**ORIGINAL ARTICLE**

# Hyponatremia in Patients with Bacterial Meningitis and its Association with in-Hospital Mortality

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## ABSTRACT

**Aim:** To determine the frequency of hyponatremia in patients with bacterial meningitis at presentation and to compare the frequency of in hospital mortality in patients with and without hyponatremia.
**Methods:** This descriptive case series study was carried out at Department of Medicine, Ch. Muhammad Akram Teaching & Research Hospital Lahore from 5th August 2015 to 4th February 2016. Clinically proven 90 cases of bacterial meningitis in adult age range were selected from the emergency department. Serum sodium level was measured and patients were followed for 7 days for in-hospital mortality. Sodium level <135 mg/dl was labeled as hyponatremia.
**Results:** The mean age of 50.02±4.681 ranged from 40 to 60 years of age. Fifty two patients (57.8%) were males and remaining 38 patients (42.2%) were females. Twenty three patients (25.6%) had hyponatremia at presentation. Seventeen patients (18.9%) died during their stay in hospital. 17.4% patients with hyponatremia and 19.4% without hyponatremia died during hospital stay. Results were not different statistically (non-significant). There was no effect of age, gender of patient, duration of disease and GCS at presentation on outcome and association in our sampled population.
**Conclusion:** It is concluded that although frequency of hyponatremia is high in patients with meningitis but it had not shown any effects on in-hospital mortality.
**Keywords:** In-hospital mortality, Hyponatremia, Bacterial meningitis, Glasgow Coma Scale (GCS)

## INTRODUCTION

Bacterial meningitis constitutes a medical emergency.[1] Vaccination against common pathogens has decreased the burden of disease.[2] Patients need to be hospitalized for early diagnosis and rapid initiation of empiric antimicrobial and adjunctive therapy are vital.[3] Therapy should be initiated as soon as blood cultures have been obtained, preceding any imaging studies. Clinical signs suggestive of bacterial meningitis include fever, headache, meningismus, and an altered level of consciousness but signs may be scarce in children, in the elderly, and in meningococcal disease. Host genetic factors are major determinants of susceptibility to meningococcal and pneumococcal disease[1,2,3].

Similarly in hospitalized patients, hyponatremia is one of the most frequently observed, but sometimes overlooked[4], electrolyte disorder with bacterial meningitis[5,6,7]. It is reported that mild hyponateremia occurs in 15–30% of hospitalized patients and moderate/severe hyponateremia in 1–7%[6]. Hyponateremia is also a known complication of acute meningitis[7]. Patients with meningoencephalitis are predisposed to develop hypovolemic hyponateremia due to dehydration (because of fever, vomits, poor oral intake). Also anti-edematous treatment (hyperosmolar fluids like mannitol) may contribute to a decrease in serum sodium concentration[4,5,6,7]. In a study of 61 patients with tick borne encephalitis, hyponateremia was observed in 25(41%) patients. In 20 patients (33%), hyponateremia was mild, in 3(5%) it was moderate, and in 2(3%) severe[8] in a recent study in paediatric population with meningitis, frequency of Hyponatremia came out 13.2% and it was significantly associated with poorer outcome (OR: 3.81; 95% CI: 1.00-14.48, p Z 0.04)[9]. Among 14 patients with hyponatremia 11 (78.6%) had poor outcome while 50 among 102 patients without hyponatremia had poor outcome (49%).

Rationale of current study is there is no local study available and sodium levels vary in population with different life styles and dietary habits. In our common practice we do not include sodium level as an indicator for severity of disease. Results of this study may help physicians to learn frequency of

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hyponatremia in bacterial meningitis patients and its importance. Its relation with hyponatremia in encephalitis and fungal meningitis is known[4,6] but no study is so far done for its effect on bacterial meningitis. This study will help to reduce mortality and morbidity associated with lower levels of sodium in patients with bacterial meningitis who may be at increased risk of complications.

