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Acid - Base Imbalance and Dyselectrolytemia in Malaria

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Abstract

Introduction: *Electrolyte imbalance and acid base imbalance is a common complication in severe infectious disease including malaria. The aim of this study was to evaluate the acid base and electrolyte imbalance in malaria.*

Material and Methods: *This descriptive observational study was carried out from March 2015 to Aug 2016 in department of medicine Gandhi medical college Bhopal. All malaria positive cases admitted in medical ward and who were willing to participate were enrolled the study and those patient who received i/v fluid before admission and associated with co morbid condition like copd acute exacerbation, diabetic ketoacidosis, chronic renal failure etc. Were excluded from the study. Serum electrolyte were analyzed using flame emission spectro photometric method and ABG analysis by ESCHWELER COMBISYS II.*

Results: *Out of 100 malaria positive cases[P. Vivax(39), P. Falciparum(46), Mixed infection(15)] hyponatremia, hypokalemia, hyperkalemia was observed 27%, 9%, 14% respectively. And metabolic acidosis and respiratory acidosis were observed as 17%, 3%, respectively and P. Falciparum had most common dyselectrolytemia [hyponatremia(16/46), hypokalemia(3/46), hyperkalemia(11/46)] and acid base imbalance[M.acidosis(12/46), M.alkalosis(3/46), R.acidosis(1/46)].*

Conclusion: *This study was aimed to electrolyte and acid base imbalance, hyponatremia was most commonly associated with pl.falciparum wherein most patients had moderate hyponatremia.The most common complicatin of severe malaria was acute renal failure.And this was associated with hyperkalemia.Among the acid base imbalances ,the most commonly observed was metabolic acidosis which had a very high correlation with falciparum malaria, other acid base imbalances common in decreasing order were metabolic alkalosis and respiratoryacidosis.*

Keywords: *Malaria, electrolyte imbalance, acid-base imbalance, hyponatremia, hyperkalemia, hypokalemia, metabolic acidosis, metabolic alkalosis, respiratory acidosis.*

Introduction

Malaria is life threatening disease, with nearly half of the world's population being vulnerable to this infection. Malaria accounts for an estimated 2-3 million deaths annually and it is also responsible for the untold morbidity in approximately 300 -500 million people annually.[1] and 1.5±2.7 million die [2,3,4]. Four species of Plasmodium cause malaria in humans. These are P.falciparum, P.vivax, P.malariae and P. Ovale. P.falciparum is responsible for most of the deaths and most of the severe complications which result from malaria. [5] which include cerebral malaria, anaemia and renal failure. [6]. Electrolyte imbalances and mineral disturbances were known to be common clinical manifestations in several infectious diseases including malaria. Hyponatremia, hyperkalaemia, usually develops

because of infection with Plasmodium species. [7]. It is observed that malaria is often associated with abnormalities of fluid, electrolytes (Na+ and K+) and acid-base balance. These can occur in any type of malaria but are more common in severe falciparum malaria, extremes of age and in patients with high degree of fever and vomiting. [8]. The pathophysiology of the hyponatraemia in malaria remains unclear, but several studies have suggested that an increased secretion of vasopr-essin, either appropriately or inappropriately, plays an important role. [9][10]. The aim of this study was to determine the prevalence of hyponatraemia and other electrolyte and acid base imbalances and their association with the severity of malaria which was caused by various Plasmodium species.

Material and Methods

The present study conducted in the department of medicine, Hamidia hospital and Gandhi Medical College Bhopal from March 2015 to September 2016.

Objectives

1. To Study Acid base imbalance in malaria.
2. To Study electrolyte imbalance in malaria

Inclusion Criteria

1. All Malaria positive cases admitted in medical ward.
2. Who were willing to participate were enrolled in the study.

Exclusion Criteria

1. Patient referred from hospitals after giving treatment like I/V fluids.
2. Other associated co morbid conditions like COPD acute exacerbation, DKA, CRF, etc.

The following data were included for analysis:

1. All malaria Positive Patients admitted in Medical ward after exclusion.
2. Question regarding symptoms like fever, onset, duration, pattern, associated with symptoms were asked.
3. Detailed history regarding other systemic diseases was taken.
4. These enrolled patients were examine thoroughly.
5. Routine investigations including PS for mp, degree of parasitemia, malarial antigen test, Serum sodium, potassium and ABG were performed.

