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Haematological Predictors of Malaria in Acute Febrile Illness

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ABSTRACT
Malaria remains a major public health problem and leading cause of mortality in tropical countries. A variety of hematological alterations like anemia, leukocytosis or leukopenia, thrombocytopenia and rarely DIC have been reported in malaria. The present study aimed to evaluate the alteration of hematological parameters in malaria and their probability to detect malaria in acute febrile illness cases. This was case-control study, conducted in the department of the medicine, ESIC Medical College and Hospital, Hyderabad for one year duration. 50 diagnosed cases of malaria as cases and 50 acute febrile illness malaria negative patients as control were enrolled and analysed. Diagnosis of malaria was made by peripheral blood smear. Clinical presentation and hematological parameters were studied in all of them. Out of total malaria cases 52% were infected with *Plasmodium vivax* (PV) and 48% was of *Plasmodium falciparum* (PF). Majority of the malaria cases (76%) were 18-30 years of age, predominantly male. Mean age±SD among cases was 25.98±10.19 years. Among clinical presentation, most of the participants (74% cases and 66% control) were observed continuous fever. Splenomegaly was found in 60% of malaria cases and only 8% of non malaria control this was statistically significant ($p<0.05$). There was a statistically significant difference in hemoglobin, platelet counts, total leucocyte count and RDW ($p<0.001$) levels in patients with malaria compared to patients without the disease. Anemia and thrombocytopenia was the most common hematological changes. They can be helpful in detecting early complications to monitor and treat them effectively. Malaria, *P. vivax*, *P. falciparum,* fever, thrombocytopenia, hematological changes.

INTRODUCTION

Malaria is a common life threatening disease in humans, it is caused by intracellular parasite which is transmitted by bite of infected female Anopheles mosquito's vectors. The other less common modes of transmission of malaria by congenital transmission, transfusion of infected blood and sharing needles[1]. Malaria remains a major public health issue in tropical countries. In the Indian subcontinent the distribution of malaria is heterogeneous, governed by many physiological and climatic risk factors[2]. There are five major species of malaria parasite, *plasmodium vivax, p. ovale, p. falciparum, p. malariae* and *p. knowlesi,* among them *p. vivax* and *p. falciparum* were most common. *p. falciparum* causes most dangerous form of malaria, lead to significant morbidity and mortality in India[3,4]. The malaria infection may cause a wide variety of clinical manifestation ranging from very mild symptoms to severe disease, due to these non specific sign and symptoms the clinical diagnosis of malaria become a challenging problem[5]. The most common complications of falciparum malaria infection are cerebral malaria, severe anemia, ARDS, circulatory collapse, hemoglobinuria, renal failure, thrombocytopenia, abnormal bleeding and disseminated intravascular coagulation[6]. The Hematological and biochemical alterations in malaria are mainly occurs during the asexual stage of the life cycle and also thought to act as an adjuvant tool in strengthening the suspicion of malaria, thereby prompting a more meticulous search for malaria parasites[7,8]. A wide variety of hematological changes seen in malaria like progressively increasing anemia, thrombocytopenia, decreasing RBC counts, atypical lymphocytosis, decreased red blood cell indices and leukopenia, had relatively good sensitivities and specificities in predicting the presence of malaria infection[9,10].

Diagnosis of malaria by Microscopic examination of peripheral blood smear is a valuable and gold standard technique but it required expertise and repeated examination to rule out malaria.

Recent serological and molecular based diagnostic approaches for malaria provide superior sensitivity and specificity. Rapid antigen detection test (RDT) Enzyme linked immunosorbent assay (ELISA) and real time polymerase chain reaction (rt-PCR) are used for diagnosis of malaria[11,12].

A prompt and early diagnosis is crucial for effective management of malaria. In India the drug policy for treatment of malaria designed according to the National Anti Malaria Program. Any fever without any other obvious cause may be considered as malaria, investigated and treated accordingly, in order to reduce morbidity and prevent death in malarial[13].

Aims and objectives: The objective of this study to analysed the alteration of hematological parameters in malaria and their role as a predictors of malaria in acute febrile illness.

MATERIAL AND METHODS

This was a case control study conducted in the Department of Medicine, ESIC Medical College and Hospital, Hyderabad for one year duration from 1st November 2018 to 31st October 2019.

We have enrolled 50 cases of malaria as diagnosed by peripheral smear examination and 50 age matched control that were negative for malarial parasites on peripheral smear examination.

Inclusion criteria:

- All adult patients age ≥18 years
- Patients with fever of less than 7 days admitted to medical word
- Participants who provides written informed consent for the study

Exclusion criteria:

- Patients ≤18 years of age
- Patients who had no fever during hospital stay
- Patients in whom a localizing skin or subcutaneous infections and systemic infection such as pneumonia or meningitis, etc
- Patients who not willing for the study
- All the Information was collected through prepared proforma for each patient

Data were collected: Age, socio-demographic status, clinical sign and symptoms. Duration, type, pattern of fever, chills, rigors and rashes was recorded. A complete clinical examination was done to rule the other possible causes of fever. Fever was categorized as per the following definitions.

