ORIGINAL ARTICLE

# FREQUENCY OF DEPRESSION AMONG PATIENTS WITH CHRONIC LIVER DISEASE

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**Background:** Psychiatric co-morbidity is a frequent finding in patients with chronic liver disease (CLD). Patients with CLD may have anxiety, depression, sleep disturbances and behavioural disorders as well as cognitive defects. Therefore, this study was designed to determine the frequency of major depression in patients diagnosed with chronic liver disease **Methods:** This descriptive cross-sectional study was conducted at the department of gastroenterology Ayub Teaching Hospital Abbottabad from January–July 2017. One hundred and eleven patients diagnosed with chronic liver disease were included in the study using consecutive non-probability sampling technique. A detailed medical history was taken and physical exam was conducted before the patients were asked to answer a questionnaire (HADS-D). The answers were marked to obtain a final score. Quantitative variables like age, HADS-D score, and duration of CLD were described in terms of mean and standard deviation. Categorical variables like gender and depression were described in terms of frequencies and percentages. Stratification was done on age, duration of CLD and gender to see the effect modifiers. Chi-Square test was used at 5% significance level for determining statistically significant difference. **Results:** Out of 111 patients, 38 (34.2%) were found to have depression on the basis of their HADS-D score. When depression was stratified according to age, gender and duration of chronic liver disease, a strong statistical association was seen with duration of chronic liver disease and increased serum ALT levels ($p$<0.05). **Conclusion:** Depression is fairly common in patients with CLD and is significantly associated with the duration of CLD and derangement of liver enzymes.

**Keywords:** Chronic liver disease; Cirrhosis; Hepatitis; Morbidity; Anxiety; Health-related quality of life

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## INTRODUCTION

Major depressive disorder or depression as it is commonly known, is known to adversely affect an individual's feelings, thinking and actions. Its common features include sadness and loss of interest in once-enjoyable day-to-day activities.[1] In addition to major features such as fatiguability, low mood and decreased activity, depression is also associated with changes in sleep habit, disturbed appetite, nonspecific body aches and pain, difficulty concentrating on topics / issues, and suicidal tendencies.[2]

Chronic liver disease, as is evident from the name, is a chronic disease that tends to run for longer periods of time. Chronic diseases are associated with development of negative perception of disease which may in turn be secondary to the disease process, the burden / cost of treatment and a forced / altered lifestyle as a result of disease process. Individuals suffering from and incapacitated by a chronic illness ultimately develop depression.[3,4] The estimated prevalence of depression in patients with chronic diseases is thought to be between 9.3–25%.[5] Depression may be diagnosed coincidentally in such patients, or may develop secondary to the burden of chronic illness as a psychological reaction or as a result of neuro-biological changes due to the chronic disease.[4,6–9]

The annual incidence of depression in adults is 6.7% and up to 16.6% individuals worldwide will experience depression at least once in their lifetime.[2] While depression can strike at any age and any person irrespective of their health status, patients with chronic hepatitis C have been reported to have 4–7 times more depression than that in general population.[10,11] Depending on the study design, sample selection and the diagnostic tool, previous estimates of depression in patients with chronic liver disease have varied from 0–82%.[10,12] A number of tools are available for screening depression in patients with chronic diseases such as the Patient Health Questionnaires 2 and 9 (PHQ-2, PHQ-9)[13], Structured Clinical Interview for DSM-IV (SCID)[14], Hospital Anxiety and Depression Scale (HADS) score[15] and Hamilton Rating Scale for Depression (HRSD)[16] to name a few.

Patients diagnosed with CLD often have

psychiatric co-morbidities such as anxiety and depression in addition to sleep disturbance, cognitive defects and other behavioural abnormalities.[1,17] The course of illness in CLD is adversely affected by depression in the form of projection of physical and functional manifestation of CLD, non or poor compliance with treatment and a reduced HRQOL.[18–22]

Presence of depression in addition to any chronic disease results in 2–3 times less likelihood of treatment adherence by that individual, and consequently more chances of an adverse healthoutcome.[23–25] Adherence to nutritional and exercise programs in depressed diabetic patients was found to be less than non-depressed diabetic patients.[26] In fact, a statistically significant association ($p < .000$) between diabetic complications and depression has been identified.[27] Depressed individuals has psychological disability and little or no productivity, and exhibit more healthcare utilization than non-depressed individuals.[28] Patients with major depression and chronic illnesses have been found to have a significantly increased utilization of healthcare, increased functional disability and decreased productivity compared to non-depressed individuals in general population.[29]

