

Severity of Depression in Hepatitis B and Hepatitis C Patients

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ABSTRACT

Objective: To assess and compare the severity of depression in chronic hepatitis B (CHB), chronic hepatitis C (CHC) and healthy subjects.

Study Design: Comparative study.

Place and Duration of Study: Shifa International Hospital, Islamabad from July 2011 to February 2012.

Methodology: A total of 206 subjects were divided in three groups. Group-I (chronic hepatitis C, n = 95), group-II (chronic hepatitis B, n = 29) and group-III (healthy subjects, n = 82). They were matched for age, gender and socioeconomic status and were compared for frequency and severity of depression as measured by Hospital Anxiety and Depression Scale (HADS).

Results: Some degree of depression was noted in all groups. Frequency of depression was 72.6% in group-I, 58.6% in group-II and 37.8% in group-III (p value < 0.001).

Conclusion: Both CHC and CHB had high frequency of some degree of depression. Hepatitis C patients had more depressive features than CHB. It is worthwhile to do more close mental health observation in them. A multidisciplinary team including a psychiatric specialist can help in this approach.

Key words: Depression. Hepatitis C. Hepatitis B. Hospital anxiety and depression scale.

INTRODUCTION

The World Health Organization (WHO) estimates that about 180 million people (some 3% of the world's population) are infected with *hepatitis C virus* (HCV), 130 million of whom are chronic carriers at risk of developing liver cirrhosis and liver cancer. The frequency of hepatitis C infection in Pakistan is high (4.7%), varying from 0.4% to 33.7%, indicating pockets of infections.¹ In fact, chronic hepatitis C (CHC) is currently the main cause of chronic liver disease (CLD) and the leading indication for liver transplantation in the western world.² On the other hand, chronic hepatitis B (CHB) infects approximately 400 million people worldwide and causes one million deaths annually of liver disease.³ Approximately 15 – 40% of infected patients eventually developing cirrhosis, liver failure, or hepatocellular carcinoma during the course of CHB infection.⁴ The overall HBsAg seroprevalence in healthy adults based on combined data from blood donors and non-donors was 2.4% ranging from 1.4% to 11.0%.⁵

Evaluation for psychiatric symptoms in hepatitis is important because they have an adverse effect upon the course of disease.⁶ Psychiatric problems in the patients with hepatitis may be responsible for functional impairment, reduced treatment compliance, and reduced quality of life. These patients often come from population groups at risk of psychiatric disorders, such as injecting drug users. Early detection of psychiatric issues in

chronic hepatitis is crucial because treatment of hepatitis C involves interferon, which itself has significant neuropsychiatric side effects.^{7,8} These psychiatric symptoms are the major reason for delay or stopping of interferon treatment.⁸ Successful medical treatment, therefore, requires detection and management of depression and other psychiatric issues before and during the treatment.⁹

Rates of depression have been reported in the range of 22 – 59% of patients with hepatitis C.^{7,10-12} Individuals with non-alcoholic fatty liver disease (NAFLD) and HCV had a higher prevalence of depression than HBV patients and general population.¹³ The most consistent correlates of depression status in CLD patients were female gender and excessive alcohol consumption.¹³ Incidence of HCV and depression is also greater in mentally ill people¹⁴ and I.V. (intravenous) drug abusers.¹⁵ It has been reported that patients with CHC have a compromised quality of life, a higher prevalence of psychiatric disorders and higher scores of fatigue and these effects do not seem to be related to the severity of liver inflammation or fibrosis.¹⁶

Little is known about the frequency of depression in patients with chronic hepatitis B and even less about its impact on the health-related quality of life of such patients. Same is true regarding depression in chronic hepatitis in Pakistan.

The aim of this study was to evaluate both hepatitis B and hepatitis C for depression and to compare this with healthy subjects.

METHODOLOGY

In this comparative study, 260 hepatitis patients and healthy subjects coming to OPD of Gastroenterology at

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Received March 07, 2012; accepted August 23, 2012.

Shifa International Hospital, Islamabad, from July 2011 to February 2012 were requested to participate. Out of these, 40 individuals were excluded and 14 did not agree to participate in the study. Thus, the study was carried out on 206 participants. All patients with diagnosis of CHC or HBV with duration greater than 6 months with age between 18 and 65 years were included in the study. Patients on anti-depressant therapy, those with any other psychiatric illness or neurological disorder (severe depression or psychosis), those with cirrhosis (Child-Pugh stages B or C), liver failure, patients with other severe chronic diseases (e.g. cancer, ischaemic heart disease or stroke), patients on treatment with interferon, patients with liver disease of aetiology other than HCV or HBV (including alcoholics) were excluded. For controls (healthy subjects), those with any significant chronic disease were also excluded from the study. Informed verbal consent was obtained from all patients and study was approved by the Ethics Committee of the Institution.

To match the socioeconomic status with the patients, the attendants of the patients were taken as controls. Age and gender were matched with the cases. Total number of controls recruited were 82. The study population was divided in three groups: group-I (CHC, $n = 95$), group-II (CHB, $n = 29$) and group-III (controls, $n = 82$). History and physical examinations were performed. Chronic viral hepatitis was diagnosed by the presence of positive serologic markers for at least 6 months including HBsAg and HBV PCR for CHB and anti-HCV anti-body and HCV PCR for CHC. Other investigations included coagulation profile, liver function tests and serum albumin.

