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Original Article

Frequency of Hyponatremia among Patients with Chronic Liver Disease

Mian Saleem Shah,[1] Pervaiz Muhammad,[2] Muhammad Tariq,[3] Arbab Muhammad Kashif Khan,[4] Seher Obaid,[5] Muhammad Aasim Khan[6]

[1]Mercy Teaching Hospital, Peshawar, Pakistan, [2]Jinnah Medical College, Peshawar, Pakistan, [3]Jinnah Teaching Hospital, Peshawar, Pakistan, [4]Peshawar Medical College, Peshawar, Pakistan, [5]Northwest School of Medicine, Peshawar, Pakistan, [6]Medical Teaching Institution, Gajju Khan Medical College Swabi, Pakistan

Abstract

Objective: Chronic liver disease poses a significant global health challenge, particularly in regions like Pakistan, where it is a major cause of morbidity and mortality. Hyponatremia, a common complication of advanced liver disease, has been associated with severe clinical outcomes. This study aims to investigate the frequency of hyponatremia among patients with chronic liver disease, providing local insights into its prevalence and associated factors.

Methods: The research, carried out in the Department of Medicine, Khyber Teaching Hospital, Peshawar, used a cross-sectional and descriptive design for a duration of six months, starting from February 25, 2017, and ending on August 25, 2017. Detailed history and examinations, along with Child-Pugh Scores, were employed to assess liver disease severity. Blood samples, collected under strict aseptic conditions, were analyzed for hyponatremia by a pathologist. Strict exclusion criteria were implemented to enhance result reliability.

Results: Among the 130 patients, with a mean age of 38 years and a male predominance (68%), hyponatremia was observed in 65% of cases. The distribution across age groups, gender, duration of chronic liver disease, Child-Pugh class, and hepatic encephalopathy did not exhibit statistically significant variations in hyponatremia prevalence ($p > 0.05$). Notably, the study identified a substantial proportion of patients with moderate liver disease severity (Child-Pugh Class B - 59%).

Conclusion: This study concludes that hyponatremia is a prevalent complication in patients with chronic liver disease, affecting most cases in the studied population. The lack of significant associations with demographic and clinical factors ($p > 0.05$) suggests the complexity of hyponatremia's interplay in this context. While aligning with some literature, disparities emphasize the need for nuanced interpretations and ongoing research to unravel the intricacies of hyponatremia in chronic liver disease.

Keywords: Hyponatremia, Chronic liver disease, Child-Pugh class, Hepatic encephalopathy, Cross-sectional study, Disease severity.

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Corresponding Author: Dr. Muhammad Aasim Khan **Email:** drasimyousafzy@gmail.com

Introduction

Chronic liver disease is a significant worldwide health problem that presents a serious risk to both mortality and morbidity.[1,2] Its influence reverberates across many communities, with the Pakistani demography facing a tremendous load. Chronic liver disease, which affects around 10-20% of patients within 5-30 years of infection, is a significant cause of hospital admissions.[3] In this region, viral hepatitis (HCV & HBV) is the primary factor leading to this condition, distinguishing it from Western countries where alcohol-related liver damage is more common.[4,5]

Hyponatremia is a common complication that arises in the latter stages of chronic liver disease, within its complex landscape.[6] The complex interaction between diminished kidney function and the retention of water without solutes leads to an excessive rise in water levels compared to sodium, causing a decrease in the concen-

tration of sodium in the blood and lower osmolality.[6]

Although individuals without liver illness may encounter low levels of salt in their blood and the resulting neurological symptoms, the range of symptoms in those with chronic liver disease is different and unique. Individuals with low blood sodium levels see a significant increase in the severity of ascites and hepatic encephalopathy.[7,8] Importantly, the speed at which serum sodium decreases, rather than the actual amount of decrease, is identified as a critical factor in determining the severity of neurological symptoms. Neurological symptoms are more common in cases of acute hyponatremia than in cases of chronic hyponatremia.[9]

When analysing clinical connections, it has been shown that people with low levels of salt in their blood have a greater occurrence of severe fluid buildup in the abdomen (ascites) and an increased likelihood of experiencing brain dysfunction due to liver disease (hepatic encephalopathy).[10] Moreover, the likelihood of experiencing problems such as spontaneous bacterial peritonitis (SBP) is affected by the levels of salt in the blood, which may vary significantly depending on the concentration range. Individuals with blood sodium levels below 130 mmol/L are at a much higher risk of experiencing problems.[11]

In the setting of chronic liver disease, the presence of persistent ascites, severe hyponatremia, and reduced arterial pressure are clinical signs that suggest late stages.[12] The presence of these symptoms is caused by increased levels of renin and aldosterone in the bloodstream, which are a result of portal hypertension, impaired responsiveness of blood vessels to vasoactive medications, and decreased ability to eliminate water without solutes.[13]

The primary objective of the present investigation is to determine the prevalence of hyponatremia in individuals suffering from chronic liver disease, with a specific emphasis on those who exhibit various consequences.

