ORIGINAL RESEARCH

Falciparum Malaria and Acute Renal Failure

Golla Vahini[1], Yerraguntla Shashidhar[1]

[1]Assistant Professor, General Medicine, Gandhi Medical College/General Hospital, Secunderabad, Telangana, India.

ABSTRACT

Background: Aim & Objectives: To study the ABG and electrolyte disturbances in severe malaria. To assess the prognostic significance of these parameters.

Materials and Methods: The present study is a prospective study of 50 patients above the age of 12 yrs. The patients were selected from those who were admitted with severe malaria in Acute Medical Care Unit, Ganndhi Hospital, Secunderabad. Patients who came with symptoms or signs of severe malaria like coma, convulsions, hypotension, decreased urine output, anemia, jaundice, respiratory distress are assessed. Out of them who fit the exclusion criteria are excluded.

Results: Acidosis is commonly seen with malaria and this most often high anion gap metabolic acidosis contributed by lactic acidosis, renal failure and other anions. Electrolyte abnormalities are common in malaria with hyponatremia, eukalemia, hypochloremia, hypocalcemia and hypophosphatemia being the commonest.

Conclusion: Finally, we conclude, Strong predictors of mortality include acidosis, high anion gap, hyperlactatemia and hyperkalemia.

Keywords: Malaria, Hypokalemia, Hyponateremia, Jaundice, Hypotension.

Corresponding Author: Dr. Yerraguntla Shashidhar, Assistant Professor, General Medicine, Gandhi Medical College/General Hospital, Secunderabad, Telangana, India. Email: shashidhary19@gmail.com

INTRODUCTION

Malaria is an acute and chronic illness characterized by paroxysms of fever, chills, sweats, fatigue, anemia, and splenomegaly. It has played a major role in human history, having arguably caused more harm to more people than any other infectious disease.

Malaria is an infection caused by the coccidian protozoan parasite of the genus Plasmodium carried by female Anopheles spp. mosquitoes. The clinical disease in humans may vary widely according to the species of parasite and the genetics, immune status and age of the host. These variables have a major influence on all aspects of the disease, including epidemiology, pathogenesis, clinical features and management.

Chronic complications of malarial infection include nephrosis, tropical splenomegaly and endemic Burkitt's lymphoma. Acute infections can be febrile episodes causing morbidity or they can be life threatening due to multiorgan failure. No organ system is immune from the affects of malaria.

The organ systems are made up of organs which are in turn a collection of tissues. Any tissue is nothing but a group of functionally similar cells. Hence cell is the smallest functional unit of the body.[1]

Inside each cell there will be physiological reactions carried out by sub cellular structures with the aid of enzymes and other proteins. These reactions and cellular integrity are disturbed with slight changes in the composition of surrounding fluids.[2]

Proper maintenance of pH, blood gases and electrolyte composition are vital for the survival of the cell. If there are derangements in these parameters one can assess the cellular functional impairment before organ dysfunction can be seen clinically. Thus these parameters provide us the information regarding cellular microenvironment which gets deranged first then progressing to organ damage.[3]

Hence the present study is undertaken to study arterial blood gases and electrolyte changes in malaria in order to identify the at risk individuals with organ failure and to provide them with effective and timely treatment.

Aim & Objectives

- To study the ABG and electrolyte disturbances in severe malaria
- To assess the prognostic significance of these parameters

MATERIALS & METHODS

The present study is a prospective study of 50 patients above the age of 12 yrs.

The patients were selected from those who were admitted with severe malaria in Acute Medical Care Unit,Gandhi Hospital, Secunderabad.

Patients who came with symptoms or signs of severe malaria like coma, convulsions, hypotension, decreased urine output, anemia, jaundice, respiratory distress are assessed. Out of them who fit the exclusion criteria are excluded.

Inclusion Criteria

- Patients with positive blood smear or positive QBc test for malaria.
- Patients with signs and symptoms of severe malaria.

