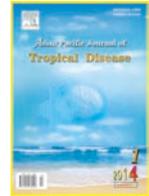




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## Hyponatremia in malaria—experience in tertiary hospital from India

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## PEER REVIEW

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## Comments

It is a good study in which authors evaluated prevalence and severity of hyponatremia in various species of malaria. This study also compared severity of hyponatremia with severity of malarial infection with appropriate statistical methods. There is good review on recent literature and evidence on pathophysiology and management of hyponatremia in malaria cases.

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## ABSTRACT

**Objective:** To determine the prevalence of hyponatremia and its association with severity and species of malaria.

**Methods:** This is a prospective study, done at Father Muller Charitable Hospital Mangalore, in Karnataka, India. Serum sodium and parasite counts were estimated in all positive cases of malaria patients under 15 years admitted in hospital between August 2010 to July 2012. Data regarding all positive cases of malaria under 15 years admitted in hospital between Jan 2010 to June 2011 were obtained. Data was analysed by *Chi*-square test, Fisher's exact test and student *t* test. *P* value less than 0.05 was taken significant.

**Results:** A total of 60 patients with malaria who met the inclusion criteria were enrolled for study. *Plasmodium vivax* was the common species causing malaria (53.3%). Hyponatremia was reported in 39 (62%) patients. Of the 39 cases, 2 (3%) patients had severe hyponatremia, 19 (31.67%) patients had moderate hyponatremia, whereas 18 (30%) patients had mild hyponatremia on admission respectively. Mean sodium for falciparum malaria (131.03±4.31) mEq/L cases was significantly lower than that of vivax malaria cases [(134.2±3.3) mEq/L, *t*=2.20, *P*=0.029]. Severity of hyponatremia increased with severity of infection.

**Conclusions:** Hyponatremia is common in children with malaria and its severity increases with severity of infection. It's more common and more severe in falciparum malaria than vivax malaria.

## KEYWORDS

Hyponatremia, Malaria, Severity

## 1. Introduction

Malaria is endemic in the tropics and subtropics causing 247 million infections worldwide. According to UNICEF, around the world one child death occurs due to malaria every 30 seconds. India contributes 75%–77% of total malaria cases in Southeast Asia region. 95% of the population of moderate to high risk of malaria in SEAR is living in India and highest numbers of death were reported from India[1,2]. It is caused by four species of plasmodium including *Plasmodium vivax* (*P. vivax*), *Plasmodium falciparum* (*P. falciparum*), *Plasmodium malariae*, and *Plasmodium ovale*.

Out of these species, studies have shown that *P. falciparum* is responsible for majority of the deaths, and severe complications like cerebral malaria, anemia and renal failure[3,4].

Hyponatremia is often been associated with malaria and is well recognised complication of severe malaria[5]. It has been show that mortality from hyponatremia is high particularly when not diagnosed and managed early. The pathophysiology of hyponatremia in malaria remains unclear but various proposed mechanisms are administration of hypotonic fluids, the syndrome of inappropriate antidiuretic hormone secretion (SIADH), cerebral salt wasting, renal

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losses and excessive sweating[6,7].

The aim of this study is to determine the prevalence of hyponatremia and its association with severity and species of malaria.

## 2. Materials and methods

This was a prospective study carried out in Father Muller charitable hospital. It is a 1200 bedded multi-specialty, tertiary referral hospital in Mangalore, a picturesque city in southern India, on the shore of the Arabian Sea. Malaria is endemic in this city and has already killed more than 300 people in the past 15 years[8]. This study was carried out from August 2010 to July 2012 for a period of 2 years. All smear positive malaria patients aged between 0–15 years who were willing to participate were included in the study. Children with pre-existing renal disease were excluded from the study. Informed written consent was taken at the time of admission. Serum sodium levels were estimated by ion selective electrode method on admission, before administering antimalarial drugs. Severity was assessed by parasite count[9].

Hyponatremia was defined as serum sodium  $\leq$ 135 mEq/L. Hyponatremia was graded as mild if serum sodium is between 131–135 mEq/L, moderate if 126–130 mEq/L, and severe if  $<$ 125 mEq/L. Available data was analysed by mean, Chi-square test, Fisher's exact test and student *t* test. A *P* value less than 0.05 was considered significant.

