided into two gender-based groups and evaluated at the beginning of the study, at the first, second, and third months of treatment, and three months after the end of therapy. We used the Hamilton depression and anxiety scales to evaluate the subject.

Marital status was significantly different among the studied groups in this study. A higher proportion of married states was observed in both male and female groups.

Also, there was a significant difference in occupation among the studied groups, where the higher proportion was non-workers. Consistent with research by Gallach and colleagues, most females were non-workers (91.8%) while all males were workers [12].

Furthermore, BMI showed significant differences among studied groups, where the female group had higher BMIs. This can be explained as differences BMI among male and female due to pertaining to body weight perception, eating attitudes and weight-loss strategies [32].

In this study, there was a significant difference among studied groups regarding hypertension. The higher percentage of hypertension and diabetes mellitus were in the male group compared to the female groups. Previously, Fabrazzo and colleagues studied the effect of DAAs on CHC patients with and without psychiatric symptoms. Consistent with our findings, the researchers found a similar percentage of diabetes mellitus in the total population. However, the percentage of hypertension in study participants was higher than in our study [3]. Women are more aware of high blood pressure than men, while men have a larger prevalence of high blood pressure until after menopause as a result of decrease female hormone protection [33].

In this study, no statistically significant difference between the mean values of SIFFM subscales and total across the groups under study. On the scales of, a greater proportion of individuals were neuroticism, extraversion, and agreeableness with moderate class than those from the low class. Consistent with our findings, previous investigation [22] found no significant of personality disorders on in tolerability, clinical efficacy, or treatment

**Table 4** The repetitive measures of ANOVA for HADS-D and HADS-A

	Baseline	After 1st month	After 2nd month	After 3rd month	After 6th month	One way ANOVA Repeated measure analysis	Two-way ANOVA Repeated measure analysis time X group interaction
<i>Hamilton depression scale assessment (HADS-D)</i>							
Male group	10.60 ± 2.01	8.83 ± 1.91	7.93 ± 1.79	5.11 ± 1.51	3.23 ± 1.41	$df=3.34, 320.906$ $F=364.105$ $P < 0.000$	$df=3.41, 572.917,$ $F=0.387$ $P=0.788$
Female group	10.74 ± 2.11	8.69 ± 2.22	8.11 ± 1.68	4.89 ± 1.80	3.16 ± 1.46	$df=3.290, 236.855,$ $F=241.584$ $P < 0.001$	
<i>Hamilton anxiety rating scale (HADS-A)</i>							
Male group	12.73 ± 3.58	12.49 ± 4.04	9.44 ± 2.94	6.49 ± 2.71	2.65 ± 1.83	$df=2.170, 208.319,$ $F=325.894$ $P < 0.000$	$df=2.227, 382.523,$ $F=0.117$ $P=0.912$
Female group	12.52 ± 4.12	12.02 ± 4.41	9.28 ± 3.12	6.15 ± 3.12	2.32 ± 1.87	$df=2.387, 171.862,$ $F=252.94$ $P < 0.000$	

ANOVA Analysis of variance, HADS-D Hamilton depression scale assessment, HADS-A Hamilton anxiety rating scale

**Table 5** Univariate linear regression for difference between pre-post treatment scores of HAD-D and HAD-A with other parameters

	B	Std. error	Beta	t	P value	95% confidence interval for B	
						Lower bound	Upper bound
<i>HAD-D</i>							
Age	0.018	0.021	0.069	0.899	0.370	- 0.022	0.059
Gender	- 0.215	0.382	- 0.043	- 0.561	0.575	- 0.969	0.540
Body mass index	- 0.039	0.046	- 0.065	- 0.844	0.400	- 0.131	0.053
Years of education	- 0.018	0.058	- 0.024	- 0.306	0.760	- 0.132	0.097
Neuroticism	- 0.005	0.064	- 0.006	- 0.079	0.937	- 0.131	0.12
Extraversion	0.090	0.044	0.155	2.039	0.043*	0.003	0.176
Openness to experience	0.035	0.037	0.072	0.936	0.350	- 0.038	0.107
Agreeableness	0.004	0.047	0.006	0.080	0.936	- 0.088	0.096
Conscientiousness	- 0.004	0.036	- 0.009	- 0.117	0.907	- 0.076	0.067
<i>HAD-A</i>							
Age	- 0.004	0.032	- 0.011	- 0.136	0.892	- 0.067	0.059
Gender	- 0.123	0.594	- 0.016	- 0.207	0.836	- 1.296	1.05
Body mass index	0.015	0.072	0.016	0.21	0.834	- 0.128	0.158
Years of education	- 0.021	0.09	- 0.018	- 0.234	0.816	- 0.199	0.157
Neuroticism	- 0.058	0.099	- 0.045	- 0.584	0.560	- 0.252	0.137
Extraversion	0.085	0.069	0.095	1.241	0.216	- 0.050	0.221
Openness to experience	- 0.022	0.057	- 0.029	- 0.378	0.706	- 0.135	0.092
Agreeableness	0.032	0.072	0.034	0.439	0.662	- 0.111	0.175
Conscientiousness	0.032	0.072	0.034	0.439	0.662	- 0.111	0.175

discontinuation; however, this study included only 19 patients with PD and interferon treatment [21]. Similarly, another study reported no difference between individuals with PD who had interferon therapy in Spanish prisoners in discontinuation rate [34]. In this study, there was no apparent explanation for this finding; however, it may be connected to the fact that a much greater proportion of people with PD were already getting psychiatric care prior to beginning HCV treatment. This could have a protective effect by reducing the likelihood of adverse mental events, as well as lead to more frequent contact with health services and a decreased risk of treatment cessation [34].

