Haematological profile of Malaria patients at a tertiary care hospital of Konkan region, Maharashtra State, India

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Abstract

Background: Malaria is a numero-uno infectious, killer disease in the developing world including India. This disease is caused by Plasmodium parasitic species with mosquitoes acting as vectors of transmission. Hematological tests include RBC, WBC and platelet parameters, peripheral blood examination which change based on parasitaemia need to be evaluated in various malaria affected regions to get prompt malarial diagnosis. Prompt diagnosis leads to prompt treatment avoiding troublesome malarial complications.

Objectives: The present observational cross-sectional study was undertaken to estimate the Hematological profile in malaria cases diagnosed in a tertiary care hospital of Konkan region, Maharashtra.

Methods: All the patients referred to Hematology section, Department of Pathology with malaria were evaluated with clinical details. The data was collected from 1st January 2017 to 31st December 2020 for three years' duration. Total malarial cases studied were 50 cases. CBC/ PBS examination was done on EDTA blood sample. The RBC parameters, WBC parameters and platelet counts were studied with respect to malarial parasitaemia. Parasite index was found on smear and malarial diagnostic confirmation was also done using rapid kit test. All the findings were filled in MS-Xcel sheet 2010 and data was analyzed manually.

Results: Malaria caused by P.vivax was predominant in present study. Patients in age range of 15-30 years were more affected in present study, that is, younger people were affected. Male predominance was seen. Fever was most common presenting symptoms followed by chills and rigor in present study. Hb, RBC count, PCV – showed that anemia was more common hematological change in present study, as these values were lower than normal level. Red cell indices like MCV, MCH, MCHC, RDW and peripheral blood smear revealed all the values in a normal range showing normocytic normochromic RBCs in the present study. Patients with malaria having normal TLC followed by leucopenia were more common in present study. Thrombocytopenia was most common hematological change seen in present study.

Conclusion: Hematological parameters are measurable indices of blood that serve as a marker for malarial diagnosis.

Key words: Malaria, Hematological profile, Complete blood count (CBC)

Introduction

The Italians believed that 'Malaria' arise due to foul air common near marshy areas[1]. Malaria has been in existence since ancient times and was first described in fourth century BC, but not until 1889 was the protozoon causing malaria described, and in 1879 female anopheles mosquito was demonstrated to be the vector for the disease[2]. Malaria is a disease of tropical and subtropical countries particularly Africa and Asia. Though Africa accounts for 90% of mortality burden of malaria, South-east Asia also still suffers considerable mortality and morbidity[3].

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Malaria is a major health concern in India and many parts of the world[1,4]. In the Indian subcontinent, malarial distribution is heterogeneous and governed by many climatic and physiological risk factors[4]. The World Health Organization (WHO) recommends that all persons of all ages in all epidemiological settings with suspected malaria should receive a parasitological confirmation of diagnosis[5].

It is caused by protozoa parasites of genus plasmodium which infect and destroy red blood cells (RBCs). The four species of plasmodium: P.vivax, P.falciparum, P.ovale, P.malariae cause malaria in humans. In India, P. vivax parasite contributes towards the majority of cases. The clinical diagnosis of malaria is challenging because of non-specific nature of signs and symptoms which overlap considerably with other febrile illness common on tropical regions[4].

Typically, microscopic slide examination of peripheral blood remains the most widely used test due to cost-effectiveness[6]. Microscopic detection and identification of plasmodium species in Giemsa or Leishman stained thick film of blood (for screening) and thin blood film (for species confirmation) is accepted worldwide as 'gold standard' for routine diagnosis of malaria[5].

Haematological changes are some of the most common complications in malaria and they play a major role in malarial pathogenesis. These changes involve the major cell types such as RBCs, leukocytes and thrombocytes[6]. Malaria infection in human is usually associated with a reduction in haemoglobin level frequently leading to anaemia. Anaemia is the major cause of death in malarial infection due to difficulty in diagnosis especially where parasitaemia and the clinical picture may be confused with other causes of anaemia[2].

