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Original Research Article

Clinical profile of malaria in children at a tertiary care hospital of Bihar and evaluation of parasite LDH based rapid diagnostic test for malaria

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ABSTRACT

Background and Purpose: Malaria is a very common infection leading to high morbidity and mortality. We aimed to evaluate the clinical profile of Malaria in Bihar. We also tried to evaluate the efficacy of pLDH based rapid diagnostic test for Malaria.

Materials and Methods : This was a hospital-based retrospective observational evaluation of record of patients diagnosed with Malaria between August 2018 to August 2020 at Indira Gandhi Institute of Medical Sciences, Patna, Bihar. Statistical significance of different clinical features was evaluated between the prevalent malarial species. pLDH based RDT was evaluated against the microscopic examination of Plasmodium species. Fischer's exact test was used to determine" p value".

Results: 92 patients had confirmed diagnosis of malaria during the study period. The number of males was more 52(56.5%) and most patients were from the age group 5-10 years (37%). Vomiting, respiratory symptoms and jaundice were found significantly higher ($p< 0.05$) in falciparum Malaria cases. Sensitivity, specificity, PPV and NPV of pLDH based RDT were 93.8%, 87.5%, 76.2%, and 97.1% respectively when compared to microscopy. The positive likelihood ratio was 7.5 and the negative likelihood ratio was 0.07

Conclusion: The present study showed the clinical profile of Malaria in the state of Bihar, India. We were able to show that P. vivax infection is more common and P.falciparuminfection more dangerous. Rapid diagnostic tests were found to be effectiveneed to look for evidence of Malaria in sick children even without typical signs and symptoms.

1. Introduction

Malaria is a protozoal disease caused by Plasmodium species and transmitted by the bite of the infected female anopheles mosquito.[1] In 2018, approximately 228 million cases of malaria were estimated worldwide against 231 million cases in 2017. WHO African region had the highest number of malaria cases (93%) followed by WHO South East Asia region (3.4%). 405000 deaths were estimated to occur worldwide due to malarial infection. Also, there was a 70% reduction in cases of malaria in WHO SEAR when compared to 2010.[2] In India, the incidence of malaria and associated mortality has declined. The API (annual parasite index) has reduced from 3.29% in 1995 to 0.9% in 2015. But still, India contributes around 80-90 % of total malaria cases in SEAR. P.vivax constitutes around 50% of total malarial cases in India.[3] Due to increasing drug resistance, there is an absolute need for accurate diagnosis and rational treatment of malaria.[4] Value of microscopic examination in the diagnosis of malaria is of questionable value often in cases with low parasitemia and especially mixed infection.[5]

The present study was done to evaluate the clinical profile of malaria depending on the causative Plasmodium species with the objective to determine the statistical significance between them. Efficacy of pLDH (parasite Lactate Dehydrogenase) based rapid diagnostic test (RDT) for malaria was also evaluated against peripheral blood

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smear microscopy (taking microscopy as the gold standard).

2. Materials and Methods

This was a hospital-based observational retrospective study done at Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India. This is a tertiary care teaching hospital catering to patients from all parts of Bihar, adjoining states of India and Nepal. Records of patients either admitted to the Pediatrics ward or evaluated and treated in OPDs with a confirmed diagnosis of Malaria (ICD 10 code 50-54) were evaluated. The study period was between August 2018 to August 2020 (a total of 2 years).

2.1. Inclusion criteria

1. Children of age up to 14 years
2. Having a confirmed diagnosis of malaria based on the detection of Plasmodium species on RDT (pLDH based) or peripheral blood microscopy, or both.

2.2. Exclusion criteria

1. Proper and complete records not available
2. Diagnosis of malaria without confirmatory isolation of Plasmodium species.