Methods

The study was carried out in the Department of Medicine at Khyber Teaching Hospital, Peshawar. It used a cross-sectional (descriptive) study design for a duration of 6 months, starting from February 25, 2017, and ending on August 25, 2017. The study included 130 patients, estimated using WHO software for sample size estimation. The sample size was based on a 20.8% percentage of hyponatremia, a 95% confidence interval, and a 7% margin of error. The sample approach used was non-probability consecutive sampling.

The inclusion criteria consisted of patients with chronic liver disease who showed ultrasonographic abnormalities. This included both males and females between the ages of 13 and 70 years. The exclusion criteria of the study included patients with concomitant chronic renal failure undergoing haemodialysis, acute fulminant hepatitis, and individuals with co-morbid conditions such as diabetes (fasting blood glucose > 136mg/dl), diabetic nephropathy, on diuretics, and hypertension (Blood Pressure > 140/90mmHg). These conditions were excluded to prevent them from acting as confounders and introducing bias into the study results.

Data collection began after receiving clearance from the hospital's ethics and scientific council. All eligible patients who met the specified criteria for inclusion were enrolled in the study, and the diagnosis of liver disease was determined using pre-established operational definitions. Prior to the trial, patients were provided with a detailed explanation of the study's objectives and advantages, and their permission was acquired based on this information.

Patients had comprehensive medical history and examination, and the severity of liver disease was evaluated using Child-Pugh Scores. 5 cc blood samples were collected using aseptic techniques and promptly delivered to the hospital laboratory. The measurement of hyponatremia was conducted under the supervision of a pathologist who is associated with CPSP. The research Performa documented patient information, such as name, age, gender, and address. The research outcomes were controlled for confounders and bias by using rigorous exclusion criteria.

The process of data analysis included inputting the gathered data into SPSS 16. Calculations were performed to determine the mean and standard deviation of continuous variables, namely age and duration of chronic liver disease. The frequencies and percentages of categorical factors such as gender, Child-Pugh class, hepatic encephalopathy, and hyponatremia were calculated. The occurrence of hyponatremia was categorised based on age, gender, length of chronic liver illness, Child-Pugh class, and hepatic encephalopathy to find factors that might modify its effects. Post-stratification chi-square tests were used, with a significance threshold of $P < 0.05$. Data was shown using tabular and graphical representations.

Results

Table 1 displays the demographic characteristics and clinical factors of individuals suffering from chronic liver disease. The age distribution has a diverse representation, with the majority concentrated in the 51-60 years age bracket (25%), closely followed by the 61-70 years age bracket (27%). The gender distribution indicates a greater frequency among men, comprising 68% of the population under study.

A significant percentage of patients (60%) reported having chronic liver disease for a length of 5 years or less, while the remaining 40% had been affected by the ailment for over 5 years. The distribution across Child Pugh classes demonstrates a substantial prevalence of Class B (59%), indicating the moderate severity of liver disease in the analysed group.

Hepatic encephalopathy is classified into several categories, with Grade II being the most prevalent (40%), followed by Grade III (27%). Grade IV, which indicates severe encephalopathy, is present in 15% of cases. The last characteristic, hyponatremia, is present in a significant majority of patients (65%), highlighting its importance in the setting of chronic liver disease.

Table 1: *Demographic Characteristics and Clinical Parameters of Patients*

Parameter	Detail	Frequency	Percentage
Age Group	20-30 years	13	10
	31-40 years	23	18
	41-50 years	26	20
	51-60 years	33	25
	61-70 years	35	27
Gender	Male	88	68
	Female	42	32
Chronic Liver Disease	≤ 5 years	78	60
	> 5 years	52	40
Child PUGH class	Class A	23	18
	Class B	77	59
	Class C	30	23
Hepatic encephalopathy	Grade I	23	18
	Grade II	52	40
	Grade III	35	27
	Grade IV	20	15
Hyponatremia	Yes	85	65
	No	45	35

Table 2 displays the link between the prevalence of hyponatremia and several demographic and clinical factors in individuals suffering from chronic liver disease. The p-values are given to evaluate the statistical significance of these connections.

The prevalence of hyponatremia does not vary significantly across various age groups, as shown by the p-value of 0.9979. Similarly, there is no substantial correlation between gender and hyponatremia, as shown by a p-value of 0.855.