Exclusion Criteria

- Patients with history of smoking and alcoholism.
- Patients with pre existing lung disease, heart disease and renal disease.
- Patients with endocrine disorder like Cushing's disease. Conn syndrome, hypothyroidism etc.
- Patients with vomiting and diarrhea.
- Other concurrent illness.

A consent form is signed by the patient or close relative after he or they are well informed about the risks of obtaining an arterial blood sample. Consent form also includes the permission for using the patients details in medical books and journals.

Soon after admission blood samples are withdrawn for testing for presence of malaria (blood smear/QBc) and also for arterial blood gas analysis and electrolytes. Arterial sample is taken from radial artery and if not posterior tibial, dorsalis pedis, brachial or femoral arteries. A venous sample is also taken for estimating serum electrolytes (arterial sample may give errors in estimating serum electrolytes.

A proforma of detailed history, physical examination and investigations was prepared. Patient or his/her attendants were interviewed elaborately and the details entered into a designed format.

RESULTS

A total of 50 patients are included in the study.

ISSN 2515-8260 Volume 09, Issue 03, 2022

Dermographic Charactristics of the Study Population

A) Male Female Ratio

Males (32) were more than females (18) and they are in a ratio of 1.8:1. This indicates the high outdoor activity of males when compared to females and hence more prone for mosquito bites.

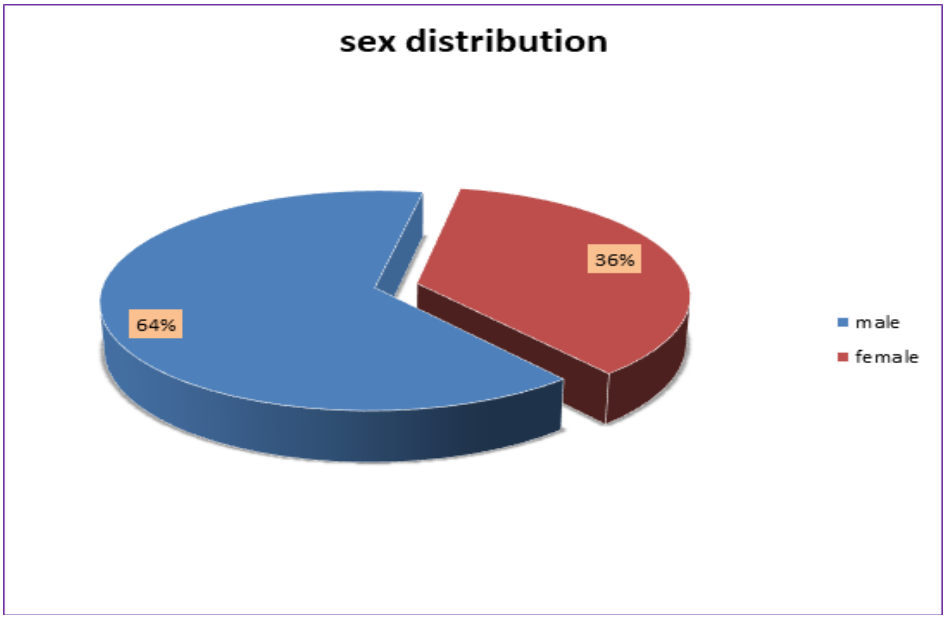

Figure 1: Male and female ratio

B) Age Distribution of the Study Population

Table 1: ?

Age	Male	Female	No.	%
12_22	7	3	10	20
23 - 33	12	8	20	40
34 - 44	8	4	12	24
45 - 55	5	3	8	16
	32	18		

The age of the study population ranges from 14 – 52 yrs with a median age of31.92 yrs. Majority of the study population (40%) are in the 23 -33 age group followed by 34 – 44 age group(24%). 60% of the patients were below the age of 34 yrs.

