DEPRESSIVE ILLNESS AMONG CHRONIC LIVER DISEASE PATIENTS: A CROSS-SECTIONAL STUDY

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ABSTRACT

OBJECTIVES

This study investigated the association between chronic liver disease and major depressive disorder (MDD) in Pakistani adults. The prevalence of MDD among chronically ill patients admitted to a medical unit was examined, focusing on the impact of age, income, education level, and comorbidities on depression severity.

METHODOLOGY

A descriptive cross-sectional survey was conducted over two months at the Khyber Teaching Hospital in Peshawar. A total of 410 patients with chronic liver disease were included. Depression severity was assessed using the Patient Health Questionnaire-9 (PHQ-9). Data analysis was performed using SPSS version 25, utilizing statistical tests such as Pearson correlation, ANOVA and chi-square.

RESULTS

The study investigated depression severity among 410 patients with chronic liver disease, focusing on demographic characteristics and comorbidities. The mean age of participants was 54.244 years, with a moderate level of depressive symptoms indicated by a mean PHQ-9 score of 10. Income showed a weak but significant negative correlation with depression severity (-0.138, p = 0.005), while age did not show a significant correlation (-0.053, p = 0.288).

CONCLUSION

This study enhances the understanding of the intricate relationship between chronic liver disease and major depressive disorder (MDD). The results indicate that income level, education level, and the presence of comorbidities significantly influence the manifestation of depression in this population. Healthcare professionals can leverage these insights to identify high-risk patients and tailor interventions to enhance mental well-being and treatment outcomes for individuals with chronic liver disease.

KEYWORDS: *Chronic Liver Disease, Major Depressive Disorder, Prevalence, Age, Income, Education, Comorbidities, Depression Severity, Targeted Interventions*

INTRODUCTION

Major depressive disorder (MDD) is a psychiatric condition classified by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), characterized by at least five out of nine diagnostic criteria, including depressed mood, sleep impairment, guilt or worthlessness, loss of energy, impaired concentration, and suicidal thoughts for at least two weeks. Major depressive disorder is a common and disabling illness with an annual prevalence of 2%-4% in the general population.[1] The prevalence of major depressive disorder is doubled in medically ill patients compared to the general population, with an annual prevalence of 5%-10%.[2] This higher prevalence of MDD is associated with worsening symptoms, greater healthcare utilization, and poor adherence to treatment.[3] Depression is often overlooked in medical settings, and differentiating it from conditions like delirium, personality disorders, and medication-induced depressive disorders poses diagnostic challenges. The presence of comorbid medical conditions and major depressive disorders is linked to adverse medical outcomes. Three patients with chronic liver disease frequently present with psychiatric comorbidities such as depression.[4] Gallo et al. reported a reduction in all

causes of mortality in primary care in elderly patients given evidence-based treatments for MDD, compared with treatment as usual. Seven multiple medical conditions (e.g., 'multimorbidity') appear to be associated with even higher rates of depression and poorer medical and psychiatric outcomes.[5] Chronic medical illnesses and MDD have a bidirectional relationship, as MDD is independently associated with an increased prevalence of chronic medical disorders. Depression is associated with a more significant physical symptom burden, poorer treatment adherence and quality of life, increased healthcare utilization, and increased all-cause mortality in individuals with chronic illnesses.[6] Key factors contributing to depression in the Pakistani population include financial crises, social stressors, limited education, and inadequate access to necessities. Finding these inciting factors in patients with MDD is a crucial cornerstone of cognitive behavior therapy (CBT), the first line of therapy for MDD. Other treatment options include selective serotonin receptor inhibitors (SSRIs), serotonin norepinephrine receptor inhibitors (SNRIs), tricyclic antidepressants (TCAs), and monoamine oxidase inhibitors (MAOIs).[7] This study fills a crucial gap in research by examining the prevalence of major depressive disorder (MDD) in patients with chronic liver disease, a subgroup that has been underrepresented in existing literature. Its novelty is examining a relatively understudied population within the broader chronic illness demographics. By shedding light on this frequently overlooked area, the study aims to offer valuable insights that can guide clinical practice and stimulate further academic inquiry. Through meticulous investigation and thorough analysis, the research endeavors to elucidate the extent of depression among individuals with chronic liver disease.

