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Original article

Association between esophageal varices severity and psychological distress in cirrhotic patients

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ABSTRACT

BACKGROUND: Patients with liver cirrhosis are highly vulnerable to psychological disorders; however, the implications of these mental health issues on the severity of esophageal varices remain unclear.

OBJECTIVES: This study aimed to investigate the correlation between the grading of esophageal varices and the occurrence of anxiety and depression in cirrhotic patients experiencing upper gastrointestinal bleeding.

METHODS: This study was conducted on inpatients at Dr. Saiful Anwar General Hospital, Malang, who were diagnosed with liver cirrhosis and experienced upper gastrointestinal bleeding over a six-month period using a consecutive sampling method. The grading of esophageal varices from endoscopic data was categorized according to the First Baveno International criteria. Anxiety and depression levels were assessed using the Hospital Anxiety and Depression Scale (HADS). Statistical analysis was performed using the Chi-Square test with a significance level of p-value < 0.05.

RESULTS: Out of 53 respondents, 46 had large-grade esophageal varices and 7 had small-grade varices. Based on HADS scores, 38 respondents exhibited symptoms of anxiety, 10 were within the normal range, and 5 exhibited symptoms of depression. A significant moderate correlation was found between the grading of esophageal varices and the presence of anxiety and depression in cirrhotic patients with upper gastrointestinal bleeding ($p = 0.001$; $r = 0.445$).

CONCLUSION: There is a significant correlation between large-grade esophageal varices and the occurrence of anxiety in cirrhotic patients experiencing upper gastrointestinal bleeding.

KEYWORDS: Anxiety; depression; liver cirrhosis; upper gastrointestinal bleeding; grading varices.

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INTRODUCTION

Liver cirrhosis is a chronic condition that can lead to various serious complications, one of which is upper gastrointestinal bleeding. Gastrointestinal bleeding associated with portal hypertension is among the most life-threatening complications in cirrhotic patients.[1] Portal hypertension, a consequence of liver cirrhosis, results in the formation of varices in the upper digestive tract, particularly in the esophagus and stomach. The rupture of esophageal or gastric varices represents a severe and potentially fatal complication of chronic liver disease, often leading to significant upper gastrointestinal hemorrhage.[2] Although the global prevalence of liver cirrhosis remains uncertain, it is estimated to range between 0.15% and 0.27% in the United States. In 1998, cirrhosis accounted for over 25,000 deaths and 373,000 hospital discharges. By 2010, it was responsible for approximately 49,500 deaths and ranked as the eighth leading cause of mortality in the country. These numbers are likely underestimates due to the high prevalence of undiagnosed cirrhosis, particularly in patients with non-alcoholic steatohepatitis (NASH) and hepatitis C.[3] Because compensated cirrhosis often remains

asymptomatic for extended periods, it is estimated that up to 1% of the population may have histologically confirmed but undiagnosed cirrhosis. Globally, cirrhosis caused approximately 1.48 million deaths in 2019—an 8.1% increase compared to 2017.[4] As an incurable disease, cirrhosis has a profound impact on patients' quality of life. Consequently, patients with liver cirrhosis are particularly vulnerable to psychological issues such as anxiety, depression, restlessness, negative attitudes toward treatment and care, and even suicidal ideation.[5]

Numerous studies have shown that prolonged emotional stress can impact the human immune system, leading to diminished immune function and accelerating disease progression. Mental health disorders such as depression and anxiety are frequently observed in patients with liver cirrhosis.[6,7] A study involving veterans with cirrhosis indicated that symptoms of depression and anxiety are common in this population.[8] Furthermore, a systematic review and meta-analysis revealed that the prevalence of anxiety and depression among patients with end-stage liver disease varies between 4.5% and 64%.[9] Other studies have also reported that depression and anxiety are the most prevalent psychological disorders affecting liver disease patients, with anxiety affecting 25% to 45% of patients with chronic liver disease and depression affecting 29% to 72%.[10,11] These disorders not only significantly reduce health-related quality of life in patients with chronic diseases but also influence various aspects of care, including medication adherence and social behaviors such as alcohol and substance use.[12] The most common depression and anxiety have occurred in decompensated cirrhosis and liver transplant candidates, but their treatment remains poor.[11] Therefore, the current study aims to evaluate the association between the severity of esophageal varices and the prevalence of psychological distress in patients with liver cirrhosis.

