ISSN 2515-8260 Volume 09, Issue 07, 2022

A STUDY OF ELECTROLYTE DISTURBANCE IN PATIENTS WITH TUBERCULAR MENINGITIS IN CENTRAL RAJASTHAN

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Abstract

Hyponatremia is the most common, electrolyte abnormality out of all in critically ill neurological patients. TBM is a common cause of sub-acute and chronic meningitis in developing countries like India. It is an important cause of stroke in young individuals in India. Hyponatremia in TBM is multifactorial and may be due to anorexia, nausea, vomiting, poor intake of sodium, diarrhoea, drugs and associated comorbidities.

Method: This study was a six-month cross-sectional study of consenting patients admitted with a diagnosis of TBM at our hospital. Patients were labelled as having hyponatremia, SIADH and CSWS as per operational definitions. The findings were noted in the Performa along with other demographic Patients were classified as per BMRC stage I/II/III and duration of symptoms.

Results: A total of 135 patients were admitted with the diagnosis of Tubercular Meningitis. Out of 135 patients with TBM, 48.88% (n=66) had hyponatremia. It was found that 13.33% (n=29) had SIADH and 19.26% (n=37) had CSWS. The age range of the patients was from 22 years to 60 years with mean age of 43.78±2.64. There were 61.48% (n=83) male and 38.51% (n=52) were female. Maximum number of patients were in age group 51 – 60 years with 31.19% (n=42). The most common presenting complaint of the patients was fever

followed by headache, vomiting, and altered sensorium. It is observed that occurrence of hyponatremia was not dependent on age group (p-value=0.47), gender (p-value=0.106) and Grade of disease (p-value=0.188). CONCLUSION: Electrolyte disturbance adds to morbidity and mortality in TBM patients. It is thus important to investigate serum electrolytes early in such patients and to differentiate the cause of hyponatremia., so that electrolyte imbalance can be detected early and proper management can be initiated to prevent morbidity and mortality due to electrolyte imbalance.

Introduction

The human body is 60–70% water. Water in human body is divided into two major compartments, extracellular compartment which makes 1/3 and intracellular which makes 2/3 of total body water. Sodium is the major electrolyte, which normally ranges between 135 and 145 mEq/L. Hyponatremia is defined as a serum sodium of <135 mEq/L and is the commonest electrolyte abnormality occurring in 3–35% of hospitalized patients. [1]. Hyponatremia is a disorder of water balance. The severity of hyponatremia has been categorized as mild (130–134mEq/L), moderate (120–129 mEq/L) and severe (<120 mEq/L)[2], and serum sodium <125 mEq/L is regarded as an independent predictor of mortality, especially in critically ill patients. In a review of hospitalized patients with hyponatremia, mortality increases by 1.5–60 times in the patients with hyponatremia compared to controls [3].

Tuberculosis is a common infectious disease in developing countries. Central nervous system tuberculosis (CNS TB) is the most severe form of TB and accounts for approximately 5%‑10% of all extrapulmonary cases and around 1% of all TB cases. [4] Considering that a diagnosis of TBM is difficult to ascertain and, therefore, the incidence rate might be underestimated, the global burden of TBM is estimated to be at least 100,000 cases per year [5]. TBM is the most lethal form of tuberculosis, resulting in death or severe disability in around 50% of the affected patients [6].

Electrolyte imbalance is frequently seen in patients with CNS disorders in ICU. Hyponatremia is the most common, electrolyte abnormality out of all in critically ill neurological patients. Amongst the central nervous system disorders, hyponatremia is commonly noted in subarachnoid haemorrhage, encephalitis, meningitis, and head injury. Hyponatremia may also be due to recurrent vomiting, diarrhoea, nutritional deficiency and drug toxicity such as osmotic agents, diuretics and carbamazepine. Cerebral salt wasting (CSW) was first reported in 1950. In majority of neurological patients, hyponatremia with normal renal functions was attributed to the syndrome of inappropriate secretion

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of antidiuretic hormone (SIADH) which was described seven years later than CSW. CSW was reintroduced to the medical literature by Nelson et al. in 1981 [7]. Subsequently, there are several reports of CSW as a cause of hyponatremia in neurological patients [7-9]. CSW has been reported to be more common than SIADH in some studies [10].

