

FREQUENCY OF DEPRESSION IN PATIENTS OF CHRONIC HEPATITIS C BEFORE STARTING TREATMENT

MUHAMMAD OWAIS FAZAL¹, GHULAM ABBAS TAHIR², AHMED BILAL³, YASIR YAQOOB⁴,
KAMRAN AHMED⁵, AYESHA IZZAT⁶

¹⁻⁵Faisalabad Medical University, Punjab, Pakistan.

⁶Musarrat Medical Centre, Jaranwala, Punjab, Pakistan.

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CORRESPONDENCE: DR. MUHAMMAD OWAIS FAZAL E-mail: owais.fazal@pmc.edu.pk

ABSTRACT

OBJECTIVE

To quantify the prevalence of depression among Hepatitis C patients not receiving treatment.

STUDY DESIGN

Cross-sectional study.

PLACE & DURATION OF STUDY

Medical Department, Faisalabad Medical University and affiliated Allied Hospital, Faisalabad, from 30th December 2021 to 29th June 2022.

METHOD

A total of 310 patients having Hepatitis C infection, with an age range of 20 years to 60 years, were included, while the patients suffering from an additional underlying chronic medical disease like CKD, COPD, and diabetes, which can cause depression, were excluded. Demographic data, including age, gender, residence (rural or urban), education of patient (Primary, middle or higher education), marital status (single, married or separated), income of patient and duration of Hepatitis C infection were recorded. The selected patients were interviewed by using Beck Depression Inventory.

RESULTS

The mean age of participants was 41.75 ± 8.62 years. One hundred and sixty-three patients (52.58%) were in the 20–40 age range. 166 (53.55%) of the 310 patients were men, and 144 (46.45%) were women, for a male-to-female ratio of 1.2:1. The frequency of depression in patients with Hepatitis C infection not receiving any treatment was found in 187 (60.32%) patients.

CONCLUSION

The frequency of depression in patients suffering from Hepatitis C infection not receiving any treatment is very high.

KEYWORDS

Beck Depression Inventory; Cross-sectional Studies; Depression; Hepatitis C; Prevalence.

INTRODUCTION

The Flaviviridae family includes the Hepatitis C virus. The genome of the HCV virion is a single-stranded positive RNA.¹ It has several subtypes and six genotypes. Worldwide, there are 175 million HCV patients, that comprise 3% of the world's population.² The highest incidence rate has been seen in Egypt (15–20%), while the United Kingdom has the lowest occurrence (0.01–0.1%).³ Hepatitis C infection is present in 25% of people with hepatocellular carcinoma, and 27% of people with cirrhosis, according to estimates.⁴ Hepatitis C virus (HCV), which has a significant morbidity and mortality rate in Pakistan, is present in over 10 million people among the Pakistani population.⁵

Unsterilised sharp objects or needle stick injuries, blood and blood products transfusion, and tattooing are risk factors for spreading the hepatitis C virus. The possibilities of contribution from sexual and perinatal transmission have been estimated to be close to 5%. The other modes of spread are vertical transmission and sexual transmission.⁶ Previous research revealed that the use of non-disposable needles for frequent medical parenteral injections was strongly linked to HCV seropositivity and that most people who tested positive for the anti-HCV did not have a history of blood transfusions. Hepatitis C is one of the most widespread causes of chronic liver disease worldwide.⁷ There are an estimated 71 million chronic hepatitis C infections worldwide. Those who get chronic hepatitis C infection run a 15%–20% chance of developing liver cirrhosis within 20 years.⁸ According to the World Health Organisation, the Eastern Mediterranean and European regions, with 2.3% and 1.5% prevalence rates, respectively, are the most affected regions.⁷ In Pakistan, which has a population of 190 million people, the hepatitis C virus has infected about 10 million people.¹