Malaria infected patients tends to have significantly lower platelets, white blood cells (WBCs), lymphocytes, eosinophils, RBCs and HB levels, while monocyte and neutrophil counts were significantly higher in comparison to non- malaria infected patients. The most common complication during malaria infection is thrombocytopenia[6].

The present observational cross-sectional study was undertaken to study the Hematological profile in malaria cases diagnosed in a tertiary care hospital of Konkan region, Maharashtra. This is first such study conducted in coastal Maharashtra after extensive research.

Materials and Methods

A cross-sectional observational study was conducted from 1st January 2017 to 31st December 2020 for three years' duration. Fifty (n=50) cases who were positive for malaria with both rapid malarial card test and on peripheral smear were included in the study while cases with other infectious diseases were excluded.

Patients detailed history regarding age, sex, nature and duration of illness, blood transfusion history, clinical findings, history of anti-malarial therapy were recorded. Venous blood was collected in EDTA vacutainers. Hemoglobin (Hb), Packed cell volume (PCV) or Hematocrit, RBC indices (MCV, MCH, MCHC), Total leukocyte count (TLC), Absolute leukocyte count, platelet count and RDW were measured in EDTA sample using Horiba's 5-part hematology analyzer.

Peripheral blood smear were prepared using fresh blood sample stained with Leishman stain and stained for blood picture to evaluate Differential leukocyte count (DLC), species identification and for estimation of parasitaemia. Rapid malarial visual antigen test card was used to identify the positivity of type of plasmodium species. This kit is called 'Mal Card' by J.Mitra and Co. Pvt. Ltd. (New Delhi).

Results

Total malarial cases studied were 50 cases. The number of cases is less over three year study period due to low population density in the Ratnagiri district of Maharashtra.

Patients affected with malaria having P.vivax species were 45/50 cases (90%) which was more frequent than P. falciparum that is, 4/50 cases (8%). Single case of mixed infection was seen (2%). Patients affected with malaria infection were more in age group of 15-30 yrs (42% cases or 21/50 cases).This was followed by those aged >45 years of age (30% cases or 15/50 cases) and 31-45 yrs (24% cases or 12/50 cases). No malarial cases were detected <5 yrs of age, while 6-14 yrs comprised 4% cases or 02/50 cases). Male predominance was seen with malaria infection (46/50 cases). Male: Female ratio of malarial infection was 11.5.

Table 1: Presenting signs and symptoms in different Malarial infections

Symptoms	Falciparum	Vivax	Mixed	Total	Percentage (%)
Fever	03	43	01	47	94 %
Chills & Rigor	01	18	00	19	38 %
Nausea	00	14	00	14	28 %
Vomiting	00	09	00	09	18 %
Abdominal pain	03	13	00	16	32 %
Back pain	00	01	00	01	2 %
Muscle pain	00	01	00	01	2 %
Diarrhoea	00	05	01	06	12 %
Cough	01	20	01	22	44 %
Breathlessness	00	02	00	02	4 %
Headache	02	13	00	15	30 %
Fatigue	01	06	00	07	14 %
Profuse sweating	00	05	00	05	10 %
Hepatomegaly	01	00	00	01	2 %
Hepatospleenomegaly	00	02	00	02	4 %
Bloody stool	00	01	00	01	2 %
Oedema	00	01	00	01	2 %
Jaundice	00	01	00	01	2 %

Fever (94 % cases or 47/50 cases) was the most common presenting symptom in P.vivax and P.falciparum malaria, followed by chills and rigor (38% cases or 19/50 cases) and abdominal pain (32% cases or 16/50 cases) (Table 1).