TBM is a common cause of sub acute and chronic meningitis in developing countries like India. It is an important cause of stroke in young individuals in India. Hyponatremia in TBM is multifactorial and may be due to anorexia, nausea, vomiting, poor intake of sodium, diarrhea, drugs (diuretic, osmotic agents, carbamazepine, oxcarbazepine) and associated comorbidities.

Material and Methods

This study was a six-month cross-sectional study of consenting patients admitted with a diagnosis of TBM at the Department of Internal Medicine, JLN Medical college and associated group of hospitals, Ajmer, Rajasthan. Revevent permission was taken from the ethical and research committee. The patients were enrolled as per the inclusion and exclusion criteria.

Inclusion Criteria

1. All patients of either sex aged 18 to 60 years who presented to the department with signs and symptoms of tubercular meningitis.

Exclusion Criteria

1. Patients who did not provide written informed consent.
2. Patient with history of other chronic diseases which may affect body electrolyte levels like lung carcinoma, hypothyroidism or hyperthyroidism, Addison's disease, head trauma, multiple sclerosis, asthma, renal impairment, congestive heart failure, myocardial infarction, and chronic liver disease.

A brief history of the duration of illness and demographic information was taken from each patient and confirmed by an attendant. Blood samples were drawn and sent for the measurement of all routine blood investigations including serum urea, electrolytes, thyroid function tests, and urinary sodium at the time of admission. Patients were labelled as having hyponatremia, SIADH and CSWS as per operational definitions. The findings were noted in the Performa along with other demographic characteristics. The TBM was graded as per BMRC (British Medical Research Council Contemporary Clinical Criteria for TBM) in stage I/II/III and duration of symptoms.

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Diagnostic criteria for TBM

1. Clinical features - if presenting with any two or more of the clinical features in one week: Fever ≥ 99°F occurring about at least 6 hours/day for more than one week, headache dull in nature persisting, on VAS (visual analog scale) ≥ 6 for at least three hours/day per day for more than one week or history of contact with TB patient in last two years.
2. Laboratory data - positive acid-fast bacilli (AFB) smear on cerebrospinal fluid (CSF), positive AFB culture on CSF, CSF pleocytosis (20-500 lymphocytes per cubic mm) with increased CSF protein ≥ 100 mg/dl and decreased CSF glucose concentration <60% of corresponding plasma level checked at the same time as CSF examined.

Patients having serum sodium level ≤135 mEq/L were labeled as having hyponatremia. Patients with hyponatremia was evaluated for the etiology of hyponatremia and patients was labeled as having SIADH or CSWS based on following criteria

1. The volume status; Euvolemia (absence of supine heart rate more than 100 and systolic BP less than 100 mmHg) was labeled SIADH and hypovolemia (presence of supine heart rate more than 100 and systolic BP less than 100 mm Hg) was labeled as CSWS, plus having any two or more of the following:
    i. Plasma sodium concentration ≤135 mmol/L,
    ii. Plasma osmolality ≤280 mOsmol/kg,
    iii. Urine osmolality ≥100 mOsmol/kg,
    iv. Urinary sodium concentration ≥30mmol/L,
    v. absence of clinical or biochemical features of adrenal and thyroid dysfunction or no history of diuretic use within the past three months.

RESULTS

During the study period, a total of 135 patients were admitted with the diagnosis of Tubercular Meningitis satisfying the inclusion criteria. The age range of the patients was from 22 years to 60 years with mean age of 43.78±2.64. In terms of gender distribution 61.48% (n=83) of our patients were male and 38.51% (n=52) were female.[Image 1]

Maximum number of patients were in age group 51 – 60 years with 31.19% (n=42), followed by 27.42% (n=37), 24.44% (n=33) and 17.05%

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(n=23) patients in the age group 31-40 years, 41-50 years, and 21-30 years respectively as presented in Image 2.