Continuous fever: The temperature remained above normal throughout the day and did not fluctuate more than 1°C in 24 hrs.

Remittent fever: The temperature remained above normal throughout the day with more than 1°C fluctuation.

Intermittent fever: The fever was present only for some hrs of the day and was normal during remaining hours. Diagnosis of malaria parasite was done by peripheral blood smear examination. Peripheral smear positivity was taken as the gold standard for diagnosis of malaria. All patients were investigated with Hemoglobin level (Hb%), complete blood counts, chest X ray, urine microscopy, urine culture, serum biochemistry, blood culture, serology for typhoid and other relevant tests.

Peripheral blood smear, both thick and thin smears were stained with the JSB staining and examined by experienced epidemiology department personnel. Malaria was diagnosed when any one of the smears was positive for malaria parasite.

Statistical analysis: The data were analysed using SPSS version 22 statistical software. Means, percentages, standard deviations and ranges were calculated. Statistical analysis was performed using student t-test. $p<0.05$ was considered as significant.

RESULTS

A total of 100 suspected patients of acute febrile illness who satisfied the inclusion criteria were enrolled in present study. 50 patients diagnosed as smear positive for malaria (cases) and 50 patients are smear negative for malaria (control) were taken for comparison.

Majority of the malaria cases (76%) were 18-30 years of age, Mean age±SD among cases was 25.98±10.19 years and control were 28.54±7.97 years. Most of the participants were male 80% in malaria cases and 78% in control. Malaria was common amongst the younger population who are commonly exposed to mosquitoes by way occupation, travel etc. there were no statistically significant difference in age and gender among cases and control ($p>0.05$). It was revealed that *Plasmodium vivax* infection are slightly higher (52% case) than *plasmodium falciparum* (48% cases).Table 1 Among clinical presentation, most of the participants (74% cases and 66% control) were observed continuous fever. Chills and rigors during the febrile episode occurred in 36% cases and 24% of the controls There are no significant difference between them ($p>0.05$). Splenomegaly was found in 60% of malaria cases and only 8% of non malaria control this was statistically significant ($p<0.05$) Table 2. Out of the total 50 malaria cases, 33 (66%) cases had anemia, 37 (74%) of thrombocytopenia, TLC counts between 4000-11000 in 66% of cases and 72% were RDW more than 15%.

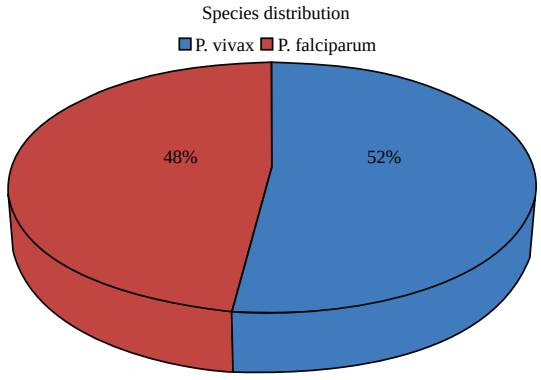

Fig. 1: Distribution of cases as per types of species of malaria

There was a statistically significant reduction in hemoglobin and platelet counts ($p<0.001$) levels in patients with malaria compared to patients without the disease. RDW was significantly increased in cases as compared to control. Statistically significant difference were seen in total leukocyte count of cases and control ($p<0.05$) Table 3.

DISCUSSIONS

Malaria poses a significant health burden in the temperate and tropical regions of India. Hematological alteration in malaria is mainly representing indices of prognostic and follow-up value. Prompt and accurate diagnosis of malaria plays a critical role towards the effective management of malaria.

In the current study incidence of *Plasmodium vivax* was slightly higher than *plasmodium falciparum* but statistically not significant, concordance finding also reported by Malik *et al*.[14] and Beg *et al.*[15], whereas much higher incidence of *p. vivax* were found by many other Indian studies. Chandra *et al.*[16] and Verma *et al.*[17] reported *p. vivax* positive cases were 69.8% and 76.7% respectively. *p. vivax* malaria is difficult to detect and treat because the parasitemia is typically low in comparison to that of *p. falciparum*.

In our study the mean age of the malaria patients was 25.98±10.2 years and the highest proportion of cases (76%) was seen in the younger adult (18-30) years age group, almost similar results were obtained by Zeeba *et al.*[18] and Kumbhar *et al.*[19]. It has been reported that the incidence of malaria in endemic areas falls as people grow older, suggesting that advancing age contributes to immunity.

Current study observed that males were affected more from the malaria parasite than female, comparable with the many other researchers. Jiero, *et al.*[20], Abdussalam, *et al.*[21] and Sudheer, *et al.*[22]. Increased chance of malaria infection in male subjects may be due to more outdoor activities.

