

Hyponatraemia in Cerebral Malaria and Association with Outcome

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Abstract

Cerebral malaria is a severe and potentially fatal neurological manifestation of malaria. Hyponatremia is observed in the majority of adult and pediatric patients with severe malaria. The importance of correcting the hyponatremia that complicates severe malaria is debated. A total of 60 cases of Cerebral Malaria studied in the Department of Paediatrics, Bal Chikitsalaya, MB Hospital, RNT Medical College, Udaipur, Rajasthan in between March 2015 to February 2016 for a period of one year. Total 40 (66.7%) was positive for *P. falciparum*, 11 (18.3%) for *P. vivax* and 9 (15%) for both *P. falciparum* and *P. vivax*. Total 44 (73.3%) patients were hyponatremic (<135 Meq/L), 28 (46.7%) had sodium level < 130 Meq/L and 2 (3.3%) patients had very low sodium (< 120 Meq/L). Total 30 patients of *P.falciparum* positive had low sodium (< 135 Meq/L). All patients had GCS < 11 and out of them maximum patients i.e. 42 (70%) belonged to low sodium group (121-134 Meq/L). 23 (38.3%) patients had deep coma (GCS ≤ 7) and out of them 13 (21.6%) were from low sodium group (121-134 Meq/L). Mortality was 7 (11.7%) and 6 were from low sodium group (< 135 Meq/L). In conclusion, this study showed that hyponatremia is a common feature in children presenting with Cerebral Malaria and it is associated with increased mortality. There is direct relationship between serum sodium and GCS. Thus, early detection, prompt management and adequate supportive therapy are key steps to reduce morbidity and mortality due to Cerebral Malaria.

Keywords: Cerebral malaria, hyponatremia, GCS

1. Introduction

Malaria is a protozoan disease transmitted by the bite of infected *Anopheles* mosquitoes.[19] Malaria, a major public health problem in tropical areas, is responsible for infecting 300-500 million people and 1-3 million deaths annually.[3] Malaria is one of the most common parasitic infections in our country and has been a serious problem in some parts poor control.[12] In India 1.06 million malarial cases was found in 2012, out of which 0.53 million were caused by *P. falciparum* causing 519 deaths.[1] *P. falciparum* malaria causes more severe disease as compared to *P. vivax* malaria which is often benign.[13] But few evidences from the studies done in past decades in Asian countries suggest that *P. vivax* is also capable of causing severe disease. [2, 11, 15- 17]

Cerebral malaria is a severe and potentially fatal neurological manifestation of infection with *Plasmodium* species. [20] The case-fatality rate of cerebral malaria in most hospital settings is high, often over 30 percent. [4]

Hyponatremia is observed in the majority of adult and pediatric patients with severe malaria. The pathophysiology of the hyponatraemia in malaria remains

unclear, but a number of underlying mechanisms have been proposed, including the administration of hypotonic fluids, SIADH (syndrome of inappropriate antidiuretic hormone secretion), cerebral salt wasting (CSW), losses through sweat, gastrointestinal tract and kidneys.[8,14] The importance of correcting the hyponatremia that complicates severe malaria is debated. Some authors, noting that hyponatremia is associated with adverse outcomes in other clinical situations, have suggested that it should be specifically and aggressively treated. Others have argued that it is a physiological response to hypovolemia requiring no specific therapy beyond rehydration, although the extent of hypovolemia in patients with severe malaria remains controversial. [8]

Cerebral malaria is a common and potentially fatal clinical disorder in children requiring urgent ICU management. There is paucity of systemic study from this part of Rajasthan (India). Therefore we prospectively examined children presenting with Cerebral Malaria to Bal chikitasalya, Maharana Hospital, Udaipur to examine the prevalence of hyponatremia in Cerebral malaria and to see

association between serum levels of sodium and level of sensorium and outcome of patients.

2. Material and methods

Children over 1 month of age, with a primary diagnosis of Cerebral Malaria admitted during March 2015 to February 2016 were included in the study. Cerebral Malaria was defined as WHO criteria plus *P. vivax* infected also included. The level of consciousness was assessed using the modified Glasgow Coma Scale in patients age <12 months and Glasgow Coma Scale in patients age >12 months. Other causes of coma, such as meningitis and encephalitis, were meticulously excluded.