A. Blood Analysis

1. Blood haemoglobin was measured by sahli's haemoglobinometer
2. Blood urea was measured by nesslers method.
3. Serum creatinine was estimated by picric acid method.
4. Serum sodium and potassium

Venous blood samples (10ml) OF malaria positive patient were collected into sample tube without the addition of anticoagulant. The blood samples were centrifuged at 1500 rpm for 20 minutes; the serum was separated and immediately used for the determination of the electrolytes, sodium, potassium was analyzed using flame emission spectrophotometric method.

B. ABG Analysis

1.Using ESCHWELER COMBISYS - II (Microprocessor -controlled Automatic Analysis system for quantitative measurements and calculation) PH, Electrolytes and Blood gas status were measured - (Na, K, Cl, Hco3, Po2, Pco2, Ph. BE.)

Normal blood gas parameters and electrolyte levels are:

PH = 7.35 – 7.45, PaO2 = 80 – 100 mmHg, PaCO2 = 35

– 45 mmHg, HCO3 = 24 ± 2 mEq/L, BE = 0 ± 2 mEq/L,

S. Na+ = 135-145 mEq/L, S. K+ = 3.5 – 5.0 mEq/L, S. Cl- 102-109 mEq/L

C. Malaria parasite detection method

1. The malaria parasite density determines by examine a thick blood film stained by the Giemsa stain.

2. Detection in patient samples of malaria parasite antigens such as histadine rich protein II (HRP-II) plasmodium lactate dehydrogenate (pLDH) performed by rapid tests based on immune-chromatographic methods.

Other investigation

1. Ultrasonography:-USG abdomen was done to see size of kidney, Renal Parynchymal disease etc.
2. CT HEAD:- when needed

Results

Table 1 Showing Distribution Of Electrolyte Imbalances Among Patients Of Malarial Fever

Electrolyte Imbalance	P. vivax	P. falciparum	Mixed	Total	P value	Mean	S.D.
Hyponatremia	6	16	5	27	0.1528	0.27	6.0827
Hypokalemia	3	3	3	9	0.0302	0.09	0
Hyperkalemia	0	11	3	14	0.000	0.14	5.686

Table 2 Showing Distribution of Acid Base Imbalance Among Cases of Malarial Fever

Acid Base Imbalance	P. vivax	P. falciparum	Mixed	Total	P value	Mean	S.D.
Metabolic acidosis	2	12	3	17	0.07	0.2	5.5075
Metabolic alkalosis	0	3	0	3	0	0.03	1.732051
Respiratory Asidosis	0	1	1	2	0	0.02	1.532052

Table 3 Showing Correlation of Degree of Hyponatremia With Malarial Infection

Degree of hyponatremia	P. vivax	P. falciparum	Mixed	Total	P value	SD	Mean
Mild (130-134)	6	0	1	7	0.05	3.2451	0.07
Moderate (126-129)	0	10	3	13	0	501316	0.13
Severe (less than 126)	6	0	1	7	0	0.5733	0.08

Table 4 Showing Correlation of Degree of Metabolic Acidosis with Malarial Fever

Degree of metabolic acidosis	p. vivax	P. falciparum	Mixed	Total	Mean	S.D	P value
Mild (ph 7.25-7-34)	2	4	1	7	0.08	0.8146	0.0354
Moderate (ph 7.1-7.24)	0	6	3	9	0.09	2.5098	0
Severe (pH less than 7.1)	0	2	1	3	0.03	0.08366	0
Total	2	12	5	19			

Discussion

Electrolyte imbalance

Hyponatremia

In the current study hyponatremia was observed in 27 patients (27%). Of which 6 patients were positive for p. vivax. 16 were positive for p. falciparum and 5 patients had mixed infection. For patients suffering from falciparum infection 34.78% patients were found to be having hyponatremia in contrast to 15.38 % patient of p. vivax having hyponatremia. This relatively higher incidence of hyponatremia in p. falciparum patients has been observed and also supported a study by Jasmin H. et al (2012)[11], which

observed 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.In current study it is similar to what has been reported by Jasmin H. et al (2012) [11], Kakkilaya (2002) [12], also reported mild hyponatremia in the malaria patients.The cause of hyponatremia in current study is proposed to be due to ARF, vomiting and severe dehydration. This etiology has been supported by Das et al (2014) [13], Who observed that may be due to hypovolemia following vomiting, decrease intake either orally or through nasogastric tube in unconscious patients or due to ARF.A study by Viroj Wiwanitkit [14] proposed that hyponatremia may be due to host vasopressin, however the current study is limited to ascertain this hypothesis.