Clinical Presentation of the Patients

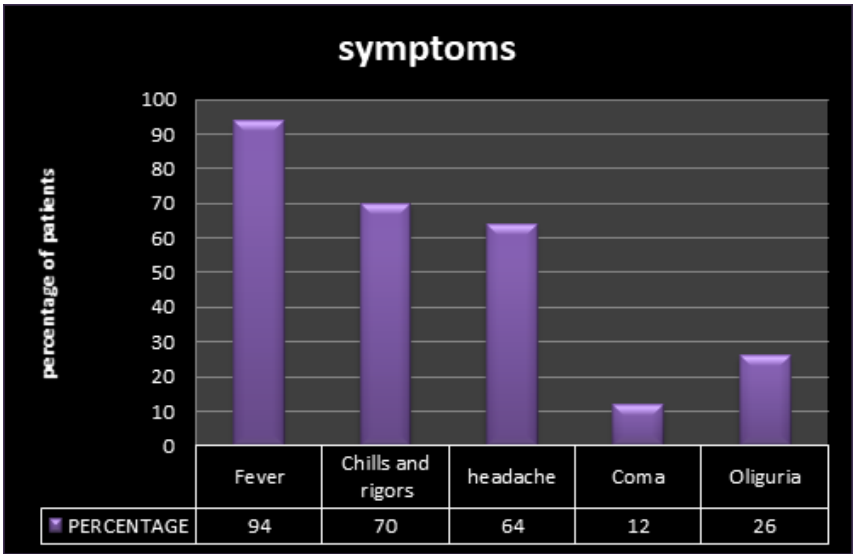

Figure 2: Symptons

Fever with chills and rigors, headache are the common symptoms and jaundice, anemia and shock are the common signs in study population.

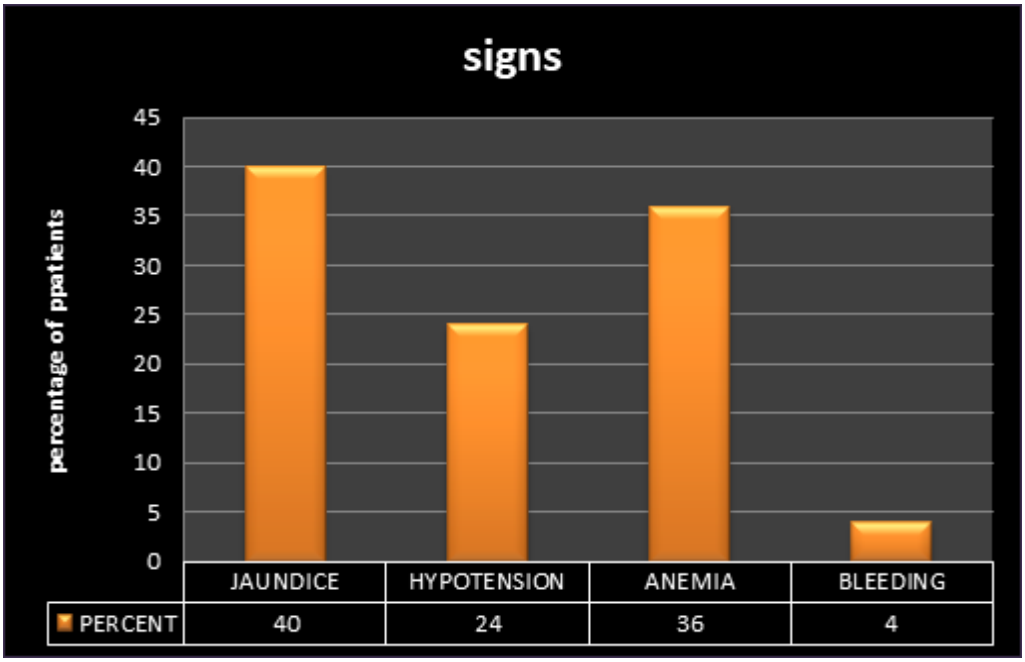

Figure3: Signs

pH CHANGES

Table 2: ?

