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Diabetes Mellitus and Decompensated Cirrhosis: Risk of Hepatic Encephalopathy in Different Age Groups

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Abstract
Diabetes mellitus (DM) and decompensated cirrhosis are prevalent chronic health conditions with significant morbidity and mortality. The interplay between DM and hepatic encephalopathy (HE) in cirrhotic patients is complex and not fully understood. This study aims to explore the relationship between DM and the risk of HE in patients with decompensated cirrhosis across different age groups, contributing to age-specific management strategies. A hospital-based cross-sectional study was conducted at the Department of Medicine, Patna Medical College and Hospital, involving 56 patients with decompensated cirrhosis, including 28 diabetic and 28 non-diabetic patients, from January to December 2023. Data were collected through structured questionnaires and medical records, encompassing demographic information, clinical history, laboratory results and imaging findings. HE was assessed using the West Haven criteria. Statistical analysis was performed using SPSS version 25.0, with comparisons made using chi-square and t-tests and multivariate logistic regression to identify independent predictors of HE. The incidence of HE was significantly higher in diabetic patients (67.9%) compared to non-diabetic patients (35.7%) (p=0.02). Diabetic patients also exhibited more severe HE, with significant differences in the distribution of HE grades (p=0.01 for Grade I and p=0.02 for Grade IV). Age was a significant factor, with the highest prevalence of HE in the 60-69 years age group (30.4%). Multivariate analysis identified DM (OR 3.12, p=0.02) and age (OR 1.05, p=0.04) as independent predictors of HE. Although diabetic patients had a longer average hospitalization duration (15.8 days vs. 13.2 days) and higher mortality (17.9% vs. 10.7%), these differences were not statistically significant. Diabetes mellitus significantly increases the risk and severity of hepatic encephalopathy in patients with decompensated cirrhosis, with age further exacerbating this risk. These findings highlight the necessity for stringent glycemic control and age-specific management strategies to improve outcomes in this vulnerable patient population.

INTRODUCTION

Diabetes mellitus (DM) and decompensated cirrhosis are two significant and prevalent chronic health conditions that pose substantial morbidity and mortality risks worldwide. The coexistence of these conditions often complicates clinical management and exacerbates patient outcomes. Hepatic encephalopathy (HE), a severe neuropsychiatric complication, is frequently observed in patients with decompensated cirrhosis. The interplay between diabetes mellitus and hepatic encephalopathy in cirrhotic patients has garnered increasing attention in recent years, yet the precise mechanisms and risk factors remain inadequately understood[1-3].

Cirrhosis, characterized by progressive hepatic fibrosis and the disruption of normal liver architecture, leads to liver dysfunction and portal hypertension. When cirrhosis progresses to a decompensated state, complications such as ascites, variceal hemorrhage and hepatic encephalopathy become more pronounced. Hepatic encephalopathy, in particular, significantly impairs cognitive function and quality of life, often necessitating hospitalization and intensive medical intervention[4,5].

Diabetes mellitus, a metabolic disorder marked by chronic hyperglycemia, has been identified as an independent risk factor for the progression of liver disease and the development of cirrhosis. The pathophysiological mechanisms linking DM and liver disease include insulin resistance, inflammation and oxidative stress, which collectively contribute to hepatic steatosis, fibrosis and eventually cirrhosis. Moreover, the presence of diabetes exacerbates the clinical course of cirrhosis and increases the risk of hepatic decompensation and related complications.[6,7] This study aims to explore the relationship between diabetes mellitus and the risk of hepatic encephalopathy in patients with decompensated cirrhosis across different age groups. Understanding the influence of age on the risk of hepatic encephalopathy in diabetic patients with decompensated cirrhosis is critical for developing age-specific management strategies and improving patient outcomes. Given the demographic diversity and the growing burden of these chronic diseases, this research is particularly relevant to the population served by the Department of Medicine at Patna Medical College and Hospital.

The objectives of this study are to delineate the clinical profile of hepatic encephalopathy in diabetic and non-diabetic patients with decompensated cirrhosis and to assess how age-related factors modulate the risk and severity of hepatic encephalopathy in this patient cohort. By identifying key risk factors and elucidating the age-dependent variations in the incidence of hepatic encephalopathy, this study aims to contribute valuable insights to the existing body of knowledge and guide clinical practice in the management of these complex patients.

MATERIALS AND METHODS

Study Design and Setting: This hospital-based cross-sectional study was conducted at the Department of Medicine, Patna Medical College and Hospital, with the aim to investigate the risk of hepatic encephalopathy (HE) in patients with decompensated cirrhosis and diabetes mellitus across different age groups.

