HYPONATREMIA IN PATIENTS WITH TUBERCULOUS MENINGITIS: A CLINICAL OVERVIEW

Husnain Ahmed[1], Muhammad Ishfaq[2], Alvina Ahmed[3], Filza Ajmal[4], Iman Aly[5], Afsheen Mehmood[6]

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[1]Postgraduate Trainee, Department of Medicine, Hayatabad Medical Complex, Peshawar
[3]Postgraduate Trainee, Department of Medicine, Hayatabad Medical Complex, Peshawar
[4]Postgraduate Trainee, Department of Medicine, Hayatabad Medical Complex, Peshawar
[5]Postgraduate Trainee, Department of Medicine, Hayatabad Medical Complex, Peshawar
[6]Associate Professor, Khyber Girls Medical College, Peshawar

Correspondence

[2]Muhammad Ishfaq, Associate Professor, Department of Medicine, Hayatabad Medical Complex, Peshawar
: +92-333-9005472
: dashfaq@gmail.com

ABSTRACT

OBJECTIVES

This study aims to determine the frequency of hyponatraemia in patients suffering from tuberculous meningitis in a tertiary care hospital.

METHODOLOGY

A cross-sectional study was conducted from January to June 2024 at the Department of Medicine, Hayatabad Medical Complex, Peshawar. We conducted this study on 219 patients. Presenting with tuberculous meningitis, having an age between 18 to 60 years of either gender. Patients with bipolar affective disorder, posttraumatic stress, lung carcinoma, hypothyroidism, or hyperthyroidism and pregnant women were excluded. The frequency of hyponatraemia was determined.

RESULTS

This study was conducted on 219 patients presenting with tuberculous meningitis. The mean age of the study patients was 42.41 ± 11.38 years. The frequency of hyponatremia in our study was 75 (34.2%). Stratification of hyponatremia with age, gender, diabetes, hypertension and duration of disease was not significant with a p-value> 0.05.

CONCLUSION

Hyponatremia is a fairly common occurrence in Tuberculous meningitis patients, and its early detection and management are crucial to patient management.

KEYWORDS: *Hyponatremia, Tuberculous meningitis, Tertiary Care hospital, Central Nervous System*

INTRODUCTION

Tuberculosis is a leading cause of infection-related mortality worldwide. The most typical type of CNS tuberculosis is tuberculous meningitis (TBM). The most frequent electrolyte abnormality seen in TBM patients who have been admitted is hyponatraemia.[1] There is a significant link between sodium problems and morbidity and mortality. Before any treatment intervention, the differential diagnosis of hyponatraemia must be considered because of its high prevalence and associated neurological limitations.[1] The main mechanism for hyponatraemia in CNS infection is SIADH (syndrome of inappropriate antidiuretic hormone secretion); however, there are other potential causes as well. Cerebral salt wasting syndrome (CSWS) is considered an alternative mechanism.[2] Due to the enhancement of renal water retention by antidiuretic hormone, SIADH lead to volume expansion. Following renal salt depletion, CSWS is characterized by a reduction in effective arterial blood volume.[3] It is still uncertain what the exact mechanism is that causes cerebral salt-wasting syndrome. It has been linked to natriuretic peptides, such as brain natriuretic peptides and C-type natriuretic peptides. The pathophysiology of SIADH is associated with injury to hypothalamus cells that result in ADH leakage into the bloodstream.[4] The osmoreceptors in the hypothalamus are reset as part of another pathway. A clinician should be able to distinguish between SIADH and CSWS because both have the same incidence of hyponatremia. Moreover, it is significant because these two disorders have similar environmental influences.[5] In cases of tuberculous meningitis (TBM), a study observed that among patients with hyponatremia, 50% were attributed to cerebral salt wasting (CSW), and 8.82% were related to the syndrome of inappropriate antidiuretic hormone secretion (SIADH).[6] Additionally, another study reported that 40 % of patients with TBM had hyponatremia.[7] Severe hyponatremia may lead to complications like lethargy, seizure, and coma due to brain edema.[8] There is a notable scarcity of literature

available on the rate of hyponatremia in tuberculosis meningitis (TBM) cases in Pakistan. Hence, this study aims to determine the frequency of hyponatremia among TBM patients in our local healthcare setting. By analyzing the data collected, this study aimed to fill the existing knowledge gap. The results of this study will not only contribute to the existing body of research but will also be instrumental in facilitating the timely diagnosis of hyponatremia in TBM patients. Early detection and appropriate management of hyponatremia can play a crucial role in preventing adverse outcomes and improving the overall prognosis of TBM patients. In a recent large cohort study, moderate to profound hyponatremia was associated with significantly high mortality and hence required more intense medical care.[9] Consequently, this research holds significant potential for enhancing clinical practice and patient care in our region.

