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Original Article

Study of Hematological Alterations in Malaria at a Tertiary Health Care Center of South Gujarat, India

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Abstract

Background: Malaria is a disease with a great global burden. It is one of the most prevalent parasitic infection common in tropical, subtropical countries, particularly Asia and Africa. Malaria causing plasmodia is parasites of blood and hence induces hematological alterations. The hematological changes that have been reported to accompany malaria include anemia, thrombocytopenia, leukocytosis as well as leukopenia, mild-to-moderate atypical lymphocytosis, monocytosis, eosinophilia, and neutrophilia. Hence, the present study is undertaken to evaluate the various hematological parameters affected in malaria and to observe the variations, if any, in *Plasmodium falciparum*, *Plasmodium vivax,* and mixed infections.

Materials and Methods: The present study was carried out in the Department of Pathology at Tertiary Health Care Center of South Gujarat from August 2018 to October 2018. A total of 480 smear-positive malaria cases were analyzed and various hematological parameters were studied.

Results: Out of 480 smear-positive cases, *P. vivax* was positive in 77% of cases, *P. falciparum* was positive in 22% of cases and mixed infection in 1% of cases. Most of the cases were seen in the age group of 21–40 years. Anemia was seen in 53.1% of cases. Normocytic normochromic blood picture was the most common type in anemic patients (46.6%). Thrombocytopenia was seen in 84.58% of the patients. Out of which, 75.86% were affected by *P. vivax*, 23.15% were affected by *P. falciparum*, and 0.98% were affected by the mixed infection. About 28.75% of cases showed hematological features of leukopenia, and 5.2% of cases were having leukocytosis.

Conclusions: Various hematological findings can help in early diagnosis of malaria which is essential for timely and appropriate treatment which can limit the morbidity and prevent further complications

Key words: Anemia, Hematological parameters, Malaria, Prevention, Thrombocytopenia

INTRODUCTION

"Malaria" received its name from Italian, as it was believed to arise due to foul air common near marshy areas. It is one of the most prevalent parasitic infection common in tropical, subtropical countries, particularly Asia and Africa.[1,2] It is a protozoan disease transmitted by the bite of infected Anopheles mosquito, and the incubation period varies from 8 to 30 days depending on species. Despite enormous control efforts, an increase in the drug resistance of the parasite, the insecticide resistance of its vectors, human travel, and migration has contributed to its resurgence and is a leading cause of mortality and morbidity in developing areas of the world.[3]

According to the WHO World Malaria Report 2018, an estimated 219 million cases of malaria occurred worldwide in 2017, compared with 216 million cases in 2016, 214 million cases in 2015. Most malaria cases in 2017 were in the WHO African Region (200 million or 92%), followed by the WHO Southeast Asia Region with 5% of the cases and the WHO Eastern Mediterranean Region with 2%. Fifteen countries in Sub-Saharan Africa and India carried almost 80% of the global malaria burden. Five countries accounted for nearly half of all malaria cases worldwide: Nigeria (25%), the Democratic Republic of the Congo (11%), Mozambique (5%), India (4%), and

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Uganda (4%).[1] In India, in the year 2017, a total of 8.76 million malaria cases had occurred, out of which about 48% of cases were *Plasmodium vivax* malaria.[1] The annual parasite index of India for the year 2015 was 0.9. Annual Blood Smear Examination (ABER) of India for the year 2015 was 9.6.