Variable estimates of depression in patients with chronic liver disease in Pakistan have been put forward in literature, for example, a study from Karachi reported that the frequency of depression in patients with chronic liver disease was 31.47%.[4] On the other hand, a study from Rawalpindi reported that depression was diagnosed in 41.8% in patients with chronic hepatitis C.[30] While the general prevalence of depression in Pakistan has been reported to be 4.2%[31], prevalence rates of depression and anxiety as high as 71.6% and 70.6% respectively have been reported in Pakistani patients with chronic liver disease.[32] Yet another study published recently reported that the frequency of depression in patients with CLD was 29.2%.[33] Keeping in view these wide ranging estimates, the lack of previous studies from this region and the effect of depression on treatment adherence in chronic diseases, we decided to undertake this cross sectional study to estimate the frequency of depression in patients with chronic liver disease and to determine any associations that could be addressed as an intervention to reduce the prevalence of depression in this patient population.

## MATERIAL AND METHODS

Following approval of hospital ethics committee, the study was conducted at the Ayub Teaching Hospital Abbottabad from January 2017 to July 2017. The study design was cross sectional, and we enrolled 111 patients with CLD using 17%' proportion of depression among patients with CLD. 95% confidence interval and 7% margin of error using WHO sample size calculator. Non probability (consecutive) sampling technique was used for enrolling study participants. All patients with CLD aged 25–70 years and belonging to either gender was included. Patients with a prior diagnosis of depression or another major psychiatric illness, patients with history of emotional trauma such as sudden loss of assets or near relative in the last 6 months, patients presenting in a state of shock or coma, patients with hepatic encephalopathy (Grade II or more), patients with other chronic debilitating diseases like COPD, asthma, CKD, CCF, stroke, etc, and patients with substance abuse except alcohol were excluded from the study.

All patients presenting to Gastroenterology unit and meeting the selection criteria were included in the study after obtaining a written informed consent. Patients were subjected to a detailed history and clinical examination. Interview using HADS-D in a calm environment to detect depression was carried out. The HADS-D score was calculated for each patient after the interview to ascertain the presence of depression.

Depression was diagnosed on the basis of Hospital Anxiety and Depression Scale (HADS- D) attached as Annexure II. A cut-off score of ≥11 on the HADS-D was used to diagnose depression. Since the chronic liver disease is a spectrum of illnesses, therefore, patients were labelled as CLD if they presented with deranged liver function tests due to any cause for at least 6 months or if the ultrasound examination of abdomen suggested any one or more features of chronic liver disease.

All the above-mentioned information including name, age and address were recorded on pre designed *pro forma*. Care was taken during extraction of information from all patients to avoid responder bias. Confounders and other bias were controlled by strictly following the exclusion criteria. Data was analysed using SPSS 20.0. Quantitative variables like age, HADS-D score, and duration of CLD were described in terms of mean and standard deviation. Categorical variables like gender and depression were described in terms of frequencies and percentages. Stratification was done on age, duration of CLD and gender to see the effect modifiers. Chi-Square test was used at 5% significance level for determining statistically significant difference.

## RESULTS

A total of one hundred and eleven patients with chronic liver disease were enrolled in this study. Males comprised majority of study population (n=60; 54.1%). The mean age of patients was 52.25±6.91 years. The youngest study participant was 42 years

old while the age of oldest was 65 years. The mean duration of chronic liver disease was 4.35±2.26 years. The shortest duration of chronic liver disease was one year while the longest duration of disease was nine years. The mean HADS-D score was 8.51±3.46. The lowest score among study participants was two while the highest HADS-D score was fourteen. According to the HADS-D score cut-off value, 38 (34.2%) study participants were found to have depression. There was no statistically significant association of depression with the age and gender of study participants ($p$>0.05). However, a statistically significant association between depression and the duration of chronic liver disease was noted in the study population ($p$<0.05). All the results are being presented as tables. Independent sample t-test was used to compare the HADS-D score in different groups of study population and it was found that there was a significant association with the duration of CLD ($p$<0.05). Depression was diagnosed more frequently in patients with minimum five years duration of chronic liver disease.

Among the study participants, majority had chronic hepatitis (n=86; 47.48%) and 25 (22.52%) patients had cirrhosis of liver. Of the 25 who had cirrhosis of liver, 13 (52%) had Child-Pugh class A, 7 (28%) had Child-Pugh class B and 5 (20%) had Child-Pugh class C. 45 (40/54%) had hypertension and 15 (13.52%) had diabetes mellitus. Mean ALT level in study participants was 85.2±60.8 IU/L with a range of 24.0-345. Among 86 patients with chronic viral hepatitis, 75 had chronic hepatitis C and of these, genotype 3a was the commonest, detected in 45 patients, followed by 3b in 23 and 1a in 7 patients. Depression was significantly associated with increased ALT levels ($p$<0.05). The mean±SD viral load was 1,972,094±3, 912, 465 IU/mL.

