

Frequency of depression in chronic Hepatitis C naïve patients

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ABSTRACT

Objectives: To determine frequency of depression in chronic hepatitis C naïve patients before interferon therapy using CES-D questionnaire.

Methodology: Patients testing positive antibodies to HCV by EIA of more than 6 months duration and who have not taken interferon therapy previously were included after taking informed consent. Patients who had co-infections such as hepatitis B and D virus or human immunodeficiency virus, or patients with other coexisting chronic liver disease like primary biliary cirrhosis, chronic autoimmune hepatitis and Wilson disease were excluded from study. Urdu version of CES-D a self-reporting questionnaire in public domain was administered. A score of >10 was taken consistent with depression.

Results: Ninety-six patients were included and 59.4% were depressed. These included 57.9% males and 42.1% females. Highest frequency was seen in under-graduates and positive correlation was seen with duration of hepatitis C infection.

Conclusions: This study showed that 59.4% of patients with hepatitis C have depression before initiation of therapy and this should be evaluated and treated if necessary before starting interferon therapy.

KEY WORDS: Depression, Hepatitis, Hepatitis C, Interferon.

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INTRODUCTION

Hepatitis C (HCV) is one of the major health related problem being faced by Pakistan, with prevalence as high as 16% in certain localities.¹ It is estimated that more than 170 million people in the world are infected by HCV, this represents about 2.5% of world population and about 32.3 million are in South East Asia.^{2,3} Due to unavailability of vaccine the world wide prevalence of HCV has not shown a downward trend as seen in hepatitis B (HBV) although both share the same modes of spread, about 3-4 million new cases of HCV are reported each year.^{4,5} Depression is the third common adverse effect of HCV infection reported in 70% of HCV patients who have not received Interferon therapy, preceded by physical fatigue (86%) and irritability (74%).⁶

Prevalence of depression is reported to be much higher in HCV patients (24-70%) as compared to general population (6-10%).^{7,8} A recently published systematic review of depression occurring during interferon therapy showed considerable variation in frequency and extent of interferon induced depression from 0 to 82% due to difference in criteria, treatment protocol and cutoff values.⁸ But this highlights the importance of recognition of this disorder while managing HCV. Not only do the interferon based therapies induce de-novo depression but it also aggravates the scores of already existing depression.⁹ Early virological responses (EVR) were significantly lower in patients with depressive symptoms as compared to those without them.¹⁰ The use of anti depressive therapy in such patients significantly improves sustained virological response (SVR).¹¹ Because of the increased risk of poor treatment outcomes, active depression should be treated before HCV therapy is initiated.¹²

This study was designed to document the frequency of depression in chronic hepatitis C naïve patients before interferon therapy using CES-D questionnaire. The results will help to document the magnitude of this problem in our settings and thus help in formulating strategies to effectively deal with this issue.

METHODOLOGY

Adult patients were enrolled from the hepatitis clinic at Civil Hospital Karachi. Patients testing positive antibodies to HCV by EIA of more than 6 months duration who have not taken interferon therapy previously were included after taking informed consent. Patients who had co-infections such as hepatitis B and D virus or human immunodeficiency virus, or patients with other coexisting chronic liver disease like primary biliary cirrhosis, chronic autoimmune hepatitis and Wilson disease were excluded. Patients who were on interferon therapy or those who have earlier received such a therapy were also excluded. Patient with diagnosis of uncontrolled neurological, cardiovascular, endocrine, hematological, hepatic or renal disease and patients with schizophrenia, manic depression, on antidepressant drug induced mental disorder, dementia, stroke were also excluded from study as these diseases have their own impacts on depression.

CES-D Questionnaire is a self-reporting questionnaire for diagnosing of depression that has been validated previously.¹³ This questionnaire was translated to Urdu and retranslated back to English by different person to check validity of translation. The

CES-D scale is designed to measure depressive symptoms in the general population (i.e., non-psychiatric persons older than 18). The 20-item self-administered scale measures the major components of depressive symptomatology, including depressive mood, feelings of guilt and worthlessness, psychomotor retardation, loss of appetite, and sleep disturbance. The scale is in the public domain. Therefore, it may be used without copyright permission. A score of >10 was taken consistent with depression.

Sample size: Various studies with different diagnostic criteria and methods have reported frequency of depression in HCV at 24-70%.^{6,7} For sample size calculation the mean value of 47 was taken (P), confidence interval (1- α) 95%, absolute precision (ϵ) 0.10 and the sample size with these values was determined as 96.

Data Collection Procedure: After taking informed consent for the study, selected patient's venous blood was collected for anti-HCV test, which was analyzed by using EIA at Lab 2000 laboratory in Civil Hospital Karachi. The CES-D questionnaire was given to them while waiting for consultation in waiting room. The questionnaire had questions written both in English and Urdu languages for self-answering. Patients were provided help by a researcher.