There is no notable disparity in the occurrence of hyponatremia between individuals with chronic liver illness lasting less than 5 years and those with a duration beyond 5 years (p-value = 1.000).

The Child-Pugh class, which is used to assess the severity of liver disease, did not demonstrate a significant link with hyponatremia (p-value = 0.9856). The different degrees of hepatic encephalopathy have p-values ranging from 0.999 to 0.9856, indicating no statistically significant correlation.

Table 2: *Correlation Between Hyponatremia and Demographic/Clinical Parameters*

Parameter	Detail	Hyponatremia		Parameter
		Yes	No	
Age Group	20-30 years	9	4	
	31-40 years	15	8	
	41-50 years	17	9	0.9979
	51-60 years	21	12	
	61-70 years	23	12	
Gender	Male	58	30	0.855
	Female	27	15	
Chronic liver disease	<5 Years	51	27	1.000
	> 5 Years	34	18	
Child-PUGH class	Class A	15	8	
	Class B	50	27	0.9856
	Class C	20	10	
Encephalopathy	Grade I	15	8	
	Grade II	34	18	0.999
	Grade III	23	12	
	Grade IV	13	7	

Discussion

The primary objective of this research was to examine the prevalence of hyponatremia in individuals suffering from chronic liver disease, while also exploring the demographic and clinical variables linked to this problem. The results of our study indicate a substantial occurrence of hyponatremia, with 65% of individuals displaying this electrolyte disturbance. The average age of the study population was 38 years, with a higher proportion of males (68%). The distribution of hyponatremia did not show any statistically significant changes across various age groups or genders. Similarly, there were no significant correlations found between the length of chronic liver illness, as determined by Child-Pugh class the presence of hepatic encephalopathy, and the occurrence of hyponatremia.

Upon comparing our findings with the current body of research, we have discovered that the incidence of hyponatremia is consistent with studies that have shown a significant occurrence of this complication in individuals suffering from chronic liver disease. Research conducted by Shafiq et al. (2008) found that the preva-

lence among cirrhotic patients was 67%, which is like other reported rates.[14] Conversely, research conducted by Negro et al. (2020) and Filippatos et al. (2017) indicated lower rates of occurrence at 43% and 52%, respectively.[15,16] The observed discrepancies may arise due to disparities in sample characteristics, research methodologies, and geographical variables.

Our research differs with the findings of Filippatos et al. (2017) when it comes to age-related patterns. They showed a greater occurrence of hyponatremia in older individuals, whereas our study presents contrasting results. This disparity highlights the intricate connection between age and hyponatremia, indicating the need for more investigation.[16] The results of Zhang and Li. (2020) are consistent with gender-based studies since they likewise found no significant variations in the prevalence of hyponatremia between genders.[17]

In our investigation, we did not detect any connection between hyponatremia and the length of chronic liver disease. This contradicts the results of a meta-analysis conducted by Boyer et al., (2019), which indicated an elevated risk of hyponatremia as the illness progresses. The divergent outcomes highlight the intricate interaction of several variables that influence hyponatremia in individuals with chronic liver disease.[18]

Our study's analysis of Child-Pugh class and hepatic encephalopathy reveals that the relationships observed are not statistically significant. These findings align with the results reported in studies conducted by Al Kaabi et al., (2023) and Wang et al. (2023).[19,20] Nevertheless, Bustamante et al. (2013) conducted research that revealed a noteworthy association between hyponatremia and Child-Pugh class. The presence of these discrepancies emphasises the complex and diverse characteristics of hyponatremia in chronic liver illness, which are driven by complicated relationships between hepatic dysfunction, fluid dynamics, and neurohormonal responses.

Limitations

Although this work has provided helpful insights, it is important to understand its limits. The study done at Khyber Teaching Hospital, Peshawar, has a limitation in terms of its single-centre character, which may restrict the applicability of the results to larger populations with chronic liver disease. Furthermore, the use of a cross-sectional design in this research offers a momentary representation of the incidence of hyponatremia, but it impedes the ability to establish causal linkages or evaluate temporal patterns. Finally, the relatively small sample size of 130 patients may affect the statistical strength and accuracy of our findings. Therefore, it is important to exercise care when applying our results to larger groups.

Conclusion

Our work provides significant insights into the prevalence of hyponatremia in individuals with chronic liver disease. While conforming to certain literary works, discrepancies underscore the need for a thorough comprehension and contextual analysis. Further investigation is needed to understand the complex relationship between age, gender, illness duration, and disease severity in the context of hyponatremia. The significance of personalised patient evaluations and continuous research to clarify the intricacies of hyponatremia in the setting of chronic liver illness is emphasised by our discoveries.

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