## SUBJECTS AND METHODS

This descriptive case series study was carried out at Department of Medicine, Ch. Muhammad Akram Teaching & Research Hospital Lahore from 5th August 2015 to 4th February 2016. Age 18–60 years, both genders, new cases of bacterial meningitis diagnosed during last 72 hours were included. History of recent drug intake changing serum sodium level e.g. hypertonic saline and hydrocholthiazide, chronic liver disease diagnosed by elevated ALT more than 100 IU/ml, end stage renal disease (creatinine clearance < 15 mL/min), diagnosed cases of ulcerative colitis, diabetes mellitus (BSR >200mg/dl) and malignant hypertension (> 180/110 mm of Hg) by medical record and history of diarrhea in last 15 days were excluded. Data was collected in structured questionnaire containing background information like age, sex, serum sodium level and duration of meningitis by date of start of fever more than 101F. Under aseptic conditions, venous blood samples were obtained from cases at the time of presentation in emergency department. Serum sodium level was measured by using standard chemical analyzer and hyponateremia was labelled. Frequency of hyponatremia was calculated. Patients were followed for seven days for in hospital mortality. Presence of in hospital mortality was recorded in hyponatremic and non hyponatremic patients. Confounding variables like duration of disease > 2 days and Glasgow coma score less than 12/15 at time of presentation were recorded additionally to cater their effect.

Data collected was entered and analyzed in the SPSS version 17. Mean with standard deviation was calculated for quantitative variables like age, mean GCS and serum sodium level and frequency and percentages in case of categorical variables like gender, hyponatremia, in hospital mortality, duration of disease > 2 days and Glasgow coma score less than 12/15 at time of presentation. In hospital mortality in both groups was compared using chi square test. A p value $\leq$.05 was taken as significant.

## RESULTS

Fifty four patients (60%) in our study population were below 50 years whereas 36 patients (40%) were either 50 years or more in age with mean age of 50.02±4.681 ranged from 40 to 60 years. Fifty patients (57.8%) were male and remaining 38 patients (42.2%) were female. Seventeen patients (18.9%) died during their stay in hospital. Twenty three patients (25.6%) had hyponatremia at presentation. Eighty three patients (92.2%) among sampled population had GCS level above 12 while 7 (7.8%) had GCS level below 12. In 41 patients (45.6%) duration of disease was more than 24 hours (Table 1). When we cross tabulated hyponatremia with in hospital mortality and applied fisher exact test, result came up non-significant (p=0.832). 4 patients died with hyponatremia during their stay in hospital (Table 2).

When we stratified gender regarding in-hospital mortality among patients with hyponatremia and applied fisher exact test, we came up with non-significant results for both male and female patients that showed statistically equal distribution of hyponatremia male and female patients with in-hospital mortality (Table 3).

When we stratified GCS regarding in-hospital mortality among patients with hyponatremia and applied fisher exact test, we came up with non-significant results for both above and below 12 level of GCS that showed statistically equal distribution of hyponatremia patients with high and low GCS level with in-hospital mortality (Table 4).

When we stratified duration of disease more than 24 hours regarding in-hospital mortality among patients with hyponatremia and applied fisher exact test, we came up with non-significant results that showed statistically equal distribution of hyponatremia with duration of disease above and below 24 hours (Table 5). When we stratified age group regarding in-hospital mortality among patients with hyponatremia and applied fisher exact test, we came up with non-significant results for both above and below 50 years age groups that showed statistically equal distribution of hyponatremia patients between both age groups with in-hospital mortality (Table 6).

## DISCUSSION

Bacterial meningitis is a serious illness. Clinical signs suggestive of bacterial meningitis include fever, headache, meningismus, and an altered level of consciousness but signs may be scarce in children, in the elderly, and in meningococcal disease. Host genetic factors are major determinants of susceptibility to meningococcal and pneumococcal disease.[1-3] Hyponateremia is also a known complication of acute meningitis.[7] Patients with meningoencephalitis are predisposed to develop hypovolemic hyponateremia due to dehydration

(because of fever, vomits, poor oral intake). Also anti-edematous treatment (hyperosmolar fluids like mannitol) may contribute to a decrease in serum sodium concentration[4,5,6,7].

