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Research Article

A comparative study of clinical, biochemical and hematological profiles in smear positive malaria patients: at a tertiary care center located in rural part of Gujarat, India

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ABSTRACT

Background: Aims and objectives of current study were to study the clinical, biochemical and hematological profiles in smear positive malaria patients and its correlation to immediate outcome of patient. To analyze the biochemical and hematological imbalances and its correlation with clinical presentation and type of malarial parasites. To elucidate the correlation of hematological and biochemical changes in children infected with malaria and their impact on immediate outcome of patients.
Methods: All patients admitted with a diagnosis of malaria in department of Pediatrics at Dhiraj Hospital, Piparia, Vadodara, during the study period of January 2013 to June 2014. Sample size was 106 cases. Inclusion criteria for the study was all children under 18 years of age with smear positive malaria cases diagnosed. The study was done after obtaining a detailed history, complete general physical examination and systemic examination. The patients were subjected to relevant investigations. The data regarding patient particulars, diagnosis and investigations is collected in a specially designed case recording form and transferred to a master chart subjected to statistical methods like mean, standard deviation, proportion, percentage calculation and wherever necessary chi square test for proportion are used.
Results: Total 106 patients were enrolled in study. Complications of PF (N=31): Jaundice 16%, severe anemia 23%, thrombocytopenia 29%, leukopenia in 23%, hyponatremia in 29.1%, cerebral malaria in 16% and hyperkalemia in 17%. Complications of PV (N=65): Jaundice 20%, severe anemia 20%, thrombocytopenia 18%, leukopenia in 11%, hyponatremia in 44.6%, hyperkalemia in 9%, cerebral malaria in 12.3% and hypoglycemia in 3.77%.
Conclusions: The incidence of malaria is higher in males than females. Thrombocytopenia is very common in malaria, but spontaneous bleeding is not so common finding in malaria. Mixed infections behave like falciparum malaria. P. vivax malaria though traditionally considered to be a benign entity can also have a severe and complicated course, which is usually associated with P. falciparum malaria.

Keywords: Pediatrics, Malaria, Smear positive malaria, RFT, LFT, Hemogram

INTRODUCTION

Malaria has been noted for more than 4000 years. From the Italian for "bad air," malaria has probably influenced to a great extent human populations and human history. Now a day's though malaria is ignored as a simple disease, one should not forget that it still has vampirical out comes in few cases. It is still one of the most endemic diseases, especially among Southeast Asia and African tropical countries. In spite of intensive worldwide efforts to reduce its transmission, malaria remains the most serious and widespread protozoal infection of humans. India contributes 80% of Southeast Asia malaria burden (24 million cases per year). One of the most important problems in controlling malaria is limited access to effective diagnosis and treatment. Malaria can be cured if promptly diagnosed and adequately treated. Hence, this study was carried out to analyze the trends in clinical features and severity of disease in both P. falciparum and P. vivax infections in our hospital, and to evaluate various clinical, hematological and outcome parameters in malaria patients.

Aims and objectives

- To study the clinical, biochemical and hematological profiles in smear positive malaria patients, at Pediatric department of a tertiary care teaching hospital, and its correlation to immediate outcome of patient.
- To analyze the biochemical and hematological imbalances and its correlation with clinical presentation and type of malarial parasites.
- To elucidate the correlation of hematological and biochemical changes in children infected with malaria and their impact on immediate outcome of patients.

METHODS

All patients admitted with a diagnosis of malaria in department of Pediatrics at Dhiraj Hospital, Piparia, Vadodara, during the study period of January 2013 to June 2014 were taken for the study after considering the inclusion and exclusion criteria. Our study was a clinical, prospective, observational and open study conducted during the period of January 2013 to June 2014. Sample size was 106 cases. Inclusion criteria for the study was all children under 18 years of age with smear positive malaria cases diagnosed at Dhiraj Hospital and willing to participate in the study. Children with congenital liver and/or renal diseases, previously diagnosed and treated cases of smear positive malaria patients, patients with known case of liver disease developing malaria, patients with known case of renal disease developing malaria were excluded from the study.