Current study classifies severity of hyponatremia into mild (130-134), moderate (125-129) and severe (less than 126). The incidence of severe hyponatremia was found in 7 patient (7%) of which 6 were p. falciparum and 1 patient was having mixed severe infection. Association of mild hyponatremia with malarial fever was significant in the present study(p value – 0.05). Das et al (2014) [13]:In his study shows 3 patients (5%) of p. falciparum suffering from severe hyponatremia (<120). This finding is similar to current study. Jasmin H. et al (2012) [11] shows in their study that 64 cases of severe malaria had hyponatremia in comparison to 22 cases of non severe malaria having hyponatremia, out of 64 cases 50 were suffering from severe p. falciparum. This is well supported by the current study.

Hypokalemia

The current study shows the incidence of hypokalemia in 9 patients (9%) of which 20% were mixed infections. 6.52% of plasmodium falciparum and 7.69 % of plasmodium vivax were having hypokalamia. This cause of hypokalemia is likely to be due to excessive vomiting. Heindricks et al (19171)[15] 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 association of hypokalemia with malarial fever was significant in the present study (p value – 0.03). The incidence of hypokalemia in study by Das et al(2014) [13] shows 2 patients (3.3%) having hypokalemia. The incidence is slightly lower than current study. Dworak et al (1975) [16], stated that there was a progressive decrease in the Na+ and K+ levels within 12 hrs of the parasite's occupancy. Ebele J Ikekpeazu et al (2010) [17], reported that there was a reduction in the Na+ and K+ level in the cases of malaria. Asiama Rani et al (2015) [18], In this study, blood samples were used for the evaluation of electrolytes in malaria patients and healthy individuals. This study indicates that malarial infection led to reduction in the levels of Na i.e., hyponatraemia. The pathophysiology of hyponatraemia in malaria remains unclear, but several studies have reported that an increased secretion of vasopressin (ADH), either appropriately or inappropriately, plays an important role in the low level of sodium in malaria because sodium may enter into the infected cells and result in loss of blood. Hyponatraemia has been identified as a common outcome of malaria. Enhanced urinary removal of K and hypokalemia has been reported as common outcomes of malaria. Plasmodium presence may lower the K levels and aggravates the complications associated with malaria disease. P. falciparum infected individuals were frequently observed with hypokalaemia as compared to P. vivax infected individuals. No significant variation in the levels of K was found in thisstudy among P. falciparum infected and P.vivax infected cases.

Hyperkalemia

In the Current study hyperkalemia was associated with 14% patients of which 11 patients (23.91%) were p. falciparum positive and 3 patient (23%) had mixed infection no p. vivax patient was found to be having hyperkalemic which may be due to less incidence of severity in p. vivax. In current

study mild to moderate hyperkalemia (5.5-6meq/lit) was found in 10 patients (10%). And severe hyperkalemia (>6.0) found in 4 patient (4%). All these patientst were found to be having severe malaria with 11 patient (78.57%) of severe plasmodium falciparum and 3 patients (21.43%) of severe mixed infection. The association of severe hyperkalemia with malarial fevar was significant(p value – 0.04). In current study all patients were also having ARF and 12 patient (85.71%) were having metabolic acidosis. This attributing the cause of hyperkalemia. Further supported by Das et al(2014)[11] where the cause of hyperkalamia was related to acute renal failure. And reported increase incidence of hyperkalemia due to delayed referral and late hemodialysis. He reported 10 patients (16.6%) had hyperkalemia and2 patient (3.3%) had hypokalemia of whom 33.3% died to ARF and metabolic complication. Among the metabolic complication hyperkalemia and hypokalemia were the common cause of death. But incidence of hyperkalemia of this study was 16.6% as compared to hypokalemia (3.3%), it is supported by the current study. Maitland et al (2005) [19], reported hyperkalemia in 16% cases of whom 78% were Die at the time of admission.

