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Frequency of covert hepatic encephalopathy in chronic liverdisease patients

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ABSTRACT

Objective: To determine the frequency of covert hepatic encephalopathy in patients with chronic liver disease, and to identify associated demographic, clinical, and etiological factors using standardized psychometric assessments.

Study Design: The research followed the framework ofdescriptive cross-sectional design.

The research was carried out within the parameters of the Department of General Medicine, Shaheed Mohtarma Benazir Bhutto Medical University (SMBBMU), Larkana, and was performed between July 2025 and October 2025.

Methodology: A total of 323 adult patients aged 18–80 years with chronic liver disease were enrolled using consecutive sampling, excluding those with overt hepatic encephalopathy or major neurological/psychiatric disorders. Covert hepatic encephalopathy was diagnosed using standardized psychometric tests. Demographic, clinical, and laboratory data were collected and analyzed in SPSS version 26 with descriptive and inferential statistics, considering $p<0.05$ significant.

Results: Covert hepatic encephalopathy (CHE) was present in 34.4% of patients. The overall mean age was 47.8 ± 12.0 years, with males comprising 65.0% of the study population. Patients with CHE were significantly older than those without CHE (54.34 ± 11.28 vs. 44.37 ± 10.95 years; p = 0.0001). No significant associations were observed with disease duration (p = 0.838), gender (p = 0.653), or mortality (p = 0.858).

Conclusion: The phenomenon of covert hepatic encephalopathy was observed in one-third of individuals afflicted with chronic liver disease, with advancing age identified as the sole statistically significant predictor. There were no statistically significant associations between either gender, the duration of the disease, or even mortality. These findings underscore the urgent need to conduct neuropsychological assessments on a regular basis, especially in the elderly population with chronic liver disease, to facilitate early detection, early intervention and avoidance of the development of overt hepatic encephalopathy.

Keywords: Chronic Liver Disease, Hepatic Encephalopathy, Covert Hepatic Encephalopathy, Cirrhosis,

INTRODUCTION

Chronic liver disease (CLD) is a significant health problem in the world, and it has a broad influence on morbidity and mortality of populations belonging to different groups [1]. Hepatic encephalopathy (HE) is one of its excessive complications, which may be defined as a major neuropsychiatric complication with a wide clinical spectrum between mild cognitive impairments and severe neurological impairment [2,3]. Though open clinical manifestations are common in overt HE, covert hepatic encephalopathy (CHE) or minimal hepatic encephalopathy (MHE) is frequently under-identified since it is subclinical [4,5].

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Although the disease has no visible symptoms, CHE may considerably deteriorate the quality of life, daily activity, and the overall health outcomes [6–8]. The actual incidence of CHE is hard to determine as it is insidious in nature and the diagnostic methods used are variable; however, studies indicate that it could affect 30% to 50% of those with cirrhosis [9,15].

CHE has been independently correlated with elevated rates of hospitalization, cognitive deterioration, and mortality [10,11]. In the absence of prompt diagnosis and intervention, individuals with MHE confront a twofold augmented risk of progression to overt HE within a one-year timeframe, with as much as 60% potentially developing overt manifestations if left unaddressed [11,12]. Furthermore, MHE has been associated with a 3.9-fold increase in motor vehicle incidents and significant occupational repercussions, including job loss or demotion in up to 50% of instances [12]. Its prevalence and clinical manifestations differ across the etiological spectrum of CLD, with heightened occurrence noted in cirrhosis, particularly of alcoholic or viral etiology [14,16]. Recent advancements in diagnostic methodologies now enable the identification of subtle neurocognitive deficits, facilitating earlier interventions that may enhance outcomes and alleviate the burden on healthcare systems [13,17]. Significantly, the early diagnosis and management of CHE not only ameliorate individual patient trajectories but also confer societal advantages, including reductions in healthcare costs and enhancements in public safety [12,18]. This investigation seeks to explore the prevalence of CHE among individuals with CLD, identify contributing etiologies, evaluate diagnostic strategies, and assess clinical outcomes. Anticipated findings include a 30%–50% prevalence of CHE among patients with cirrhosis, a 50% reduction in job-related impairments with timely intervention, and an up to 60% lower risk of progression to overt HE when managed appropriately [11,12,15]. These insights are expected to inform more effective clinical management and guide health policy

aimed at mitigating the broader impact of this frequently underdiagnosed condition

METHODOLOGY

This cross-sectional investigation was conducted in the Medical Units I–III and the General