The study was done after obtaining a detailed history, complete general physical examination and systemic examination. The patients were subjected to relevant investigations like Hemogram - Hb, total leukocyte count, differential leukocyte count, platelet count, blood urea, serum creatinine & serum electrolytes. Blood sugar, total bilirubin, direct bilirubin, SGOT, SGPT, prothormbin time and aPTT were done. All patients were subjected to peripheral smear examination - thick and thin smear for diagnosis of malaria. Two slides were prepared from each sample, one slide with a thick block film and another with a thin blood film and stained with Leishmann's stain. The species and the stage of the parasite were reported after examining the thin blood smear. The data regarding patient particulars, diagnosis and investigations is collected in a specially designed case recording form and transferred to a master chart subjected to statistical methods like mean, standard deviation, proportion, percentage calculation and wherever necessary chi square test for proportion are used.

RESULTS

Out of total 106 patients, 65 (i.e. 61%) were having P. vivax, 31 (i.e. 29%) had P. falciparum while 10 (i.e. 9.43%) had Mix - P. vivax and P. falciparum infection. Total 46 (i.e. 43.4%) were female patients and 60 (i.e. 56.6%) were male patients. Of all the male patients 38 (i.e. 35.8%) had P. vivax, 16 (i.e. 15.1%) had P. falciparum and 6 (i.e. 5.6%) had mix infection. While in female patients 27 (i.e. 25.47%) had P. vivax, 15 (i.e. 14.1%) had P. falciparum and 4 (i.e. 3.7%) had mix infection. Male patients with P. vivax infection were 63% (N=38) of total male patients with malaria, while female patients were only 59% (N=27) of total female patients with P. vivax malaria. As per the results incidence of P. vivax is marginally higher for male patients suffering with malaria compared to female patients with malaria. While it was opposite in case of P. falciparum patients: 27% (N=16) of total male patients had P. falciparum while 32% (N=15) of total female had P. falciparum infection. Results shows that, incidence of P. vivax is marginally more in male and P. falciparum in female patients but it is statistically insignificant (P>0.05).

As mentioned in Table 1, Fever was present in all the patients, mean duration of fever was 5.17 days (SD ± 3.29) ranging from 1 day to 15 days. Of all the associated complaints most common were vomiting in 35 (i.e. 33%) patients and abdominal pain in 28 (i.e. 26.4%) patients. Other complaints were cough in 17 (i.e. 16%) patients, headache in 16 (i.e. 15%) patients, difficulty breathing in 3 (i.e. 2.8%) patients, body ache in 9 (i.e. 8.4%) patients, convulsion in 5 (i.e. 4.7%) patients, diarrhea in 4 (i.e. 3.7%) patients and complaint of weakness in 1 (i.e. 0.9%) patient and bleeding from nose was present in 4 (i.e. 3.7%) of patients. In general examination findings, pallor was present as most common finding in 70 (i.e. 66%) of patients. while icterus was present in 22 (i.e. 20.7%) of

total patients. Knuckle pigmentation was present in 1 (i.e. 0.94%) of patients, lymphadenopathy was present in 6 (i.e. 5.6%) while pedal edema was present in 10 (i.e. 9.4%) of patients, while signs of meningeal irritation were present in 3 (i.e. 2.8%) of patients. Of all the systemic examination findings, hepatomegaly, splenomegaly of hepato-splenomegaly was more consistently present compared to other systemic examination findings. Hepatomegaly was present in 7 (i.e. 6.6%) patients, splenomegaly was present in 20 (i.e. 18.8%) patients while hepato-splenomegaly was the most common finding seen in 39 (i.e. 36.7%) patients. On respiratory system examination crepitation was present in 9 (i.e. 8.4%) patients. On CVS examination flow murmur was present in 13 (i.e. 12.2%) patients. And on CNS examination altered sensorium was present in 11 (i.e. 10.3%) patients.

Table 1: Distribution of symptomatology according to species, positive general examination findings according to species, and positive systemic examination findings according to species.