Cirrhosis, hepatocellular carcinoma (HCC), and end-stage liver disease requiring liver transplantation are the most common outcomes of chronic hepatitis C infection.⁹ A considerable global disease burden is a result of both rising mortality and morbidity from HCV-related advanced liver illnesses and patient-reported outcomes, such as quality of life or mental health status.¹⁰

Pre-existing psychiatric illnesses, such as mood and psychotic disorders, are 3–4 times more common and frequently go undetected in HCV patients. This could be brought on by a diminished desire to use or access mental and primary health care services, actual or imagined stigma against HCV patients, or denial of their psychiatric symptoms. As comorbid depression is linked to decreased adherence to HCV

medication, it can impact prognosis. Between 20 and 50% of HCV patients report having depression, compared to 10% of the general population.¹¹

Before beginning treatment, 264 Hepatitis C patients were enrolled in a local study in Karachi.¹² The subjects' average ages ranged from 17 to 71 and mean age was 39.82 ± 10.61 years. 127 (48.1%) were men, and 223 (84.5%) were married. Hepatitis C was present for an average of 3.665 ± 2.445 (0.1 to 12) years. 191 (72.3%) of the participants had depression.

The rationale of this study was to find the prevalence of depression in those patients with Hepatitis C who have not been given any treatment yet (pretreatment prevalence in hepatitis C patients). Seeing the magnitude of the disease will help us find the burden of the disease and make policy for routine psychiatry evaluation in all patients of Hepatitis C infection before starting treatment. Without addressing depression, physicians cannot complete the treatment of chronic disease. Depression results in poor compliance and poor outcomes of medical treatment. Finding the frequency of depression and treating the undiagnosed depression will help improve the quality of life in patients suffering from Hepatitis C infection.

METHOD

This is a descriptive, cross-sectional study, conducted in the Medical Department, Faisalabad Medical University and affiliated Allied Hospital, Faisalabad, from 30th December 2021 to 29th June 2022.

Hepatitis C infection is defined as patient having positive ELISA report anti-HCV antibodies. Depression is operationally defined as symptoms meeting the Beck's Depression Inventory. (Performa will be filled for the selected sample in the Urdu language).

Sample size was calculated using the WHO sample size calculator, $P = 72.3\%$,³ Confidence Interval= 95%, Absolute precision required= 5%. Thus, the sample size was = 310 patients. A non-probability, consecutive sampling technique was used.

Sample Selection

a. Inclusion Criteria

- Patients of female and male genders
- Patients aged 20 to 60 years.
- Patients were suffering from Hepatitis C infection as per the operational definition.

b. Exclusion Criteria

- Already diagnosed cases of depression (Determined on medical record)
- Patients with underlying chronic diseases like CKD, COPD and diabetes can cause depression. (Determined by medical history).

Data Collection Procedure

After the approval from the hospital's ethical review committee, via letter No.F.4ERC/FMU/2020-21/, 310 patients with Hepatitis C infection were enrolled in the OPD of the Medical Unit of Allied Hospital Faisalabad. Patients were enrolled after matching the inclusion and exclusion criteria. Written informed consent was taken from patients or guardians. Demographic data, including age, gender, residence (rural or urban), education of patient (Primary, middle, or higher education), marital status (single, married or separated), income of patient and duration of Hepatitis C infection were recorded. The researcher interviewed the selected patients by using the Beck Depression Inventory.⁴ All the pieces of information were collected on specially designed proforma. Patients with depression were treated as per hospital protocols.

Data Analysis

All the data were entered into SPSS V-23. The mean and standard deviation were calculated for all quantitative variables like age, duration of disease and Beck Depression Inventory score. Frequency and percentage were calculated for all qualitative variables like gender, income status, educational level, residence status and depression.

Effect modifiers like age, gender, duration of disease, educational status, residence status, income and marital status were controlled by stratification. Post-stratification chi-square test was applied, and a p-value ≤ 0.05 was taken as significant.