Table 1: Demographic information of the sampled population

| Variable | No. | % |
|---|---|---|
| **Age (years)** | | |
| <50 | 54 | 60.0 |
| ≥50 | 36 | 40.0 |
| **Gender** | | |
| Male | 52 | 57.8 |
| Female | 38 | 42.2 |
| **In-hospital mortality** | | |
| Yes | 17 | 18.9 |
| No | 73 | 81.1 |
| **Hyponatremia** | | |
| Yes | 23 | 25.6 |
| No | 67 | 74.4 |
| **Glasgow Coma Scale** | | |
| >12 | 83 | 92.2 |
| <12 | 7 | 7.8 |
| **Duration of diseases >24 hours** | | |
| Yes | 41 | 45.6 |
| No | 49 | 54.4 |

Table 2: Comparison of hyponatremia according to in-hospital mortality

| Hyponatremia | In-hospital Mortality | |
|---|---|---|
| | Yes | No |
| Yes | 4 | 19 |
| No | 13 | 54 |
| Using fisher exact test = 0.832 (non-significant) | | |

Table 3: Stratification of gender regarding in-hospital mortality among patients with hyponatremia

| Gender | Hyponatremia | In-hospital Mortality | | P value |
|---|---|---|---|---|
| | | Yes | No | |
| Male | Yes | 1 | 14 | .197 |
| | No | 8 | 29 | |
| | Total | 9 | 43 | |
| Female | Yes | 3 | 5 | .199 |
| | No | 5 | 25 | |
| | Total | 8 | 30 | |

Table 4: Stratification of GCS regarding in-hospital mortality among patients with hyponatremia

| GCS | Hyponatremia | In-hospital Mortality | | P value |
|---|---|---|---|---|
| | | Yes | No | |
| < 12 | Yes | 0 | 3 | .14 |
| | No | 2 | 2 | |
| | Total | 2 | 4 | |
| > 12 | Yes | 4 | 16 | .42 |
| | No | 11 | 52 | |
| | Total | 15 | 68 | |

Table 5: Duration of disease >24 hours stratification regarding in-hospital mortality among patients with hyponatremia

| Duration of diseases > 24 hours | Hyponatremia | In-hospital Mortality | | P value |
|---|---|---|---|---|
| | | Yes | No | |
| Yes | Yes | 1 | 6 | .494 |
| | No | 9 | 25 | |
| | Total | 10 | 31 | |
| No | Yes | 3 | 13 | .534 |
| | No | 4 | 29 | |
| | Total | 7 | 42 | |

Table 6: Age group stratification regarding in-hospital mortality among patients with hyponatremia

| Age groups (years) | Hyponatremia | In-hospital Mortality | | P value |
|---|---|---|---|---|
| | | Yes | No | |
| ≥ 50 | Yes | 1 | 5 | .720 |
| | No | 7 | 23 | |
| | Total | 8 | 28 | |
| <50 | Yes | 3 | 14 | .890 |
| | No | 6 | 31 | |
| | Total | 9 | 45 | |

Hyponatremia is also a known complication of acute meningitis. [7] Patients with meningoencephalitis are predisposed to develop hypovolemic hyponatremia due to dehydration (because of fever, vomits, poor oral intake). Also anti-edematous treatment (hyperosmolar fluids like mannitol) may contribute to a decrease in serum sodium concentration[45,6,7]. In our study, 23 patients (25.6%) had hyponatremia at presentation. 17 patients (18.9%) died during their stay in hospital. 17.4% patients with hyponatremia and 19.4% without hyponatremia died during hospital stay. Results were not different statistically (non-significant).

Our results do not match with previous studies. In a study of 61 patients with tick borne encephalitis, hyponateremia was observed in 41% (25 patients). In 20 patients (33%), hyponateremia was mild, in 3(5%) it was moderate, and in 2(3%) severe.[8] In a recent study in pediatric population with meningitis, frequency of Hyponatremia came out 13.2% and it was significantly associated with poorer outcome (OR: 3.81; 95% CI: 1.00e14.48, p Z 0.04)[9]. Among 14 patients with hyponatremia 11(78.6%) had poor outcome while 50 among 102 patients without hyponatremia had poor outcome (49%).

The resultant difference may be secondary to different sampled population. In our study population 90 patients were included with mean age of 50.02±4.681 ranged from 40 to 60 years of age. 52 patients (57.8%) were male and remaining 38 patients (42.2%) were female. More male were

included. This may be secondary to treatment seeking behavior or undiagnosed female population.

There was no effect of age, gender of patient, duration of disease and GCS at presentation on outcome and association in our sampled population. Limitation of current study includes non-representative sample and non probability sampling technique.

## CONCLUSION

It is concluded that although frequency of hyponatremia is high in patients with meningitis but it had not shown any effects on in-hospital mortality. There was no effect of age, gender of patient and time elapsed since diagnosis relationship between hyponatremia and in-hospital mortality in sampled population.

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