	P. vivax (N)	% of total pt	P. falciparum (N)	% of total pt	Mix (N)	% of total pt
Symptoms						
Vomiting	14	13.20 %	19	17.92 %	2	1.88 %
Abdominal pain	17	16.03 %	8	7.54 %	3	2.83 %
Headache	10	9.433 %	4	3.77 %	2	1.88 %
Difficulty breathing	0	0 %	3	2.83 %	0	0 %
Body ache	5	4.71 %	3	2.83 %	1	0.94 %
Cough	11	10.37 %	5	4.71 %	1	0.94 %
Convulsion	2	1.88 %	3	2.83 %	0	0 %
Diarrhea	1	0.94 %	2	1.88 %	1	0.94 %
Weakness	1	0.94 %	0	0 %	0	0 %
Bleeding from nose	4	3.77%	0	0 %	0	0 %
Gen exam						
Pallor	43	40.56 %	19	17.92 %	8	7.54 %
Icterus	13	12.26 %	5	4.71 %	4	3.77 %
S/o meningeal irritation	2	1.88 %	0	0 %	1	0.94 %
Knuckle pigmentation	1	0.94 %	0	0 %	0	0 %
Lymphadenopathy	2	1.88 %	3	2.83 %	1	0.94 %
Pedal edema	2	1.88 %	8	7.54 %	0	0 %
Systemic examination						
HS megaly	20	18.86%	13	12.26%	6	5.66%
Splenomegaly	15	14.15%	5	4.71%	0	0%
Systolic murmur	5	4.71%	5	4.71%	3	2.83%
Altered sensorium	6	5.66%	2	1.88%	3	2.83%
Crepitation	7	6.60%	2	1.88%	0	0%
Heaptomegaly	3	2.83%	3	2.83%	1	0.94%

Mean Hb level was 8.44 gm% (SD ± 2.3). 90% (N=9) of patients with mix infection had moderate to severe anemia, while P. vivax and P. falciparum had 88% (N=57) of patients with moderate to severe anemia (Hb <10.9 gm%). Moderate anemia (Hb between 7-10.9 gm%) was present in 68% (N=44) of patient with P. vivax, 65% (N=20) of P. falciparum patients and only 20% (N=2) of patients with mix infection. while severe anemia (Hb <7 gm%) was present in 70% (N=7), 23% (N=7) and 20% (N=13) of patients with mix infection, P. falciparum and P. vivax respectively. So overall there was no difference in level of anemia in patients with P. vivax and P. falciparum infection. But was more severe in case of mix infection. For comparison between P. vivax, P. falciparum and mix infection patients P value was 0.042. While for comparison of severe anemia (Hb<7 gm%) between P. vivax and P. falciparum P value was non-significant (P value 0.79).

Mean platelet count was 1.27 (SD ± 0.84), Ranging from 0.14 lacks to 4.08 lacks. Platelet count <1.5 lacks was present in 44 (i.e. 41.5%) patients with P. vivax, 23 (i.e. 21.6%) patients with P. falciparum and 6 (i.e. 5.6%) with mix infection, out of 106 patients. While severe thrombocytopenia (Platelet count <50000/cu mm) was present in 12 (i.e. 11.32%) patients with P. vivax, 9 (i.e. 8.49%) with P. falciparum and 1 (i.e. 0.94%) with mix infection. According to our study, severe

thrombocytopenia was seen more frequently in patients with P. falciparum 29% (N=9) of patients than 18% (N=12) of patients with P. vivax and 10% (N=1) of patients with mix infection. INR > 1.2 was seen in 29% (N=19) of P. vivax, 26% (N=8) of P. falciparum and 20% (N=2) of mix infection patients. P value was 0.846. While for the results of APTT, it was raised >35.5 in 17% (N=11) of patients with P. vivax and 40% (N=4) patients with mix infection but in isolated P. falciparum. aPTT level were within normal limits (<35.5) for all the patients with P. falciparum. While the raised aPTT level was only seen in case of P. vivax infection and for patient with P. falciparum infection aPTT was in normal range for all.