METHODS

Study design

The research employed a cross-sectional design and was conducted at Saiful Anwar General Hospital, Malang, Indonesia, from January 2024 to December 2024. The goal of the current study was to evaluate the psychological status of patients with cirrhosis and esophageal varices using the Hospital Anxiety and Depression Scale (HADS) as a measurement instrument.[13] The protocol of the study was designed and implemented in accordance with the recommendations of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE).[14]

Ethical approval

This study was approved by the Saiful Anwar General Hospital Ethics Committee and conducted in accordance with the Declaration of Helsinki.[15] A complete explanation of the purpose of the study, potential risks, and benefits was given to all subjects prior to participation. Voluntary written informed consent was obtained from each participant. Participants were given the freedom to withdraw from the study at any moment without penalty. There was no reward for participation.

Participants and eligibility criteria

Participants were recruited using a consecutive sampling method, a type of non-probability sampling, where all patients meeting the inclusion criteria and presenting sequentially were enrolled in the study. The minimum required sample size was 50 patients. Inclusion criteria were adults aged ≥18 years, diagnosed with liver cirrhosis, conscious at the time of data collection, and experiencing upper gastrointestinal (GI) bleeding. Participants were also required to have endoscopy data related to their upper GI bleeding episode. Exclusion criteria included cirrhotic patients with upper GI

bleeding who were unconscious and/or clinically unstable (experiencing hemodynamic instability or receiving inotropic and/or vasopressor therapy), patients with limited physical mobility or a history of stroke, patients with a prior diagnosis of depression or anxiety disorders, those with comorbidities such as diabetes mellitus or autoimmune disease, and individuals with a history of tumors or malignancy outside the gastrointestinal system.

Data collection

The study was carried out at Saiful Anwar General Hospital, Malang, Indonesia, between January and December 2024. Collected data included clinical characteristics of patients during hospitalization and vital sign measurements to ensure that patients were conscious and hemodynamically stable. Psychological assessment was conducted using the HADS, which consists of items evaluating symptoms of anxiety and depression potentially experienced by cirrhotic patients.[13] Data collection was performed by SM, AF, ACYS, and LV. In the event of disagreements during data collection or analysis, discussions were held to reach consensus.

Covariates

The predictor variable in this study was the severity of esophageal varices, assessed according to the First Baveno International Consensus. Esophageal varices were categorized into two grades: small varices and large varices.[16] The primary outcome was psychological distress, assessed using the HADS questionnaire. Based on the scores, participants were classified into one of three psychological categories: depression, anxiety, or normal.[13]

Statistical analysis

Categorical variables were presented as frequencies and percentages (n, %), while normally distributed numerical variables were presented as mean ± standard deviation (SD), and non-normally distributed numerical variables were presented as median with interquartile range (IQR). The Kolmogorov–Smirnov test was used to assess the normality of data distribution. Baseline characteristics were summarized descriptively. The chi-square test was used to examine the association between the severity of esophageal varices and psychological distress among cirrhotic patients. A p-value of less than 0.05 was considered statistically significant. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software (IBM Corporation, New York, USA).

RESULTS

Baseline characteristics of patients

Table 1 presents the baseline characteristics of patients included in this study. The mean age of the participants was 42.28 years with a SD of 12.40 years. Regarding sex distribution, 27 patients (50.9%) were male and 26 patients (49.1%) were female. Psychological status, assessed using the HADS, revealed that 10 patients (18.9%) had a normal psychological profile, 38 patients (71.7%) experienced anxiety, and 5 patients (9.5%) showed signs of depression.