In cases where both the slide examination and the rapid diagnostic test results are negative for malaria, the diagnosis of malaria is extremely unlikely and other causes of illness should be looked for and treated.[6]

Indoor record sheets and outdoor records were looked for age, sex, date of admission, date of discharge, outcome, presenting symptoms, examination findings like pallor, hepatosplenomegaly, etc. The presence of any comorbidity was also recorded. Patients were labeled as severe malaria based on the definition of severe malaria by the working group of WHO. Characteristics of severe malaria include impaired consciousness, severe anemia, pulmonary edema, jaundice, acute renal failure, hypoglycemia, ARDS, bleeding manifestations, hypotension, and metabolic acidosis.[7]

A comparative analysis of diagnostic tests was also done between pLDH based rapid diagnostic test for malaria and routine peripheral blood smear examination (considering blood film as the gold standard for diagnosis of malaria).

2.3. Statistical analysis

MS Excel was used for data entry. SPSS 20 was used for statistical analysis. Fisher's exact test was used to compare clinical features between P. falciparum and P. vivax groups. pLDH based RDT and microscopy for diagnosis of malaria were compared based on sensitivity, specificity, positive predictive value, negative predictive value, and other statistical measures. Tables, Bar diagrams, and Flow charts were used to present the data.

3. Results

During the analysis of records of admitted and OPD patients, a total of 162 patients were found to be treated with a diagnosis of Malaria. 92 patients out of them had a confirmatory diagnosis of Malaria, based on either peripheral blood microscopy, or rapid diagnostic test for malaria (pLDH based test, which is used at our center), or both of the tests. The clinical profile of these patients was analyzed. 70 patients were treated empirically for Malaria without a confirm diagnosis, or complete records were not available for these patients. They were excluded from the study.

Record of 160 patients who had both pLDH based rapid test and microscopy done, were used to evaluate the usefulness of pLDH based RDT for malaria, considering peripheral blood examination as the gold standard for diagnosis of Malaria (Chart 1).

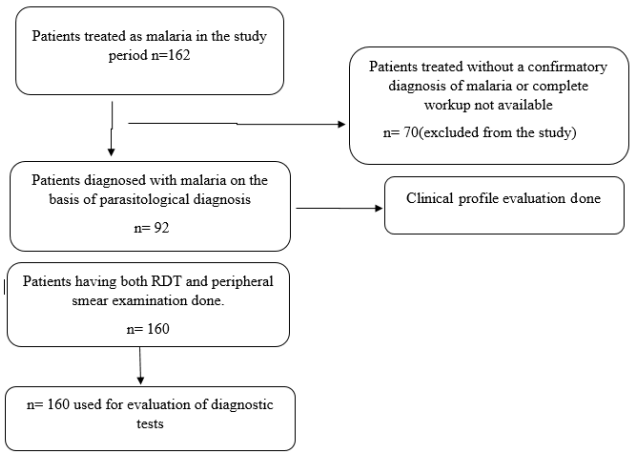

Chart 1: Showingselection of cases

Out of 92 patients under study, 52(56.5 %) were male and 40(43.5%) were female. There were 5(5.4 %) patients in the age group 0-1 year, 25(27.1%) patients in the age group 1-5 year, 34(37%) in the age group 5-10 years, and 28(30%) patients in the age group 10-14 years. So, we can see that maximum (37%) patients belonged to the age group 5-10 years. The mean age of the patients was 7.31 years with SD of ± 4.04 years (Table 1).

There was a seasonal variation in the distribution of cases, the maximum number of cases occurring in August, and other months of rainy season. There were very few cases in the winter season (Figure 1)

Out of 92 cases with parasitological diagnosis, 51(55.4%) cases were found to be infected with P. vivax, 37(40.2%) cases with P. falciparum, and 4(4.3%) cases were found to be having a mixed infection. For the study of clinical features and their significance in between Plasmodium species, the mixed infection was categorized under the falciparum infection group. The

Table 1: Demographic profile of Patients

Age group	No. of Patients (n)	Percent (%)	Male (n)	Female (n)	Mean age(±SD) yr
0-1 year	5	5.4%	3	2	
1-5 year	25	27.1%	12	13	7.31(± 4.04)
5-10 year	34	37%	21	13	
10-14 year	28	30%	16	12	
Total	92	100%	52	40	