The incidence rate (i.e., the number of cases per 1000 population) of malaria globally reduced between 2010 and 2017; it fell from 72 in 2010 to 59 in 2017. India reported more than 3 million fewer cases (24%) from 2016 to 2017.[1]

Clinical presentations of malaria include – fever with chill and rigor, headache, diarrhea, vomiting, abdominal distension, cough, hepatomegaly, and splenomegaly.[2]

Malaria causing plasmodia is parasites of blood and hence induces hematological alterations. The hematological changes that have been reported to accompany malaria include anemia, thrombocytopenia, leukocytosis as well as leukopenia, mild-to-moderate atypical lymphocytosis, monocytosis, eosinophilia, and neutrophilia. Platelet abnormalities are both qualitative as well as quantitative.[4]

The high mortality rate in malaria infection is usually associated with heavy parasite load, anemia, low platelet count, jaundice, and delay in diagnosis.[2]

Hence, the present study is undertaken to evaluate the various hematological parameters affected in malaria and to observe the variations, if any, in *Plasmodium falciparum*, *P. vivax,* and mixed infections. The aim of the study is to find out changes in different hematological parameters in smear-positive malaria cases and to compare these changes in *P. vivax* and *P. falciparum* infection.

MATERIALS AND METHODS

Study Setting

The present study was carried out in the Department of Pathology at Tertiary Health Care Center of South Gujarat from August 2018 to October 2018. A total of 480 smear-positive malaria cases were analyzed.

Study Period

August 2018 to October 2018.

Study Design

This was a cross-sectional descriptive study.

Inclusion Criteria

The laboratory confirmed that smear-positive malaria cases from August 2018 to October 2018 were included in this study.

Exclusion Criteria

NIL.

Sample Size

The sample size was 480 cases.

Control(s)

Not required.

Methods of Collection of Data

All malaria positive cases were analyzed. Routine laboratory work, thin, and thick blood films were prepared and examined for defining the species involved. The thin and the thick smears were made on the same slide and stained with Giemsa stain. A minimum of 200 fields (oil immersion) were assessed to label a negative smear.

Hematological profile by a three-part cell counter was performed in all patients. Anemia and thrombocytopenia were labeled when hemoglobin was <11.0 g%, and platelet counts were <1.5 lakh/mm^3, respectively. Leukopenia and leukocytosis were labeled when the total WBC count was $<4.0 \times 10^3/mm^3$ and $>11.0 \times 10^3/mm^3$, respectively.

Blood film examination was also performed in all patients, and they were classified according to the morphologic type of anemia in the following category: Normocytic normochromic, normocytic hypochromic, microcytic hypochromic, and dimorphic (normocytic to macrocytic and microcytic to macrocytic).

Statistical Analysis

Qualitative data are presented as frequencies and percentages. All the data were analyzed using Microsoft Excel 2013.

RESULTS

The present study was carried out in the Department of Pathology at Tertiary Health Care Center of South Gujarat from August 2018 to October 2018. A total of 480 smear-positive malaria cases were analyzed, and hematological parameters were studied.

Out of 480 malaria positive cases, *P. vivax* was the most common observed species in our study accounting for 370 cases (77%) followed by *P. falciparum* accounting for 106 cases (22%) followed by 4 (1%) cases of mixed infection [Table 1].

Most of the cases were seen in the age group of 21–40 years (50%) with the highest prevalence between the age group of 21 and 30 years (32.5%). There were 28.2% of cases that were below the age of 20 years. Youngest case

was 6 months old, and the oldest case was 75 years old and both cases were having *P. vivax* infection [Table 2].

There were 312 cases of males (65%) and 168 cases of females (35%). In our study, male:female ratio was 1.8:1 [Table 3].

Anemia was seen in 255 (53.1%) cases. Out of which, 196 (76.9%) cases were of *P. vivax*, and 56 (21.9%) cases were of *P. falciparum* and 3 (1.2%) cases were of mixed infection [Table 4].

Blood picture was normocytic normochromic in 224 (46.6%) cases, which was the most common finding in the study followed by a microcytic hypochromic picture in 102 (21.2%) cases followed by normocytic hypochromic picture in 65 (13.5%) cases [Table 5].