pH	**fatal group**	**nonfatal group**		
6.95 - 7.05	1	0	no. of patients	%
7.06 - 7.15	3	0		
7.16 - 7.25	4	1		
7.26 - 7.35	6	7	22	44
7.36 - 7.45	4	23	27	54
7.46 - 7.55	0	1	1	2
MEAN	7.27	7.37		
STD DEV×2	0.10	0.05		

(P VALUE 0.0008)

Acidosis is seen in 44% of the patients while 54% of the patients have a normal pH. Two patients have mixed acid base disturbance(metabolic acidosis and respiratory alkalosis). The mean pH of those who died is 7.27±0.10 and those who survived is 7.37 ± 0.05. (p = 0.0008).

$PaCO_2$ CHANGES

Table 3: ?

PACO2	**fatal**	**non-fatal**		
13 _17	1	0		
18 - 22	3	1		
23 - 27	4	0		
28- 32	4	2	NO.	%
33 - 37	3	12	30	60
38 - 42	3	15	18	36
43 - 47	0	2	2	4
mean	28.83	37.06		
std dev×2	8.11	4.96		

Arterial partial pressure of CO2 ranged from 16 – 48 mm of Hg. PaCO2 levels are in normal range in 36% of patients and they are elevated in 60% of patients. Mean value of PaCO2in those who died is 28.83±8.11 and it is 37.06±4.96 in those who survived.

PAO_2 CHANGES

Table 4: ?

PAO2	**Fatal**	**Non-fatal**		
51 - 60	1	0		
61-70	3	0		
71 - 80	2	5	NO.	%
81 - 90	7	19	37	74
91- 100	5	8	13	26
	18	32		
MEAN	82.56	86.63		
STD DEV×2	12.43	5.07		
P VALUE	0.20			

Hypoxia is seen in 74% of the patients. Those who survived had a mean value of 86.63±5.07 compared to the mean value of 82.56±12.43 of those who died (p value > 0.05).

HCO_3 CHANGES

Table 5: ?

Hco3	**Fatal**	**Non-fatal**	
1 _ 6	1	0	
7_11	3	1	

12_16	9	3	No.	%
17 -21	4	14	35	70
22 -26	1	12	13	26
27 - 31	0	1	2	4
32-36	0	1		
	18	32		
mean	14.32	21.15		
std dev×2	5.40	4.67		

Hco3 levels are reduced in 70% of the patients. They were normal in 26% of the patients. Hco3 ranges from 5 to36 mmol/L. Themean value in fatal vs. non fatal group is 14.32±5.40 vs 21.15±4.67.

BASE DEFICIT

Base deficit ranges from 19 to -12. Normal values are seen in 38% of patients. Base deficit is high in 60% of the patients. Mean values of base deficit in fatal and non-fatal groups are 14 and 3 respectively.

Table 6: ?

Base deficit	**Fatal**	**Non-fatal**	**NO**	**%**
_13 _ -4	0	1		
_3 _ +3	1	18	19	38
4_9	6	10	30	60
10_18	10	3		
19 - 27	1	0		
	18	32		
MEAN	14	3		
STD DEV×2	5.40	4.74		
P VALUE	<0.01			

Anion Gap Changes

About 38% have normal anion gap and high anion gap acidosis is present in 62% of the cases. The mean value of anion gap in those who died is 17.06± 4.08 whereas it is 11.88±3.69 in those who survived. (p value <0.001)

Table 7: ?

Anion gap	**Fatal group**	**Nonfatal group**	**No.**	**%**
8 _ 12	2	17	19	38
13 _17	6	11	31	62
18 -22	8	4		
23 - 27	2	0		
	18	32		
MEAN	17.06	11.88		
standard deviation×2	4.08	3.69		

Lactate Levels

Lactate levels are elevated in all the patients with a range of 2.1 – 5.6. Lactate levels are more than 3.0 mmol/l in 64% of the patients. In fatal vs. non fatal group the mean lactate levels are 4.08±0.90 vs. 3.10±0.50 (p value = 0.0003).

Table 8: ?

