Original Article

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Study of Routine Hemogram And Serum Electrolytes (Na+, K+) Changes in Malaria Patients at Tertiary Care Hospital of Western India

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ABSTRACT

Background: Malaria is still a major health problem accounting for more than 2 million lives around the globe. This study aims to assess the routine hemogram and serum electrolytes changes enabling early detection of malaria and thereby alerts the clinician to start early treatment.

Methods: A total of 325 smear positive Malaria cases at indoor and outdoor patient departments of V.S. General Hospital, Ahmedabad were analyzed by performing complete blood count (CBC) in automated cell counter and serum electrolytes estimation in biochemistry analyzer. Results were analyzed for species specificity and compared with the other relevant studies.

Results: P.Vivax cases (74.8%) were more common than P.falciparum cases (25.2%) with Male predominance. Anemia (80%) and thrombocytopenia (85.8%) were most significant findings in malaria patients in routine hemogram. Mean hemoglobin was 10.3 Gram/dl; Mean Total WBC count was 6314.8/cumm and Mean Platelet count was 89628.2/cumm. Serum electrolytes showed hyponatremia (59.7%), hypokalemia (29.9%) and hyperkalemia (20.6%). All these electrolyte derangements were found more common with P.falciparum cases.

Conclusions: In patients presenting with fever, low hemoglobin and platelet count must trigger high index of suspicion of malaria. Serum electrolytes should be regularly monitored in all malaria positive cases as their derangements may indicate disease severity and timely correction of it may prevent deadly complications improving morbidity and mortality in high grade infections.

Keywords: Malaria, Anemia, Thrombocytopenia, Serum Electrolytes

Introduction

Malaria has worldwide distribution in tropical and subtropical regions and poses a major public health challenge. [1] In spite of worldwide efforts to reduce its transmission, malaria still remains a major cause of morbidity and mortality. [2] Around 1.5 million laboratory confirmed cases of malaria are annually reported in India. Transmission season for malaria in the city of Ahmedabad is believed to be from May to August with significant rise in the number of cases of Plasmodium vivax (P.Vivax) over plasmodium falciparum (P.Falciparum) has been observed. [3] Direct visualization of parasite on peripheral blood smear examination is the "gold standard" and cost effective for the diagnosis of malaria.[4] Malaria has a significant impact on routine hemogram comprising of hemoglobin(Hb) percentage, Red blood cell(RBC) count, RBC indices, Total white blood cell(WBC) count, Platelet count, Differential WBC Count with Peripheral Smear findings and some of these changes are species specific. The hemogram abnormalities are anemia and thrombocytopenia which is most marked and have been reported invariably. Others include atypical lymphocytosis, leukopenia, leukocytosis, neutropenia, neutrophilia, eosinophilia, monocytosis, serum electrolyte changes and rarely bone marrow suppression to fulminant disseminated intravascular coagulation (DIC).[5] Serum electrolyte changes comprise hyponatremia, hypokalemia and hyperkalemia.[6] Detection of the hemogram as well as serum electrolyte changes in patients of malaria enable the clinician to establish an effective and early therapeutic intervention, in order to prevent the occurrence of major complications and death. The present study was carried out to assess the changes in routine hemogram and serum electrolyte levels in proven cases of malaria in western part of India in the city of Ahmedabad, Gujarat state and to correlate and determine the association of above changes with respect to specific malaria parasite species.

Materials and Methods

This prospective study was conducted from September 2014 to august 2016 at a Smt. NHL Municipal Medical College, V.S General Hospital, Ahmedabad after obtaining Ethical committee approval of Institutional Review Board.

Indoor and outdoor malaria positive cases satisfying following criteria were included in the study:

- Age > 1 year of either sex
- Slide positive malaria cases (P.vivax or P.falciparum)
- Previously untreated for present episode of malaria.

Patients with clinical history and or finding suggestive of chronic liver disease, bleeding disorder, thrombocytopenia, drug intake or conditions which might have contributed in blood changes were excluded from study.

The clinical diagnosis of malaria was confirmed by peripheral blood smear examination which is gold standard for the diagnosis of malaria. For this 5ml of venous blood was collected from each patient in EDTA tube for complete blood count (CBC) and in plain tube for serum electrolytes (Sodium and Potassium) estimation. For microscopic examination of peripheral blood thin and thick films were made on different slides and stained with Field's stain. Grading of parasitemia (by semi quantitative scale) was done from thick film examination. 325 samples were tested on automated 5 part cell counter (Cell dyn Ruby – Abott Diagnostics) for CBC including Hb, total WBC count, RBC count, hematocrit, red cell indices (MCV, MCH, MCHC), and platelet count. In all samples differential WBC count was done from peripheral blood film by counting 100 WBCs. Samples for serum elecvtrolytes were tested in Automated Biochemistry Analyzer- Abbott Architect c8000 after centrifugation of the sample.