RESULTS

The age range in this study was from 20 to 60 years, with a mean age of 41.75 ± 8.62 years. Most of the patients, 163 (52.58%), were between 20 to 40 years of age (Table 1).

Of 310 patients, the male-to-female ratio was of 1.2:1 (Figure 1). Our study's mean disease duration was 5.84 ± 2.16 years (Table 1). The distribution of patients according to place of living is shown in Table 1. The distribution of patients according to education, income & marital status is shown in Table 2.

In our study, the frequency of depression in patients with Hepatitis C infection not receiving any treatment was found in 187 (60.32%) patients (Figure 2).

The Stratification of depression concerning age groups and gender & duration of illness is shown in Table 3. Table 4 shows the stratification of depression concerning the income, education & marital status, while stratification of depression for residence is shown in Table 5.

Table 1
Distribution of patients according to age, duration of disease, place of living, education, income, and marital status. (N=310 each group)

	No. of patients	%	Duration of disease (years)	No. of patients	%	Place of living	No. of patients	%
20-40	163	52.58	>5	177	57.10	Rural	110	35.48
41-60	147	47.42	<5	133	42.90	urban	200	64.52
Mean ± SD = 41.75 ± 8.62 years			Mean ± SD = 5.84 ± 2.16 years					

Table 2
Distribution of patients according to education, income, and marital status, (N=310 each group)

Education	No. of patients	%	Income status	No. of patients	%	Marital Status	No. of patients	%
Primary	50	61.13	Lower	98	31.61	Unmarried	66	21.29
Middle	128	41.29	Middle	138	44.52	Married	224	72.26
Higher	132	42.58	Affording	74	23.87	Separated	20	6.45

Table 3
Stratification of depression based on age group, gender and duration of illness.

Age	Depression		Gender	Depression		Duration	Depression	
	Yes	No		Yes	No		Yes	No
20-40	99 (60.4%)	65 (39.26%)	Male	112 (67.47%)	54 (32.53%)	>5 years	100 (56.50%)	77 (43.50%)
40-60	89 (60.54%)	58 (39.46%)	Female	75 (52.08%)	69 (47.92%)	<5 years	87 (65.41%)	46 (34.59%)
P-value	0.974		p-value	0.006		p-value	0.112	

Table 4
Stratification of depression concerning income, education, marital status.

Income	Depression		Education	Depression		Marital Status	Depression	
	Yes	No		Yes	No		Yes	No
Lower	62 (63.27%)	39 (35.45%)	Primary	32 (64.0%)	18 (36.0%)	Unmarried	45 (68.18%)	21 (31.82%)
Middle	82 (59.42%)	84 (42.0%)	Middle	75 (58.59%)	53 (41.41%)	Married	130 (58.04%)	94 (41.96%)
Affording	43 (58.11%)	31 (41.89%)	Higher	80 (60.61%)	52 (39.39%)	Separated	12 (60.0%)	8 (40.0%)
p-value	0.758		p-value	0.799		p-value	0.334	

Table 5
Stratification of depression concerning residence.

Residence	Depression		p-value
	Yes	No	
Rural	71 (64.55%)	39 (35.45%)	0.259
Urban	116 *58.0%	84 (42.0%)	

DISCUSSION

A frequent mental disorder and the main contributor to disability globally is depression.⁵ Major depression has been linked to long-term hepatitis C (HCV) exposure and prior interferon-alpha antiviral therapy.^{6,7} In over 80% of instances, HCV infection results in chronic hepatitis C (CHC), and in one in five people within 20 to 50 years of the initial condition, liver cirrhosis; of these, 5 to 10% will develop hepatocellular carcinoma or decompensated liver disease.⁵ It is now known that chronic hepatitis C (CHC) is a systemic illness with a wide range of extrahepatic symptoms, such as anhedonia, lethargy, irritability, anxiety, sleeplessness, and heightened pain sensitivity.¹ There is proof that HCV directly invades the brain⁹ and that the immune system has been chronically stimulated.¹⁰ These elements may work in conjunction with several neuronal pathways, neurotransmission, and neurotrophic mechanisms to cause neuropsychiatric symptoms in CHC.^{6,7}

