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Assessment of electrolyte imbalance and its association with different malaria types: An observational study

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Abstract
Aim: The aim of this study was to determine the severity of hyponatraemia and hypokalaemia and their association with the severity of malaria which was caused by the *P. falciparum* and the *P. vivax* species of Plasmodium.
Methods: This investigation was conducted prospectively for a duration of 1 year. The research included all hospitalized patients who had clinical symptoms consistent with malaria, as determined by the World Health Organization's criteria, and who expressed their willingness to participate. A total of 200 cases of *P. falciparum* and *P. vivax* malaria were identified (100 instances of each). The patients were categorized into two cohorts: severe (100) and non-severe (100) instances of malaria, in accordance with the standards and criteria established by the World Health Organization (WHO).
Results: Prevalence was higher among men than females. *P. falciparum* exhibited higher prevalence among individuals aged 13 to 30 years, whereas *P. vivax* showed higher prevalence among those aged 31 to 50 years. *P. falciparum* malaria exhibited a higher prevalence of hyponatremia and hypokalemia compared to *P. vivax* malaria. The prevalence of hyponatremia and hypokalemia was higher in severe cases of malaria compared to non-severe cases.
Conclusion: Hyponatremia and hypokalemia are often seen in cases of malaria, particularly in the severe manifestations of falciparum and vivax malaria, as opposed to non-severe cases. *P. falciparum* malaria is more often associated with hyponatremia and hypokalemia compared to *P. vivax* malaria. It is advisable to assess the serum electrolyte levels in patients of all age groups with malaria to avoid potential problems arising from electrolyte depletion, since these might have serious repercussions.

Keywords: Malaria, sodium, potassium, severity

Introduction
Malaria is one of the most prevalent infectious diseases in the world. The pandemic has impacted individuals from over 100 nations and has wreaked havoc on the healthcare systems of these countries. The highest occurrence of this condition is found in Africa and Southeast Asia [1]. Annually, there were approximately 300-500 million cases of illness and 2-3 million cases of death reported as a result of malaria [2]. The World malaria report, published in November 2018, indicated a rise in malaria cases from 217 million in 2016 to 219 million in 2017. In 2017, the estimated malaria mortality rate was 435,000, which was comparable to the previous year [3].
According to the records of the National Vector Borne Disease Control Programme (NVBDCP), the annual parasite incidence (API) in most parts of India was less than 2. In scattered regions, the API ranged from 2 to 5, while regions with an API greater than 5 were found in the states of Rajasthan, Karnataka, Southern Madhya Pradesh, Chhattisgarh, Gujarat, Jharkhand, Goa, Orissa, and the northeastern states [4]. Malaria is a vector-borne disease transmitted by mosquitoes and it is a prevalent disease in Mangalore, a region in the state of Karnataka. Malaria is a disease caused by single-celled eukaryotic protozoan parasites belonging to the Plasmodium spp. genus. There are five species known to be capable of infecting humans: *P. falciparum*, *P. vivax*, *P. ovale*, *P. malariae*, and *P. knowlesi*.

The complex epidemiology of malaria in India is a result of the diverse geographical, ethnic, and widespread distribution of nine Anopheles vectors that transmit three types of Plasmodia, namely *P. falciparum*, *P. vivax*, and *P. malariae* [4]. Electrolytes are minerals present in blood and other body fluids. There optimum range is essential for proper physiological activities [5]. Electrolyte imbalances and mineral disturbances were known to be common clinical manifestations in several infectious diseases including malaria. Hyponatraemia, hyperkalaemia, hypocalcaemia and hypomagnesaemia usually develops because of infection with Plasmodium [6]. Sodium (Na) is known as the major cation of extracellular fluid. It regulates the normal distribution of water and osmotic pressure in various body fluids. Various health problems occur due to Na+ ion disturbance [7]. Hyponatraemia, the decline in the Na concentration, is considered as an important clinical manifestation of malaria. De-creased level of Na exaggerates the disease symp-toms and results in severe malaria [8]. Potassium (K) is identified as a crucial electrolyte for accurate functioning of all body cells, tissues and organs. It maintains blood pH and water levels in the body. It is particularly important in skeletal and smooth muscle contraction. Hypokalaemia is a frequent consequence of severe malaria. Decreased level of K is an evident correction of acidosis in malaria [9].