Thrombocytopenia was regarded mild if platelets counts were (50-150 $x10^3/\mu L$), moderate if platelets counts were (20-50 $x10^3/\mu L$), and severe if platelets counts were (< 20 $x10^3/\mu L$).

Analysis: The data was entered in Microsoft Excel sheet to evaluate the results. Percentage analysis was carried out. The results were tabulated as cross tables and graphs.

Results

Out of total 325 cases, 82 patients were affected with P.falciparum (25.2%), and 243 patients (74.8%) were affected with P.vivax. There were 25(7.7%) pediatric patients in the study with 16 P.falciparum and 9 P.vivax cases. In both the species, majority of patients were adults (figure 1). Males (72.3%) were more affected than females (27.7%). Male: Female ratio was 2.6: 1. There was no significant difference between two species of malarial parasites gender wise.

80% of the malaria patients had anemia. 82.9% of P.falciparum positive cases were anemic; anemia was mild in 24.4 % cases, moderate in 36.6% cases and severe in 21.9% cases. 72.4% of P.vivax positive cases were anemic; anemia was mild in 39.9 % cases, moderate in 20.9% cases and severe in 11.6% cases. (Table 1). So there is significant association between malaria and anemia; it is more common in P.falciparum than P.vivax affected patients.

RBC Count- Out of total malaria positive cases RBC Count was normal in 41.5% of patients; low in 49% of patients and high in 9.5% of patients. Overall 65.2% of patients had low (<35) hematocrit level. 80.5% of P.falciparum cases and 60.1% of P.vivax cases had low hematocrit level.

RBC Indices- In present study majority (66.2%) of patients had normal MCV and 28.3% of patients had low MCV. Species wise, 31.7% of P.falciparum and 27.2% of P.vivax cases had low MCV. Overall MCH was low in 68.3% of cases**.** 27.4% of cases had normal and 4.3% of cases had high MCH. No significant difference in values of MCH was found among the two species. Overall MCHC was low in 67.7% of cases**,** while 27.4% of cases had normal and 4.9% of cases had high MCH. 56.1% of P.falciparum cases and 71.6% of P.vivax cases had low MCHC.

Majority of malaria patients (85.8%) had low platelet count (thrombocytopenia). With relation to severity of thrombocytopenia, 56.9%, 24.3% and 4.6% of patients had mild, moderate and severe thrombocytopenia. Overall thrombocytopenia was more common in P.falciparum (93.9%) than P.vivax (83.1%) patients.Mild thrombocytopenia was more seen with P.vivax (59.7%) than with P.falciparum (48.9%) patients and moderate thrombocytopenia was more seen with P.falciparum (40.2%) than with P.falciparum (18.9%) patients. There was no significant difference in both species in the incidence of severe thrombocytopenia (P.falciparum -4.9% and P.vivax-4.5%). (Figure 2)

Total WBC count was normal in 69.8% of malaria cases while it was low (leucopenia) in 22.5% of cases. Species wise, high Total WBC Count (leucocytosis) was found in 46.3% of P.falciparum cases and 35.8% of P.vivax cases & low total WBC count was found in 29.3% of P.falciparum cases and 20.2% of P.vivax cases. Mean values of hemoglobin, Total WBC count, Platelet count, and RBC count in P.falciparum cases are lower than those of P.vivax infection. These shows that P.falciparum infection has more effect on routine hemogram baseline parameters than P.vivax infection.(Table 2)

Serum Sodium was predominantly low (hyponatremia) in 59.7% of all cases. Species wise 65.9% of P.falciparum & 57.6% of P.vivax patients had hyponatremia. Thus in the present study, hyponatremia was found to be more frequent in P.falciparum cases. Serum Potassium was normal in about half (49.5%) of malaria cases. Remaining cases had hypokalemia (29.9%) and hyperkalemia (20.6%). Hypokalemia was found in 34.1% of P.falciparum patients

and 28.4% of P.vivax patients. Hyperkalemia was seen in 20.8% of P.falciparum patients and 20.6% of P.vivax patients. So both hypokalemia and hyperkalemia were found to be more common in P.falciparum patients in present study. (Table 3) Both hyponatraemia and hypokalaemia were present in 27.7% of all patients in present study.

Table 1: Relation between severity of Anemia in P.falciparum and P.vivax cases.