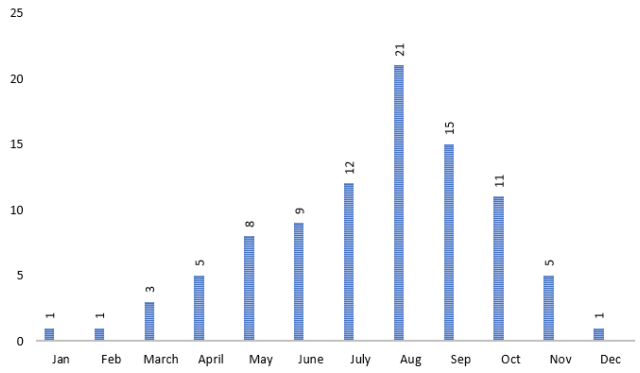

Fig. 1: Month-wise distribution of Malaria cases (n)

different common clinical features, complications, and their statistical significance is shown in Table 2. Fever was the most common symptom (96.7%). Anemia and thrombocytopenia were very common, present in 64% and 67% cases respectively. The presence of vomiting, respiratory symptoms, and jaundice was significantly higher in P.falciparum Malaria than P.vivax Malaria (Table 2).

pLDH based strip test (rapid diagnostic test for malaria) was evaluated in comparison to peripheral smear microscopy for the diagnosis of Malaria. Out of 160 cases in which both RDT and peripheral blood microscopy were done, 48 cases were diagnosed by microscopy, while RDT diagnosed 59 cases. 3 cases missed by RDT were diagnosed by microscopy, while RDT diagnosed an additional 14 cases. When peripheral blood smear microscopy was considered as the gold standard, sensitivity, specificity, positive predictive value and negative predictive value of pLDH based RDT were respectively 93.8%, 87.5%, 76.2%, and 97.1%. The positive likelihood ratio was 7.50[95% CI 4.57-12] and the posterior probability (odds) for the positive test was 76% (3.2). The negative likelihood ratio was 0.07[95%CI 0.02-0.21] and the posterior probability(odds) for a negative test was 3% (0.0) {Table 3}.

4. Discussion

Out of 162 patients treated with the diagnosis of malaria during the study period at our institute, 92 cases which had a confirmed parasitological diagnosis were included for analysis of the clinical profile and their significance. Furthermore, 160 patients who had undergone both rapid diagnostic test (pLDH based strip test) and microscopy, were included for evaluation of RDT in comparison to microscopy for diagnosis of malaria.

52(56.5%) patients were male and 40(43.5%) patients were female in the study group. Most studies from India have shown an increased incidence of Malaria in males. Desai PD et al in their study from Gujarat found the incidence of Malaria in males and females to be 67.8% and 32.1% respectively.[8] Similar outcomes were found in the study by Kaushik JS et al.[9] The reason for this gender difference can be a more outdoor activity done by male subpopulation and more care for male children by their respective families.

The mean age of the patients was 7.31 years with SD of ± 4.04 years in this study. The highest number of patients, 34(37%) were found in the 5-10 year subgroup. Kwenti TE et al in their study on malaria at Cameroon had similar findings with 23% of children in the age group 5-10 years being found positive for Malaria.[10]Most studies from India show the highest number of Malaria patients in 0-5 year age group. The findings of our study may be explained by the fact that we included outdoor patients also. The severity of Malaria is more in the lower age group. So, a study based on admitted patients of Malaria may show an increased incidence in lower age groups as generally sick malarial patients are admitted. Most cases of Malaria were found in August and September. This seasonal variation may be explained by increased breeding of mosquitoes during the rainy season which is the vector for this disease. Most studies from the north and eastern India shows this seasonal variation including the study by Savargaonkar D et al in Delhi.[11]