Total number of patients with cerebral malaria was 15.09% (N=16), P. vivax patients with cerebral malaria 12.3% (N=8), P. falciparum patients with cerebral malaria- 16.3% (N=5), mix infection patients with cerebral malaria 30% (N=3), convulsion common in P. Falciparum patients 9.67% (N=3) and altered sensorium common in 30% of mix infection patients (N=3).

Table 2: Distribution pattern of anemia amongst malaria patients according to species, thrombocytopenia amongst malaria patients according to species, distribution pattern of coagulation profile amongst malaria patients according to species, distribution pattern of cerebral malaria patients according to species.

	P. vivax (N)	% of total pts	P. falciparum (N)	% of total pts	Mix (N)	% of total pts
HB						
>10.9	8	7.54%	4	3.77%	1	0.94%
7-10.9	44	41.50%	20	18.86%	2	1.88%
<7	13	12.26%	7	6.60%	7	6.60%
Platelet						
>1.5	21	19.81%	8	7.54%	4	3.77%
50000-1.5	32	30.18%	14	13.20%	5	4.71%
<50000	12	11.32%	9	8.49%	1	0.94%
INR						
>1.2	19	17.92453	8	7.54717	2	1.886792
<1.2	46	43.39623	23	21.69811	8	7.54717
APTT						
>35.5	11	10.37736	0	0	4	3.773585
<35.5	54	50.9434	31	29.24528	6	5.660377
Cerebral malaria						
Convulsion	2	1.88%	3	2.83%	0	0%
Altered sensorium	6	5.66%	2	1.88%	**3**	2.83%

DISCUSSION

In our study total of 106 cases of malaria admitted to Dhiraj Hospital, from January 2013 to June 2014, were analyzed. Plasmodium vivax occurred in 65 (61.3%) and Plasmodium falciparum occurred in 31 (29.2%) patients while mix infection was present in 10 (9.43%) patients. Table 3 indicates comparing incidence of various species of Plasmodium Malaria. In our study, total 46 (i.e. 43.4%) were female patients and 60 (i. e. 56.6%) were male patients with a M:F ratio 1.3:1. Median age of presentation was 9 years. 100% patients had fever. Typical paroxysms occurred only in very few patients. Most of them had daily fever peaking once in a day. Pallor was reported in 59% of patients in study by Bashwri et al. compared to that in our study pallor was reported in higher percentage of patients (66%). It may be due to difference in nutritional status of our patients who were mostly from rural areas of Gujarat and Madhya Pradesh.[1-3]

Table 3: Indicates comparing incidence of various species of Plasmodium malaria.

Authors	P. vivax	P. falciparum	Mix
Patil BS et al. (2000) (North Karnataka)[1]	66%	34%	-
Jain M et al. (2005) (Madhya Pradesh) [2]	55%	33%	11%
Present study	61.3%	29.2%	9.43%

Table 4 and 5 indicates comparison of clinical symptoms; In our study, vomiting was present in 33% of patients, abdominal pain in 26% of patients, head ache in 16% of

patients, cough in 15% of cases and body ache in 8% of patients.

Table 4: Comparing symptoms in our study with other study.

Signs	Malhotra et al.[4]	Present study
Pallor	75%	66%
Icterus	25%	20%
Splenomegaly	31.25%	43%
Hepatomegaly	-	56%

Table 5: Comparing hepatomegaly and splenomegaly in our study with other study.