Lactate	fatal	non fatal	No.	%
0.6 -1.7	0	0	0	0
1.8 - 2.9	3	15	32	64
3.0 - 4.1	8	16		
4.2 - 5.3	5	1		
5.3 - 6.4	2	0		
mean	4.08	3.10		
STDDEV×2	0.90	0.50		

Serum Creatinine Levels

Table 9: ?

S- Creatinine	fatal	non-fatal	no	%
0.6 - 1.5	4	16	20	40
1.6 - 3.0	3	11	30	60
3.1 - 4.5	8	3		
4.6 -6.0	3	2		
mean	3.14	2.05		
std dev×2	1.45	1.14		

About 60% of the patients had elevated renal parameters. The creatinine values ranged from 0.6 to 5.9. Among 60% only 4% had pre renal renal failure. The mean values of creatinine in fatal and nonfatal groups are 3.14±1.45 and 2.05±1.14 with a p value0.01.

Sodium Levels

Sodium levels are low, high and normal in 52%, 6% and 42% respectively. Those who died had a mean value of 122.72±12.51 and those who survived had a mean value of 133.97±8.51. (p value = 0.07).

Table 10: ?

Sodium	Fatal group	Nonfatal group		
96- 105	1	0		
106 - 115	2	1		
116 - 125	4	5		%
126 - 135	4	9	26	52
136 -145	6	15	21	42
146 -155	1	2	3	6
	18	32		
mean	127.72	133.97		
Std deviation×2	12.51	8.51		

Potassium Levels

Table 11: ?

Potassium	**fatal group**	**nonfatal group**	**no.**	**%**
2.6- 3.5	2	5	7	14
3.6 - 4.5	5	22	27	54
4.6-5.5	9	5	16	32
5.6-6.5	2	0		
	18	32	50	
mean	4.63	4.09		
std dev×2	0.73	0.53		

Potassium levels are normal in majority of the patients (54%). Low and high levels are seen in 14% and 32% of the patients respectively. Fatal group had a mean value of 4.63±0.73 and non fatal group had a mean value of 4.09±0.53 (p value 0.009).

Serum Chloride Changes

Table 12: ?

Chloride	**Fatal**	**Nonfatal**		
62 - 70	1	0		
71 - 79	1	0		
80 -88	2	6	No.	%
89 - 97	5	3	18	36
98 - 106	6	14	20	40
107 -115	2	9	12	24
116 - 124	1	0		
	18	32		
MEAN	96	101		
STD DEV×2	13.10	8.84		

Chloride levels are high, normal and low in 24%, 40% and 36% of patients respectively. There is no significant difference in the means of fatal and nonfatal groups (p value = 0.20).

Calcium Levels

Serumcalcium levels are low (58%)or normal (40%). Mean value of calcium in those who survivedis 8.93±0.77 is not significantly different from the mean value of those who died i.e. 8.79±0.80 (p value 0.56).

Table 13: ?

Calcum	**Fatal**	**Non-fatal**	**No.**	**%**
7.6 - 8.1	4	6	29	58
8.2 - 8.9	7	12		

9.0 - 9.7	4	9	20	40
9.8 -`10.5	3	4		
10.6 - 11.3	0	1		
MEAN	8.79	8.93125		
STDDEV×2	0.80	0.77		

Phosphate Levels

Table 14: ?

Phosphate	**Fatal**	**Non-fatal**	**NO**	**%**
1.5 - 3.0	9	7	16	32
3.1 - 4.5	7	22	29	68
4.6 - 6.0	2	3	5	10
MEAN	3.07	3.49		
STD DEV×2	0.98	0.56		

Phosphate levels are normal, low or high in 68%, 32% and 10% respectively. 3.07±0.98 vs. 3.49±0.56 are the mean values of phosphate in fatal and nonfatal groups (p value =0.104).

DISCUSSION

The results in our study are compared with studies in India and abroad.