Table 2 : Hb (Haemoglobin) concentration in malarial cases

Hb (gm/dl)	Vivax	Falciparum	Mixed	Percentage (%)
<5	00	00	01	02 %
5-8	02	00	00	04 %
8-10	39	04	00	86 %
>10	04	00	00	08 %

About 86 percent (43/50 cases) of patients with P.vivax and P.falciparum malaria had Hb in the range of 8-10 gm/dl. This indicates moderate anemia was present in these patients (Table 2).

Table 3 : Red Blood Cell (RBC) count in our malarial cases

RBC Count (millions/ cu.mm)	Vivax	Falciparum	Mixed	Percentage (%)
<3	03	00	01	8 %
3-4	15	00	00	30 %
4-5	24	03	00	54 %
>5	03	01	00	08%

About 54% patients (27/50 cases) with P.vivax and P.falciparum had RBC count in a range of 4-5 millions /cu mm. 30% patients (15/50 cases) with P.vivax and P.falciparum had RBC count in a range of 3-4 millions /cu mm. 8% malarial patients (4/50 cases) had RBC count <3 millions /cu mm and >5 millions /cu mm, respectively (Table 3).

Table 4 : HCT (Haematocrit) in percentage

HCT [%]	Vivax	Falciparum	Mixed	Percentage (%)
<20	01	00	01	04 %
20-35	25	03	00	56 %
>35	19	01	00	20 %

In 56% (28/50 cases) of malarial patients had P.vivax and P.falciparum with hematocrit (HCT) in a range of 20-35%. 4% (2/50 cases) of malarial patients had malaria with hematocrit (HCT) of <20% and this indicates that anemia was present. The rest of the 20% malarial cases (20/50 cases) had hematocrit as >35% (Table 4).

Table 5 : Mean Corpuscular Volume(MCV) (fL)

MCV (femtolitres)	Vivax	Falciparum	Mixed	(%)
<80	08	00	01	18 %
80-100	37	04	00	82 %
>100	00	00	00	00 %

In patients having malaria of P.vivax and P.falciparum, MCV was in range of 80-100 fL in 82% cases (41/40 cases). This indicates normocytic population of RBCs by MCV parameters in malarial cases. The malarial cases with MCV <80 fL were 18% (9/50 cases). MCV > 100 fL/cell were not seen in our malarial cases (Table 5).

Table 6 : Mean Corpuscular Hemoglobin(MCH) (pg)

MCH (pg)	Vivax	Falciparum	Mixed	Percentage (%)
<27	10	01	01	24 %
27-32	31	03	00	68 %
>32	04	00	00	08 %

In patients having malaria of P.vivax and P.falciparum, MCH was more commonly seen in a range of 27–32 pg in 68% cases (34/50 cases). This indicates presence of normochromia of RBCs by MCH parameters. About 24% malarial cases (12/50 cases) had MCH <27 pg while 8% malarial cases (4/50 cases) had MCH >32 pg (Table 6).

Table 7 : Mean Corpuscular Hemoglobin Concentration(MCHC) (%)

MCHC (%)	Vivax	Falciparum	Mixed	Percentage (%)
<31	03	00	00	06%
31-35	26	02	01	58%
>35	16	02	00	36%

MCHC was seen in normal range of 31-35 g/dl in 58% of malarial cases (29/50 cases) in both P.vivax and P.falciparum affected patients. This indicates normochromia of RBCs. Also 6% malarial cases had MCHC <31 g/dl while 36% had MCHC value of >35 g/dl (Table 7).

Table 8 : Red Cell Distribution width (RDW)

RDW (%)	Vivax	Falciparum	Mixed	Percentage (%)
10-15	37	04	00	82 %
>15	08	00	01	18 %

In 82% (41/50) patients with malaria were having RDW within normal range of 10-15% which shows that there was no anisocytosis in RBC population. RDW of >15% were seen in 18% (9/50 cases) of malarial cases (Table 8).