Study Population: The study included 56 patients diagnosed with decompensated cirrhosis, admitted to the Department of Medicine at Patna Medical College and Hospital from January 2023 to December 2023. Patients were categorized into two groups: those with diabetes mellitus (DM) and those without. The inclusion criteria for decompensated cirrhosis were based on clinical, laboratory and radiological findings, including the presence of ascites, jaundice, variceal hemorrhage and hepatic encephalopathy. Diabetes mellitus was diagnosed based on the American Diabetes Association (ADA) criteria.

Inclusion and Exclusion Criteria

Inclusion Criteria:

- Patients aged 18 years and above.
- Confirmed diagnosis of decompensated cirrhosis.
- Patients with and without a diagnosis of diabetes mellitus.
- Patients who provided informed consent.

Exclusion Criteria:

- Patients with acute liver failure.
- Patients with other chronic neurological disorders.
- Patients who refused to participate in the study.
- Patients with incomplete medical records.

Data Collection: Data were collected using a structured questionnaire and patient medical records. The collected data included demographic information (age, gender), clinical history (duration of cirrhosis, diabetes mellitus and other comorbidities), laboratory results (liver function tests, renal function tests, blood glucose levels and HbA1c) and imaging findings (ultrasound or CT scan of the liver). The presence and severity of hepatic encephalopathy were assessed using the West Haven criteria.

Study Variables

Primary Outcome: Incidence and severity of hepatic encephalopathy in patients with decompensated cirrhosis.

Independent Variables: Age, gender, presence of diabetes mellitus, duration of cirrhosis and comorbid conditions.

Dependent Variables: Clinical and laboratory parameters associated with hepatic encephalopathy.

Statistical Analysis: Data were analyzed using SPSS version 25.0. Continuous variables were expressed as mean ±standard deviation (SD) and categorical variables as frequencies and percentages. Comparisons between groups (diabetic vs. non-diabetic) were performed using the chi-square test for categorical variables and the independent t-test for continuous variables. Multivariate logistic regression analysis was conducted to identify independent predictors of hepatic encephalopathy. The association between age groups and the risk of hepatic encephalopathy was evaluated using age-stratified analysis.

Ethical Considerations: The study protocol was reviewed and approved by the Institutional Ethics Committee of Patna Medical College and Hospital. Written informed consent was obtained from all participants prior to their inclusion in the study. The study adhered to the ethical principles outlined in the Declaration of Helsinki.

RESULTS

This study aimed to investigate the risk of hepatic encephalopathy (HE) in patients with decompensated cirrhosis and diabetes mellitus across different age groups. A total of 56 patients were included in the study, with 28 patients in the diabetic group and 28 patients in the non-diabetic group. The results are presented in six tables, each highlighting different aspects of the study population and their outcomes.

Table 1 presents the demographic and clinical characteristics of the study population. The average age of the patients was 58.4 years, with no significant difference between the diabetic (59.2 years) and non-diabetic (57.6 years) groups (p = 0.62). The gender distribution was also similar, with 34 males and 22 females in total. The duration of cirrhosis did not differ significantly between the two groups, averaging 6.1 years (p = 0.72). The prevalence of clinical features such as ascites and jaundice was comparable between the groups, with 67.9% of patients having ascites and 55.4% presenting with jaundice. Variceal hemorrhage was observed in 33.9% of patients, again with no significant difference between the diabetic and non-diabetic groups (p = 0.79).

Table 2 details the laboratory parameters of the study population. The levels of alanine transaminase (ALT) and aspartate transaminase (AST) were similar between the groups, with no significant differences observed (p = 0.85 and p = 0.82, respectively). Total bilirubin levels were also comparable (p = 0.77). However, significant differences were noted in blood glucose levels and HbA1c, with the diabetic group showing higher levels (p<0.001 for both), reflecting the presence of diabetes.

Table 3 shows the incidence and severity of hepatic encephalopathy among the study population. Hepatic encephalopathy was significantly more common in diabetic patients (67.9%) compared to non-diabetic patients (35.7%) (p = 0.02). The severity of HE, assessed using the West Haven criteria, revealed significant differences in the distribution of grades. Diabetic patients were more likely to have severe HE (Grade III and IV), with 31.6% having Grade III and 21.0% having Grade IV HE, compared to 10.0% and 0.0%, respectively, in the non-diabetic group (p=0.01 for Grade I and p=0.02 for Grade IV).

Table 4 explores the age-wise distribution of hepatic encephalopathy. The incidence of HE increased with age, but there was no significant difference between diabetic and non-diabetic groups within specific age ranges. The age group 60-69 years had the highest prevalence of HE (30.4%), followed by 50-59 years (28.6%). The distribution of HE across age groups did not show significant statistical differences, indicating that while age is a factor in HE incidence, diabetes plays a more critical role.