METHODOLOGY

A descriptive cross-sectional survey design was employed to investigate the association between chronic liver disease and major depressive disorder (MDD) among Pakistani adults. The study was conducted at the Khyber Teaching Hospital in Peshawar, Pakistan. The study comprised 410 participants who met the predefined inclusion criteria. Depression severity was assessed using the Patient Health Questionnaire-9 (PHQ-9), a validated self-report questionnaire that covers various aspects of depression, including mood, anhedonia, sleep disturbances, appetite changes, concentration difficulties, feelings of worthlessness or guilt, energy levels, and suicidal ideation. Response options for each question typically range from 0 to 4, representing levels of depression severity: "no, "depression," "mild depression," "moderate depression," "moderately severe depression," and "severe depression." The inclusion criteria were the participants who had received a clinical diagnosis of chronic liver disease, confirmed through medical records, imaging studies, or histopathological findings. The age inclusion criterion was restricted to adults 18 or older admitted to the medical unit. Informed consent was obtained from all participants, indicating their willingness to engage in the study procedures and data collection-individuals possessing the cognitive ability and linguistic proficiency necessary to complete the required assessments accurately. The exclusion criteria Individuals with acute liver diseases, such as acute viral hepatitis or acute liver failure, were excluded from the study to maintain the focus on chronic liver disease. Participants with severe psychiatric disorders other than major depressive disorder, such as schizophrenia or bipolar disorder, were excluded due to potential confounding effects on depression severity and study outcomes. Substance abuse disorders, including alcohol or drug dependence, led to exclusion due to their potential impact on mental health outcomes and treatment responses. Significant cognitive impairment or neurological disorders affecting cognition also served as exclusion criteria to ensure reliable data collection. Pregnant or lactating women were excluded from the study due to potential confounding factors related to hormonal changes and pregnancy-related complications. Ethical approval was granted by Khyber Medical College Peshawar, Institutional Research and Ethical Review Board, via letter No. 115/DME/KMC.

RESULTS

Our result shows the demographic characteristics of the 410 patients included in the study. (table.1) The mean age of the participants was 54.244 years, with a standard deviation of 11.856, indicating a relatively homogeneous age distribution within the sample. The mean total score on the Patient Health Questionnaire-9 (PHQ-9), which assesses depression severity, was 10, with a standard deviation 5.917. This suggests a moderate level of depressive symptoms among the patients. Additionally, the table provides information on the income levels of the participants, with a mean income of 27 04.878 Pakistani rupees and a standard deviation of 28,357.842.

Table 1: The mean age, PHQ9 score, and income were calculated for the 410 patients

	Mean	Std. Deviation	N
Age (Years)	54.244	11.856	410
Total Score	10	05.917	410
Income	27804.878	28357.842	410

The correlation coefficients between age and total PHQ-9 scores and between income and total PHQ-9 scores for the 410 patients included in the study are shown in Table 2. The correlation between age and total PHQ-9 scores was -0.053, with a 95% confidence interval ranging from -0.149 to 0.044. This indicates a weak, non-significant negative correlation between age and depression severity, suggesting that older age may not necessarily be associated with higher levels of depressive symptoms among patients with chronic liver disease (p = 0.288). Conversely, the correlation between income and total PHQ-9 scores was -0.138, with a 95% confidence interval ranging from -0.232 to -0.042. This suggests a weak but statistically significant negative correlation between income and depression severity, indicating that higher income levels may be associated with lower levels of depressive symptoms among these patients (p = 0.005).

Table 2: The correlation between age and PHQ9 scores and income and PHQ9 scores was calculated

	Correlation	Confidence Interval	Significance
Age & Total score	-0.053	(-0.149, 0.044)	0.288
Income & total score	-0.138	(-0.232, -0.042)	0.005

The comparison of mean PHQ-9 scores between two groups based on educational attainment: the uneducated group and the educated group among the uneducated participants, the mean PHQ-9 score was 10.182, with a standard deviation of 6.066, based on a sample size of 370 individuals. In contrast, among the educated participants, the mean PHQ-9 score was lower at 8.250, with a smaller standard deviation of 3.947, based on a smaller sample size of 40 individuals. This suggests a potential difference in depression severity between the two groups, with the educated group exhibiting lower mean PHQ-9 scores compared to the uneducated group. A comprehensive overview of depression severity across different comorbidities among the 410 patients shown (Table 3) provides a comparison of depression severity among patients with different comorbidities. The table categorizes patients based on the severity of their depression, ranging from "no depression" to "severe depression," and lists the number of patients in each category for various comorbidities. Among patients with diabetes mellitus (DM), 20 individuals had "no depression," 20 had "moderate depression," and 20 had "severe depression," resulting in a total of 60 patients. Similarly, the table lists the distribution of depression severity for other comorbidities such as hypertension (HTN), ischemic heart disease (IHD), and hypothyroidism.