Out of 135 patients with TBM, 48.88% (n=66) had hyponatremia. It was found that 13.33% (n=29) had SIADH and 19.26% (n=37) had CSWS. The most common presenting complaint of the patients was fever followed by headache, vomiting, and altered sensorium. The presenting complaints is shown in Table No. 1.

Distribution of patients with hyponatremia and without hyponatremia according to different characteristics like age group, gender and Grade was analysed [Table 2]. The results are shown in table no. 2. It is observed that occurrence of hyponatremia was not dependent on age group (p-value=0.47), gender (p-value=0.106) and Grade of disease (p-value=0.188).

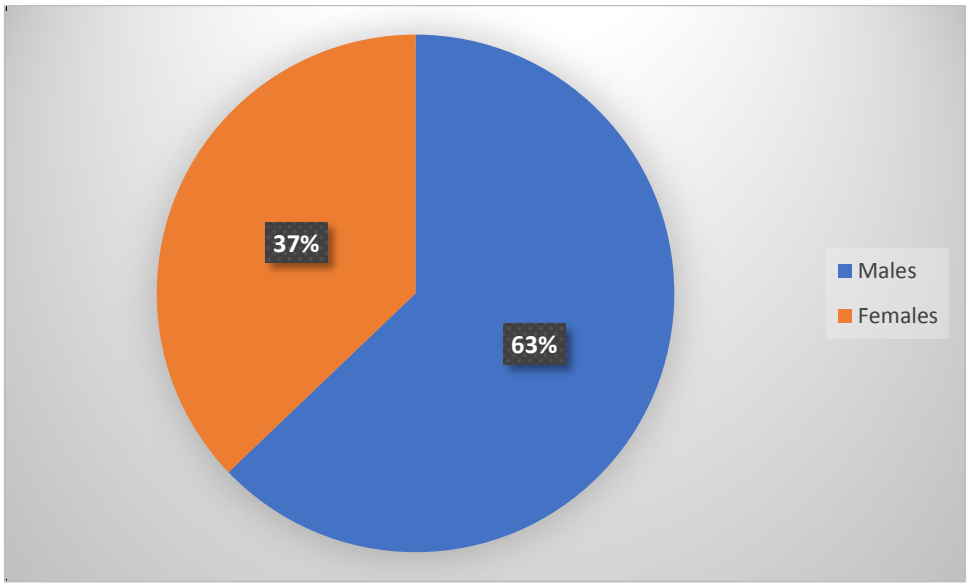

Image 1: Gender wise distribution of cases.

Table 1: Clinical features

Symptom	No. of cases	Percent
Fever	124	91.85%
Headache	110	81.48%
Vomiting	84	56.30%
Seizures	7	5.19%
Anorexia	49	36.30%
Coma	2	1.48%
Altered sensorium	79	58.52%

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Neck rigidity	34	25.19%
Cranial nerve palsy	5	3.70%

