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Clinico-Hematological Profile of Malaria Cases in a Tertiary Care Hospital

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ABSTRACT

Background: Malaria is a major public health problem in most countries of the tropics and sub tropics. Malarial parasitemia causes wide-ranging hematological alterations and may lead to life threatening complications if not diagnosed and treated in time. Alterations in the hematological parameters are also thought to have the capacity to act as an adjuvant tool in strengthening the suspicion of malaria, thereby prompting a more meticulous search for malaria parasites. Therefore the aim of the present study was to assess malaria parasitemia and its association with clinico-hematological parameters.

Methods: The present study was observational and analytical and of two years. 59 diagnosed cases of malaria on peripheral blood smear were included in the study and clinical presentation and hematological parameters were studied in them.

Observations: 58 (98.3%) were infected with Plasmodium vivax (PV) and only one case was of Plasmodium falciparum (PF). 52 (88.14%) had a parasite index (PI) of <2%. 76.3% of cases were presented with fever with chills and rigors. 49 (83%) had thrombocytopenia and 36 (61.0%) cases had anemia. Leucocytosis was observed only in 8 (13.5%) cases and leucopenia in 10 (17%) cases. Elevated ESR was observed in 78% of malaria cases.

Conclusion: Plasmodium vivax was predominant species in our region. As majority of the cases had fever and thrombocytopenia, in every case of fever with thrombocytopenia malaria should be considered in differential diagnosis in malaria endemic regions.

Hematological investigations are helpful in detecting early complications, to monitor and treat them effectively

Keywords: Malaria, vivax, falciparum, fever, thrombocytopenia, anemia

INTRODUCTION

Malaria is a life threatening infection in humans caused by intracellular protozoa of the genus plasmodium which is transmitted by bite of infected female Anopheles mosquitoes called malaria vectors. In addition, reports showed that malaria could also be transmitted by transfusion of infected blood, sharing needles and congenital transmission. There are five species of plasmodium viz. p. vivax, p. falciparum, p. ovale, p. malariae and p. knowlesi. Among these p. vivax and p. falciparum pose the greatest threat. *P. falciparum* is the most prevalent malaria parasite on the African continent. It is responsible for most malaria-related deaths globally. *P. vivax* is the dominant malaria parasite in most countries outside of sub-Saharan Africa.[1]

P. vivax and P. falciparum infections can cause complications like severe anemia, cerebral malaria with convulsions, ARDS, renal failure, circulatory collapse, hemoglobinuria, abnormal bleeding, thrombocytopenia, disseminated intravascular coagulation (DIC) and jaundice.[2]

According to the latest WHO estimates, released in December 2016, there were 212 million cases of malaria and 429 000 deaths in 2015 and nearly half of the world's population were at risk of malaria. An estimated 6.8 million malaria deaths have been averted globally since 2001. India

accounts for 75% of all malaria cases in South-East Asia. (WHO-2017)[1]

Studies have revealed that wide-ranging haematologic changes occur in malaria.[3,4,5,6] Alterations in the hematological parameters are also thought to have the capacity to act as an adjuvant tool in strengthening the suspicion of malaria, thereby prompting a more meticulous search for malaria parasites.[4,5,7] Previous studies involving patients with complicated malaria had demonstrated that a reduced platelet count, reduced white blood cell counts, and decreased red blood cell indices had relatively good sensitivities and specificities in predicting the presence of malaria infection.[5]

Changes in physicochemical parameters of P. falciparum infested blood may vary with level of malaria endemicity, presence of haemoglobinopathies, nutritional status, demographic factors and level of malaria immunity.[3]

In the last 3 decades, big strides have been made in refining, modifying, or inventing highly sensitive and specific diagnostic tools for parasitic infections.

For malaria diagnosis, these newer tests are based on serology based assays [ELISA (FAST-ELISA)], and rapid antigen detection systems (RDTs), molecular based approaches [real time polymerase chain reaction, loop-mediated isothermal amplification (Lamp), and luminex], and proteomics technology (mass spectrometry).

The newer serological and molecular based malaria diagnostic approaches provide superior sensitivity and specificity, but it is at a huge cost, in terms of equipment, infrastructure, and personnel which makes most of the newer diagnostic methods inapplicable to many areas in developing countries, where malaria is highly prevalent. Some of the hospitals in the region, however, can afford to carry out a complete blood count for hematological parameters in patients suspected to have an infection. Because microscopy is still considered by many as an imperfect gold standard, efforts have been made to examine role of hematological parameters in the diagnosis of malaria infection.

Hematological profile together with microscopy will enable rapid diagnosis, prompt treatment and further complications can be avoided. The studies reported on this are sparse and data is limited. This study will add more information.