Table 3: Comparison of depression severity for each comorbidity

	Depression					
	None	**Mild**	**Moderate**	**Moderately severe**	**severe**	**Total**
Adenocarcinoma lung with peritoneal metastases	00	10	00	00	00	10
Ca head of the pancreas	00	00	10	00	00	10
DM	20	00	20	00	20	60
DM + CKD	00	00	10	00	00	10
DM + HTN	30	40	10	10	00	90
HTN	00	30	10	00	10	50
HTN + IHD	00	00	10	00	00	10
Hypothyroid	00	10	0	00	00	10
MCTD	00	00	0	10	00	10
None	30	30	60	20	10	150

For each of the 410 patients, the analysis of variance (ANOVA) test, the mean PHQ-9 score, the standard deviation, the number of patients, and the comorbidity group are all used to compare the scores. (table.4) The mean PHQ-9 score for each comorbidity group varies, with the highest mean score observed in the MCTD (mixed connective tissue disease) group at 17, followed by the CKD (Chronic Kidney Disease) and IHD (Ischemic Heart Disease) groups at 14 and 12, respectively. On the other hand, the lowest mean PHQ-9 scores were observed in the hypothyroidism and adenocarcinoma with peritoneal metastases groups, at 5 and 6, respectively. There were big differences in the PHQ-9 scores between the groups with MCTD ($F(1,408)=13.830$, $p<0.001$), hypothyroidism ($F(1,408)=7.434$, $p=0.007$), high blood pressure ($F(1,408)=7.815$, $p=0.005$), CKD ($F(1,408)=4.727$, $p=0.030$), and adenocarcinoma with peritoneal metastases ($F(1,408)=4.727$, $p=0.030$) conditions. However, no significant differences were found between the DM (Diabetes Mellitus), Ca head of the pancreas, and IHD groups.

Table 4: PHQ9 scores were compared by comorbidity group.

Comorbidity	Mean	Standard Deviation	Count	F(df between groups, df within groups)	ANOVA significance
MCTD	17	00	10	F(1,408)=13.830	<0.001
Hypothyroidism	05	00	10	F(1,408)=7.434	0.007
DM	9.875	6.643	160	F(1,408)=0.117	0.733
HTN	8.933	5.879	150	F(1,408)=7.815	0.005
CKD	14	00	10	F(1,408)=4.727	0.030
Ca head of the pancreas	11	00	10	F(1,408)=0.292	0.589
adenocarcinoma with perioneal metastases	06	00	10	F(1,408)=4.727	0.030
IHD	12	0	10	F(1,408)=1.172	0.280

Table 5: The mean PHQ9 scores were compared for those with no comorbidities, any number of comorbidities present, one comorbidity present, and two comorbidities present.

	Mean Depression Score	Standard Deviation	Count
No Comorbidities	9.800	5.286	150
1 or 2 Comorbidities	10.115	6.259	260
1 Comorbidities	11.267	6.660	150
2 Comorbidities	8.546	5.305	110

Our result further reveals a comparison of the mean PHQ-9 scores among different groups based on the presence and number of comorbidities among the 410 patients included in the study. Table 5 categorizes patients into four groups: those with no comorbidities, those with one or two comorbidities present, those with only one comorbidity present, and those with two comorbidities present. Among patients with no comorbidities, the mean PHQ-9 score was 9.800, with a standard deviation of 5.286, based on a sample size of 150 individuals. For patients with one or two comorbidities present, the mean PHQ-9 score was slightly higher at 10.115, with a standard deviation of 6.259, based on a larger sample size of 260 individuals.