Hemoglobin(Gm/dL)	P.FALCIPARUM CASES	P.VIVAX CASES	TOTAL
NORMAL (>12.5)	12(17.1%)	53(27.6%)	65(20%)
MILD (>10-12.5)	21(24.4%)	110(39.9%)	131(40.3%)
MODERATE (7-10)	31(36.6%)	53(20.9%)	84(25.8%)
SEVERE (<7)	18(21.9%)	27(11.6%)	45(13.9%)
TOTAL	**82(100%)**	**243(100%)**	**325(100%)**

Table 2: Comparison of mean of baseline hemogram parameters between P.falciparum and P.vivax cases:

		Number of cases	Mean Value	Std. Deviation	Minimum Value	Maximum Value
Hemoglobin	P.falciparum	82	9.4	2.8	4.2	16
	P.vivax	243	10.7	2.6	3.2	17.1
	Total	325	10.3	2.7	3.2	17.1
WBC Count	P.falciparum	82	7009.5	5107.3	1620	32700
	P.vivax	243	6080.3	3010.8	1390	27400
	Total	325	6314.8	3668.2	1390	32700
Platelet Count	P.falciparum	82	66258.3	45947.7	6000	227000
	P.vivax	243	97514.4	59971.6	8000	382000
	Total	325	89628.2	58301	6000	382000
RBC Count	P.falciparum	82	3.7	1.1	1.5	5.9
	P.vivax	243	4.3	0.9	1.5	6.5
	Total	**325**	**4.1**	**1.0**	**1.5**	**6.5**

Table 3: Relationship of S. Sodium and S. Potassium with P.falciparum & P.vivax Malaria

	Sodium Level		Potassium Level	
	P.falciparum	P.vivax	P.falciparum	P.vivax
Normal	28(34.1%)	103(42.4%)	37(45.1%)	124(51%)
Low	54(65.9%)	140(57.6%)	28(34.1 %)	69(28.4%)
High	-	-	17(20.8%)	50(20.6%)
Total	**82(100%)**	**243(100%)**	**82(100%)**	**243(100%)**

Table 4: Comparison of present study with other studies in India:

		Agravat et al[7] (2010)	Shamim Akhtar et al[8](2012)	Shyamsundar Rao et al[9] (2013)	Gohil et al[10] (2013)	Present study (2015)
Species	P.falciparum	71 %	52.7 %	23.6 %	35.5 %	25.2 %
	P.vivax	29 %	36.5 %	46.5 %	54.5 %	74.8 %
	Mixed	-	10.8 %	39.9 %	10 %	-
Age	1-15 Yrs	12.2 %		17.6 %	19.1 %	7.7 %
	16-60 Yrs	82.6 %		82.4 %	76.3 %	87.4 %
	>60 Yrs	5.2 %		-	4.5 %	4.9 %

		Agravat et al[7] (2010)	Shamim Akhtar et al[8](2012)	Shyamsundar Rao et al[9] (2013)	Gohil et al[10] (2013)	Present study (2015)
Sex	Female			41.5 %	24.5 %	27.7 %
	Male			58.4 %	75.5 %	72.3 %
	M:F ratio			1.5:1	3.07:1	2.6:1
Anemia	Total (pf+pv)		86.5 %	60.2 %		80 %
	P.falciparum		89.7 %	84.6 %		85.4 %
	P.vivax		85.2 %	34.6 %		78.2 %
Thrombocytopenia	Total (pf+pv)	81.5 %	71.6 %	69.9 %	45.5 %	85.8 %
	Mild	26 %			54.6 %	56.9 %
	Moderate	31 %			34.6 %	24.3 %
	Severe	21.3 %			10.9 %	4.6 %

Pf - P.falciparum, Pv- P.vivax

Table 5: Comparison of Serum Electrolyte levels in Malaria cases.

	Thanachartwet et al[11] (2008)	Present study (2015)
Normal S.Sodium	61.7%	40.3%
Hyponatremia	37%	59.7%
Hypernatremia	1.3%	-
Normal S.Potassium	56.6%	49.5%
Hypokalemia	43%	29.9%
Hyperkalemia	0.4%	20.6%
Hyponatremia & Hypokalemia	17%	27.7%