Impact of esophageal varices severity on psychological well-being

Table 2 summarizes the association between the severity of esophageal varices and psychological outcomes (anxiety and depression) among cirrhotic patients, as measured by the HADS. Of the 53 patients, the majority of those presenting with anxiety had large esophageal varices, accounting for 37 patients (69.8%), while only 1 patient (1.9%) with small varices reported anxiety symptoms. This finding indicates a

statistically significant association between the severity of esophageal varices and anxiety in cirrhotic patients (p = 0.001). Conversely, normal psychological status was observed in 6 patients (11.3%) with large varices and 4 patients (7.5%) with small varices, though this relationship was not statistically significant (p = 0.445). Regarding depressive symptoms, 3 patients (5.7%) with large varices and 2 patients (3.8%) with small varices were identified as experiencing depression, but no significant association was found between variceal severity and depression (p = 0.408).

Table 1. Baseline characteristics of patients in our study

Characteristics	Mean ± SD or n (%)
Age	42.28 ± 12.40
Gender	
Male	27 (50.9)
Female	26 (49.1)
Psychological condition	
Normal	10 (18.9)
Anxiety	38 (71.7)
Depression	5 (9.5)

Note, data were presented in mean ± SD or n (%).

DISCUSSION

The results of this study indicate that patients experiencing anxiety symptoms are at a greater risk of having large-grade esophageal varices compared to those without anxiety. This finding is consistent with previous studies, which have reported that psychological disturbances such as depression and anxiety are among the most common comorbidities in patients with liver disease.[11] One study noted that anxiety affects approximately 25% to 45% of patients with chronic liver disease, while depression is present in 29% to 72% of cases.[10] Other research has also emphasized the complex and tightly linked relationship between stress, mental health, and the healing process, including that of esophageal varices.[17] Accordingly, our findings strengthen the existing body of evidence and support the hypothesis that psychological conditions are significantly associated with the severity of esophageal varices.

Although the mechanisms behind this correlation are uncertain, several theoretical paths have been proposed. Hepatic immune cells as well as the pro-inflammatory cytokines released by the liver, such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interleukin-1β (IL-1β), are all documented to be involved in shifts in behavior.[18] These cytokines are able to gain access to systemic circulation and cross the central nervous system through regions with a compromised blood-brain barrier, thereby influencing neural transmission and modulating central nervous system function. These changes, particularly within the basal ganglia, can influence neurotransmission and result in symptoms such as fatigue, depression, anxiety, sleep disorders, and social withdrawal.[19] Economic stressors are similarly believed to produce anxiety and depression in cirrhotics. The high cost of hospital care and chronic therapy can create considerable anxiety, especially in patients out of the hospital but still requiring ongoing therapy. Economic costs to relatives may reinforce anxiety.[11] Third, the psychic impact of the disease itself is a basic concern. Fear of potentially life-threatening outcomes such as cancer or death, and uncertainty of disease outcome, may lead to extreme emotional distress. Emotional and social support from family and friends is, therefore, essential in the healing process. Feeling cared for and not alone in confronting the illness may have positive effects on patients' mental well-being and enhance their quality of life.[20]

Several important clinical implications are found in this study. First, the paper highlights the value of routine screening for psychological disorders—namely, anxiety—during standard evaluation of cirrhotic patients with esophageal varices. Neglecting attention to anxiety may jeopardize clinical outcomes and reduce quality of life. Second, these results underscore the significance of having a multidisciplinary team for the treatment of cirrhotic patients, including hepatologists, psychiatrists, and clinical psychologists to bring the entire person into care. Third, patients with large esophageal varices, also at higher risk of anxiety, need to be prioritized for psychological intervention, e.g., counseling or supportive therapy. Fourth, these findings serve as the basis for patient and family education on the psychological effect of liver cirrhosis and the necessity of emotional support upon recovery. Lastly, this study lays the groundwork for further research into the relationship between psychological disorders and the severity of cirrhotic complications, and provides justification for the incorporation of psychosocial elements into the clinical practice guidelines for managing patients with cirrhosis.