METHODS

The present study was observational and analytical study conducted at a tertiary care centre, Karad, Maharashtra from January 2016 to December 2018. Total of 59 cases were studied. All the diagnosed cases of malaria on peripheral blood smear during the study period were included in the study.

The Ethical Committee clearance was taken prior to start study.

Written informed consent for prospective cases was taken.

Data collection and laboratory methods-

- For previous years cases –

From archival of data, hematology records and stored Peripheral smears were studied and analyzed.

- For prospective cases-

Material used: EDTA vacutainers, 3cc disposable syringe, glass slides, cover slips, DPX mountant, Leishman stain, Hematology analyzer.

Method

Socio-demographic, clinical details, investigations were recorded.

3ml venous blood specimen was collected by venipuncture in EDTA vacutainer tubes and was analyzed using a Nihon Kohdein hematology analyzer.

Hemoglobin level (Hb%), total white blood cell count (TWBC), differential WBC count, red blood cell count (RBC), hematocrit (Hct), mean cell volume (MCV), mean cell hemoglobin (MCH), mean cell hemoglobin concentration (MCHC) and platelet count (PC) were recorded.

According to WHO guidelines, hemoglobin level <13 gms% in males and < 12 gms% in females was categorized as anemia, WBC < 4000/ cumm, as leucopenia, > 11000/cumm as leucocytosis and platelet count < 1,50,000/ cumm as thrombocytopenia.[8]

Two drops of capillary blood sample was added on a glass slide to prepare a thin and thick smear.

Thick smear was de-hemoglobinised before staining. For this purpose the slide was kept in distilled water for 10 minutes, taken out and dried.

Both thin and thick smears were stained by Leishman stain, studied under the microscope under oil immersion.

Thin blood smear was studied for RBC morphology, differential count, platelets, detection of malaria parasite, its type and density.

Parasite density (Parasite Index- PI): Parasitemia is number of parasitized RBCs / 1000 RBCs and is expressed as percentage. In a thin smear number of parasitized RBCs seen in 1000 RBCs (in 100Xobjective) were counted and the percentage was expressed. In this study 1µl of blood was considered to be equivalent to $5X10^6$ red blood cells and hence 1% PI is equivalent to 50000 parasites/ µl. Hyperparasitemia was categorized as > 100000 parasites / µl (i.e. >2%).Thus cases were categorized as < 2% (Low parasitemia) and > 2% (high parasitemia [9]

Inclusion criteria –

All diagnosed cases of malaria by peripheral blood smear in tertiary care hospital

Exclusion criteria – Nil

RESULT

In the present study a total of 59 cases of malaria were obtained within a period of 3 years- January 2016 to December 2018.

Table-1 Distribution of cases as per types of species of malaria

Types of species	Number of cases	Number of cases (%)
P. Vivax	58	98.3
P. Falciparum	01	1.7

Almost all cases i.e. 58 (98.3%) out of 59 were of P. Vivax with only 1 (1.7%) case of P. Falciparum

Table– 2 Distribution of malaria cases according to parasite index

Type of species	Parasitic index	
	<2%	>2%
P. Vivax	51	07
P. Falciparum	01	
Total	52	07

Out of 59 cases, 52 (88.14%) cases had a parasite index of <2% and 7 (11.86%) cases had >2% parasite index.

Table– 03 Distribution of malaria cases as per Socio-demographic characteristics

Parameters	Number of patients	Number of patients (%)
Sex:		
Male	47	79.7
Female	12	20.3
Age(yrs)		
<=15	01	1.7
16-30	34	57.6
31-45	13	22
>=46	11	18.7
Occupation		
Government worker	07	11.9
Merchant	09	15.3
Daily Laborer	13	22
Farmer	30	50.8
Residence		62.7
Rural	37	37.3
Urban	22	

Males were affected more than females in the ratio of 3.9:1 and highest occurrence of malaria was in the age group of 16-30 years. It was more common in farmers followed by daily labourers, merchants and government workers. It is more common in rural area than urban.

Table – 04 Seasonal variation in malaria

Month	Year 2016	Year 2017	Year 2018	Total
January	0	1	0	1
February	1	1	1	3
March	2	1	0	3
April	1	2	3	6
May	0	2	1	3
June	0	2	2	4
July	3	0	5	8
August	1	7	3	11
September	5	3	2	10
October	3	0	2	5
November	0	0	3	3
December	2	0	0	2

Majority of cases 33(55.9%) were occurred in rainy season followed by 15(25.42%) in summer and 11(18.64%) in winter season.