The clinical manifestations of malaria are variable among patients according to the severity of the infection. Sign and symptoms of malaria usually appear 10-15 days after the bite of infective mosquito. The common clinical presentation were fever with chills and rigors, headache, weakness (malaise), nausea/vomiting, pain in abdomen, breathlessness, pallor, Splenomegaly and bleeding manifestations.

Continuous fever was seen in most of the patients in our study, accordance to the Patel, *et al.*[23] and Tangpukdee, *et al.*[24].

Table 1: Age and gender wise comparison of malarial (cases) and non malarial (control)

Baseline characteristics	Cases (n = 50)	Control (n = 50)	p-value
Age group (years)			
18-30	38 (76%)	37 (74%)	>0.05
31-40	8 (16%)	9 (18%)	
41-50	3 (6%)	4 (8%)	
≥50	1 (2%)	0 (0%)	
Mean age±SD (years)	25.98±10.19	28.54±7.97	
Gender			
Male	40 (80%)	39 (78%)	>0.05
Female	10 (20%)	11 (22%)	

Table 2: Comparison of clinical profile among malarial (cases) and non malarial (control)

Clinical profile	Cases (n = 50)	Control (n = 50	p-value
Type of fever			
Continuous	37 (74%)	33 (66%)	>0.05
Intermittent	13 (26%)	17 (34%)	
Fever with chills and rigors			
Present	18 (36%)	12 (24%)	> 0.05
Absent	32 (64%)	38 (76%)	
Fever with Splenomegaly			
Present	30 (60%)	4 (8%)	< 0.001
Absent	20 (40%)	46 (92%)	

Table 3: Comparison of hematological parameters among malarial (cases) and non malarial (control) Clinical profile

Hemoglobin (g %)	Cases (n = 50)	Control (n = 50)	p-value
≤10	33 (66%)	21 (42%)	<0.001
≥10	17 (34%)	29 (58%)	
Mean±SD (g%)	8.53±2.86	10.66±2.63	
Total count cells mm^{-3}			
≤4000	14 (28%)	0 (0%)	<0.001
4000-11000	33 (66%)	44 (88%)	
≥11000	3 (6%)	6 (12%)	
Mean±SD cells mm^{-3}	6022±3409	8392±2794	
RDW			
≤15%	14 (28%)	31 (62%)	<0.001
≥15%	36 (72%)	19 (38%)	
Mean±SD (%)	17.43±4.23	15.02±2.29	
Platelet count			
Thrombocytopenia	37 (74%)	1 (2%)	<0.001
Normal count	13 (26%)	49 (98%)	
Mean±SD (lakh)	1.17±0.97	2.61±0.75	

Present study found significantly higher percentage of Splenomegaly among malaria cases as compared to control, our finding correlate with the Khuraiya *et al.*[25].

The incidence of malaria was higher among. Rural population, low socioeconomic strata, laborers or daily wagers working without using any protective measures. Chances of malaria are more in the rainy (June-August) and post-rainy (September) seasons, this could be related to more water accumulations occurs which is favorable for breeding of female anopheles mosquitoes, the warm stagnant water and hot humid climatic conditions also raised the biting rates and transmission rate of malaria parasites[26].

Hematological changes are well recognized in malarial infection and considered a hallmark of clinical suspicion of malaria. The nature of hematological abnormalities depends on the duration of infection. Anemia and thrombocytopenia are the major hematological change were seen in the present study, similar finding observed by several other studies, Srivastava, *et al.*[27], Antwi, *et al.*[28] and Lathia *et al.*[29] reported that thrombocytopenia has been emerged as a strong predictor of malaria. The suggested mechanisms for thrombocytopenia include disseminated intravascular coagulation or excessive removal of platelets by reticulo-endothelial system.

In our study a statistically signi cant reduction in hemoglobin levels (HGB≤ 10 g dL^{-1}) in those with malaria, in comparison to those without malaria, in agreement with the Omarine, *et al.*[30] and Maina, *et al.*[31].

The current study has revealed that there were statistically significant differences in total leucocytes counts between malaria-infected and non infected patients, consistent with the earlier reports. Adedapo *et al.*[32].

Red cell distribution width (RDW) describes the population dispersion of red cell volume or the range of changes in size of red blood cells which mostly present as enlarged after malarial invasion. In present study RDW, values were found to be higher in the malaria group than the non-malarial cases in concordance with other study findings, Koltas, *et al.*[33]. Lower mean values for hemoglobin, leukocyte count and platelet count in the malaria group compared to

the control group was observed in our study. This was in concordance with other studies[33,34].

CONCLUSION

We have concluded that hematological changes such as anemia, thrombocytopenia, red cell distribution width and leucopenia showed a statistically significant correlation with malarial infection. All these parameters provide a diagnostic clue in a patient with acute febrile illness and play role as a predictors of malaria. Anemia and thrombocytopenia can be used as a prognostic indicator of malaria infection in endemic areas.

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