

FREQUENCY OF ANXIETY AND DEPRESSION IN CHRONIC HEPATITIS C PATIENTS VISITING A TERTIARY CARE HOSPITAL AT GADAP TOWN, KARACHI

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Date Received:

September 10, 2018

Date Revised:

May 26, 2019

Date Accepted:

June 02, 2019

ABSTRACT

Objective: To determine the frequency of anxiety and depression in chronic hepatitis C patients.

Methodology: In this cross sectional study conducted at a private medical college hospital, adult subjects of either sex with positive antibodies to hepatitis C of more than 6 months' duration were enrolled after taking informed consent. After implementation of inclusion and exclusion criteria subjects were interviewed for the presence and severity of anxiety and depression by Beck anxiety inventory and Beck depression inventory questionnaires respectively.

Results: The mean age of 264 naïve hepatitis C subjects was 39.826 ± 10.6121 (ranging from 17 to 71) years. Among those, 127 (48.1%) were males while 137 (51.9%) were female. Mean duration of hepatitis C was 3.665 ± 2.445 (range 0.1 to 12) years. Anxiety was found in 177 (67%) subjects and males had higher frequency as compared to females (70.9% versus 63.5%). Depression was found in 191 (72.3%) subjects, In contrast to anxiety, depression was more prevalent in females 106 (77.4%) as compared to males 85 (66.9%).

Conclusion: Anxiety and depression were found in a significantly high number of naïve hepatitis C patients.

Key Words: Anxiety, Depression, Hepatitis C

This article may be cited as: Bhutto AR, Jat MI, Rafi S, Washdev W, Arsalan M, Amanullah. Frequency of anxiety and depression in chronic hepatitis C patients visiting a tertiary care hospital at Gadap Town, Karachi. *J Postgrad Med Inst* 2019; 33(2): 125-9.

INTRODUCTION

Attributable to global non-availability of vaccination, the incidence of hepatitis C virus (HCV) has not appeared into a steadily worsening situation as seen in hepatitis B (HBV) and consequently hepatitis C virus (HCV) is a foremost cause of chronic liver disease¹. According to WHO, approximately 3% of the world population (about 180 million people) are infected with hepatitis C, of which 130 million (50-80%) are chronic carriers and are at risk of liver cirrhosis and hepatocellular carcinoma². The frequency of HCV is 16% in Pakistan indicating far above the ground percentile in certain areas¹.

There is slow and sinister course of chronic hepatitis C infection³. In chronic hepatitis C, patients may or may not be symptomatic, and can present with hepatic and extra hepatic manifestations with fatigue and chronic pain being the predominant symptom⁴. Extra-hepatic manifestations include cerebrovascular events, encephalopathy, cognitive dysfunction and myelitis

among depression and fatigue are the chief cause of psychiatric disarray. Diversity of extra-hepatic consequences of HCV conditions may heighten the clinical parameters of hepatic infection despite of liver disease manifestations⁵. In HCV, depression is often associated with physical symptoms like chronic pain and fatigue⁶. Seventy percent of HCV infected patients develop Depression even those who didn't receive interferon therapy and this is the most common undesirable effect of HCV infection preceded by physical fatigue (86%) and irritability (74%)¹. Prognostic factors of fatigue in HCV patients are old age, female, and single status. It causes intrusion with patient ability to execute daily activities and mutilation of quality of life⁵. Due to impairment of friendly and family interaction, reduced sense of interest, changes in dietary habits, because of fear of prognosis, hopelessness, anger, HCV serological status information is itself a significant motive for poor health related quality of life⁷.

Early detection of psychiatric issues in chronic hepatitis is crucial because treatment of hepatitis C involves interferon, which itself has significant neuropsychiatric side effects. In some cases psychiatric symptoms are one of the reason reasons for holding interferon treatment. Successful treatment, therefore, requires detection and management of depression and other psychiatric issues before and during the treatment.