Out of 480 cases, 138 (28.75%) cases showed hematological features of leukopenia and 25 (5.2%) cases were having leukocytosis. Out of 138 leukopenia cases, 90 cases (65.2%) were having *P. vivax* infection, and 48 cases (34.8%) were having *P. falciparum* infection. Out of 25 leukocytosis cases, 20 cases (80%) were having *P. vivax* infection, two cases (8%) were having *P. falciparum* infection, and three cases (12%) were having mixed infection [Table 6].

Out of total of 480 cases, the majority – 406 cases (84.58%) were having thrombocytopenia. Out of which, 308 cases (75.86%) were affected by *P. vivax*, 94 cases (23.15%) were affected by *P. falciparum*, and four cases (0.98%) were affected by mixed infection [Table 7].

DISCUSSION

Malaria is transmitted by the female anopheles mosquito, which causes clinical illness and pathological changes in various body organs with the parasites invading and multiplying in the circulating red blood cells. Malaria causes

Table 1: Total malaria positive cases

Total case	*Plasmodium vivax*		*Plasmodium falciparum*		Mixed infection	
	Number of cases	Percentage	Number of cases	Percentage	Number of cases	Percentage
480	370	77	106	22	4	1

Table 2: Age-wise distribution of malaria

Age group (years)	*Plasmodium vivax*		*Plasmodium falciparum*		Mixed infection		Total	
	Number of cases	Percentage	Number of cases	Percentage	Number of cases	Percentage	Number of cases	Percentage
0–10	61	16.4	09	8.5	00	00	70	14.6
11–20	53	14.4	12	11.3	00	00	65	13.6
21–30	126	34.0	28	26.4	2	50	156	32.5
31–40	62	16.7	22	20.8	00	00	84	17.5
41–50	33	8.9	20	18.9	00	00	53	11.0
51–60	26	7.1	13	12.3	2	50	41	8.5
61–70	8	2.1	02	1.8	00	00	10	2.1
71–80	1	0.4	00	00	00	00	01	0.2
Total	370	100	106	100	4	100	480	100

Table 3: Sex-wise distribution of malaria

Sex	*Plasmodium vivax*		*Plasmodium falciparum*		Mixed infection		Total	
	Number of cases	Percentage	Number of cases	Percentage	Number of cases	Percentage	Number of cases	Percentage
Male	233	63.0	78	73.6	1	25	312	65
Female	137	37.0	28	26.4	3	75	168	35
Total	370	100	106	100	4	100	480	100

Table 4: Anemia in malaria cases (hemoglobin <11 g%)

Total case	*Plasmodium vivax*		*Plasmodium falciparum*		Mixed infection	
	Number of cases	Percentage	Number of cases	Percentage	Number of cases	Percentage
255	196	76.9	56	21.9	03	1.2

numerous hematological alterations, of which anemia and thrombocytopenia are the most important.[4]

The results of the present study and its correlation with other studies are discussed as follows: [Table 8].

The most common species of malaria in the present study was *P. vivax* (77%) followed by *P. falciparum* (22%). Findings are compatible with studies done by Jadhav *et al.*[5] and Ca *et al.*[3] However, Bashawri *et al.*[6] reported higher falciparum prevalence and Jairajpuri *et al.*[7] reported a higher prevalence of mixed infection (47.1%).

P. falciparum is associated with serious complications such as severe anemia, malarial hepatitis, and renal failure; hence, *P. falciparum* infection on suspicion of complication should be further evaluated.

Mixed infections behave like falciparum malaria, but its incidence and severity are less than severe *P. falciparum* malaria. In mixed infection, *P. vivax* malaria has a protective role against the severity of falciparum malaria.

In the present study, 50% of cases were in the age group between 21 and 40 years and were found to be similar with the studies done by Agrawal *et al.*,[8] in which 75% of cases were in the age group between 21 and 40 years and Jairajpuri *et al.*,[7] in which 46% of cases were in the age group between 20 and 30 years.