Table 2. The impact of esophageal varices grade on patients' anxiety and depression

HADS score	The first baveno international consensus on esophageal varices		Total (n = 53)	p
	Large (n = 46)	Small (n = 7)		
Anxiety	37 (69.8)	1 (1.9)	38 (71.7)	0.001
Normal	6 (11.3)	4 (7.5)	10 (18.9)	0.445
Depression	3 (5.7)	2 (3.8)	5 (9.4)	0.408

Note, data were presented in n (%); HADS, hospital anxiety and depression scale.

Despite its utility, this study has certain limitations that need to be taken into consideration in interpreting the results. First, cross-sectional design only allows for association to be evaluated, not causality between the severity of esophageal varices and psychiatric disorders. Second, the sample size employed (n = 53) is comparatively small and may decrease statistical power as well as the generalizability of the results, particularly for subgroups such as depressed patients or those with small varices. Third, the study was done in a single center—Saiful Anwar General Hospital, Malang—such that the results may not be applicable to cirrhotic patients elsewhere or in different healthcare facilities. Fourth, there was no control for potential confounding factors like socioeconomic status, family support, and alcohol or substance use history. Fifth, psychological status was also assessed with the HADS questionnaire, a self-report and subjective measure that is open to perception bias and misunderstanding. Lastly, since there was no long-term follow-up, it is not clear whether the symptoms of anxiety or depression seen are transient, chronic, or change with time.

CONCLUSION

This study demonstrates a significant correlation between the severity of esophageal varices and the presence of anxiety in patients with liver cirrhosis. Those with large-grade varices had a greater chance of experiencing anxiety than patients who have small-grade varices. Though the correlation between the severity of varices and depression was not found to be statistically significant, the outcomes still demonstrate the interplay between physical and psychological conditions in cirrhotic patients. These results highlight the need for an integrated management strategy for liver cirrhosis that addresses not just clinical and physical sequelae but also psychological well-being. Continued assessment of mental health status, particularly anxiety, needs to be incorporated into the care of cirrhosis in order to improve both quality of life and successful long-term treatment.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The protocols of our study have been approved by local ethical committee.

CONFLICTS OF INTEREST

We have no conflict of interest

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We have no source of funding

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AUTHOR CONTRIBUTION

Conceptualization: SM; Data Curation: AF, ACYS, LV; Formal Analysis: AF, ACYS, LV; Investigation: AF, ACYS, LV; Project Administration: AF, ACYS, LV; Resources: AF, ACYS, LV; Methodology: AF, ACYS, LV; Software: AF, ACYS, LV; Visualization: AF, ACYS, LV; Supervision: SM; Validation: SM; Writing – Original Draft Preparation: AF, ACYS, LV; Writing – Review & Editing: SM. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