Age:

In the present study maximum number of patients (40%) is encountered in the age group of 23 – 33 yrs followed by 34 -44 yrs age group (26%) and the mean age of cases is 31.92 yrswith a range of14 -52 yrs. The mean age in AIIMS studyis 33.2 years and a range of 12 – 65 yrs.

Sex:

In our study males constitute 64% and females constitute 36% of study population. There were 71.4% males and 28.6% females in AIIMS study.

Arterial pH:

In the present study, 44% patients are in the acidic range, 54% are in normal range. In the study conducted in AIIMS,[4] 46.4% of patients had acidosis. 67% of patients had acidosis in the study by Day NP etal,[5] 22% of patients had acidosis in the study by Oguche et al.[6]

The mean pH in fatal vs. non-fatal cases in the present study is 7.27±0.10 vs. 7.37±0.05 as compared to AIIMS study which is 7.26 vs. 7.37.

Acidosis is significantly associated with mortality in our study (p value 0.0008, relative risk 4.29).Thisfinding is similar to the studies conducted by Day NP et al (relative risk 5.0) and Oguche et al (p value <0.05).[5,6]

Majority of the patientshad low levels (60%).most of the patients developed metabolic acidosis. very few developed mixed disturbances. 3 patients and 2 patients developed respiratory acidosis and respiratory alkalosis respectively in addition to metabolic acidosis. In the study by Day NP et al,[3] patients developed respiratory acidosis ($PaCO_2$ > 45 mm of Hg). In the present study $PaCO_2$ is found to be significantly associated with mortality. The mean value in fatal vs. non fatal patients is 28.83mm of Hg vs. 37.06 mm of Hg (p value 0.0006).

PaO_2:

In the present study, 74% of the patients are found to be hypoxic at the time of admission .29.7% of the patients had PaO2 <80 mm of Hg. No significant association with mortality is present (p value 0.20). These data suggest hypoxia is common regardless of disease severity.

Bicarbonate:

In the AIIMS study arterial bicarbonate is low in 85.7% and <8mmol/l in 14.3% of patients. 70% patients in our study developed low levels of bicarbonate with <8 mmol/l seen only in 6% of patients.

Mean value in fatal vs. nonfatal patients is 14.32±5.40 mmol/l vs. 21.15±4.67 mmol/l and this is found to be significant in our study (p value <0.05).mean values in AIIMS study were 13.8 vs. 18.9 mmol/l in fatal vs. nonfatal group respectively.

Anion GAP

62% of patients had high anion gap metabolic acidosis. Significant association is found with mortality (p value0.001). Mean values in fatal vs. non fatal groups are 17.06 vs. 11.88 in our study. Dondrop et al study had a mean anion gap value of 11.1 which strongly predicted mortality independent of lactate and creatinine concentrations.

Lactate:

Hyperlactatemia is seen in all patients in our study. Lactate levels >4 mmol/l is seen in 64% of patients compared to 35% of patients in Day NP et al study.[5] Significant association is found with mortality in our study (p value 0.003) which is similarly seen in studies by Day NP et al and Dondrop et al.[5,7]

Sodium:

In our present study low sodium levels are seen in 52% of the patients. Serum sodium levels are low in 42.8% in AIIMS study,4 16% in Oguche et al study, 76.4%.[6]

In fatal vs. non fatal group the mean sodium level is 127.72±12.51 vs. 133.97±8.51. In AIIMS study the mean value of sodium is 133 vs. 134.[3]

No significant association is found between low sodium levels and mortality in our study. This finding is similar to the study by Oguche et al.[6]

Potassium:

Serum level of potassium is found to be normal in majority of the patients (54%). Elevated potassium levels are seen in 16 (32%) of patients of whom 11(68.75%) died. Hypokalemia is seen in 14% of patients. Potassium levels are normal in 77% of patients in Maitland et al study and 50% in AIIMS study.[9]

The mean values of potassium in fatal vs. nonfatal group are 4.63±0.73 vs. 4.09±0.53 in the present study and in AIIMS study the values are 4.5 vs. 3.5 respectively.