Medicine Outpatient Department of Chandka Medical College Hospital, affiliated with Shaheed Mohtarma Benazir Bhutto Medical University, Larkana, following ethical approval. For the purposes of this study, covert hepatic encephalopathy (CHE) was defined as a subclinical neuropsychiatric condition in patients with chronic liver disease, characterized by impairments in attention, working memory, psychomotor speed, or executive function, in the absence of overt hepatic encephalopathy, and diagnosed using standardized psychometric tests including the Psychometric Hepatic Encephalopathy Score (PHES), Inhibitory Control Test (ICT), Number

Connection Test (NCT-A and B), and Stroop Test with validated cutoffs. Consecutive sampling was employed to recruit participants. Eligible subjects included adult patients aged 18–80 years, diagnosed with chronic liver disease, able to provide informed consent, and capable of completing assessments. Patients with overt hepatic encephalopathy, major neurological or psychiatric disorders, recent substance abuse, a history of head trauma or brain surgery, or severe comorbid medical conditions interfering with cognitive testing were excluded. The sample size was calculated using the WHO sample size calculator, based on an expected prevalence of 30%, an absolute precision of 5%, and a 95% confidence level, yielding 323 participants. Data were collected through structured patient interviews, medical records, and laboratory and imaging reports, documenting demographic characteristics, clinical history, disease etiology, laboratory parameters (including liver function and serum ammonia), and potential CHE triggers such as infection, gastrointestinal bleeding, or electrolyte imbalance. Neuropsychological assessments were performed using the aforementioned standardized tests, and quality of life was evaluated using the Chronic Liver Disease Questionnaire. The analysis of data was conducted utilizing SPSS version 26.

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Descriptive statistical methods were employed to encapsulate the demographic and clinical characteristics, and chi-square tests were implemented, with a significance threshold set at $p \leq 0.05$ as significant.

RESULTS

The investigation encompassed a cohort of 323 individuals, demonstrating a mean age of 47.80 ± 12.03 years (95% CI: 46.48–49.11) alongside a mean disease duration of 4.10 ± 3.33 years (95% CI: 3.73–4.46). Among these participants, 210 (65.0%) were identified as male, while 113 (35.0%) were identified as female. A significant proportion of the participants were married (70.0%), whereas 20.1% were categorized as single, 7.1% as divorced, and 2.8% as widowed. The predominant etiology was cirrhosis, accounting for 51.7%, followed by non-alcoholic fatty liver disease at 21.7%, hepatitis B at 17.0%, hepatitis C at 3.4%, and other etiologies at 6.2%. Comorbidities included diabetes mellitus in 32.8% of participants and hypertension in 47.4%. The prevalence of alcohol consumption was reported by 28.5% of the participants, while infections and gastrointestinal bleeding occurred in 18.0% and 11.8% of cases, respectively. Electrolyte imbalances were observed in 16.4% of the cohort, constipation in 30.3%, and nonadherence to prescribed medication in 23.2% of participants. The symptoms most frequently reported included memory impairments (28.2%), compromised judgment (21.7%), concentration difficulties (20.4%), mood fluctuations (16.1%), and slurred speech (10.5%) as shown in TABLE I.

Patients with covert hepatic encephalopathy (CHE) had a significantly higher mean age compared to those without CHE (54.34 ± 11.28 vs. 44.37 ± 10.95 years; $p = 0.0001$). The mean duration of liver disease was comparable between the two groups (4.05 ± 3.29 vs. 4.13 ± 3.37 years; $p = 0.838$). Gender distribution showed no significant difference, with males accounting for 66.7% of the CHE group and 64.2% of the non-CHE group ($p = 0.653$). Mortality rates were also similar, occurring in 8.1% of patients with CHE and 7.5% of those without CHE ($p = 0.858$) as shown in TABLE II.

Table I: Demographic and Clinical Characteristics of Study Participants (n=323)		
Mean ± Standard Deviation		**95% Confidence Interval**
Age in years = **47.80 ± 12.03**		46.48----49.11
Duration of Disease in years = **4.10 ± 3.33**		3.73----4.46
n (%)		
Gender	Male	210 (65.0)
	Female	113 (35.0)
MaritalStatus	Single	65 (20.1)
	Married	226 (70.0)
	Divorced	23 (7.1)