REFERENCES

1. Biecker E. Gastrointestinal bleeding in cirrhotic patients with portal hypertension. ISRN Hepatol 2013;2013(1):541836.doi: 10.1155/2013/541836. PMID: 27335828
2. Maruyama H, Yokosuka O. Pathophysiology of portal hypertension and esophageal varices. Int J Hepatol 2012;2012(1):895787.doi: 10.1155/2012/895787. PMID: 22666604
3. Wang Y, Wang M, Liu C, et al. Global burden of liver cirrhosis 1990-2019 and 20 years forecast: results from the global burden of disease study 2019. Ann Med 2024;56(1):2328521.doi: 10.1080/07853890.2024.2328521. PMID: 38727511
4. Schuppan D, Afdhal NH. Liver cirrhosis. Lancet 2008;371(9615):838-851.doi: 10.1016/S0140-6736(08)60383-9. PMID: 18328931
5. Zimbrean PC, Jakab SS. Depression and anxiety management in cirrhosis. Hepatol Commun 2025;9(1):e0600.doi: 10.1097/HC9.0000000000000600. PMID: 39670879
6. Jiao W, Lin J, Deng Y, et al. The immunological perspective of major depressive disorder: unveiling the interactions between central and peripheral immune mechanisms. J Neuroinflammation 2025;22(1):10.doi: 10.1186/s12974-024-03312-3. PMID: 39828676
7. Ishikawa Y, Furuyashiki T. The impact of stress on immune systems and its relevance to mental illness. Neurosci Res 2022;175(1):16-24.doi: 10.1016/j.neures.2021.09.005. PMID: 34606943
8. Alshehri A, Alshehri B, Alghadir O, et al. The prevalence of depressive and anxiety symptoms among first-year and fifth-year medical students during the COVID-19 pandemic: a cross-sectional study. BMC Med Educ 2023;23(1):411.doi: 10.1186/s12909-023-04387-x. PMID: 37277742
9. Peng JK, Hepgul N, Higginson IJ, et al. Symptom prevalence and quality of life of patients with end-stage liver disease: A systematic review and meta-analysis. Palliat Med 2019;33(1):24-36.doi: 10.1177/0269216318807051. PMID: 30345878
10. Holmes R, Patel A, Desai AP. Psychiatric disorders and their treatment: Impact of outcomes in patients with chronic liver disease. Clin Liver Dis (Hoboken) 2022;20(2):32-37.doi: 10.1002/cld.1204. PMID: 36033426
11. Hernaez R, Kramer JR, Khan A, et al. Depression and anxiety are common among patients with cirrhosis. Clin Gastroenterol Hepatol 2022;20(1):194-203.doi: 10.1016/j.cgh.2020.08.045. PMID: 32835845
12. Olvera-Cruz SI, Cano-Estrada A, Hernandez-Mariano JA, et al. Association between medication adherence and health-related quality of life among type 2 diabetic adults in Mexico. J Family Med Prim Care 2024;13(10):4521-4527.doi: 10.4103/jfmpc.jfmpc_399_24. PMID: 39629420
13. Snaith RP. The hospital anxiety and depression scale. Health Qual Life Outcomes 2003;1(1):29.doi: 10.1186/1477-7525-1-29. PMID: 12914662
14. Cuschieri S. The STROBE guidelines. Saudi J Anaesth 2019;13(Suppl 1):S31-S34.doi: 10.4103/sja.SJA_543_18. PMID: 30930717
15. Goodyear MD, Krleza-Jeric K, Lemmens T. The Declaration of Helsinki. BMJ 2007;335(7621):624-625.doi: 10.1136/bmj.39339.610000.BE. PMID: 17901471
16. de Franchis R, Bosch J, Garcia-Tsao G, et al. Baveno VII - Renewing consensus in portal hypertension. J Hepatol 2022;76(4):959-974.doi: 10.1016/j.jhep.2021.12.022. PMID: 35120736

17. Sara JDS, Toya T, Ahmad A, et al. Mental stress and its effects on vascular health. Mayo Clin Proc 2022;97(5):951-990.doi: 10.1016/j.mayocp.2022.02.004. PMID: 35512885
18. Pratim Das P, Medhi S. Role of inflammasomes and cytokines in immune dysfunction of liver cirrhosis. Cytokine 2023;170(1):156347.doi: 10.1016/j.cyto.2023.156347. PMID: 37639845
19. Popko K, Gorska E, Stelmaszczyk-Emmel A, et al. Proinflammatory cytokines Il-6 and TNF-alpha and the development of inflammation in obese subjects. Eur J Med Res 2010;15 Suppl 2(Suppl 2):120-122.doi: 10.1186/2047-783x-15-s2-120. PMID: 21147638
20. Rodriguez-Gonzalez A, Velasco-Durantez V, Martin-Abreu C, et al. Fatigue, emotional distress, and illness uncertainty in patients with metastatic cancer: Results from the prospective neoetic_seom study. Curr Oncol 2022;29(12):9722-9732.doi: 10.3390/curroncol29120763. PMID: 36547177