The purpose of this research was to assess the severity of hyponatraemia and hypokalaemia and their connection with the severity of malaria which was produced by the *P. falciparum* and the *P. vivax* species of Plasmodium.

Materials and Methods

This investigation was conducted prospectively for a duration of 1 year. The research included all hospitalized patients who had clinical symptoms indicative of malaria, as determined by the World Health Organization (WHO) criteria, and who expressed their willingness to participate. Prior to their enrollment in the trial, all participants were provided with a detailed explanation of the nature and objectives of the study. The diagnosis of malaria was confirmed by the evaluation of peripheral smears (both thick and thin) and by using the malarial antigen detection fast card test.

There were 200 diagnosed cases of *P. falciparum* and *P. vivax* malaria (100 + 100). The patients were divided into two groups of severe (100) and non-severe (100) cases of malaria, based on the WHO guidelines and criteria.

Severe Malaria

The patients were considered as having severe *P. falciparum* malaria, if they met the predefined, modified World Health Organization (WHO) criteria for severe malaria on admission or during hospitalization ("severity criteria") :

- A Glasgow Coma Scale (GCS) score of < 11 (which indicated cerebral malaria) or
- Anaemia (haematocrit -< 0.20 L/L with a parasite count of > 100.000/μL) or
- Jaundice (serum bilirubin -> 50 μmol/L with a parasite count of > 100.000/μL)
- Renal impairment (urine output- < 400 mL/24 h and serum creatinine- > 25 μmol/L) or
- Hypoglycaemia (blood glucose -< 2.2 mmol/L) or
- Hyperparasitaemia (> 10% parasitaemia) or
- Shock (systolic blood pressure- < 80 mm Hg with cold extremities)
- Fulfilment of any one of the above criteria was considered as suggestive of severe malaria.

Inclusion Criteria

1. All the confirmed patients of malaria above 1year of age.
2. Willingness in giving an informed consent.

Exclusion Criteria

1. Unwillingness in giving an informed consent.
2. Already enrolled in the study.

For all the patients who were willing to participate in the study, their demographic profile, their complete history with vitals and relevant system examination with relevant laboratory investigations was recorded in a preformed proforma and they were subjected to the following investigations:

- Complete Blood Count (CBC) : [Hb, TC, DC and platelet]
- Peripheral Smear examination for the malaria parasite
- Serum billirubin
- Serum Creatinine
- Serum electrolyte (Na+, K+)

The methodology of the procedures to be followed:

- CBC by using ("Sysmex KX-21 Three Part Differential Automated Haematology Analyser").
- PSMP by the thick and thin smear methods; staining with the Giemsa stain.
- Evaluation of serum billirubin and creatinin by using a semi- automated biochemistry analyser.
- Evaluation of serum electrolyte (Na^+, K^+) by using a Prolyte fully automated electrolyte analyser.

Statistical Analysis: The data from the study was analyzed separately by using the Statistical Package for Social Sciences. The results were presented as Mean ± SD (Standard deviation) and a p value of <0.05 was considered as significant.

Results

Males were more commonly affected than females. *P. falciparum* was more prevalent in the 13 to 30 years age group and *P. vivax* was more prevalent in the 31-50 years age group.

Table 1: Age and Sex wise distribution of cases of *P. falciparum* and *P. vivax*.

Age/ Gender	0-10 year	6–12 Year	13-20 year	21-30 year	31-50 year	>50 Year
P. falciparum						
Male	10	7	18	13	11	1
Female	6	7	10	9	7	1
P. vivax						
Male	6	9	15	8	28	1
Female	4	6	8	5	9	1

Table 2: Comparison of Mean ± SD of serum Na+ and K+ level in *P. falciparum* and *P. vivax*.