51(55.4%) patients had evidence of P.vivax infection, 37(40.2%) had P.falciparum infection and 4(4.3%) patients had findings of mixed infection. Chery et al in their study from Goa in India also observed similar findings with evidence of P.vivax infection in 77% of patients, though government data suggests the equal incidence of both P.vivax and falciparum infection.[3,12]Fever was the most common presenting symptom (96.7%). Chills and rigor, hepatosplenomegaly, and anemia were found in 53.2%, 57.6%, and 69.5% of cases. To our surprise, thrombocytopenia was found in 72.8% of cases. Saravu K et al from a study in Karnataka, India also documented thrombocytopenia in 88% of cases.[13]Features of severe malaria namely respiratory symptoms, vomiting, and

Table 2: Clinical features in differentmalaria species

Clinical features	P.v (n= 51)	P.f (n=41)	Total (n=92)	p value
Fever	50(98.04%)	39(95.12%)	89(96.7%)	0.488
Chills & Rigor	29(56.8%)	20(48.7%)	49(53.2%)	0.321
Vomiting	14(27.5%)	22(53.6%)	36(39.1%)	0.002
Respiratory symptoms	5(9.8%)	11(26.8%)	16(17.3%)	0.003
Anemia	33(64.7%)	31(75.6%)	64(69.5%)	0.12
Thrombocytopenia	35(68.6%)	32(78%)	67(72.8%)	0.199
Jaundice	4(7.8%)	8(19.5%)	12(13%)	0.023
Hepatosplenomegaly	32(62.7%)	21(51.2%)	53(57.6%)	0.116

V=Plasmodium vivax, P f=Plasmodium falciparum

Table 3: Evaluation of efficacy ofRDT (considering Microscopy as gold standard)- 2x2 table

pLDH based RDT	Microscopy		Total
	Positive	Negative	
Positive	45	14	59
Negative	3	98	101
Total	48	112	160

jaundice were found to be significantly higher with the infection by P.falciparum. The presence of more severe symptoms in falciparum malaria can be explained by hyperparasitemia, clogging of blood vessels, sequestration, and hemolysis. Most studies around the world including the study by Geleta G and Mangal Pet al suggest higher chances of severe malaria with falciparum infection, though many cases of severe malaria are also being diagnosed with vivax malaria recently.[14,15]

pLDH based strip rapid diagnostic test (RDT) for malaria was evaluated against peripheral blood film microscopic examination for malaria. We know that peripheral blood film examination is still considered the gold standard for diagnosis of malaria, but RDTs are recommended alternative being almost equally efficacious and many times better than microscopy, especially in resource-limited settings.[16,17] Sensitivity, specificity, PPV, and NPV of pLDH based RDT were 93.8%, 87.5%, 76.2%, and 97.1% respectively when compared to microscopy. The positive likelihood ratio was 7.5 and the negative likelihood ratio was 0.07. All parameters are showing that RDTs are quite effective when compared to microscopy in the diagnosis of malaria with especially high negative predictive value. Khan SA et al in their study from Pakistan found pLDH based test (OptiMAL) to be 95% sensitive and 94.5% specific.[18] Lower specificity in our study may be explained by the fact that RDT was actually able to diagnose more cases of malaria than the gold standard microscopic examination. Congpuong K et al found optiMAL test detected more accurately than blood film ($p< 0.005$) and is simple, easy to perform, and rapid. RDTs are especially useful in resource-limited settings.[19,20] Alkhiary W stated that optiMAL-IT malaria test is especially good as a negative test and can be considered as a quick screening test for blood donors.[21] Marcel NM et al showed that predictive values of positive tests were highly comparable between light microscopy(90.09%[95% CI 83.61-94.18]) and RDT for Malaria (90.91%[95% CI 84.50-94.83]).[22]

5. Conclusion

The present study showed the clinical profile of Malaria in the state of Bihar, India. We were able to show that P. vivax infection is still commoner and P. falciparum infection more dangerous. Rapid diagnostic tests were found to be effective, simple, and rapid to perform and they can be used as an alternative to routine microscopic examination for malarial parasites. Our study may reinforce the dictum to keep Malaria as a differential diagnosis with atypical features like thrombocytopenia and even without evidence of fever in sick children.

6. Source of Funding

No financial support was received for the work within this manuscript.

7. Conflict of Interest

The authors declare they have no conflict of interest.

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