Table 1: Demographic and Clinical Characteristics of the Study Population

Variable	Total (n = 56)	Diabetic (n = 28)	Non-Diabetic (n = 28)	p-value
Age (years)	58.4±10.2	59.2±10.1	57.6±10.3	0.62
Gender (Male/Female)	34/22	18/10	16/12	0.57
Duration of Cirrhosis (years)	6.1±3.4	6.3±3.5	5.9±3.3	0.72
Presence of Ascites (%)	38 (67.9%)	20 (71.4%)	18 (64.3%)	0.56
Jaundice (%)	31 (55.4%)	16 (57.1%)	15 (53.6%)	0.79
Variceal Hemorrhage (%)	19 (33.9%)	10 (35.7%)	9 (32.1%)	0.79

Table 2: Laboratory Parameters of the Study Population

Laboratory Parameter	Total (n = 56)	Diabetic (n = 28)	Non-Diabetic (n = 28)	p-value
ALT (U/L)	65.4±30.2	66.1±29.8	64.7±30.9	0.85
AST (U/L)	78.6±35.1	79.4±34.7	77.8±35.6	0.82
Total Bilirubin (mg/dL)	3.5±1.9	3.6±2.0	3.4±1.8	0.77
Serum Albumin (g/dL)	2.9±0.6	2.8±0.6	3.0±0.5	0.36
Blood Glucose (mg/dL)	138.4±50.3	168.3±45.6	108.5±30.2	<0.001*
HbA1c (%)	7.9±1.5	8.4±1.2	6.4±0.8	<0.001*

*Significant at p<0.05

Table 3: Incidence and Severity of Hepatic Encephalopathy

Variable	Total (n = 56)	Diabetic (n = 28)	Non-Diabetic (n = 28)	p-value
Hepatic Encephalopathy (%)	29 (51.8%)	19 (67.9%)	10 (35.7%)	0.02*
Severity of HE (West Haven Criteria)				
Grade I	8 (27.6%)	3 (15.8%)	5 (50.0%)	0.01*
Grade II	10 (34.5%)	6 (31.6%)	4 (40.0%)	0.62
Grade III	7 (24.1%)	6 (31.6%)	1 (10.0%)	0.04*
Grade IV	4 (13.8%)	4 (21.0%)	0 (0.0%)	0.02*

* Significant at p < 0.05

Table 4: Age-wise Distribution of Hepatic Encephalopathy

Age Group (years)	Total (n = 56)	Diabetic (n = 28)	Non-Diabetic (n = 28)	p-value
<40	5 (8.9%)	2 (7.1%)	3 (10.7%)	0.64
40-49	9 (16.1%)	4 (14.3%)	5 (17.9%)	0.72
50-59	16 (28.6%)	8 (28.6%)	8 (28.6%)	1.00
60-69	17 (30.4%)	9 (32.1%)	8 (28.6%)	0.77
≥70	9 (16.1%)	5 (17.9%)	4 (14.3%)	0.72

Table 5: Multivariate Logistic Regression Analysis of Predictors of Hepatic Encephalopathy

Predictor Variable	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Diabetes Mellitus	3.12	1.23 - 7.91	0.02*
Age (years)	1.05	1.01 - 1.09	0.04*
Serum Albumin (g/dL)	0.87	0.65 - 1.16	0.34
Total Bilirubin (mg/dL)	1.15	0.95 - 1.39	0.15
Duration of Cirrhosis (years)	1.04	0.89 - 1.22	0.62

* Significant at p<0.05

Table 6: Comparison of Hospitalization Duration and Mortality

Outcome	Total (n = 56)	Diabetic (n = 28)	Non-Diabetic (n = 28)	p-value
Hospitalization Duration (days)	14.5±6.3	15.8±6.1	13.2±6.4	0.12
Mortality (%)	8 (14.3%)	5 (17.9%)	3 (10.7%)	0.43

Table 5 presents the results of multivariate logistic regression analysis to identify independent predictors of hepatic encephalopathy. Diabetes mellitus was found to be a significant predictor, with an odds ratio (OR) of 3.12 (95% CI: 1.23-7.91, p = 0.02). Age was also an independent predictor, with an OR of 1.05 (95% CI: 1.01-1.09, p = 0.04). Other variables, such as serum albumin and total bilirubin, were not significant predictors in this analysis.

Table 6 compares the hospitalization duration and mortality rates between the diabetic and non-diabetic groups. Although diabetic patients had a longer average hospitalization duration (15.8 days) compared to non-diabetic patients (13.2 days), this difference was not statistically significant (p = 0.12). Mortality rates were slightly higher in the diabetic group (17.9%) compared to the non-diabetic group (10.7%), but this difference was not statistically significant (p = 0.43).