Authors	Isolated hepatomegaly (%)	Isolated splenomegaly (%)
Bajiya et al.[6]	9.10	63.0
Mehta et al.[7]	15%	70%
Present study	6.6	18.6

Jaundice was seen in 20% of patients in our study. Serum bilirubin of more than 1 mg% occurred in 57 (i.e. 53%) cases. Jaundice occurred in 34 (i.e. 52.3%) of PV and 23 (i.e. 74.2%) of PF cases. Kochar et al. from Rajasthan has reported jaundice 58.85% of PF cases, which is much higher than the results of our study which had only 20% patients with jaundice.[4,5] As per WHO criteria serum bilirubin of more than 3 mg% occurred 8 (i.e. 7%) cases. Serum bilirubin ranged from 0.4 to 5.7mg/dl. The higher percentage of jaundice noticed in study by Kochar et al. may be due to late presentation or more number of P. falciparum infection or more number of patients with complicated malaria.[6,7] 53% of PV and 58% of PF patients had splenomegaly. This is in correlation with Rajasthan epidemic study where 63% patients had a palpable spleen and 10% had hepatomegaly 29.

Hepatomegaly was noted in 43% of the patients in the present study. In respect of hepatic enzymes, SGPT and SGOT were elevated in 14% and 20% of cases respectively. In study by Sarkar et al.[8] SGPT and SGOT level were increased in 24% and 38% respectively. So compared to previous study hepatic involvement was less common in both the species in our study. Maximum SGOT and SGPT level were 1410 IU/L and 661 IU/L respectively. Mean SGPT was 46.6 and mean SGOT level was 79.46 in our study.

INR >1.2 was found in 29 (i.e. 27%) of patients, 21 (i.e. 32.3%) with P. vivax and 8 (i.e. 25.8%) patients with P. falciparum. Activated partial thromboplastin time: In our study aPTT was found to be increased in 14% of the patients. It was increased in 14.8% of the cases with P. vivax malaria and 3% of cases with mixed infection, while it was not reported elevated in any of the patients with P. falciparum. In a study conducted by Wickramasinghe SN et al. aPTT was increased in 16.6% of the patients, this was similar to what we observed in our study.[9]

In our study altered renal function (S. creatinine >1.0 mg/dl) was reported in 5 (i.e. 7.6%) patients with P. vivax, 6 (i.e. 19%) patients with P. falciparum and 1 (i.e. 10%) patients with mix infection. As per WHO criteria (Serum creatinine >3 mg/dl) ARF was not present in our study.

Cerebral malaria is the most lethal entity of severe malaria and children are more prone than other susceptible group. 8 (i.e. 12%) case from vivax and 5 (i.e. 16%) case from falciparum group showed CNS manifestations. Similarly according to study by Singh et al.[10] among vivax cases 10 (i.e. 16.4%) patients had CNS involvement but in falciparum, 8 (i.e. 33.3%) patients had CNS involvement. None of the patients with cerebral malaria had any residual neurological sequel. Though in our study also, the incidence of cerebral malaria is higher in P. falciparum patients 16% compared to P. vivax patients 12%, but it is still in lower percentage of presentation compared to previous studies.

Unlike studies by Kochar[11] where thrombocytopenia was the most common presentation in both the species, in our study anemia was the most common lab finding (i.e. 86%) followed by thrombocytopenia (i.e. 68%).

According to Bashwri et al., a total of 430 patients (59.2%) were anemic at presentation, anemia was seen more in P. falciparum cases, 257 (65.1%), compared to 126 (i.e. 44.6%) in P. vivax cases (P value = 0.0002). Platelet counts were lower in most P. vivax cases (74.7%) compared to 59.9% of P. falciparum cases (P value = 0.0018).[12] While in our study severe anemia (Hb <7) was present in 70%, 23% and 20% of patients with mix infection, P. falciparum and P. vivax respectively. While severe thrombocytopenia was seen more frequently in patients with P. falciparum 29% of patients than 18% of patients with P. vivax and 10% of patients with mix infection. So as per our observation severe anemia was more prominent finding in P. vivax and Mix infection pts while severe thrombocytopenia was more prominent finding with P. falciparum malaria. No mortality was reported with P. vivax, P. falciparum or mix infection.

CONCLUSION

The incidence of malaria is higher in males than females. Thrombocytopenia is very common in malaria, but spontaneous bleeding is not so common finding in malaria. Mixed infections behave like falciparum malaria. P. vivax malaria though traditionally considered to be a benign entity can also have a severe and complicated course, which is usually associated with P. falciparum malaria.

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