Depression was assessed by Hospital Anxiety and Depression Scale (HADS) questionnaire. This questionnaire included 14 questions. Each question had 4 choices (0 – 3). Maximum score of depression in this questionnaire was 21. Scores from 0 – 7 were taken as no depression, 8 – 11 as mild depression while 12 – 21 were taken as moderate to severe depression. The study employed a translated and validated Urdu version of this scale.¹⁷ Demographic characteristics (age, gender, socio-economic status) and clinical features (receiving treatment, type and duration of therapy) were noted. All the findings were documented in a well designed proforma that included age, gender, etiology of disease, child score and score of depression (using HADS). Data was analyzed using Statistical Package for Social Sciences (SPSS) version 17. Data was expressed in the form of frequencies and percentages. Age, gender and severity of depression was categorized separately for all groups. For statistical analysis, significance of age difference, gender and severity of depression in three groups was assessed by chi-square test. For all tests, significance was defined as $p < 0.05$.

RESULTS

A total of 206 patients completed the study. Out of these, 91 (44%) were male while 115 (55.6%) were female.

Table I: Age and gender distribution of study population ($n = 206$).

	Groups			p-value
	Group-I N = 95	Group-II N = 29	Group-III N = 82	
Age in years				0.431
21-35	14 (14%)	5 (17%)	17 (20%)	
36-50	48 (50%)	16 (55%)	47 (57%)	
50 and above	33 (34%)	8 (27%)	18 (22%)	
Gender				0.644
Male	41 (43%)	11 (38%)	39 (47%)	
Female	54 (56%)	18 (62%)	43 (52%)	

Table II: Incidence of depression in three groups.

Degree of depression	Groups			p-value
	Group-I ($n = 95$)	Group-II ($n = 29$)	Group-III ($n = 82$)	
No	26 (27.36%)	12 (41.37%)	51 (62.19%)	< 0.001
Mild	50 (52.6%)	11 (37.9%)	27 (32.9%)	
Moderate-severe	19 (20%)	06 (20%)	04 (4.87%)	
Total depression	69 (72.6%)	17 (58.6%)	31 (37.80%)	

P-value showing significant depression in group-I as compared to other groups.

Ninety five patients (46%) had CHC (group-I), 29 patients (14%) had CHB (group-II), while 82 patients (39%) were of control group (group-III). The demographic profiles are shown in the Table I.

Out of the 206 patients, 117 (56.7%) were found to have some degree of depression, more belonging to mild and some to moderate to severe class (Table II). Comparing three groups, the percentage of depression was greater in group-I as compared to group-II and group-III.

In group-I, 69 patients (72.6%) were depressed. In group-II, 17 patients (58.6%) were found to be depressed, while in group-III, 31 patients (37.8%) were found to be depressed (Table II, $p < 0.001$).

DISCUSSION

Most of the patients with liver diseases experience anxiety and depression symptoms.^{10,18} The number of people with co-morbid HCV and depressive disorder (including minor depression) increased significantly between 1995 and 2005 from 18% to over 35% of all people with diagnosed HCV.¹⁹ The results of this study reveal that patients with hepatitis C had more depression compared with those suffering from hepatitis B and controls (72.6% in HCV group, 58.6% in HBV group and 37.8% in the control group). These results are in accordance with a previous study that demonstrated that hepatitis C positive patients had more psychiatric disorders than hepatitis B positive patients.²⁰ In another study, hepatitis C patients exhibited more anxiety, depression and mood disorders in comparison with other liver diseases.²¹ It has also been demonstrated that the quality of life is lower in CHC patients as compared to CHB patients.²²

It is hypothesized that multiple factors are responsible for depression in hepatitis patients. Complexity, ambi-

guity, inconsistency and unpredictability of the course of illness, alterations in brain metabolites as evident by magnetic resonance imaging spectroscopy, and emotional factors and perception of stigma are thought to be the causes of depression in this population.^{23,24} Diagnosis of the psychiatric disorders at the commencement of interferon therapy seems to be very important as some severe psychiatric disorders like depression have been a contraindication for prescribing these agents necessitating a close monitoring of these patients.²⁵

Incidence of depression and mortality following interferon therapy has been reported to be as high as 17% and 0.02% to 3.4%, respectively.²⁶ Taking into consideration that psychiatric disorders usually occur in the first month following commencement of interferon therapy, early assessment of patient's mental health seems to be desirable in most cases. Early treatment of depression does affect response and adherence to treatment.²⁷ The frequency of depression in hepatitis patients in this study was even higher, especially in CHC. A multi-disciplinary team should be consulted to develop complex physical and psychological treatments for patients with CHC.

CONCLUSION

Higher prevalence of depression in patients with hepatitis C in comparison with patients with hepatitis B and normal controls indicates need for more attention to psychiatric monitoring of these patients. A multi-disciplinary approach is desirable for favourable outcome.