We conducted this study to determine the prevalence of depression in Hepatitis C patients who were not receiving therapy. The study's participants ranged in age from 20 to 60, with a mean age of 41.75 + 8.62 years. 163 (52.58%) of the patients, or the majority, were in the 20–40 age range. 166 (53.55%) of the 310 patients were men, and 144 (46.45%) were women, for a male-to-female ratio of 1.2:1. In our study, 187 patients (60.32%) with hepatitis C infection who were not receiving therapy frequently experienced depression. Before beginning treatment, 264 Hepatitis C patients from Karachi were included in a local study.³ The subjects' average ages ranged from 17 to 71 and were 39.82 ± 10.61 years. 127 (48.1%) were men, and 223 (84.5%) were married. Hepatitis C was present for an average of 3.665 ± 2.445 (0.1 to 12) years. 191 (72.3%) of the participants had depression.

In a substantial American cohort (n=4,781) with a prior history of intravenous drug use (IVDU) in 51.4%, the prevalence of depression in chronic HCV-infected patients was reported to be 29.7%, which is higher than the 9% prevalence in the general population using the personal health questionnaire (PHQ-8) with a cutoff score of 10,13 which was consistent with the findings of the other studies.^{1,8} In contrast to chronic hepatitis B, chronic hepatitis C (CHC) was independently related to depression, according to data from the National Health and Nutrition Examination Survey (2005–2010, n=10,231). Major depressive disorder occurred in 11.4% of HCV patients, with a 54.6% prevalence of depression, according to the Patient Health Questionnaire (PHQ-9).^{9–13} Among Australian CHC patients (n=395), the Hospital Anxiety and Depression Scale (HADS-D 8) depression prevalence was 27%, which is 2.4 times higher than community norms and linked with single status.¹⁴ In a nationwide survey carried out in Japan, 7.1% of patients reported having depression. Even though a substantial prevalence (51.6%) of depression by Beck depression inventory (BDI-II) was identified in 67 Chinese IVDUs, there are data on the majority of depression in CHC patients from Asian countries.¹⁵

One hundred thirty-five individuals with chronic hepatitis C and 76 patients with chronic hepatitis B were assessed for major depressive disorder by Mauro G. Carta et al.¹⁶ When compared to chronic hepatitis B and the control group, they found that major depressive disorder was more common in people with chronic hepatitis C. Ultimately, interferon therapy did not affect the association between chronic hepatitis C and major depressive disorder (based on international diagnostic criteria). There is a considerable range in the commonness of depression among Hepatitis C patients. Compared to the general population (6–10%), it ranges from roughly 24–70%.¹⁸ The wide variety of prevalence estimates made by various studies may be due to the complexity of the disease itself, the racial and population makeup of the study participants, and other factors related to depression and anxiety. According to Kenny-Walsh, 376 Irish women who had contracted iatrogenic hepatitis C had a 16% prevalence of sad mood documented in their medical records.¹⁹ In 500 patients evaluated at a tertiary referral centre, a majority of 24% were diagnosed with depression, according to Lee et al. Using a standardised psychiatric interview, Dwight et al discovered a 28% frequency in 50 individuals.²⁰

Uncertain factors may be at play in the increased rate of depression among hepatitis C patients. However, it has been hypothesised that several factors may be at play, including disease characteristics, such as changes in brain metabolites as shown by dynamic brain imaging and unpredictable, inconsistent, and complex disease progression. The reasons for depression in this population have also lately been linked to affective variables, stigma perception, and the involvement of platelet 5-HT.²¹ As seen in numerous studies in Pakistan, where the prevalence of depression is twice as high in female patients compared to male patients, gender differences also play a crucial role.²²⁻²⁴ However, this study's HCV patients did not exhibit this gender disparity.