Data Analysis Procedure: PASW Statistics version 18.0 was used for statistical analysis with significance level set at <0.05.

RESULTS

Ninety-six patients with naïve hepatitis C satisfying the inclusion/exclusion criteria were included in this study. Fifty-seven (59.4%) patients were male and 39 (40.6%) were female. Mean \pm SD of age patients was 38.2 \pm 9.2 years. Mean age of males was 36.9 \pm 8.9 years and that of females was 38.3 \pm 9.3 years ($p=0.4$; 95% CI -4.7 to 1.9).

Twelve (12.5%) patients were uneducated, 26 (27.1%) had education up to matric, 31 (32.3%) were intermediate, 24 (25%) were graduates and 3 (3.1%) cases had postgraduate degree. Most of the patients had history of HCV infection for less than 2 years.

Mean \pm SD of CES-D rating scale was 16.3 \pm 6.2. Out of 96 HCV cases, depression was seen in 57 (59.4%) patients out of 57 depressed patients, 32 (36.8%) patients had mild to moderate depressive symptoms and 27 (63.2%) had severe depressive symptoms.

Frequency of depression was high in males as compared to females, out of 57 depressive cases, 33 (57.9%) were male and 24 (42.1%) were female

(P-value = 0.51). Frequency of depression was high in undergraduate patients. Out of 57 depressive cases, 15 (26.3%) cases were undergraduate, 22 (38.5%) cases from intermediate, 11 (19.29%) cases had education up to matric while 7 (12.2%) cases were uneducated.

The correlation of CES-D Scores with age was studied by Pearson correlation test and it did not show any significant correlation of CES-D Scores with age of the patients (R^2 Linear = 0.02, $P = 0.171$). The correlation of CES-D scores with duration of history was studied by Kendell's Test and found to be positively correlated (correlation coefficient = 0.256, $P = 0.001$). This showed that higher depression scores were found in patients with longer history of HCV infection. A similar test of correlation was also done with level of education but it did not reveal any significant correlation (correlation coefficient = 0.09, $P = 0.255$).

DISCUSSION

Like many chronic medical illnesses, hepatitis C is associated with an increased prevalence of psychiatric disorder particularly depression.^{14,15} The presence of depressive symptoms in hepatitis C, as in other chronic medical illnesses, is important because they have an adverse effect on the course of illness, with amplification of physical symptoms, functional impairment, reduced treatment compliance and reduced quality of life.¹⁶ The association is also of particular importance in hepatitis C because patients often come from population groups at risk for psychiatric disorder, such as injecting drug users (IDUs).

In addition, treatment for hepatitis C involves interferon alfa, which has neuropsychiatric side effects. Psychiatric disorder is the main reason for delay or discontinuation of interferon alfa treatment.¹⁷ Successful medical treatment of hepatitis C therefore requires detection and management of depression both before and during treatment.¹⁶ The reasons for the high prevalence of depression in persons with hepatitis C are not clear; these have been hypothesized to arise from the disease itself, or from the high proportion of persons at risk for psychiatric disorder among those affected by hepatitis C, or to the stigmatizing nature of the diagnosis, recently a role of platelet 5-HT has also been suggested.¹⁸

Studies of psychiatric symptoms in hepatitis C have frequently relied on self-administered scales rather than a formal psychiatric assessment, making it difficult to assess the clinical significance of their findings. They have also tended to focus on depression

and omit anxiety disorders. Finally, studies have for the most part reported on the prevalence of psychiatric disorder without making the important distinction between previously diagnosed and hitherto-unrecognized disorder.

In common with persons with other significant medical illnesses, persons with hepatitis C have high rates of psychological symptoms and reduced quality of life compared with the general population.^{15,19,20} Kenny-Walsh, reported a 16% prevalence of depressed mood noted in the medical charts of 376 Irish women with iatrogenic hepatitis C.²¹ Lee et al reported a prevalence of 24% for depression in 500 patients seen at a tertiary referral center, and Dwight et al using a standardized psychiatric interview, found 28% prevalence in 50 patients.^{16,22}

Depression prevalence in HCV-infected patients ranges from about 24% to 50%, we found significant levels of depression in persons with hepatitis C. The prevalence of 59.4% in our sample agrees well with that reported by other studies that used standardized psychiatric interview. Another study reported 47.2% prevalence of depression in HCV positive cases. Gender difference is also very important factor, as noticed in various studies in Pakistan where the prevalence of depression is twice in female patients as compared to male patients.²³⁻²⁵ However in this study this gender difference is not seen in HCV patients.