Children aged under 5 years are the most vulnerable group affected by malaria. In 2017, they accounted for 61% of all malaria deaths worldwide.[1] Malaria can affect any age group. However, most studies show more adults as compared to children. The adult age group is more affected due to their greater mobility and greater risk of exposure due to more outdoor activity.[3]

The present study had 65% male patients as compared to 35% female patients. Other studies with comparable results include Surve *et al.*[4] with 57% males, Jadhav *et al.*[5] with 58.3% males, Erhart *et al.*[9] with 69% males, Bashawri *et al.*[6] with 75.9% males, Agrawal *et al.*[8] with 58.5% males, and Saha and Das[2] with 55.4% males.

Anemia was present in 53.1% of cases in our study. Other studies with comparable results include Igbeneghu and Odaibo[10] with 63.5% cases of anemia, Ca *et al.*[3] with 63% cases of anemia, Kashinkunti and Alevoor[11] with 69% cases of anemia, Sharma[12] with 86.7% cases of anemia, and Bhawna *et al.*[13] with 65.5% of cases of anemia.

There is a wide variation in anemia due to malaria infection depending on the geographical location of the study. Report of the year 2017 includes a section on malaria-related anemia, a condition that, left untreated, can result in death, especially among vulnerable populations such as pregnant women and children aged under 5 years. Recent years have seen a decline in awareness of the burden of malaria-associated anemia.[1]

Anemia was normocytic-normochromic in the majority (46.6%) of cases, which is concordant with other studies done by Bhawna *et al.*,[13] Bashawri *et al.*,[6] and Facer.[14] However, the microcytic hypochromic picture was seen in 21.2% cases, results are similar to other studies.[6,13,15] This is due to the geographical location of the study, where patients have Iron and Folate deficiency due to inadequate dietary intake, along with parasitic and bacterial infections which themselves cause a significant amount of anemia. Hence, practically it becomes difficult to determine the extent to which malaria alone contributes to the anemia.

Table 5: Type of blood picture in malaria cases

Type of blood picture	Number of cases	Percentage
Normocytic normocromic	224	46.6
Normocytic hypochromic	65	13.5
Microcytic hypochromic	102	21.2
Dimorphic (normocytic to macrocytic)	42	8.8
Dimorphic (microcytic to macrocytic)	47	9.9

Table 6: Leukopenia and leukocytosis in malaria cases

TC	*Plasmodium vivax*		*Plasmodium falciparum*		Mixed infection		Total	
	Number of cases	Percentage	Number of cases	Percentage	Number of cases	Percentage	Number of cases	Percentage
Leukopenia	90	65.2	48	34.8	00	00	138	28.75
Leukocytosis	20	80	2	8	3	12	25	5.2

Table 7: Thrombocytopenia in malaria cases

Total case	*Plasmodium vivax*		*Plasmodium falciparum*		Mixed Infection	
	Number of cases	Percentage	Number of cases	Percentage	Number of cases	Percentage
406	308	75.86	94	23.15%	04	0.98

Table 8: Comparative analysis of different malarial species

Study	*Plasmodium vivax* (%)	*Plasmodium falciparum* (%)	Mixed (%)
Present study	77	22	1
Jadhav *et al*.[5]	62.17	37.69	0.04
Ca *et al*.[3]	60	30	10
Surve *et al*.[4]	55	45	-
Erhart *et al*.[9]	59	38	2
Jairajpuri *et al*.[7]	51.6	1.1	47.1
Bashawri *et al*.[6]	39	54.1	2.33

Table 9: Frequency of thrombocytopenia in different studies

Study	Incidence of thrombocytopenia (%)
Present study	84.58
Agrawal *et al*.[8]	85.5
Horstmann *et al*.[18]	85
Saha and Das[2]	82.43
Akhtar *et al*.[19]	71.06
Sharma[12]	70
Richards *et al*.[20]	67
Gill *et al*.[21]	63.33

We observed normal WBC count in 66.05% of the patients and leukopenia in 28.75% patients, leukocytosis (5.2%) was seen rarely in some cases. Leukopenia was present more frequently in *P. vivax* – infected patients (65.21%) than in *P. falciparum* – infected patients (34.78%) in our study.