Table 9: Red cell morphology on peripheral smear in malaria species

Blood picture	P.vivax	P.falciparum	Mixed	(%)
Normocytic normochromic	32	3	0	70 %
Normocytic hypochromic	4	0	0	8 %
Microcytic hypochromic	4	1	1	12%
Macrocytic	4	0	0	8%
Dimorphic	1	0	0	2%

Predominantly normocytic normochromic (32/50 cases or 70% cases) was the RBC morphology of patients having malaria with both P.vivax and P.falciparum. Microcytic hypochromic RBC picture was seen in 12% (6/50) cases while Macrocytic RBC picture was seen in 8% (4/50) cases which were all P.vivax cases (Table 9).

Table 10: Parasite count (%) with respect to type of malaria

Parasite count In %	Vivax	Falciparum	Mixed	Percentage (%)
<1	25	01	01	54%
1-5	18	03	00	42%
>5	02	00	00	04%

54 percent of malarial patients (27/50 cases) had parasitic index <1% indicating low parasitaemia. 42 percent of malarial patients (21/50 cases) had parasitic index between 1-5% indicating low parasitaemia (Table 10). In our study, there was no specific correlation of high parasite index with increased severity of thrombocytopenia and vice versa.

Table 11: White blood cell count (cells/cu.mm)

Total Leucocyte Count cells/ mm3	Vivax	Falciparum	Mixed	(%)
<4000	09	00	00	18 %
4000-11,000	33	04	01	76 %
>11,000	03	00	00	06 %

TLC (Total leucocyte count) was within normal range, that is between 4000 – 11000/cu mm in 76% (38/50 cases) in both P.vivax and P.falciparum affected malarial patients.

This was followed by leukopenic malarial cases with TLC <4000 cu mm in 18 % (9/50) cases. All these 18% cases were due to P.vivax. This indicates normal TLC range was seen more common in P.vivax infection followed by leucopenia.

Only 6% malarial cases (3/50 cases) had leukocytosis with TLC >11000/ cu mm. All these 6% cases were due to P. vivax infection.

In our study, leucopenia and leukocytosis were all caused by P. vivax (Table 11).

Table 12: Absolute counts of types of WBCs in malarial cases

Absolute Count	Vivax	Falciparum	Mixed	(%)
Neutrophilia	12	00	00	24%
Neutropenia	07	01	01	18%
Lymphocytosis	10	01	01	24%
Eosinophilia	05	00	00	10%
Normal Count	11	02	00	13%

In patients with malaria, positive for P.vivax, neutrophilia and lymphocytosis was predominantly seen (24% cases each or 12/50 cases each). P.falciparum cases mainly showed neutropenia and lymphocytosis based on absolute counts (Table 12).

Table 13: Platelet Count in Malarial cases

Platelet Count/mm3	Vivax	Falciparum	Mixed	Percentage (%)
<50,000	20	00	00	40 %
50,000-1.5 lakhs	24	04	01	58 %
>1.5 lakhs	01	00	00	2 %

In 58% (29/50 cases) of patients with malaria of P.vivax and P.falciparum were having platelet count in a range of 50,000 – 1.5 lakhs/ cu mm of blood.

Platelet count was <50000/cu mm in 40% (20/50 cases) malarial cases.

This indicates thrombocytopenia was present in majority of malarial cases.

Only 2% malarial cases had normal platelet count due to earlier diagnosis (Table 13).

Discussion

Malaria has been in existence since ancient times and was first described in 4 BC. The levels of endemicity of malaria vary from country to country. In 1880, the French army surgeon named Alphonse Lavern, in Algeria first saw and described malaria parasite in the RBCs of human beings. In 1898, Italians found that human malaria was transmitted by female Anopheles species mosquitoes[2].

The World Health Organization (WHO) established criteria for severe malaria that assisted clinical and epidemiological studies. This project was begun in 1990 and was then revised in 2000 to include other clinical manifestations and laboratory values that portend a poor prognosis based on clinical experience in semi-immune patients[7].