REFERENCES

1. World Health Organization. Hepatitis C [Internet]. [updated 2009 Apr 16]. Available from: http://www.who.int/vaccine_research/viral_cancers
2. Alter HJ, Seeff LB. Recovery, persistence, and sequelae in hepatitis C virus infection: a perspective on long-term outcome. *Semin Liver Dis* 2000; **20**:17-35.
3. Lavanchy D. Hepatitis B virus epidemiology, disease burden, treatment, and current and emerging prevention and control measures. *J Viral Hepatol* 2004; **11**:97-107.
4. Lavanchy D. Worldwide epidemiology of HBV infection, disease burden, and vaccine prevention. *J Clin Virol* 2005; **34**:S1-S3.
5. Ali SA, Donahue RMJ, Qureshi H, Vermund SH. Hepatitis B and hepatitis C in Pakistan: prevalence and risk factors. *Int J Infect Dis* 2009; **13**:9-19. Epub 2008 Oct 2.
6. Gadit AA. Mood disorder associated with gastrointestinal and liver diseases: are there many challenges? *J Pak Med Assoc* 2010; **71**:1064-5.
7. Majeed S, Memon A, Abdi MA. Frequency of depression among hepatitis C patients. *Kust Med J* 2009; **1**:42-5.
8. Zdilard D, Franco-Bronson K, Bucher N, Locala JA, Younossi ZM. Hepatitis C: interferon alfa and depression. *Hepatology* 2000; **31**:1207-11.
9. Dogar IA, Siddiqui N, Bajwa A, Bhatti A, Haider N, Hashmi ZY. Relationship between liver diseases and levels of anxiety and depression. *J Pak Psych Soc* 2009; **6**:61.

10. Gill ML, Atiq M, Sattar S, Khokhar N. Psychological implications of hepatitis C virus diagnosis. *J Gastroenterol Hepatol* 2005; **20**:1741-4.
11. Gleason OC, Yates WR, Philipsen MA. Major depressive disorder in hepatitis C: an open-label trial of escitalopram. *Prim Care Companion J Clin Psychiatr* 2005; **7**:225-30.
12. Memon SA, Zuberi BF, Ashfaq MN, Kiran Z, Qadeer R, Memon AR, et al. Frequency of depression in chronic hepatitis C naive patients. *Pak J Med Sci* 2011; **27**:780-3.
13. Weinstein AA, Kallman Price J, Stepanova M, Poms LW, Fang Y, Moon J, et al. Depression in patients with non-alcoholic fatty liver disease and chronic viral hepatitis B and C. *Psychosomatics* 2011; **52**:127-32.
14. Rosenberg SD, Goodman LA, Osher FC, Swartz MS, Essock SM, Butterfield MI, et al. Prevalence of HIV, hepatitis B, and hepatitis C in people with severe mental illness. *Am J Public Health* 2001; **91**:31-7.
15. Alavian SM, Adibi P, Zali MR. Hepatitis C virus in Iran: epidemiology of an emerging infection. *Arch Iranian Med* 2005; **8**:84-90.
16. Abdo AA. Hepatitis C and poor quality of life: Is it the virus or the patient? *Saudi J Gastroenterol* 2008; **14**:109-13.
17. Mumford DB, Tareen I, Bajwa M, Bhatti MR, Kareem R. The translation and evaluation of Urdu version of hospital anxiety and depression scale. *Acta Psychiatr Scand* 1991; **83**:81-5.
18. Yates WR, Gleason O. Hepatitis C and depression. *Depress Anxiety* 1998; **7**:188-93.
19. Yawn BP, Rocca LG, Wollen PC. 10-year-trends in the diagnosis and treatment of hepatitis C and concomitant mental health disorders: 1995 to 2005. *Prim Care Companion J Clin Psychiatry* 2008; **10**:349-54.
20. 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.
21. Wessley S, Pariente C. Fatigue, depression and chronic hepatitis C infection. *Psychol Med* 2002; **32**:1-10.
22. Foster GR, Goldin RD, Thomas HC. Chronic hepatitis C virus infection causes a significant reduction in quality of life in the absence of cirrhosis. *Hepatology* 1998; **27**:209-12.
23. 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. Epub 2008 Apr 25.
24. Janke EA, McGraw S, Garcia-Tsao G, Fraenkel L. Psychosocial issues in hepatitis C: a qualitative analysis. *Psychosomatics* 2008; **49**:494-501.
25. Ho SB, Nguyen H, Tetrick LL, Optif CA, Basara ML, Dieperink E. Influence of psychiatric diagnoses on interferon-alpha treatment for chronic hepatitis C in a veteran population. *Am J Gastroenterol* 2001; **96**:157-64.
26. Olsson I, Mykletun A, Dahl AA. The hospital anxiety and depression rating scale: a cross-sectional study of psychometrics and case finding abilities in general practice. *BMC Psychiatr* 2005; **14**:5:46.
27. Hauser P, Khosla J, Aurora H, Laurin J, Kling MA, Hill J, et al. A prospective study of the incidence and open-label treatment of interferon-induced major depressive disorder in patients with hepatitis C. *Mol Psychiatr* 2002; **7**:942-4.