METHODOLOGY

This cross-sectional study was conducted at the Department of Medicine, Hayatabad Medical Complex Peshawar. The study spanned six months, from January to June 2024. It was a cross-sectional study. The sample size was calculated using the WHO calculator, with a 40% frequency of hyponatraemia in patients with tuberculous meningitis, a 6.5% margin of error, and a 95% confidence level. The sample consisted of 219 patients, who were selected using the non-probability consecutive sampling technique. The study included patients with tuberculous meningitis of both genders, aged 18 to 70. World Health Organization (WHO) criteria for the diagnosis of tuberculous meningitis (TBM) is made if any two or more of the following clinical characteristics are observed within one week: a fever of 99°F or higher persisting for more than one week; a headache with a visual analogue scale (VAS) score of 6 or higher for at least three hours a day for over a week, where 0 represents no pain and 10 indicates the most severe pain; or vomiting for at least three times daily for up to three successive days. In addition to these symptoms, any of the following laboratory results are considered indicative of TBM: a positive acid-fast bacilli (AFB) smear on cerebrospinal fluid (CSF), a positive AFB culture on CSF, elevated protein levels in the CSF (greater than 100 mg/dl), or low glucose levels in the CSF (less than 60% of the plasma level), measured simultaneously with the CSF assessment. A blood test diagnosed hyponatraemia when the serum sodium level was less than 130 mEq/L. Patients with bipolar affective disorders, posttraumatic stress, lung carcinoma, hypothyroidism or hyperthyroidism, and pregnant women were excluded. These patients may be using certain drugs that can affect their sodium levels. Pregnancy causes physiological changes in fluid balance and sodium regulation, which can influence sodium levels. Upon receiving approval, data collection commenced following authorization by the hospital ethics committee. All patients meeting the inclusion criteria were enrolled, and informed consent was obtained from all participants. Demographic information, medical history, and physical examination findings were documented for each patient. Data was recorded using a predetermined proforma and analyzed with SPSS v.23 software. Numerical variables, such as age and disease duration, were presented as mean ± standard deviation. In contrast, categorical variables, including gender, hyponatremia, diabetes, hypertension, and residence area, were presented as frequencies and percentages. Hyponatremia was categorized according to age, gender, presence of diabetes, hypertension status, and residential areas to determine potential effect modifiers. A post-stratification chi-square test was applied.

RESULTS

This study included 219 patients who presented with tuberculous meningitis. The study population's mean age was 42.41 ± 11.38 years, and the mean duration of the disease was 3.95 ± 1.98 days. The age distribution of the patients in our study was as follows: 18 to 30 years (40 patients, 18.3%), 31 to 40 years (44 patients, 20.1%), 41 to 50 years (73 patients, 33.3%), and 51 to 60 years (62 patients, 28.3%). Regarding gender distribution, the study included 119 male patients (54.3%) and 100 female patients (45.7%). The frequency of hyponatraemia in our study was 75 (34.2%) (Table 1). The frequency of diabetes in our study was 29 (13.2%). The frequency of hypertension in our study was 19 (8.7%). According to the residence area, there were 126 (57.5%) patients from rural areas, and 93 (42.5%) patients were from urban areas. Hyponatremia in tuberculous meningitis patients showed no significant association with age, gender, diabetes, hypertension, or disease duration ($p > 0.05$). Although more frequent in males, non-diabetics, and those with shorter disease duration, these differences were not statistically significant. Figure 1;

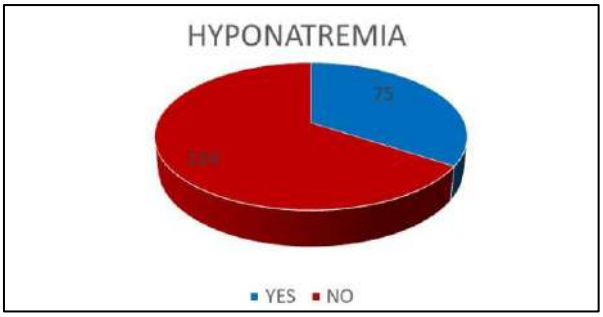

Figure 1: Frequency of Hyponatremia

Table 2: Stratification of Hyponatremia with Age Distribution, Gender, Diabetes, Hypertension and Duration of Disease

	Age Distribution				Gender		Diabetes		Hypertension		Duration of Disease	
Hyponatremia	18 to 30 years	31 to 40 years	41 to 50 years	51 to 60 years	Male	Female	Yes	No	Yes	No	1-5 days	>5 days
Yes	12	18	28	17	43	32	12	63	8	67	55	20
No	28	26	45	45	76	68	17	127	11	133	106	38
Total	40	44	73	62	119	100	29	190	1	200	161	58
P-Value	0.38				0.52		0.38		0.45		0.96	