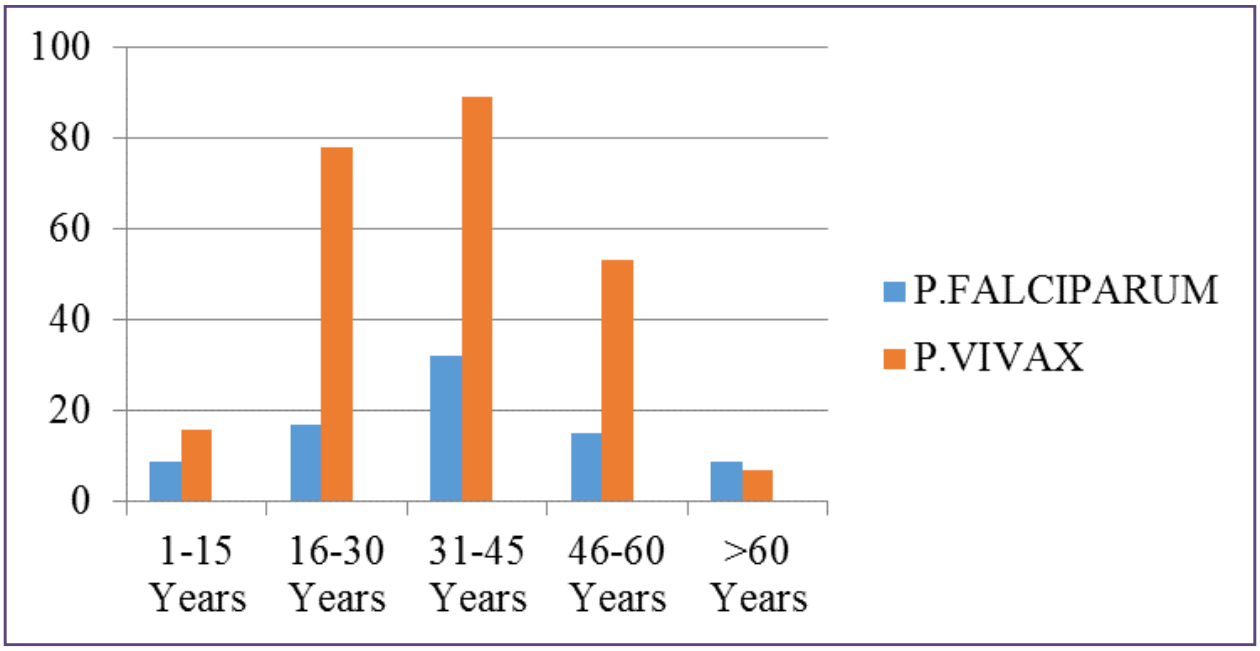

Fig. 1: Age wise distribution of malaria cases.

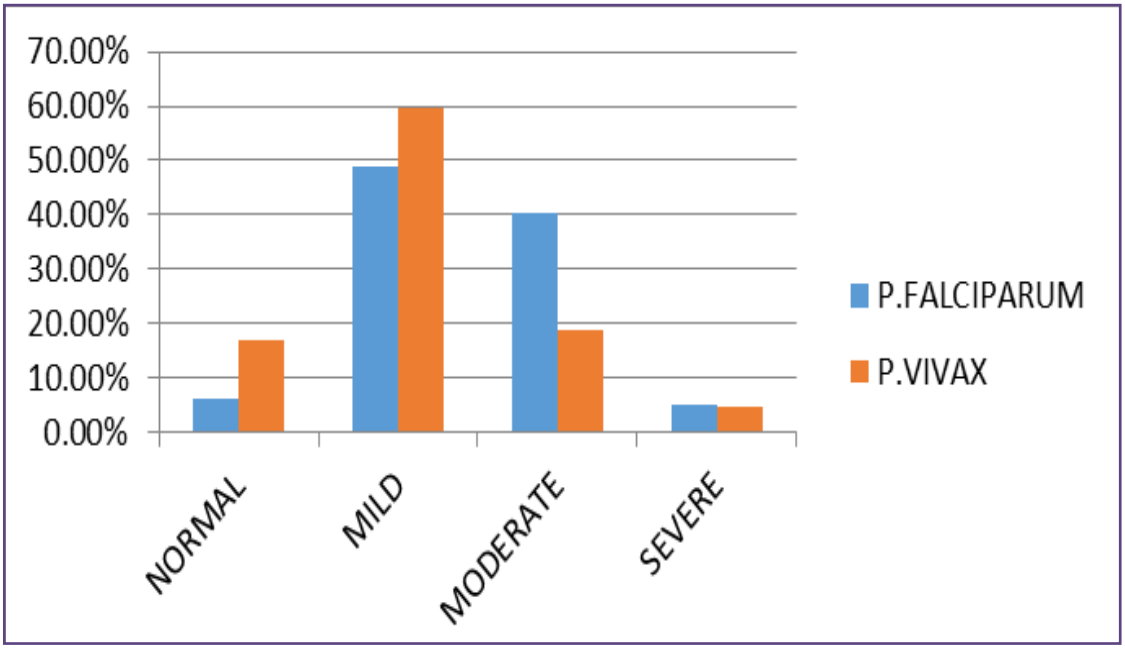

Fig. 2: Relationship of thrombocytopenia with P.falciparum & P.vivax cases.