**Table-1: Crosstabulation of depression and different variables in study population**

| | | **Age of patients** | | | |
|---|---|---|---|---|---|
| | | **≤ 53 years** | **> 53 years** | **Total** | ***p* value** |
| Depression | Yes | 19 | 19 | 38 | |
| | No | 46 | 27 | 73 | **0.19** |
| Total | | 65 | 46 | 111 | |
| | | **Sex** | | | |
| | | Male | Female | Total | *p* value |
| Depression | Yes | 22 | 16 | 38 | |
| | No | 38 | 35 | 73 | **0.59** |
| Total | | 60 | 51 | 111 | |
| | | **Duration of CLD** | | | |
| | | ≤ 5 years | > 5 years | Total | *p* value |
| Depression | Yes | 18 | 20 | 38 | |
| | No | 58 | 15 | 73 | **0.001** |
| Total | | 76 | 35 | 111 | |
| | | **Serum Alt Levels** | | | |
| | | ≤ 100 IU/L | > 100 IU/L | Total | *p* value |
| Depression | Yes | 18 | 20 | 38 | |
| | No | 58 | 15 | 73 | **0.001** |
| Total | | 76 | 35 | 111 | |

*p*-value<0.05

# DISCUSSION

The frequency of depression in this study was 34.2% and it was found to be statistically significant with duration of CLD. The prevalence of depression in patients with chronic liver disease varies from as low as 29.2% to as high as 71.6%.[4,30–33] Almost all of these studies, including this one, have been single centre-based cross-sectional studies. Depression has been found to associated more with chronic hepatitis C than with other causes of chronic liver diseases.[34]

Depression is frequently encountered in CLD patients and it plays an important role in determining the health-related quality of life in these patients. In patients with chronic hepatitis C, for example, presence of depression adversely affects the course of disease, amplifies the physical symptoms of chronic hepatitis C, augments functional impairment and decreases treatment compliance ultimately decreasing the health-related quality of life in these patients.[35]

A number of risk factors have been identified to have a significant association with depression in patients with CLD such as increased age, unemployment, at least one episode of upper GI bleed, being female and non-alcoholic causes causing CLD.[4,12] In contrast, we found a statistically significant association between duration of CLD and depression. We did not observe any statistically significant association between depression and age and gender of study participants.

There are conflicting reports about association of age and female gender with depression in patients with CLD. While some authors[12,36], report an association with depression in CLD patients, others report no such association.[30,37]

A recently published study from Brazil observed that in patients diagnosed with Hepatitis C, the presence of depression was associated with an adversely affected quality of life.[38] The authors observed an independent but statistically significant association between a poor quality of life and elevated transaminase and major depression.[38]

A recent study from Egypt which assessed the cognitive functions of patients with CLD reported that among the many aetiologies of CLD, chronic hepatitis C was associated with more anxiety and depression when compared with other etiologies.[39] The study compared patients with hepatitis B and Hepatitis C with controls. Neurological functions relating to memory, naming, attention, abstraction, fluency, and orientation as assessed in MoCA score, were worse in patients with Chronic HCV and HBV infections in addition to increased levels of anxiety and depression. Similarly, the impairment of cognitive function was worse in patients with chronic

HCV and HBV infections.[39]

Similarly, a study from Karachi, Pakistan reported that depression and anxiety were found to be common in CHC patients who had been or are being treated with antiviral treatment leading to increased risk of morbidity and mortality.[40] The authors concluded that screening for risk of depression, proper education and timely treatment through anti-depressant followed by close monitoring is mandatory to achieve success in antiviral treatment. Similar results were reported in a study from Faisalabad, Pakistan reported which showed a relatively high frequency of anxiety, loss of emotional control and depression in patients diagnosed with Hepatitis B.[41] While gender was found to be associated with an increase of depression in the study with depression being more common in females, there was no significant association of depression with gender and age in our study.

## CONCLUSION

Depression is a common comorbid in patients with chronic liver disease and it is important to diagnose and manage depression in such patients since presence of concomitant depression adversely affects the treatment outcome, disease prognosis as well as the quality of life of an individual with chronic disease. The study has its own limitations as it was a single-centre based study of a small sample size, therefore the results cannot be generalized onto the general population. Moreover, since depression and anxiety often co exist, the prevalence of anxiety was not determined in this study. In addition, the association of depression with the specific type of viral hepatitis or CLD due to any specific cause was not studied. These are important venues for future research in patients with chronic liver disease in our region.

## AUTHORS' CONTRIBUTION

ANK, MAA, AG: Conceived idea, design, research methodology, literature search, data collection, write-up. AA, MZH, JH: Literature review, data interpretation. AR: Proof reading.

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