DISCUSSION

Tuberculosis (TB) remains a significant global health concern, ranking among the top infectious diseases in terms of morbidity and mortality. According to the World Health Organisation's Global TB Report, approximately 10.8 million people were affected by tuberculosis (TB) in 2023. Within the category of extrapulmonary TB, central nervous system (CNS) tuberculosis is identified as the second most prevalent form of the disease.[9,10] TBM is the most common presentation of CNS tuberculosis.[11] Hyponatraemia is the most common electrolyte irregularity observed in admitted patients with TBM. Significant morbidity and mortality are associated with sodium disorders.[7] Considering the high prevalence and potential for neurological complications, it is crucial to evaluate the differential diagnosis of hyponatremia before commencing any therapeutic interventions. Hyponatremia can arise from multiple mechanisms, such as the syndrome of inappropriate antidiuretic hormone secretion (SIADH) and cerebral salt wasting (CSW). This condition has the potential to cause significant neurological impairments. In our study, the frequency of hyponatraemia in TBM patients was 34.2%, indicating that it's a relatively common electrolyte abnormality in TBM patients. This is consistent with the reported prevalence of 30-50% of TBM patients, emphasizing its clinical significance. A hospital-based prospective study involving 76 patients with tuberculous meningitis (TBM) found that 34 patients (44.7%) had hyponatraemia. Further analysis revealed that hyponatraemia was attributed to cerebral salt wasting in 17 cases, the syndrome of inappropriate secretion of antidiuretic hormone in 3 cases, and other miscellaneous causes in 14 cases.[6] The prevalence of hyponatraemia was higher in the 41-50 years age group (38.4%); however, the association between the age group and hyponatraemia was not significant, indicating that age alone is not a factor in causing hyponatraemia in TBM. The high frequency in middle-aged groups could be due to disease severity. A retrospective analysis by Xaiolin and colleagues found that hyponatraemia is more common in older people with TBM.[12] Hyponatremia exhibited a marginally higher prevalence in males compared to females; however, this difference was not statistically significant. The male predominance could be due to a potential difference in disease severity among genders. Similarly, patients with diabetes and hypertension have a higher prevalence of hyponatraemia, which could be attributed to renal involvement or vascular complications in these diseases. Diabetes can lead to hyponatraemia by the dilutional effect of glycosuria. Thus, results can be misleading.[13] Wasay et al. found that patients with hypertension are more likely to experience cerebral infarction and, therefore, can lead to altered sodium homeostasis in TBM patients.[14] Similarly, hyponatremia has been reported in cirrhotic patients, and its correlation with severity of hepatic encephalopathy has been documented.[15,16] Frequency of hyponatraemia was also more common in those patients who presented earlier. The study highlights the importance of early sodium monitoring in TBM patients. Electrolyte management is essential in such patients as hyponatraemia develops in 30% of cases.[17,18] The two most common causes of hyponatraemia are SIADH and CSWS, so for appropriate management, differentiated theses are essential. CSWS is a significant issue affecting children.

LIMITATIONS

While the study provides valuable information, some limitations need to be addressed. Firstly, there is a lack of differentiation between the Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) and Cerebral Salt-Wasting Syndrome (CSWS). Further research, including detailed investigations such as urine osmolality and urine sodium measurements, would be essential to distinguish between these two conditions. This differentiation is crucial as it impacts the management and treatment strategies for patients. Secondly, it is crucial to stratify hyponatremia assessment based on the severity of tuberculosis meningitis (TBM). Analyzing the severity of TBM in conjunction with hyponatremia levels would provide deeper insights into the correlation between the two conditions. This stratification could help identify patterns and outcomes associated with varying degrees of TBM severity. By addressing these limitations, future studies can enhance the understanding and management of hyponatremia in TBM patients, leading to improved patient care and outcomes.

CONCLUSIONS

Because hyponatraemia is so common in TBM patients

(34.2%) and can lead to serious problems, all TBM cases, no matter what their age, gender, or other health issues, should have their blood sodium levels checked as part of the standard diagnostic and therapeutic protocols. To stop neurological decline and enhance patient outcomes, it is important to find and fix hyponatraemia as soon as possible. Also, doctors should learn how to spot and treat the numerous causes of hyponatraemia, such as SIADH and cerebral salt wasting, so that they can give the right medication.

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AUTHORS CONTRIBUTION

Husnain Ahmed - *Concept & Design; Data Acquisition; Data Data Analysis/Interpretation: Drafting Manuscript; Critical Revision; Supervision; Final Approval*

Muhammad Ishfaq- *Concept & Design; Data Acquisition; Data Analysis/Interpretation; Drafting Manuscript; Critical Revision; Supervision; Final Approval*

Alvina Ahmed – *Concept & Design; Data Acquisition; Data Analysis/Interpretation; Drafting Manuscript; Critical Revision; Supervision; Final Approval*

Filza Ajmal - *Concept & Design; Data Acquisition; Data Analysis/Interpretation; Drafting Manuscript; Critical Revision Final Approval*

Iman Aly - *Concept & Design; Data Acquisition; Data Analysis/Interpretation; Drafting Manuscript; Final Approval*

Afsheen Mehmood - *Concept & Design; Data Acquisition; Data Analysis/Interpretation; Drafting Manuscript; Critical Revision; Supervision; Final Approval*

The authors accept responsibility for all aspects of the work and will ensure that any concerns regarding the accuracy or integrity of any part are properly investigated and resolved.