Treatment of depression in associated medical disorders results in better outcomes depending upon the stage of disease and where and when the treatment of depression is received.²⁶ SSRI have shown promising results in management of depression in hepatitis with better outcome.^{19,27}

CONCLUSION

A high proportion of patients with hepatitis C naïve patients were having depression according to the CES-D scale in our study. A positive correlation was observed with duration of illness and negative correlation with educational status.

REFERENCES

1. Ahmad N, Asgher M, Shafique M, Qureshi JA. An evidence of high prevalence of Hepatitis C virus in Faisalabad, Pakistan. *Saudi Med J* 2007;28:390-395.
2. Yang YP, Liu CB, Jin DY, Zhan MY, Tang Q, Xia NS, et al. cDNA cloning of c33-c antigen gene derived from NS3 region of Chinese HCV genome, expression in *Escherichia coli* and development of HCV EIA second-generation diagnostic kit. *Sci China B* 1994;37:190-202.
3. Alter MJ. Epidemiology of hepatitis C virus infection. *World J Gastroenterol* 2007;13:2436-2441.

4. Pantazis KD, Elefsiniotis IS, Brokalaki H. New Data concerning the Epidemiology of Hepatitis B Virus Infection in Greece. *Gastroenterol Res Pract* 2008;2008:580341.
5. Walls MA, Hsiao KC, Harris LJ. Vectors for the expression of PCR-amplified immunoglobulin variable domains with human constant regions. *Nucleic Acids Res* 1993;21:2921-2929.
6. Lang CA, Conrad S, Garrett L, Battistutta D, Cooksley WG, Dunne MP, et al. Symptom prevalence and clustering of symptoms in people living with chronic hepatitis C infection. *J Pain Symptom Manage* 2006;31:335-344.
7. 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;7:105-116.
8. 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.
9. Majer M, Welberg LA, Capuron L, Pagnoni G, Raison CL, Miller AH. IFN-alpha-induced motor slowing is associated with increased depression and fatigue in patients with chronic hepatitis C. *Brain Behav Immun* 2008;22:870-880.
10. Raison CL, Broadwell SD, Borisov AS, Manatunga AK, Capuron L, Woolwine BJ, et al. Depressive symptoms and viral clearance in patients receiving interferon-alpha and ribavirin for hepatitis C. *Brain Behav Immun* 2005;19:23-27.
11. Loftis JM, Socherman RE, Howell CD, Whitehead AJ, Hill JA, Dominitz JA, et al. Association of interferon-alpha-induced depression and improved treatment response in patients with hepatitis C. *Neurosci Lett* 2004;365:87-91.
12. Zuberi BF. Hepatitis C and Depression. *JLUMHS* 2009;8:190-191.
13. Radloff L. The CES-D scale: A self report depression scale for research in the general population. *Applied Psychological Measurement* 1977;1:385-401.
14. 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;104:2949-2958.
15. 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;27:5865-5869.
16. 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;70:817-828.
17. Li YL, Zhou JF. The clinical survey of anxiety and depression for rural chronic hepatitis B patients. *Zhonghua Gan Zang Bing Za Zhi* 2009;17:474.
18. 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.
19. Falasca K, Mancino P, Ucciferri C, Dalessandro M, Manzoli L, Pizzigallo E, et al. Quality of life, depression, and cytokine patterns in patients with chronic hepatitis C treated with antiviral therapy. *Clin Invest Med* 2009;32:E212-218.
20. Fransen Van De Putte DE, Fischer K, Posthouwer D, Van Erpecum K, Mauser-Bunschoten EP. Occurrence, course and risk factors of depression during antiviral treatment for chronic hepatitis C in patients with inherited bleeding disorders: A prospective study. *Haemophilia* 2009;15:544-551.
21. Kenny-Walsh E. Clinical outcomes after hepatitis C infection from contaminated anti-D immune globulin. *Irish Hepatology Research Group. N Engl J Med* 1999;340:1228-1233.
22. 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;42:186-191.
23. Rab F, Mamdou R, Nasir S. Rates of depression and anxiety among female medical students in Pakistan. *East Mediterr Health J* 2008;14:126-133.
24. 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;56:583-586.
25. Husain N, Creed F, Tomenson B. Depression and social stress in Pakistan. *Psychol Med* 2000;30:395-402.
26. Druss BG, Rask K, Katon WJ. Major depression, depression treatment and quality of primary medical care. *Gen Hosp Psychiatry* 2008;30:20-25.
27. Sockalingam S, Abbey SE. Managing depression during hepatitis C treatment. *Can J Psychiatry* 2009;54:614-625.

Authors Contribution:

Study Design was done by SAM & BFZ. Data collection, analysis and manuscript writing were done by SAM, MNA, ZK. Proof writing was done by RQ and ARM. Final editing and approval were done by BFZ & SA.