CONCLUSION

This study concluded that the frequency of depression in patients with Hepatitis C infection not receiving any treatment is very high. So, we recommend that in every patient with hepatitis C, depression should be considered, and its early recognition and management should be done to reduce the community's morbidity.

CONFLICT OF INTEREST

None

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REFERENCES

1. Waheed Y, Shafi T, Safi SZ, Qadri I. Hepatitis C virus in Pakistan: a systematic review of prevalence, genotypes and risk factors. *World J Gastroenterol*. 2009;15(45):5647-5653. doi:10.3748/wjg.15.5647
2. Umer M, Iqbal M. Hepatitis C virus prevalence and genotype distribution in Pakistan: Comprehensive review of recent data. *World J Gastroenterol*. 2016;22(4):1684-1700. doi:10.3748/wjg.v22.i4.1684
3. Bhutto AR, Jatt MI, Rafi S, Washdev W, Arsalan M, Ullah A. Frequency of anxiety and depression in chronic hepatitis c patients visiting a tertiary care hospital at gadap town, karachi. *J Postgrad Med Inst [I]*. 2019 ;33(2). Available from : <https://jpmi.org.pk/index.php/jpmi/article/view/2447>
4. Carepatron [Internet]. [cited 2023 Sep 3]. Available from: <https://app.carepatron.com/Onboarding?redirect=?type=admin&isBusiness=true&type=admin&isBusiness=true>
5. WHO. Epidemiological update: increasing mortality calls for action 03. *Glob Hepat report*, 2017. 2017;7–20. Available from : <https://iris.who.int/bitstream/handle/10665/255016/9789241565455-eng.pdf?sequence=1>
6. Oriolo G, Egmond E, Mariño Z, et al. Systematic review with meta-analysis: neuroimaging in hepatitis C chronic infection. *Aliment Pharmacol Ther*. 2018;47(9):1238-1252. doi:10.1111/apt.14594
7. Yarlott L, Heald E, Forton D. Hepatitis C virus infection, and neurological and psychiatric disorders - A review. *J Adv Res*. 2017;8(2):139-148. doi:10.1016/j.jare.2016.09.005
8. Ashraf S, Ahmad A. Viral hepatitis in Pakistan: challenges and priorities. *Asian Pac J Trop Biomed*. 2015;5(3):190–1. doi: [https://doi.org/10.1016/S2221-1691\(15\)30004-6](https://doi.org/10.1016/S2221-1691(15)30004-6).
9. Lee K, Otgonsuren M, Younoszai Z, Mir HM, Younossi ZM. Association of chronic liver disease with depression: a population-based study. *Psychosomatics*. 2013;54(1):52-59. doi:10.1016/j.psym.2012.09.005
10. el-Serag HB, Kunik M, Richardson P, Rabeneck L. Psychiatric disorders among veterans with hepatitis C infection. *Gastroenterology*. 2002;123(2):476-482. doi:10.1053/gast.2002.34750
11. Fireman M, Indest DW, Blackwell A, Whitehead AJ, Hauser P. Addressing tri-morbidity (hepatitis C, psychiatric disorders, and substance use): the importance of routine mental health screening as a component of a comanagement model of care. *Clin Infect Dis*. 2005;40 Suppl 5:S286-S291. doi:10.1086/427442