Table -5 Clinical presentation in malaria cases

Parameter	Number of cases	Percentage(%)
Headache	16	27.1
Vomiting	41	69.5
Fever	59	100
Typical Paroxysm (Chills and rigors)	45	76.3
General weakness	43	72.9
Pain in abdomen	03	5.1
Breathlessness	04	6.8
Splenomegaly	05	8.5
Pallor	25	42.4
Hepatomegaly	03	5.1
Bleeding manifestations	5	8.5

The most common clinical feature is fever being present in 100% of cases and it was associated with chills and rigors in 76.3% of cases.

Table – 06 Platelet count and parasite index

Platelet count	Number of cases		Total	Number of cases(%)		Total(%)
	PI<2%	PI>2%		PI<2%	PI>2%	
Normal	10	00	10	19.2	00	17
Mild thrombocytopenia	16	00	16	30.8	00	27.1
Moderate thrombocytopenia	26	03	29	50	42.8	49.1
Severe thrombocytopenia	00	04	04	00	57.2	6.8

Out of total cases 49 (83%) cases showed thrombocytopenia and 10 (17%) were having normal platelet count. In cases having PI <2% platelet count was normal in 19.2%, mild thrombocytopenia in 30.8%, moderate thrombocytopenia in 50% and no severe thrombocytopenia whereas all the cases with PI >2% showed moderate or severe thrombocytopenia.

Table – 07 Hematological parameters- Hemoglobin in relation to parasite index in malaria patients

Hemoglobin %	Cases		Total
	PI <2 (%)	PI >2 (%)	
Normal	23	-	23
Mild Anemia	20	02	22
Moderate anemia	06	03	09
Severe anemia	03	02	05

Out of the total 59 cases, 36 (61.0%) cases had anemia and 23(38.98%) were having normal hemoglobin

Out of 52 cases with PI<2%, 29 (55.8%) cases had anemia and among these majority of cases- 20 (68.96%)] were having mild anemia. All the cases (100%) with PI >2% had anemia and 5/7 (71.42%) cases had moderate or severe anemia.

Table – 8 Hematological parameters in malaria patients

Parameters	cases	Percentage (%)
RBC count – Normal	26	44.06
Decreased	33	55.93
PCV - Normal	25	42.37
Decreased	34	57.62
MCV - Normal	28	47.45
Increased		
Decreased	24	40.67
	07	11.86
MCH - Normal	27	45.76
Increased	26	44.06
Decreased	06	10.16
MCHC – Normal	26	44.06
Increased		
Decreased	25	42.37
	08	13.55
RDW - Normal	49	83.05
- Increased	10	16.94
MPV - Normal	47	79.66
Increased	12	20.33

The table shows decrease in RBC count and PCV in 55.93% and 57.62% cases respectively. There is increase in MCV, MCH and MCHC in 40.67%, 44.06%, 44.06% respectively. RDW was increased in only 16.94% and MPV was increased in 20.33% of malaria cases.

Table– 9 Total WBC count and PI index in malaria cases

Total leukocyte count	Number of cases		Total	Cases(%)		Total(%)
	PI<2%	PI>2%		PI<2%	PI>2%	
Normal	38	03	41	73.1	42.8	69.5
Leukocytosis	06	02	08	11.5	28.6	13.5
leukopenia	08	02	10	15.4	28.6	17

Of the total 59 cases, 41 (69.5%) cases were having normal WBCs count and leucocytosis was observed only in 8 (13.5%) cases and leucopenia was in 10 (17%) cases. Cases with PI<2% had normal leucocyte count in 73.1%, leucocytosis in 11.5% cases and leucopenia in 15.4% cases. Cases with PI >2% had normal leucocyte count in 42.8% cases, leucocytosis in 28.6% and leucopenia in 28.6% cases.

Table– 10 Differential leukocyte count in malaria cases

Parameter	Number of cases	Percentage (%)
Neutrophils - normal	44	74.6
neutrophilia	09	15.3
neutropenia	06	10.1
Lymphocytes – normal	46	78
lymphocytosis	01	1.7
lymphopenia	12	20.3
Monocytes - normal	55	93.22
monocytosis	04	6.8
monocytopenia	00	00
Eosinophils - normal	54	91.52
increased	05	08.47
Basophils - normal	59	100

In majority of cases differential count was normal except neutrophilia in 15.3% cases, neutropenia in 10.1% cases, lymphopenia in 20.3%, lymphocytosis in 1.7% cases, Monocytosis in 6.8% cases, eosinophilia in 8.47% with normal basophils.

Table 11- ESR in malaria patients

Parameter	cases	Percentage (%)
ESR - Normal	13	22
Increased	46	78

The table shows rise in ESR in 78% of malaria cases.