Acid base imbalance

In current study, 20% patients were having metabolic acidosis of which mild metabolic acidosis (ph- 7.25-.7.34) found in 8% of cases and moderate metabolic acidosis (ph- 7.10-7.24) found in 9% of patients and severe (ph <7.1) metabolic acidosis found in 3% patient. Maximum no. of metabolic acidosis was found in severe plasmodium falciparum malaria (45.45%). Out of 3 patients of severe metabolic acidosis, 2 were associated with severe plasmodium falciparum and 1 is associated with mixed severe infection. And all cases are associated with the hyperkalemia and ARF. This contributes to the cause of metabolic acidosis. The association of mild metabolic acidosis with malarial infection was significant (p valaue- 0.03)

In current study it was also noted that 3 patients (3%) patient had metabolic alkalosis most probably due to persistent vomiting and 2 patient (2%) had respiratory acidosis might be due to development of ARDS or Pulmonary edema. This study is further supported by Maitland K (2005) [19], Reported metabolic acidosis in 17% of patients with severe falciparum malaria and 57% of patients with ARF with metabolic acidosis.Das et al (2014) [11], 12 patients (20%) had metabolic acidosis Among the patients of severe falciparum malaria with ARF, 9 patients (50%) had metabolic acidosis and compensatory respiratory alkalosis. As per this study, Increased incidence of acidosis in this study may be due to delayed referral, improper correction of fluid status, increased incidence of bacterial septicemia and judicious use of vasopressor. He also reported 3 patients (5.0%) with metabolic alkalosis and 2 patients (3.3%) had respiratory acidosis. 23 patients (57.5%) out of 40 severe falciparum malaria had normal acid base parameter. Among the patients of severe falciparum malaria with ARF. 3 patients had metabolic alkalosis reported in their study and probably due to persistent vomiting. 2 had respiratory acidosis and this might be due to development of ARDS and/or pulmonary edema.

In the current study depits ARF in a total of 20(20%) patients. Out of which 16(34.78%) patients were plasmodium falciparum and 4 patient (26.66%) were mixed infection whereas no patient of p. vivax was associated with ARF. The higher incidence of ARF in plasmodium falciparum was attributed to intravascular haemolysis, oliguria, and ATN. Incidence of ARF was reported to be 30% by Das et al (2014) [13] and the cause of ARF was due to ATN in their study.

In current study 6 patients were having ARF without hyperkalemia and total no of 14 patient (14%) had both ARF and Metabolic acidosis.

Thus the present study very well establishes electrolyte imbalance namely hyperkalemia, hypokalemia, hyponatremia and acid base imbalance mainly metabolic acidosis and ARF in

patients of malarial fever, and there is positive relation of severity and complication associated with p. falciparum and less with p. vivax, and the study of mixed infection (p. vivax and p. falciparum) provides an important reason to investigate complication associated with malaria.

Conclusion

100 patients of diagnosed malarial fever, pl.falciparum, pl.vivax, and mixed infection (pl.falciparum+ pl.vivax) admitted in hamidia hospital over period of 1 year included in study had undergone laboratory tests

The mean age of the patients were 32.47 with age wise distribution from 13-75 years .Sex distribution in study population is 1.5:1 (male:female) .Most cases were of pl. falciparum(46%) followed by pl.vivax (39%) and mixed infections were (15%).

A higher proportion of cases observed were that of uncomplicated malaria (72%) in contrast to those having severe malaria(28%).In those having severe malaria the most common cause of severity was again due to pl.falciparum followed by mixed infection.

Since this was aimed to study electrolyte and acid base imbalance, the most common electrolyte imbalance found was hyponatremia followed by hyperkalemia and hypokalemia respectively, hyponatremia was most commonly associated with pl.falciparum wherein most patients had moderate hyponatremia (125-129).

The most common complicatin of severe malaria was acute renal failure(20% cases).And this was associated with hyperkalemia. Next common complication seen was metabolic acidosis , these complications were seen to be most commonly associated with falciparum infections.

Among the acid base imbalances ,the most commonly observed was metabolic acidosis which had a very high correlation with falciparum malaria, other acid base imbalances common in decreasing order were metabolic alkalosis and respiratory acidosis respectively, the cause of metabolic acidosis was mostly due to acute renal failure.

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