12. Evon DM, Ramcharran D, Belle SH, et al. Prospective analysis of depression during peginterferon and ribavirin therapy of chronic hepatitis C: results of the Virahep-C study. *Am J Gastroenterol.* 2009;104(12):2949-2958. doi:10.1038/ajg.2009.528
13. Weinstein AA, Kallman Price J, Stepanova M, et al. Depression in patients with nonalcoholic fatty liver disease and chronic viral hepatitis B and C. *Psychosomatics.* 2011;52(2):127-132. doi:10.1016/j.psych.2010.12.019
14. Stewart B, Mikocka-Walus A, Morgan J, et al. Anxiety and depression in Australian chronic hepatitis C outpatients: prevalence and predictors. *Australas Psychiatry.* 2012;20(6):496-500. doi:10.1177/1039856212460597
15. Wang Z, Du J, Zhao M, Page K, Xiao Z, Mandel JS. Hepatitis C virus infection is independently associated with depression among methadone maintenance treatment heroin users in China. *Asia Pac Psychiatry.* 2013;5(3):191-196. doi:10.1111/j.1758-5872.2012.00209.x
16. Carta MG, Hardoy MC, Garofalo A, et al. Association of chronic hepatitis C with major depressive disorders: irrespective of interferon-alpha therapy. *Clin Pract Epidemiol Ment Health.* 2007;3:22. doi:10.1186/1745-0179-3-22
17. Kraus MR, Schäfer A, Csef H, Scheurlen M, Faller H. Emotional state, coping styles, and somatic variables in patients with chronic hepatitis C. *Psychosomatics.* 2000;41(5):377-384. doi:10.1176/appi.psy.41.5.377
18. Schäfer A, Wittchen HU, Seufert J, Kraus MR. Methodological approaches in the assessment of interferon-alfa-induced depression in patients with chronic hepatitis C - a critical review. *Int J Methods Psychiatr Res.* 2007;16(4):186-201. doi:10.1002/mpr.229
19. Kenny-Walsh E. Clinical outcomes after hepatitis C infection from contaminated anti-D immune globulin. *Irish Hepatology Research Group. N Engl J Med.* 1999;340(16):1228-1233. doi:10.1056/NEJM199904223401602
20. Lee DH, Jamal H, Regenstein FG, Perrillo RP. Morbidity of chronic hepatitis C as seen in a tertiary care medical center. *Dig Dis Sci.* 1997;42(1):186-191. doi:10.1023/a:1018818012378
21. Schäfer A, Scheurlen M, Seufert J, et al. Platelet serotonin (5-HT) levels in interferon-treated patients with hepatitis C and its possible association with interferon-induced depression. *J Hepatol.* 2010;52(1):10-15. doi:10.1016/j.jhep.2009.10.007
22. Husain N, Creed F, Tomenson B. Depression and social stress in Pakistan. *Psychol Med.* 2000;30(2):395-402. doi:10.1017/s0033291700001707
23. Quek TT, Tam WW, Tran BX, et al. The Global Prevalence of Anxiety Among Medical Students: A Meta-Analysis. *Int J Environ Res Public Health.* 2019;16(15):2735. Published 2019 Jul 31. doi:10.3390/ijerph16152735
24. Ahmed I, Banu H, Al-Fageer R, Al-Suwaidi R. Cognitive emotions: depression and anxiety in medical students and staff. *J Crit Care.* 2009;24(3):e1-e7. doi:10.1016/j.jccr.2009.06.003

AUTHOR(S) CONTRIBUTION / UNDERTAKING FORM

Sr No.	Author name	Affiliation	Contribution	Signatures
1 st Auth	Dr Muhammad Owais Fazal	Associate Professor Faisalabad Medical University	Main Author	
2 nd Auth	Dr Ghulam Abbas Tahir	Assistant Professor Faisalabad Medical University	Data collection and analysis	
3 rd Auth	Prof Dr Ahmed Bilal	Ex-Professor, Dean of Medicine, Faisalabad Medical University	Conception of idea, data collection	
4 th Auth	Dr Yasir Yaqoob	Assistant Professor Faisalabad Medical University	Discussion write up	
5 th Auth	Dr Kamran Ahmed	FCR, Medicines Faisalabad Medical University	Discussion write up	
6 th Auth	Dr Ayesha Izzat	Private Clinician	Plagiarism check, Data collection.	

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