For all the patients who gave consent, following were recorded- demographic profile, complete history with vitals and relevant systemic examination, relevant laboratory investigations: blood sugar, CBC; PBF, RDT and QBC for malaria, ESR, serum electrolytes, RFT, LFT, ABG. Other investigations were done as required. The data was recorded on daily basis. Serum sodium level was assessed on 24 hrs basis for the next 3 days. All patients were examined daily end point being regained of sensorium or death.

3. Observation

A total of 60 cases with the diagnosis of Cerebral Malaria studied. Most of the patients 40 (66.7%) were of > 5 year age group and 20 (33.3%) were of < 5 year age group with mean age group was 74.03 months. Male to female ratio was 1:1. All patients were admitted with complain of fever and loss of sensorium (GCS < 11). Majority of patients i.e. 40 (66.7%) required hospitalization within 4 days of onset of fever.

Among 60 patients, 40 (66.7%) was positive for *P. falciparum*, 11 (18.3%) for *P. vivax* and 9 (15%) for both *P. falciparum* and *P. vivax*.

Total 44 (73.3%) patients had low sodium (< 135 Meq/L). Out of them, sodium level < 130 Meq/L was seen in 28 (46.7%) patients and rest 16 patients had levels between 131-134 Meq/L. 2 (3.3%) patients had very low sodium (< 120 Meq/L). Total 30 patients of *P.falciparum* positive had low sodium (< 135 Meq/L). P value was 0.017 (< 0.05) significant. (Table-1)

Table 1: Serum Sodium level and Species of Cerebral Malaria

Sodium	<i>P. falciparum</i>	<i>P. vivax</i>	Both	Total
<130Meq/L	19	7	2	28 (46.7%)
131-134 Meq/L	11	3	2	16 (26.7%)
135-145 Meq/L	9	0	5	14 (23.3%)
≥146 Meq/L	1	1	0	02 (3.3%)
Total	40 (66.7%)	11 (18.3%)	9 (15%)	60 (100%)

P value 0.017 (< 0.05) significant

All patients had GCS < 11 and out of them maximum patients i.e. 42 (70%) belonged to low sodium group (121-134 Meq/L), 2 patients (3.3%) in very low sodium group (< 120 Meq/L) and 2 patients (3.3%) in high sodium group (> 146 Meq/L). Among total 60 patients, 23 (38.3%) patients had deep coma (GCS ≤ 7) and out of them 13

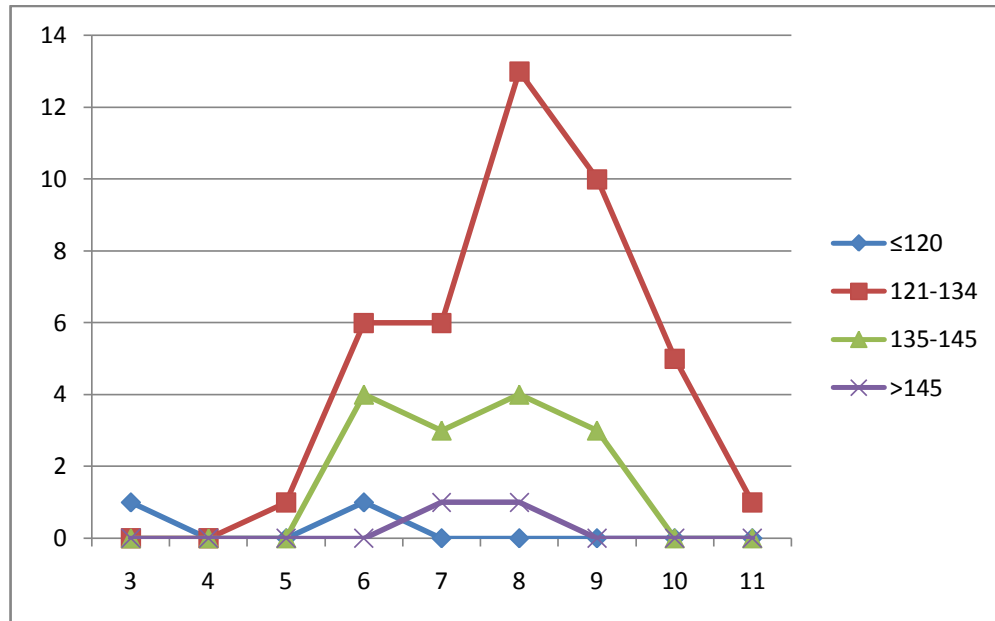
(21.6%) were from low sodium group (121-134 Meq/L), 7 (11.7%) were from normal sodium group (135-145 Meq/L), 2 (3.3%) were from very low sodium group (< 120 Meq/L) and 1 (1.7%) from high sodium group (> 146 Meq/L). (Table-2) (Figure-1)