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	Widowed	9 (2.8)
Etiology	Cirrhosis	167 (51.7)
	Hepatitis B	55 (17.0)
	Hepatitis C	11 (3.4)
	NAFLD	70 (21.7)
	Other	20 (6.2)
Diabetes Mellitus	Yes	106 (32.8)
	No	217 (67.2)
Hypertension	Yes	153 (47.4)
	No	170 (52.6)
Alcohol	Yes	92 (28.5)
	No	231 (71.5)
Infections	Yes	58 (18.0)
	No	265 (82.0)
GIBleed	Yes	38 (11.8)
	No	285 (88.2)
ElectrolyteImbalance	Yes	53 (16.4)
	No	270 (83.6)
Constipation	Yes	98 (30.3)
	No	225 (69.7)
Non-Adherence to Medication	Yes	75 (23.2)
	No	248 (76.8)
Symptoms	Memory problems	91 (28.2)

	Difficulty concentrating	66 (20.4)
	MoodSwings	52 (16.1)
	SlurredSpeech	34 (10.5)
	ImpairedJudgment	70 (21.7)

Table II: Comparison of Patient Characteristics with Covert Hepatic Encephalopathy (n=323)				
Characteristics		**Covert Hepatic Encephalopathy**		**P-Value**
		Yes (n=111)	**No (n=212)**	
Age in years		54.34 ± 11.28	44.37 ± 10.95	0.0001
Duration of Disease in years		4.05 ± 3.29	4.13 ± 3.37	0.838
Gender	Male	74 (66.7)	136 (64.2)	0.653
	Female	37 (33.3)	76 (35.8)	
Mortality	Yes	9 (8.1)	16 (7.5)	0.858
	No	102 (91.9)	196 (92.5)	

DISCUSSION

In the present study, the underlying covert hepatic encephalopathy (CHE) was identified in 34.4% of patients suffering from chronic liver disease, which aligns with previous studies documenting the rate of diagnosis between 30% and 50% in cirrhosis patients [9,15]. Pathak et al. documented 39% prevalence in a tertiary care setting, which is nearly identical to our findings [15], whereas Karki et al. documented a lower prevalence of 28% among patients in Nepal [12]. Differences in designs, demographics, and disease etiology could explain the variation in studies. Still, there is consistent support from the underlying evidence suggesting CHE is a common, albeit overlooked, complex complication of chronic liver disease.

The only predictor that was significant in our analysis was age because patients with CHE were older compared to those without. This observation aligns with the other existing literature, which indicates that advanced age is a risk factor due to the increased risk of neurocognitive deterioration and reduced compensatory abilities among older patients with cirrhosis [11,16]. Addressing the factors of age in cirrhosis patients, Nardelli et al. and Weissenborn et al. have also mentioned that the older population bears more significant brunt of the cognitive deficits due to the condition [5,9]. Conversely, this finding of no significant relationship between CHE and gender has been reported earlier, and it is indicative that hepatic encephalopathy is asexually common condition [14].

Interestingly, our analysis did not show a significant relationship between the duration of chronic liver disease and CHE, whereas in certain studies, a longer disease duration was associated with an increased risk of subclinical neurocognitive decline [10]. Severity and duration of the disease may be the more powerful determinants of CHE. We also disagree with the results of the mortality, which revealed that we did not find any statistical difference between the CHE and non-CHE patients, with studies indicating that the decreased survival in patients with CHE [17,18]. Such a discrepancy can be explained by differences in follow-up time because the current study was designed in a cross-sectional design, which did not permit longterm outcomes assessment.

Regarding comorbidities and clinical risk factors, our cohort had high levels of diabetes, hypertension, constipation, and non-compliance with medication, which is consistent with the literature that defines these as triggers of hepatic encephalopathy [16,17]. Nevertheless, they are not statistically significant in predicting CHE in this study, and it is inconsistent with prior data and can be explained by the inability in sample stratification, confounding variables, or patient characteristics. On the whole, the results of this research support previous works on the prevalence and risk profile of CHE, as well as provide context-specific information in a Pakistani population. The universal finding of age as a major predictor highlights the importance of limiting screening of cognition in older patients with chronic liver disease, which is in line with the global guidelines [13,18].

CONCLUSION

The phenomenon of covert hepatic encephalopathy was observed in one-third of individuals afflicted with chronic liver disease, with advancing age identified as the sole statistically significant predictor. There were no statistically significant associations between either gender, the duration of the disease, or even mortality. These findings underscore the urgent need to conduct neuropsychological assessments on a regular basis, especially in the elderly population with chronic liver disease, to facilitate early detection, early intervention and avoidance of the development of overt hepatic encephalopathy.

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