The objective of this study was to determine the frequency of anxiety and depression in hepatitis C patients and associated factors in our local population. As in our set up the research over these common problems is very scarce. This study would prove beneficial in early diagnoses and management of comorbid depression and anxiety in chronic hepatitis patients, thus improving the quality of life of these patients and reduction of morbidity burden on overall health care system.

METHODOLOGY

This cross-sectional research directed at outpatient division of a tertiary care hospital at Karachi; Al-Tibri Medical College & Hospital, Isra University Karachi campus, from June 2017 to December 2017. Adult subjects of either sex with positive antibodies to HCV of more than 6 months' duration were enrolled after taking informed consent.

Detailed History and physical examinations were performed. In addition to anti-HCV antibodies other laboratory investigations like coagulation profile, liver function tests and serum albumin were advised for implementation of inclusion and exclusion criteria as well as assessment of disease status. Patients were excluded if they were on interferon therapy, had other hepatitis viral infections like hepatitis B, hepatitis D virus or human immunodeficiency virus, or those with other co-existing chronic liver disease like chronic autoimmune hepatitis, primary biliary cirrhosis and Wilson disease. Patients with primary psychiatric diseases or other systemic diseases/factors having impact on depression like renal disease, hypo/hyperthyroidism, stroke, dementia, patients on anti-depressants, drug induced mental disorder, schizophrenia and manic depression were also excluded from study. Prior ethical approval was obtained from institute ethical committee. For anxiety and depression Beck anxiety inventory (BAI) and Beck depression inventory (BDI) questionnaires were used. Sample size was 264 and was calculated through standard sample size calculator and non-probability (consecutive) sampling technique was used.

All the data were analyzed using SPSS 22.0 for windows. Descriptive statistics were presented in mean \pm SD for numerical data while categorical data were presented in proportion (%). Statistical significance was determined by p value under 0.05.

RESULTS

The mean age of 264 naive hepatitis C subjects was 39.82 ± 10.6121 (ranging from 17 to 71) years. Among these, 127 (48.1%) were males and 223 (84.5%) were married. Mean duration of hepatitis C was 3.665 ± 2.445 (range 0.1 to 12) years. Among these, 108 (40.9%) were having 3 to 5 years. The socio-demographic profile of study subjects is presented in Table 1.

Out of 264 patients of chronic hepatitis C, anxiety was present in 177 (67%) subjects and according to severity 117 (44.3%) had mild to moderate anxiety. Depression was found in 191 (72.3%) subjects. Among these 88 (33.3%) presented with moderate depression (Table 2).

Gender based frequency of anxiety was found more in males as compare to females ($p = 0.204$). On the basis of tribe, the subjects belonged to Sindhi caste had higher frequency of anxiety as compared to other castes ($p < 0.001$). Duration of hepatitis C had also significant relation with anxiety ($p = < 0.001$). In contrast to anxiety, depression was more prevalent in females ($p = 0.058$). Duration of disease had significant relation with depression ($p = 0.008$) Details are given in Table 3.

DISCUSSION

In this study, anxiety was prevalent as 67% and it is higher than that reported by previous study by Luciana et al⁸. The reason for high prevalence of anxiety in naive hepatitis C patients is not clear but it has been hypothesized that changes in neurotransmission might have some role in this context. Weissenborn et al⁹ reported that changes in both striatal dopaminergic and midbrain serotonergic systems are in parallel with increased anxiety and depression irrespective of HCV viral load and severity of liver disease. Furthermore, a competitive serotonin receptors antagonist, Ondansetron, has shown efficacy in reducing hepatitis C related anxiety and depression¹⁰, hence substantiating the opinion of serotonergic pathway dysfunction.