It was found in the present study that hyperkalemia is significantly associated with mortality (p value=0.0098).Similar finding is observed in Maitland et al study.[9] Hypokalemia is not associated with mortality as is also seen in Oguchi et al study.[6]

Mean value of calcium in fatal group is 8.79±0.80 mg/dl and the mean value in non fatal group is 8.93±0.77 mg/dl in the present study. In AIIMS study the mean values of calcium in fatal vs. nonfatal group are 8.3 vs. 8.78 mg/dl.

No significant association is found between hypocalcemia and mortality (p value = 0.56). Similarly no significant association is found in studies by Maitland et al 9, and Davis et al.[10]

3.07±0.98 mg/dl and 3.49±0.56 mg/dl are the mean values of phosphate in fatal and nonfatal cases in our study. In AIIMS study fatal and nonfatal cases had mean values of 4.66 mg/dl and 2.66mg/dl respectively.

Significant association between serum phosphate and mortality is not found in our study and also in Maitland et al, Avoola et al and Davis et al studies.

Strong predictors of mortality in our study are acidosis, high anion gap and elevated lactate levels. This finding is similar to the studies by Dondrop et al and Day NP et al.[5,7]

CONCLUSION

- Acidosis is commonly seen with malaria and this most often high anion gap metabolic acidosis contributed by lactic acidosis, renal failure and other anions.
- Electrolyte abnormalities are common in malaria with hyponatremia, eukalemia, hypochloremia, hypocalcemia and hypophosphatemia being the commonest.
- Prognostic information can be obtained from ABG and electrolyte analysis
- Strong predictors of mortality include acidosis, high anion gap, hyperlactatemia and hyperkalemia.
- No relation with mortality is seen with hypoxia, hyponatremia, hypocalcemia and hypophosphatemia.

Acknowledgment

The author is thankful to Department of General Medicine for providing all the facilities to carry out this work.

REFERENCES

1. Bruce- Chwatt LJ. History of malariafrom prehistory to eradication. Malaria: principles and practice of malariology. Churchill livingstone,1988;1-59
2. Laveran CLA. Note sur un nouveau parasite trouve dans le sang de maladies attaints de fievre palustrr. Bull Acad MED 1880;9:1235
3. N J White; Manson's textbook of tropical medicine ,Malaria (chap 71), 21st edition 2003;1205-1285.
4. Manish guptaK,piyush jain et al, JAPI year book ,2002.Poster session APICON 2002.
5. Day NP, Phu NH, Mal NT, et al. The pathophysiologic and prognostic significance of acidosis in severe adult malaria.Crit Care Med 2000;28:1833-1840.
6. Oguche S, Omokhodion SI, Adeyemo AA, Olumese PEWest. Low plasma bicarbonate predicts poor outcome of cerebral malaria in Nigerian children. Afr J Med. 2002 Oct-Dec; 21(4):276-279.
7. Dondorp AM, Chau TT, Phu NH, Mai NT, Loc PP, Chuong LV, Sinh DX, Taylor A, Hien TT, White NJ, Day NP.Unidentified acids of strong prognostic significance in severe malariaCrit Care Med. 2004 Aug;32(8):1683-8
8. Fryatt RJ, Teng JD, Harries AD, Moody AH, Hall AP, Forsling ML.Plasma and urine electrolyte concentrations and vasopressin levels in patients admitted to hospital for falciparum malaria.Trop Geogr Med. 1989 Jan;41(1):57-60
9. Maitland K, Pamba A, Fegan G, Njuguna P, Nadel S, Newton CR, Lowe B.Perturbations in electrolyte levels in kenyan children with severe malaria complicated by acidosis.Clin Infect Dis. 2005 Jan 1;40(1):9-16. Epub 2004 Dec 6
10. Davis TME,Pukrittayakamee S, Woodhead JS et al. Calcium and phosphate metabolism in acute falciparum malaria.Clin Sci 1991; 81:297-304.