In the repetitive ANOVA measures of the HADS-A and HADS-D scores, no gender difference regarding psychiatric problems when patients were treated with DAAs. We observed a progressive decline in the mean HADS-A and HADS-D scores between baseline (before treatment) and consequence follow-up (during and after treatment) measurements.

Similar to our study, Sundberg and colleagues measured symptoms of depression in HCV patients (cirrhotic and non-cirrhotic) treated with DAAs using the self-rating version of the Montgomery Åsberg Depression Rating Scale (MADRS-S). Psychiatric assessment, and patient self-report measures were administered at

baseline, after 1 month, 2 months of treatment, at the end of treatment, and three months after treatment. Three months after treatment, the MADRS-S score was significantly lower than at the beginning [4].

According to previous research that published the results of the Hamilton Depression Rating Scale (HAM-D) and the Hamilton Rating Scale for Anxiety (HAM-A) before and three months after therapy with DAAs, most CHC patients were diagnosed with mixed anxiety-depressive disorder. However, with treatment, both HAM-D and HAM-A scores decreased significantly [3, 35].

Moreover, a study conducted by Kesen and colleagues administered the Hospital Anxiety and Depression (HAD) questionnaire to measure the severity of the anxiety and depression symptoms at the beginning and at the end of the treatment by DAAs [36]. Both HAM-D and HAM-A scores decreased significantly with treatment. In addition, Nardelli and colleagues who examined the prevalence of neuropsychiatric disorders, found that their incidence decreased after HCV eradication but without reaching statistical significance [37].

On the one hand, in a study done by Gallach and colleagues that measured the anxiety and depression status of patients who completed the validated Spanish version of the Hospital Anxiety and Depression Scale (HADS-D

and HADS-A). HADS was administered at the beginning of treatment, after one month of treatment, 2 months of treatment, after treatment, and 3 months after the conclusion of treatment. Even in high-risk patients with major psychiatric disorders, DAA treatment had no effect on anxiety or depression during or after treatment for chronic hepatitis C infection [12].

Depression has been identified as a consequence for HCV infection. This correlation was associated with extrahepatic HCV manifestations in the central nervous system [38]. Additionally, the elimination of HCV with antiviral medication may reduce inflammation levels, resulting in fewer psychiatric symptoms, which may account for the observed reduction in depression ratings after treatment. In addition to the psychological effect of being healthy after virus eradication, there is also a significant physical effect [4, 6].

In this study, there were no significant gender-based differences in HADS scores when variables were analyzed by gender. Similar to our study, Gallach and colleagues and Bertine and colleagues reported that there was no statistically significant difference between the mean HADS-D and HADS-A scores for gender. In contrast, they found that depression, anxiety, and related disorders were more prevalent in female patients [36, 39].

The current study's regression model showed that individuals who had a high level of extraversion were more likely to have an increase in depression. Chronic HCV patients received INF in a previous trial had a statistically significant connection between HADS-D, HADS-A, and neuroticism. However, unlike our study, the researchers did not divide patients by gender [40].

Our study had notable limitations, including its narrow focus on depression and anxiety symptoms rather than cognitive disorders or sleep problems. The second limitation is the exclusion of cirrhotic patients and those with previous psychiatric disorders from our sample. In addition, all patients were administered DAAs according to a single regimen (Sofosbuvir/daclatasvir). Consequently, the observed effects cannot be formally extrapolated to other treatment protocols.

## Conclusions

Anxiety and depression symptoms in CHC patients who received DAA therapy improved significantly at the end of treatment. In addition, extraversion was found to be a substantial risk factor for depression symptoms. Gender had no effect on the outcome of sofosbuvir-based DAAs in terms of psychiatric symptoms.

## Abbreviations

DAAs: Direct-acting antivirals; HCC: Hepatocellular carcinoma; SIFFM: The structured interview for the five-factor model of personality; CHC: Chronic hepatitis C; HCV: Hepatitis C virus; INF: Interferon; SVR: Sustained virological

response; NCCHC: National Community College Hispanic Council's; HIV: Human immunodeficiency virus; HBV: Hepatitis B virus; HDS: Hamilton Depression Rating Scale; HAS: Hamilton Anxiety Rating Scale; PD: Personality disorders.

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None.

## Author contributions

ZGM, DK, GA and NM recruited participants, analysis, and interpreted data, and were the contributors in writing the manuscript. IS recruited participants, helped in data entry, analyse, and generate result sheets. HK, EM and HSA revised data interpretation and manuscript. All authors have read and approved the final manuscript.

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## Availability of data and materials

All data generated or analysed during this study are available from corresponded on request.

## Declarations

### Ethics approval and consent to participate

Ethical approval for the study was granted by the institutional review board of the Faculty of Medicine, Assiut University, with approval number 17100747. The registration number for this study on ClinicalTrials.gov is NCT03894696, registered date: 28/3/2019. URL of the trial registry record: <https://clinicaltrials.gov/ct2/show/NCT03894696>. Before participating in this study, each participant signed a consent form. They were given assurances regarding the security of their data and information regarding the availability of anonymized data. There were no risks, and no sensitive, uncomfortable, or unpleasant topics were discussed. The research design adheres to the ethical principles outlined in the Helsinki Declaration of 1975.

### Consent for publication

Not applicable.

### Competing interests

The authors declare no conflicts of interests.

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