Prevalence of depression reported in Hepatitis C patients varies widely and ranges from about 24-70%, as compared to general population (6-10%)^{11,12} and the reason behind that ample range of prevalence as estimated by different researchers might be the diversity of the disease itself, population/racial difference of study subjects and other associated factors responsible for depression and anxiety. In our study we found depression in 191 (72.3%) persons with hepatitis C which agrees well with that reported by other studies¹³. Moreover, a study by Ashrafi et al¹⁴ reported that genotype has also been linked to higher risk of depression and suggested that patients with HCV genotype 3 infections might be at increased risk of depression. Although

Table 1: Socio-demographic characteristics of study subjects

Variable	Subjects	
Age (years), Mean ± SD	39.826 ± 10.612	
Duration of Hepatitis C (years), Mean ± SD	3.665 ± 2.445	
Gender	Female	137 (51.9%)
	Male	127 (48.1%)
Occupation	Household	137 (51.9%)
	Professional	22 (8.3%)
	Shopkeeper	35 (13.3%)
	Jobless	26 (9.8%)
	Laborer	42 (15.9%)
	Others	2 (0.8%)
Educational Status	Un-educated	65 (24.6%)
	Primary	75 (28.4%)
	Matric	78 (29.5%)
	Intermediate	42 (15.9%)
	Graduate	4 (1.5%)
Tribe/Race	Balochi	114 (43.2%)
	Sindhi	102 (38.6%)
	Urdu	17 (6.4%)
	Punjabi	14 (5.3%)
	Pashto	5 (1.9%)
	Others	12 (4.5%)
Marital Status	Un-married	27 (10.2%)
	Married	223 (84.5%)
	Widow	09 (3.4%)
	Separated/Divorced	05 (1.9%)
Duration of Hepatitis C	Less than 1 year	15 (5.7%)
	1 to <3 years	89 (33.7%)
	3 to 5 years	108 (40.9%)
	>5 years	52 (19.7%)

Table 2: Frequency and severity of anxiety and depression in study subjects

Variable	n (%)	
Anxiety as per BAI Score	0–9: Normal to Minimal Anxiety	85 (32.2%)
	10–18: Mild to Moderate Anxiety	117 (44.3%)
	19–29: Moderate to Severe Anxiety	38 (14.4%)
	30–63: Severe Anxiety	22 (8.3%)
Depression as per BDI Score	1-16: Normal	73 (27.7%)
	17-20: Mild	20 (7.6%)
	21-30: Moderate	88 (33.3%)
	31 and above: Severe	83 (31.4%)

Table 3: Relationship of anxiety and depression with different variables

Variable		Anxiety		P value	Depression		P Value
		Yes	No		Yes	No	
Gender	Male	90 (50.8%)	37 (42.5%)	0.204	85 (44.5%)	42 (57.5%)	0.058
	Female	87 (49.2%)	50 (57.5%)		106 (55.5%)	31 (42.2%)	
Education Status	Un-educated	47 (26.6%)	18 (20.75)	0.375	46 (24.1%)	19 (26.0%)	0.873
	Primary	47 (26.7%)	28 (32.2%)		55 (28.8%)	20 (27.4%)	
	Matric	48 (27.1%)	30 (34.5%)		59 (30.9%)	19 (26.0%)	
	Intermediate	32 (18.1%)	10 (11.55)		28 (14.7%)	14 (19.2%)	
	Graduate	03 (1.7%)	01 (1.1%)		03 (1.65)	01 (1.4%)	
Tribe/Race	Balochi	70 (39.5%)	44 (50.6%)	<0.001	80 (41.9%)	34 (46.6%)	0.147
	Sindhi	83 (46.9%)	19 (21.8%)		78 (40.8%)	24 (32.9%)	
	Urdu	10 (5.6%)	07 (8.0%)		13 (6.8%)	04 (5.5%)	
	Punjabi	03 (1.7%)	11 (12.6%)		10 (5.2%)	04 (5.5%)	
	Pashto	02 (1.1%)	03 (3.4%)		01 (0.5%)	04 (5.5%)	
	Others	09 (5.1%)	03 (3.4%)		09 (4.7%)	03 (4.1%)	
Duration of Hepatitis C	Less than 1 year	02 (1.1%)	13 (14.9%)	<0.001	06 (3.1%)	09 (12.3%)	0.008
	1 to <3 years	56 (31.65)	33 (37.9%)		63 (33.0%)	26 (35.6%)	
	3 to 5 years	80 (45.2%)	28 (32.2%)		78 (40.8%)	30 (41.1%)	
	>5 years	39 (22.0%)	13 (14.9%)		44 (23.0%)	08 (11.0%)	
ALT (iu/l)	< 40	18 (10.2%)	15 (17.2%)	0.239	26 (13.6%)	07 (9.6%)	0.122
	41- 80	99 (55.9%)	51 (58.6%)		102 (53.4%)	48 (65.8%)	
	81-120	40 (22.65)	14 (16.1%)		39 (20.4%)	15 (20.5%)	
	>120	20 (11.3%)	07 (8.0%)		24 (12.6%)	03 (4.1%)	