Discussion

The results of the present study (changes in routine Hemogram and S. electrolytes) were compared with the previous studies. (Table 5)

There was predominance of P.falciparum in studies by Agravat et al & Shamim Akhtar et al whereas there was predominance of P.vivax in recent studies of Shyamsundar et al and Gohil et al. [7,8,9,10] Mixed infection was also reported in above mentioned studies. The present study shows predominance of P.vivax infection (Table 4).

Anemia is a common feature found in present study and significantly associated with P.falciparum infection. This finding is comparable with the findings of Shyamsundar et al and Gohil et al showing similar results. [9, 10] One of the important reasons for anemia could be rapid and acute destruction of RBCs in malaria infection (Table 4).

Thrombocytopenia was found in 85.8% of cases in present study which is comparable with the finding in all other studies (table 4). Thrombocytopenia was present with almost equal frequency in both P.falciparum and P.vivax cases. Mechanism of thrombocytopenia could be immune mediated destruction of circulating platelets, decreased platelet survival, splenic uptake & sequestration in falciparum malaria.

Majority (59.7%) of malaria patients in the present study had hyponatremia and it was more common with P.falciparum infection (65.9%) which is comparable with the findings of study of Thanachartwet et al in which 37% of all malaria patients were hyponatremic and 81% of P.falciparum cases were having hyponatremia(Table 5).[11] Most probable mechanism for hyponatremia could be increased ADH secretion secondary to hypovolemia due to excessive sweating, pyrexia etc.

Total 50.5 % of malaria patients in the present study had changes in S. Potassium levels in which hypokalemia (29.9%) were more common than hyperkalemia (20.6%). Both hypokalemia and hyperkalemia were more common in P.falciparum patients in present study. This is comparable with Thanachartwet et al in which 43% of all malaria patients were hypokalemic; 58% of P.falciparum were showing hypokalemia in their study (Table 5). [11] Both hyponatremia and hypokalemia were present in 27.7% patients in present study whereas 17% of patients in the study of Thanachartwet et al. [11] Thanachartwet et al stated that hyponatremia might result from an increased secretion of antidiuretic hormones (in response to hypovolemia). He also stated volume depletion was the predominant risk factor for hypokalemia and likely pathophysiological mechanism for hypokalemia is multifactorial from a combination of intracellular translocation of potassium from extracellular fluid and urinary potassium loss. [11] This could be the main pathophysiological mechanisms behind hyponatremia and hypokalemia in present study.

Other studies on electrolyte changes in malaria patients also have similar results. [12]

Hyponatremia was observed in the majority of adult and pediatric patients with severe malaria in a study by M.C.English et al in UK. [13] Rajapurkar M M et al stated that Hypokalemia occurs because of hyperventilation due to hyperpyrexia and respiratory alkalosis and Hyperkalemia occurs in patients who have marked intravascular hemolysis and/or well established acute tubular necrosis. [14] Dworak et al stated that there was a progressive decrease in the sodium and potassium levels within 12 hrs of the parasite's entry into the host. [15]

Hanson et al reported that hyponatremia is a common feature in adult patients presenting with severe malaria and conclude that consequences of hypovolemia could be the major pathophysiological mechanism behind it. [16] Ikekpeazu et al also reported significant decrease in serum sodium and potassium levels in malaria patients. [17] Jasani et al concluded that both hyponatremia and hypokalemia were common in malaria and more common with P.falciparum cases and severe malaria cases. [18] Maitland et al reported that hypokalemia in malaria has been observed in P.falciparum cases in children where underlying cause was proposed to be the correction of acidosis seen usually in severe cases of malaria. [19]

Conclusions

Anemia and thrombocytopenia are main haemogram findings. Therefore, when used in addition to clinical and microscopy parameters, it has possible predictive value for clinician to include malaria as one of the differential diagnosis in cases of high grade fever and significantly improve patient's condition by prompt timely initiation of anti-malarial therapy. The findings of the present study also emphasize the need to manage the electrolyte derangements in the overall management of the malaria infections as electrolyte disturbances may be an indicator of the disease severity. Hence serum electrolytes should be regularly estimated in the malaria patients of all the age groups to prevent the complications which might result from electrolyte depletion, as these may produce grave consequences in otherwise ill patients of malaria.

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