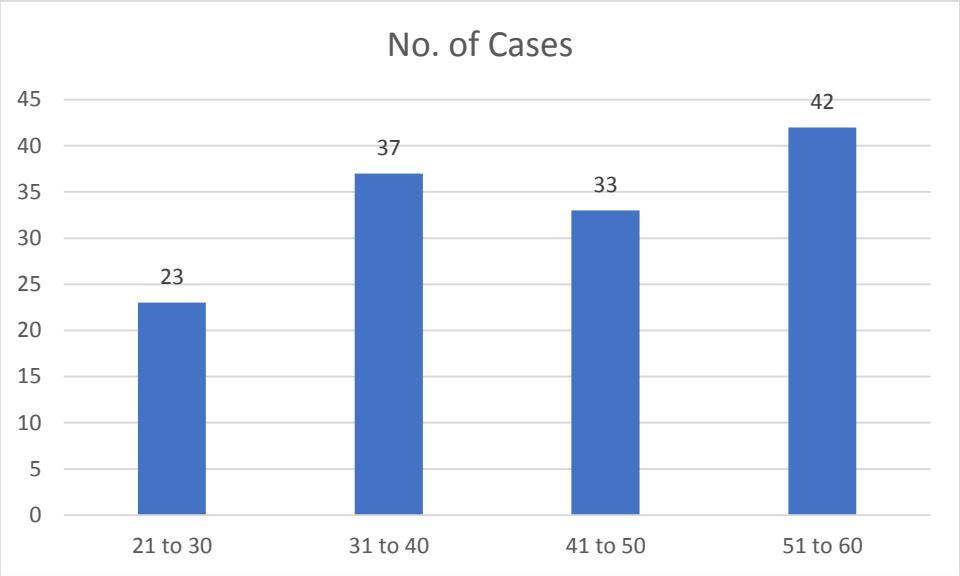

Image 2: Age group wise distribution of cases.

Table 2: Distribution of cases according to age groups, gender, and stage of TBM.

Patients Characteristics	Hyponatremia			p - value
	Yes	No	Total	
Age Group				0.47
21 to 30	8	15	23	
31 to 40	18	19	37	
41 to 50	17	16	33	
51 to 60	23	19	42	
Gender				0.106
Male	36	47	83	
Female	30	22	52	
Stage of TBM				0.188
Stage I	10	13	23	
Stage II	38	29	67	
Stage III	18	27	45	
	66	69	135	

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DISCUSSION

CSWS is defined as renal loss of sodium during intracranial diseases, leading to hyponatraemia, excessive natriuresis, volume depletion and clinical response to volume and salt replacement. It was first described by Peters et al. [11] in 1950, 7 years before the identification of SIADH [12]. As early as 1951, Rapoport et al. [13] described a salt-losing state as a possible cause for hyponatraemia in TBM. Up to 1993, however, hyponatraemia in TBM was thought to be caused by SIADH.

We conducted the prospective study to determine the frequency of hyponatremia in patients presenting with TBM in order to establish the local perspective as there is paucity of local data. A total of 135 patients diagnosed with TBM were included in this study according to the inclusion criteria. Out of 135 patients with TBM, 48.88% (n=66) had hyponatremia. It was found that 13.33% (n=29) had SIADH and 19.26% (n=37) had CSWS. In a similar study done by Ameet Kumar et al [14] on 160 patients of tubercular meningitis, they observed that out of 160 patients with TBM, 40% (64) had hyponatremia. They also reported that 14.4% (23) had SIADH and 25.6% (41) had CSWS. They analysed the relation of hyponatremia with age, gender, grade of TBM, diabetes mellitus, hypertension and duration of symptoms and reported that development of hyponatremia does not depend on these factors. Our study is in agreement with the study of Ameet Kumar et al.[14]

Other similar prospective study done by Mishra et al [15] on 76 patients with TBM reported that 34 (44.7%) TBM patients had hyponatremia, out of which, cerebral salt wasting was observed in 17, syndrome of inappropriate secretion of antidiuretic hormone in 3 and miscellaneous causes in 14 patients.[15]. Karandanis, et al. noted in his study that hyponatremia was found in 73% of cases of TBM [16].

CNS infections treatment and management is emerging as a great challenge especially in the setting of hyponatremia and its complication. Moreover, differentiating CSWS from SIADH is of paramount importance as both are managed paradoxically but present somewhat similarly. Data from our study would possibly offer new insight to clinicians that can impact the understanding of hyponatremia in TBM and aid in the improvement of active management strategies, improving quality of life and patient well-being.

CONCLUSION

Electrolyte disturbance in form of hyponatremia is common in patients with tubercular meningitis. It can occur in form of CSWS and SIADH. This also

adds to morbidity and mortality in TBM patients. It is thus important to investigate serum electrolytes early in such patients and to differentiate the cause of hyponatremia., so that electrolyte imbalance can be detected early and proper management can be initiated to prevent morbidity and mortality due to electrolyte imbalance.

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