we didn't advise genotyping of hepatitis C virus in our study population but as high prevalence of genotype 3 is well documented in our population so might be the reason for higher prevalence of depression in our study.

The reasons for the high prevalence of depression in hepatitis C patients are not clear; but it has been hypothesized that multiple factors might be responsible including the factors related to disease per se like alterations in brain metabolites as evident by dynamic brain imaging, unpredictability, inconsistency and complexity of disease course. In addition, emotional factors, perception of stigma and recently a role of platelet 5-HT has also been suggested to be the causes of depression in this population¹⁵⁻¹⁷. Our study results also revealed that females were more depressed than males (77.4% vs 66.9%) and were in accordance with findings of various previous studies conducted in Pakistan¹⁸⁻²⁰.

Many chronic medical illnesses are associated with neuropsychiatric manifestations likewise hepatitis C is also associated with an higher prevalence of psychiatric disorders like anxiety and depression^{21,22} with detrimental effects on the course of disease, augmentation

of somatic symptoms, reduced treatment compliance, functional impairment and reduced quality of life²³.

LIMITATIONS

There were a few limitations to our study. Firstly, as the study design was cross-sectional, it was difficult to directly evaluate the long-term impact of chronic hepatitis on anxiety and depression. Secondly, our study was single center based study, hence might not represent whole population.

CONCLUSION

Anxiety and depression were found in a significantly high number of naïve hepatitis C patients.

REFERENCES

1. Memon SA, Zuberi BF, Ashfaq MN, Kiran Z, Qadeer R, Memon AR et al. Frequency of depression in chronic Hepatitis C naïve patients. Pak J Med Sci 2011; 27:780-3.
2. Qureshi MO, Khokhar N, Shafqat F. Severity of depression in hepatitis B and hepatitis C patients. J Coll Physicians