DISCUSSION

Depression is frequently encountered in CLD patients, and it plays an important role in determining the health-related quality of life in these patients.[8] Some 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.[9,10] This study explored how different biological and socioeconomic factors influenced chronic liver disease patients experiences with depression. There are conflicting reports about the association of age and female gender with depression in patients with CLD.[8,11] While some authors report an association with depression in CLD patients, others report no such association.[12,13] The patients in the study were all female and had the same occupation as housewives. We first examined the severity of depression across different age groups and found that age did not have a significant correlation to the depression score (R = -0.053, p = 0.288) (Table 1). This finding was surprising, as the literature shows middle-aged populations to have disproportionately high rates of major depressive disorder. A study on the association between socioeconomic status and depression in later life found a socioeconomic gradient in depression prevalence, with older individuals in the highest wealth quintile showing the lowest rates of depression.[13] Similarly, a meta-analysis of 20 studies on anxiety and depressive disorders in the Pakistani population found that middle age was a significant risk indicator for depression.[1,14] This association between middle age and rates of depression has been reported in several low-income countries in both healthy participants and patients with chronic illnesses, which further underscores the novelty of our finding.[15] In another study, the effect of age on depression in CLD is described by Kraus et al.[16] and Theofilou, which suggest that older patients have higher levels of depression. [17] However, one possible explanation for our findings is that a confounding factor, such as the socioeconomic gradient, may exist in the prevalence of depression in older patients. On the other hand, socioeconomic factors such as income level and education level did show a statistically significant association with the severity of depression, as measured by their PHQ-9 score (Table 1, 2). This finding aligns with previous findings on the socioeconomic gradient of mental health, in which individuals with low socioeconomic positions as measured by education level, occupation, or income are more likely to have depression.[17] Patients with higher income correlated with a lower depression score (R = -0.138, p = 0.005); likewise, level of education attainment had a protective effect against depression in our sample of participants. According to Pevrol et al., there is a similar association between lower levels of education and major depression.[18] Patients with lower levels of education were significantly more likely to have major depression than those with higher education. This association of a lower educational level with more depression was reported by Timmermans IAL and Widdershoven J.[19] Because depressed people with lower education may have less access to screening and treatment.[20] Interestingly, evidence for the impact of education on rates of depression is mixed. A cross-sectional study evaluating patients with COPD in Pakistan found no significant difference in the rates of depression between patients of varying educational backgrounds.[21] However, other longitudinal studies on non-hospitalized populations worldwide have shown college-educated groups to have lower rates of depression than groups with high school diplomas.[22] Given the vast discrepancies in this area, it is essential to assess the findings of our study in the proper context. Major Depressive Disorder is a complex mental health issue influenced by many factors, and the direct effect of a singular variable is challenging to study. Further research is warranted to explore the underlying mechanisms and potential mediators between education and depression in patients with chronic liver disease. The assessment of depression severity among our patients indicates that 29.2% experienced mild depression, 37.7% experienced moderate depression, and 9.7% experienced severe depression. (table.3) Most

patients fell within the moderate range, although this may vary depending on the presence of other comorbidities. In contrast, another study found that 34% of patients had mild depression, 16.5% had moderate depression, and 12.4% had severe depression among patients with CLD. Bianchi et al. were able to obtain comparable data.[10,23] A study revealed that patients with chronic medical conditions were more likely to have a recent onset or lifetime history of psychiatric conditions.[24] The coexistence of chronic illnesses, along with other confounding factors, can affect the education level's impact on the severity of depression. A comparison of the PHQ-9 scores for patients with comorbidity and those with no comorbidities reveals that the mean PHQ-9 score for those with comorbidity was slightly higher (Table 5). Out of the comorbidities examined, the ANOVA test reveals that patients with mixed connective tissue disease, hypothyroidism, hypertension, chronic kidney disease, or adenocarcinoma with peritoneal metastases had a statistically significant impact on the likelihood of having a higher PHQ-9 score compared to those without these comorbidities (Tables 3 and 4). A study examining the relationships between chronic diseases and depression among middle-aged and older adults in China found that chronic conditions, including liver disease, were significantly associated with depression.[25] There has also been evidence that suggests patients with depression are three times more likely to be noncompliant with medication. As such, depression in patients must be considered due to its effect on overall health outcomes.[26] Furthermore, the evidence from previous studies strongly supports the use of optimal pharmacotherapy to reduce adverse outcomes associated with depression in patients with chronic liver disease (CLD). Hepatologists should approach depression management with the same level of commitment as they do for liver disease and immunosuppression. They should maintain a low threshold for suspecting depression, carefully differentiate it from hepatic encephalopathy, and confidently employ safe and effective pharmacotherapy.[27] In severe major depressive disorder (PHQ-9 $\geq$ 20), combining pharmacotherapy with psychotherapy is recommended, with electroconvulsive therapy (ECT) considered for severe suicidality. For mild-to-moderate depression (PHQ-9 < 20), initiating monotherapy with second-generation antidepressants (SGAs) or psychotherapy is reasonable, as both have demonstrated efficacy and tolerability.[28]

LIMITATIONS

The study shows that socioeconomic factors are linked to depression severity among CLD patients. Limitations include a small sample size, use of self-reported measures, and a cross-sectional design. The findings stress the need for regular depression screening for CLD patients, especially those from disadvantaged backgrounds. Tailored treatment approaches informed by socioeconomic status and comorbidities are crucial. Healthcare resource allocation should prioritize mental health services for socioeconomically disadvantaged CLD patients. Collaboration among healthcare professionals is essential for providing comprehensive care. Further research and collaborative efforts are imperative for impactful clinical practice and healthcare policy.

CONCLUSIONS

Age is not significantly correlated with depression severity in this population, unlike previous studies. However, income level, education level, and the presence of comorbidities are significantly associated with depression severity. Higher-income levels and higher education are linked to lower depression scores, indicating a potential protective effect. Additionally, the presence of comorbidities is associated with higher depression scores. This study offers critical insights into the factors impacting depression in chronic liver disease patients, highlighting the crucial roles of income, education, and comorbidities in identifying high-risk individuals and tailoring interventions. Further research is needed to understand these associations better.

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