Leukopenia was observed in a study done by Surve *et al*.[4] (18%), Bashawri *et al*.,[6] (13.3%), and Agrawal *et al*.[8] (26%).

Leukocytosis was observed in a study done by Kashinkunti and Alevoor[11] (11%), Agrawal *et al*.[8] (9%), Sharma[12] (13.3%), Biswas *et al*.[16] (12.2%), Surve *et al*.[4] (10%), and Bashawri *et al*.[6] (7.2%).

The results of leukopenia and leukocytosis in the present study were in concordance with other studies.

The reduction in circulating platelet count is consistently reported in the different types of malaria. In the present study, the percentage of patients showing thrombocytopenia was 75.86% in the case of vivax malaria and 23.15% in the case of falciparum malaria. The percentage of cases showing thrombocytopenia in falciparum infections and vivax infections varies in different studies. Studies conducted by Bashawri *et al*.[6] and Jadhav *et al*.[5] had thrombocytopenia more in vivax as in the present study, while in a study conducted by Erhart *et al*.,[9] thrombocytopenia is more in cases of falciparum malaria.

Thrombocytopenia is a common finding in cases of malaria, both vivax and falciparum, as shown by most of the studies conducted. In the present study, thrombocytopenia was seen in 84.58% of all malaria cases. Results are comparable with other studies, as shown in Table 9.

Patients who develop thrombocytopenia in malaria cases are seldom bleed whatever the grade of thrombocytopenia. The cause of thrombocytopenia in malaria cases is poorly understood; however, the researcher has proposed the following mechanisms as the cause of thrombocytopenia in malaria cases:[2]

- Decreased thrombopoiesis, however, bone marrow examination shows normal or increased number of megakaryocytes
- Peripheral destruction of platelets
- Sequestration of platelets in the spleen
- Some scientists have found disseminate intravascular coagulation (DIC) as a cause of thrombocytopenia; however, other scientists did not found DIC as a cause of thrombocytopenia.

According to Kumar *et al*.,[17] not only decreased platelet count occurs in malaria patients but also platelet dysfunction commonly encountered. According to them, two types of platelet dysfunction occur – platelet hyperactivity and platelet hypoactivity. Hyperactivity results from various aggravating agents such as immune complexes, platelet surface contact with infected RBCs, and damage to endothelial cells. Injured platelet undergoes intravascular hemolysis and releases cellular contents of the platelets that activate intrinsic coagulation cascade, as contributed to DIC. The hyperactive platelets may enhance hemostatic responses and, that is, why bleeding episodes are very rare in acute malarial infections, despite significant thrombocytopenia.

CONCLUSIONS

Malaria is one of the most common infections in the Indian subcontinent. Malaria affects mostly adults with male predominance. *P. vivax* is more common than *P. falciparum* and mixed infection. Complications associated with *P. falciparum* and mixed infection should be evaluated and the use of antibiotics along with antimalarial agents shows a better response.

The malarial infection causes various hematological and biochemical changes. Anemia and thrombocytopenia of varying severity are the most frequently observed hematological findings.

Depending on the geographical location of the study, discrimination of anemia, whether it is due to malaria or iron/FA deficiency, is difficult. However, severe anemia

is a poor prognostic factor, and malaria-related anemia, if left untreated, can cause a death, especially in women of reproductive age, pregnancy and children under 5 years.

Thrombocytopenia is another most commonly observed finding in malaria cases; however, bleeding manifestations are uncommon. In a patient with febrile illness, observation of thrombocytopenia warrants careful search for malaria parasite. The use of antimalarial agents, along with platelet transfusion in such patients, can lower the complications associated with it.

Various hematological findings can help in early diagnosis of malaria which is essential for timely and appropriate treatment which can limit the morbidity and prevent further complications.

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