Table 2: Sodium level and GCS relation in Cerebral Malaria

GCS ₁	Na Levels (Number of patients)				Total
	< 120 Meq/L	121-134 Meq/L	135-145 Meq/L	≥ 146 Meq/L	
3	01	00	00	00	01
5	00	01	00	00	01
6	01	06	04	00	11
7	00	06	03	01	10
8	00	13	04	01	18
9	00	10	03	00	13
10	00	05	00	00	05
11	00	01	00	00	01
Total	02	42	14	02	60

**GCS₁ is GCS on the day of admission*

P value 0.011 (<0.05) significant

Figure 1: Relation of Sodium level with GCS (X- axis) with respect to number of patients (Y-axis).

Mortality was 7 (11.7%). Out of 7 deaths, 6 (10%) were from low sodium group (< 135 Meq/L) and 1 (1.7%) from normal sodium group (135-145 Meq/L).

4. Discussion

A total of 60 cases with the diagnosis of Cerebral Malaria studied. In our study, total 44 (73.3%) patients had low sodium (< 135 Meq/L) while hypernatremia was seen only in 2 (3.3%) patients. Jasani *et al* [10] reported that malaria infection led to reduction in the levels of both sodium and potassium. English *et al* [6] reported 72 (55%) cases of hyponatremia (sodium < 135 mmol/L) and 4 (3%) cases of hypernatremia. They reported that if hyponatremia was left uncorrected, it may exacerbate hyponatremia in those patients who have an appropriate ant-diuretic hormone response and thus, may lead to raised intracranial pressure and predispose to seizures. Other studies also showed significant percentage of hyponatremia between 25.9% - 76.5% cases. [7- 9, 18]

Among 44 patients of hyponatremia in our study, 30 (68.2%) were positive for *P. falciparum*, 10 (22.7%) for *P. vivax* and 4 (9%) for both which was statistically significant with p value of 0.017 (< 0.05). This has been supported by Van Wolfswinkel *et al* [18] study who reported prevalence of hyponatremia in severe falciparum malaria 77%. Jasani *et al* [10] reported that mean levels of serum sodium in the cases of *P. Falciparum* malaria were significantly reduced as compared to those in the cases of *P. vivax* malaria but reduced in both. Tanwar *et al* [16] reported 4 (36.3%) *P. vivax* positive patients with hyponatremia.

Serum Sodium and Outcome

In present study, all patients had loss of sensorium at the time of admission (GCS < 11) and among them maximum patients, i.e. 44 (73.3%) belonged to low sodium group (< 135 Meq/L) which was statistically significant with p value 0.011 (< 0.05). Likewise in 7 deaths, 6 (10%) patients had low sodium (< 135 Meq/L). So our study strongly suggests

relation between low serum sodium and poor outcome. Jasani *et al* [10] and Ebele *et al* [5] reported that hyponatremia is associated with adverse outcomes and it should be specifically and aggressively treated. Hyponatremia is an indicator of the disease severity as this may produce adverse outcomes.

Hanson *et al* [8] did a study on correlation of serum sodium level and GCS that was done in adult population; reported 57% patients were hyponatremic (≤ 135 mmol/L), 30% had plasma sodium ≤ 130 mmol/L with mean plasma sodium 133 mmol/L. In comparison to patients with normal plasma sodium, those with hyponatremia had a higher Glasgow Coma Scores. This study showed that hyponatremia is a common feature with severe malaria but mortality was lower in hyponatremic than normonatremic patients (31.6% versus 51.4%). But Van Wolfswinkel *et al* [18] reported no significant correlation between sodium levels and GCS.

5. Conclusion

In conclusion, this study showed that hyponatremia is a common feature in children presenting with Cerebral Malaria and it is also associated with increased mortality. There is direct relationship between serum sodium and GCS; low serum sodium will lead to low GCS.

This study drew attention to the need to manage the electrolyte derangements for the overall management of the Cerebral Malaria. So, serum electrolytes should be watched over in malaria patients of all the age groups to prevent the complications which might result from electrolyte depletion, as these may produce grave consequences. The precise pathophysiological mechanisms of the hyponatremia in malaria need to be further studied.

Thus, early detection, prompt management and adequate supportive therapy are key steps to reduce morbidity and mortality due to Cerebral Malaria.

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