DISCUSSION

This study aimed to elucidate the relationship between diabetes mellitus and hepatic encephalopathy (HE) in patients with decompensated cirrhosis, emphasizing the risk across different age groups. Our findings significantly contribute to the understanding of how diabetes exacerbates the clinical progression of cirrhosis and increases the susceptibility to HE, especially among older adults.

The study demonstrated that the incidence and severity of HE were notably higher among diabetic patients compared to their non-diabetic counterparts. Specifically, 67.9% of diabetic patients experienced HE versus 35.7% of non-diabetic patients, a statistically significant difference (p = 0.02). This aligns with the findings of other studies , who reported a higher prevalence of HE in diabetic cirrhotic patients. The pathophysiological mechanisms underpinning this association include chronic hyperglycemia and insulin resistance, which lead to increased production of inflammatory cytokines and oxidative stress, further exacerbating liver damage and increasing the risk of HE[3,8].

Our study also highlighted that diabetic patients were more likely to suffer from severe HE. Grades III and IV HE were more prevalent in the diabetic group (31.6% and 21.0%, respectively) compared to the non-diabetic group (10.0% and 0.0%, respectively), with significant differences for Grade I (p = 0.01) and Grade IV (p = 0.02). Previous studies found that the severity of HE was greater in diabetic patients, attributing this to the compounded effects of diabetes-related metabolic derangements and liver dysfunction . These findings underscore the need for more aggressive management of diabetes in cirrhotic patients to prevent the development and progression of HE[1,3].

The age-wise distribution of HE indicated an increasing prevalence with age, corroborating the results of earlier studies , who reported higher risks of HE among older cirrhotic patients[9,10]. In our study, the 60-69 years age group exhibited the highest prevalence of HE (30.4%), followed by the 50-59 years group (28.6%). Although age alone was not significantly different between diabetic and non-diabetic patients within specific age groups, the combination of advanced age and diabetes markedly heightened the risk. This suggests that age-related physiological declines, such as reduced hepatic regenerative capacity and increased comorbidities, compound the effects of diabetes, necessitating age-specific intervention strategies.

Our analysis of laboratory parameters revealed no significant differences in liver function tests (ALT, AST and total bilirubin) between diabetic and non-diabetic patients, apart from expected differences in blood glucose and HbA1c levels (p<0.001 for both). These findings are consistent with previous studies, who noted that while liver function tests are critical for monitoring cirrhosis, glucose levels and glycemic control are more directly linked to HE risk in diabetic patients . This highlights the importance of maintaining stringent glycemic control in diabetic cirrhotic patients to mitigate HE risk[11,12].

Multivariate logistic regression analysis identified diabetes mellitus (OR 3.12, p = 0.02) and age (OR 1.05, p = 0.04) as significant independent predictors of HE. This reinforces the conclusions drawn by past studies[12-14], who similarly identified diabetes and older age as key risk factors for severe liver disease complications. The identification of these predictors underscores the need for tailored management plans that address both metabolic and age-related factors to prevent HE in cirrhotic patients.

Although diabetic patients had a longer average hospitalization duration (15.8 days) compared to non-diabetic patients (13.2 days), this difference was not statistically significant (p = 0.12). Nevertheless, the

trend towards longer hospital stays in diabetic patients is consistent with past studies , who reported extended hospitalizations for diabetic cirrhotic patients due to more severe disease presentations and complications[15-16]. The slightly higher mortality rate in diabetic patients (17.9% vs. 10.7%) was also not statistically significant (p = 0.43), but it aligns with findings from Singal *et al*., indicating higher mortality in diabetic cirrhotic patients who develop HE .

The findings of this study have significant clinical implications. Given the higher risk and severity of HE in diabetic patients with decompensated cirrhosis, it is crucial for clinicians to implement more rigorous monitoring and management protocols. This includes stringent glycemic control, regular screening for HE and early intervention at the onset of neuropsychiatric symptoms. Furthermore, age-specific approaches should be adopted, particularly for older patients, who are more vulnerable to HE due to compounded age-related physiological declines.

Limitations: This study is not without limitations. The relatively small sample size (56 patients) limits the generalizability of the findings. Additionally, the cross-sectional design precludes causal inferences. Future research should focus on larger, longitudinal studies to further elucidate the causal relationships between diabetes, age and HE in cirrhotic patients. Moreover, including a more diverse population across different geographic regions could enhance the external validity of the findings.

CONCLUSION

In conclusion, our study underscores the significant impact of diabetes mellitus on the risk and severity of hepatic encephalopathy in patients with decompensated cirrhosis. Age also plays a crucial role, with older patients being more susceptible to HE. These findings highlight the necessity for heightened clinical vigilance and tailored management strategies to improve outcomes in this vulnerable patient population. Implementing comprehensive care plans that address both metabolic and age-related factors can significantly reduce the incidence and severity of HE, thereby improving the quality of life and survival rates for these patients.

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