## 3. Results

A total of 60 cases of malaria who met the inclusion criteria were enrolled for study. Majority of the patients were between the age group of 12–15 years. *P. vivax* was the most common species causing malaria (53.3%). Hyponatremia was reported in 39 (62%) patients. Of the 39 cases, 2 (3%) patients had severe hyponatremia, 19 (31.67%) patients had moderate hyponatremia, whereas 18 (30%) patients had mild hyponatremia, on admission respectively. In the remaining 21 patients the sodium level was normal on admission. Mean serum sodium was (132.70 $\pm$ 4.10) mEq/L at admission. Mean sodium for *falciparum* malaria (131.03 $\pm$ 4.31) mEq/L cases was significantly lower than that of *vivax* malaria cases (134.2 $\pm$ 3.3) mEq/L, *t*=2.20 *P*=0.029). Though hyponatremia is prevalent in both types, it's more common and more severe in *falciparum* malaria (Table 1). Only in *falciparum* malaria cases serum sodium level  $<$ 125 mEq/L were detected. Severity of hyponatremia increased with severity of infection (Table 2).

**Table 1**

Serum sodium level in different species of malaria and their relationship.

Species	$<$ 125 mEq/L	125–130 mEq/L	131–135 mEq/L	$>$ 135 mEq/L
<i>P. vivax</i>	0	6	12	14
<i>P. falciparum</i>	2	13	6	7

$\chi^2=8.68$ , *P*=0.034.

**Table 2**

Relationship between serum sodium with severity of malaria infection.

Parasite count	$<$ 125 mEq/L	125–130 mEq/L	131–135 mEq/L	$>$ 135 mEq/L
$<$ 1000	0	0	1	0
1000–10000	0	2	6	12
$>$ 10000	2	17	11	9

Fisher's exact test, *P*=0.012.

## 4. Discussion

Malaria caused by *P. vivax* and *P. falciparum* is endemic in many parts of India including Mangalore[8]. Despite intensive efforts over the last century to understand and control malaria, it remains a leading cause of morbidity and mortality in humans. An estimated 300–500 million people infect malaria each year, resulting in 1.5–2.7 million deaths annually[10]. Hyponatremia is well recognised complication of malaria in pediatric age group. It is commonly observed with *falciparum* malaria than *vivax* malaria[10,11].

This study confirms that hyponatremia is not uncommon in pediatric malaria cases, and is associated with severe disease. Incidence of hyponatremia (62%) was comparable with other studies done by Wolfswinkel ME *et al.*[5] with 46% and Hoorn EJ *et al.*[11] with 45.5%. Whereas studies done by Viani *et al.*[12] with 25% and Ladhani *et al.*[13] with 8% had been reported lower incidence of hyponatremia in malaria. Both these studies were carried out in children with imported malaria. Our study showed hyponatremia was common and severe with *falciparum* malaria than *vivax* malaria. It is comparable with studies done in various other part of the world[5,7,11].

Even though hyponatremia in malaria is common, its pathophysiology remains unclear. Suggested mechanisms are SIADH, cerebral salt wasting, administration of hypotonic fluid, gastrointestinal loss due to vomiting or diarrhea, excessive sweating, renal loss *etc.* An understanding of the pathophysiology is of major importance because it might direct management strategies[5,11,14]. Previously it was thought that hyponatremia in malaria was associated with adverse outcome and should be managed aggressively[15], but recent study done by Hanson J *et al.*[16] showed that hyponatremia in severe malaria is associated with preserved consciousness and requires no therapy beyond rehydration.

Hyponatremia is common in children with malaria and its severity increases with severity of infection. It is more common

and more severe in falciparum malaria than vivax malaria. The precise pathophysiological mechanism of hyponatremia is unclear and requires further research.

### Conflict of interest statement

We declare that we have no conflict of interest.

### Comments

#### Background

Malaria is endemic in the tropics and subtropics causing 247 million infections worldwide. India contributes 75%–77% of total malaria cases in Southeast Asia region. Hyponatremia is a recognised complication in adult with malaria. Exact prevalence and pathogenesis of this condition in children with malaria is unknown.

#### Research frontiers

There are very few studies on hyponatremia in malaria. Exact pathogenesis of hyponatremia in malaria is unknown. This study includes all forms of malaria. It also correlates severity of malaria with severity of hyponatremia.

#### Related reports

This study confirms that hyponatremia is not uncommon in pediatric malaria cases. Results of this study are comparable with study done by Wolfswinkel ME *et al.* and Hoorn EJ *et al.* These are the two recent studies in this field.

#### Innovations & breakthroughs

Hence there is very scanty research on hyponatremia in malaria. This study provides very useful research information on hyponatremia in malaria especially in children. This study includes both vivax and falciparum malaria cases. Severity is assessed by malaria parasite count.

#### Applications

It is good to know the prevalence and severity of hyponatremia in pediatric malaria cases. Since hyponatremia in malaria is benign, there is no need of aggressive management other than dehydration correction.

#### Peer review

It is a good study in which authors evaluated prevalence and severity of hyponatremia in various species of malaria. This study also compared severity of hyponatremia with severity of malarial infection with appropriate statistical methods. There is good review on recent literature and evidence on pathophysiology and management of hyponatremia in malaria cases.

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