More than 100 countries in the world are considered malarious and more than 2.4 billion of the world's population is at risk. The worldwide annual incidence of malaria is estimated to be about 300-500 million cases. Malaria kills between 1.1 and 2.7 million people annually of which majority are children under five years[1].

The malarial parasite undergoes two cycles of development : the human cycle (asexual cycle) and the mosquito (sexual cycle). Man is the intermediate host and the mosquito is the definitive host[1-3].

Fever and other signs and symptoms are known to be sensitive measure of malaria infection but they lack specificity and positive predictive value especially in areas where malaria is less prevalent. Thus it may be difficult to distinguish the sign and symptoms of malarial disease from other viral and bacterial infections[6].

Since malaria parasites are able to attach to receptors on the red blood cell surfaces, it is expected that malaria parasite have effect on haematological parameters[8,9]. Haematological parameters are measurable indices of blood that serve as a marker for disease diagnosis[3].

Variable haematological changes in malaria are: severe persistent anaemia, red cell destruction, and thrombocytopenia, mild to moderate atypical lymphocytosis, leucopenia, leukocytosis, eosinophilia, neutrophilia and monocytosis[4,5,8].

The prevalence of plasmodium vivax infection (92%) was higher as compared to plasmodium falciparum infection (8%) in a South Indian study. Mild degree of anaemia and thrombocytopenia was observed in infected individuals. The finding of thrombocytopenia was significant in vivax infection and anaemia in falciparum infection[3].

Lab diagnosis of malaria includes Peripheral blood smears (both thick and thin smears). Alternative costlier tests to 'gold standard' microscopy are quantitative buffy coat technique (QBC), antigen detection methods, PCR, ELISA, indirect Fluorescent Antibody Test (IFAT). Alternative tests are not feasible in very lab set-up in India due to cost-restraints and high population density.

Malaria caused by P.vivax was predominant in present study. This finding was similar with other studies[1,3,6,8].

People in age range of 15-30 yrs were more affected in present study, that is, younger people were affected. These findings were similar with other studies[1,3,6,8,10].

Male predominance was seen in present study which was similar with other referenced studies[1,3,6,8,10].

Fever was most common presenting symptoms followed by chills and rigor in present study. These were similar findings with other referenced study[1].

Hb, RBC count, PCV – showed that anemia was more common hematological change in present study, as these values were lower than normal level. This was the similar finding in other studies[1,3,4,6,8,10].

Peripheral smear revealed normocytic normochromic RBCs in the present study in 70% malarial cases. MCV, MCH and MCHC was within normal range in 82%, 68% and 58% of our malarial cases. These features were similar in other study[1].

It was seen that MCV and RDW were higher level than normal in few malarial studies[4,6,8].

Patients with malaria having normal TLC followed by leucopenia were more common in present study. Other studies showed similar findings[1,8]. Few studies showed reduced leukocyte count in malarial cases[2,10]. A single study showed elevation in WBC counts in malarial cases compared to controls[11].

Thrombocytopenia was most common hematological change seen in present study. This was similar in most of the other studies[1,3,4,6-8,10].

The speculated mechanisms leading to thrombocytopenia in malaria are: coagulation disturbances, splenomegaly, bone marrow alterations, antibody-mediated platelet destruction, oxidative stress and the role of platelets as cofactors in triggering severe malaria[8,11].

Conclusion

Haematological changes can be influenced by any diseases including endemic diseases like malaria. Anaemia and thrombocytopenia may be considered as a marker of malaria infection as these are most frequently observed haematological findings.

Various haematological findings can help in diagnosis of malaria which helps the clinicians for appropriate treatment to avoid grave malarial complications. Effect on different haematological parameters were similar in patients of malaria caused P.vivax and that with P.falciparum. Haematological investigations are relatively inexpensive, reliable and competent measures to diagnose the severity of malaria.

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