- Surg Pak 2012; 22:632-4.
3. Silva LD, da Cunha CC, da Cunha LR, Araujo RF, Barcelos VM, Menta PL et al. Depression rather than liver impairment reduces quality of life in patients with hepatitis C. *Revista Brasileira de Psiquiatria* 2015; 37:21-30.
 4. Enescu A, Mitrut P, Balasoiu M, Turculeanu A, Enescu AS. Psychosocial issues in patients with chronic hepatitis B and C. *Curr Health Sci J* 2014; 40:93-6.
 5. Adinolfi LE, Nevola R, Lus G, Restivo L, Guerrera B, Romano C et al. Chronic hepatitis C virus infection and neurological and psychiatric disorders: an overview. *World J Gastroenterol* 2015; 21:2269-80.
 6. Sockalingam S, Blank D, Al Jarad A, Alosaimi F, Hirschfield G, Abbey SE. The role of attachment style and depression in patients with hepatitis C. *J Clin Psychol Med Settings* 2013; 20:227-33.
 7. Miller ER, McNally S, Wallace J, Schlichthorst M. The ongoing impacts of hepatitis c-a systematic narrative review of the literature. *BMC Public Health* 2012; 12:672.
 8. Silva LD, Cunha CC, Cunha LR, Araujo RF, Barcelos VM, Menta PL et al. Depression rather than liver impairment reduces quality of life in patients with hepatitis C. *Braz J Psychiatry* 2015; 37:21-30.
 9. Weissenborn K, Krause J, Bokemeyer M, Hecker H, Schüler A, Ennen JC et al. Hepatitis C virus infection affects the brain-evidence from psychometric studies and magnetic resonance spectroscopy. *J Hepatol* 2004; 41:845-51.
 10. Piche T, Vanbiervliet G, Cherikh F, Antoun Z, Huet PM, Gelsi E et al. Effect of ondansetron, a 5-HT₃ receptor antagonist, on fatigue in chronic hepatitis C: a randomised, double blind, placebo controlled study. *Gut* 2005; 54:1169-73.
 11. Coughlan B, Sheehan J, Hickey A, Crowe J. Psychological well-being and quality of life in women with an iatrogenic hepatitis C virus infection. *Br J Health Psychol* 2002; 7:105-16.
 12. Schafer 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; 16:186-201.
 13. Singh N, Gayowski T, Wagener MM, Masino IR. Vulnerability to psychological distress and depression in patients with end-stage liver disease due to hepatitis C virus. *Clin Transplantation* 1997; 11:406-11.
 14. Ashrafi M, Modabbernia A, Dalir M, Taslimi S, Karami M, Ostovaneh MR et al. Predictors of mental and physical health in non-cirrhotic patients with viral hepatitis: a case control study. *J Psychosom Res* 2012; 73: 218-24.
 15. Forton DM, Hamilton G, Allsop JM, Grover VP, Wesnes K, O'Sullivan C, et al. Cerebral immune activation in chronic hepatitis C infection: a magnetic resonance spectroscopy study. *J Hepatol* 2008; 49:316-22.
 16. Janke EA, McGraw S, Garcia-Tsao G, Fraenkel L. Psychosocial issues in hepatitis C: a qualitative analysis. *Psychosomatics* 2008; 49:494-501.
 17. Schafer A, Scheurlen M, Seufert J, Keicher C, Weissbrich B, Rieger P 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; 52:10-5.
 18. Rab F, Mamdou R, Nasir S. Rates of depression and anxiety among female medical students in Pakistan. *East Mediterr Health J* 2008; 14:126-33.
 19. Khan MS, Mahmood S, Badshah A, Ali SU, Jamal Y. Prevalence of depression, anxiety and their associated factors among medical students in Karachi, Pakistan. *J Pak Med Assoc* 2006; 56:583-6.
 20. Husain N, Creed F, Tomenson B. Depression and social stress in Pakistan. *Psychol Med* 2000; 30:395-402.
 21. Evon DM, Ramcharran D, Belle SH, Terrault NA, Fontana RJ, Fried MW. Prospective analysis of depression during peginterferon and ribavirin therapy of chronic hepatitis C: results of the Virahep-C study. *Am J Gastroenterol* 2009; 104:2949-58.
 22. Afsar B, Elsurur R, Eyiletan T, Yilmaz MI, Caglar K. Antibody response following hepatitis B vaccination in dialysis patients: does depression and life quality matter? *Vaccine* 2009; 27:5865-9.
 23. Castellvi P, Navines R, Gutierrez F, Jimenez D, Marquez C, Subira S et al. Pegylated interferon and ribavirin-induced depression in chronic hepatitis C: role of personality. *J Clin Psychiatry* 2009; 70:817-28.

CONTRIBUTORS

ARB conceived the idea, reviewed the literature, analyzed the data and drafted the manuscript. MIJ helped in manuscript writing and refining the script. SR helped in data management. WW reviewed the data, corresponded with editor and liaised with co-authors. MA and A supervised the study and gave final approval of the article. All authors contributed significantly to the submitted manuscript.