Gender	*P. falciparum*		*P. vivax*	
	Na+	K+	Na+	K+
Male	128.72±1.64	3.07±0.48	136.26±1.72	3.56±0.44
Female	126.84±1.24	3.06±0.42	134.46±1.64	3.54±0.40

Hyponataemia and hypokalaemia were more common in *P. falciparum* than in *P. vivax* malaria.

Table 3: Comparison of serum Na+ and K+ level in severe and non-severe cases of *P. falciparum* and *P. vivax*

Electrolyte Level		Severe Cases of malaria	Non-severe Cases of malaria	P - value
Na+	125-128	32	10	<0.05
	129-132	40	45	>0.05
	>133	27	45	>0.05
K+	<3	30	15	<0.05
	3-4	46	34	>0.05
	>4	24	51	>0.05

Hyponataemia and hypokalaemia were more common in the severe cases of malaria than in the non-severe cases of malaria.

Discussions

Malaria is a potentially fatal illness that affects approximately half of the global population [1]. Malaria causes an estimated 2-3 million deaths each year and also leads to significant illness in approximately 300-500 million individuals annually [10] Malaria in humans is caused by four species of Plasmodium. The four species are *P. falciparum*, *P. vivax*, P.malariae, and *P. ovale*. *P. falciparum* is the primary cause of mortality and severe complications associated with malaria, such as cerebral malaria, anaemia, and renal failure [11, 12]. Malaria is prevalent in numerous states of India, including Gujarat. Malaria is a vector-borne illness transmitted through the bite of an anopheles mosquito, and infrequently through blood transfusion. The predominant species found in India are *P. falciparum* and *P. vivax* [13].

Malaria is a significant contributor to both death and illness in tropical regions worldwide. Approximately 300-500 million individuals are afflicted with malaria annually, resulting in over 1 million fatalities each year [14]. *P. falciparum* is the species which is most usually connected with the severe and difficult forms of this illness [15]. Males were more commonly affected than females. *P. falciparum* was more prevalent in the 13 to 30 years age group and *P. vivax* was more prevalent in the 31-50 years age group.

Hyponataemia and hypokalaemia were more common in *P. falciparum* than in *P. vivax* malaria. Hyponataemia and hypokalaemia were more common in the severe cases of malaria than in the non-severe cases of malaria. Fryatt RJ, *et al.* [16] suggested that the mild hyponatraemia that could be seen in the acute stages of malaria did not affect the mortality and the morbidity. Some observations also suggested that in the non-severe cases, there was a very mild reduction in the sodium and potassium levels. Dworak *et al.* (1975) [17] stated that there was a progressive decrease in the Na+ and K+ levels within 12 hrs of the parasite's occupancy, whereas Kakkilaya (2002) [18] reported mild hyponetraemia in the malaria patients. Ebele J Ikekpeazu *et al.* (2010) [19] reported that there was a reduction in the Na+ and K+ level in the cases of malaria. Heindricks *et al.* [20] reported that the reduction in the K+ levels was because the host cells lost up to 75 to 80 % of their normal potassium content during the course of the malaria attack.

The observation that hyponatraemia which was seen in malaria was caused by any Plasmodium species, suggested that the hyponatraemia per se was unlikely to represent an exclusive feature of falciparum malaria, but that it merely reflected the effects of the severity of the disease.

Conclusion

Hyponatremia and hypokalemia are often seen in cases of malaria, particularly in severe types of falciparum and vivax malaria, as opposed to non-severe malaria. *P. falciparum* malaria is associated with a higher prevalence of hyponatraemia and hypokalaemia compared to *P. vivax* malaria. It is advisable to assess the serum electrolyte levels in patients of all age groups with malaria to avoid potential problems caused by electrolyte depletion, since these might lead to serious consequences.

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