Table- 12 Comparison of signs and symptoms with other studies

Clinical features	Prashant Khuraia et al (11)	Rajendra kumar Verma et al (12)	Gaurav I. Patel et al (13)	Present study
Pallor	63.46%	52.71%	66%	57.62%
Icterus	27.88%	31.78%	20%	8.47%
Hepatomegaly	26.92%	19.37%	6.6%	5.1%
Splenomegaly	32.69%	9.03%	18.6%	8.5%

DISCUSSION

Malaria is an acute febrile illness. Though it is preventable and curable disease, Malaria continues to be the major health problem in the tropics with increased morbidity and mortality.[10] As most common presentation is fever in endemic region malaria may be considered as a leading differential diagnosis in all patients presenting as acute febrile illness.[11]

In the present study in three years period a total of 59 cases were diagnosed as malaria on peripheral smear. The major species in our region was P. Vivax (PV) - 57 (98.3%) and there was only 01(1.7%) case of P. falciparum (PF) and no mixed infection. In a similar study carried by Smita Chandra and Harish Chandra in Uttarakhand, India, 69.8% cases were positive for PV and only 27.5% were positive for PF whereas 2.7% cases were reported to have mixed infection.[7] In the another similar studies by Rajendra Kumar Verma et al from Kanpur, North India[12] and Gaurav I. Patel et al from Vadodara Gujarat, India[13] reported as 76.74% cases of PV, 13.95% cases of PF and 9.3% cases of mixed infection and 61% cases of PV, 29% of PF, 9.43% of mixed infection respectively. In a similar study by Lauram M. Erhart et al from Bangkok, Thailand also reported more percentage of PV i.e. 59% and PF of 38% and mixed infection in 2% cases.[14] However in some similar other studies PF was reported as common infecting species in their regions.[4,11,15]

P. vivax malaria is difficult to detect and treat because the parasitemia is typically low in comparison to that of P. falciparum[2] In our study also out of total 59 cases, 52

(88.14%) cases had a PI of <2% and 7(11.86%) cases had a PI >2%. It is believed that PF infection is more serious than PV however recently researchers found that PV is changing its trend and it also can cause serious infections with life threatening complications.[2,12]

In our study males were affected more than female in the ratio of 3.9:1 and seen more commonly in the age group of 16 – 30 years i.e. in physically active age group. These observations are similar to some other studies.[7,10,11,12,13,14] More incidence in young age group is attributable to- 1. State of immunological balance against malaria also known as "premunition" which is achieved late in adulthood. 2. Indian demography suggests that the maximum population right now is of younger adults. 3. Increased chance of contracting the infection due to more outdoor activities in younger age group.[11]

In the present study malaria occurrence was more common in farmers (50.8%) followed by daily laborers (22%), merchants (15.3%) and government workers (11.9%). It is more common in rural region (62.7%) than urban region (37.3%) these findings are comparable with the similar study by Solmon Sirak et al[4]

In this study maximum cases 33(55.9%) were observed in rainy season i.e. June to September. In this season more water accumulations occurs which is favorable for breeding of mosquitoes and it is optimum for malaria parasite development. This finding is similar to other studies.[7,11]

The clinical presentation of malaria is variable among patients and is usually related to the severity of the infection. Malaria is an acute febrile illness. In a non-immune individual, symptoms usually appear 10–15 days after the infective mosquito bite. The first symptoms – fever, headache, and chills– may be mild and difficult to recognize as malaria. If not treated within 24 hours, *P. falciparum* malaria can progress to severe illness, often leading to death.[1]

Children with severe malaria frequently develop one or more of the following symptoms: severe anaemia, respiratory distress in relation to metabolic acidosis, or cerebral malaria. In adults, multi-organ involvement is also frequent. In malaria endemic areas, people may develop partial immunity, allowing asymptomatic infections to occur.

Patients in this study presented with fever, generalized body weakness (malaise), headache, nausea/vomiting, breathlessness, pain in abdomen, pallor, bleeding manifestations, hepatomegaly, spleno-megaly.

In all the malaria cases (100%) fever was the common clinical finding and it was associated with chills and rigors in 76.3% of cases. Typical paroxysms occurred only in few patients. Most of them had daily fever peaking once in a day. Similar findings were reported by other studies.[11,13]

The higher percentage of Hepatomegaly and splenomegaly in the study by Prashant Khuraiya et al[11] might be due to higher percentage PF infection or late presentation of the patients.

Haematological changes are well-recognised with malarial infection however background haemoglobinopathy, nutritional status, demographic factors and malaria immunity play a major role in specific changes in that geographical region. These parameters are well studied in *P. falciparum* infection, but now recent studies have indicated that these changes do occur in *P. vivax* infection also.[16] The nature of hematological abnormalities depends on the time after infection. A recent study has revealed a role of interleukins (IL–4) and interferon's (IFN–gamma) in erythropoietin suppression.[11]

In the present study the major haematological change seen was thrombocytopenia. Several other studies observed the similar finding.[4,5,7,10,11,12,13,14,16] in some studies thrombo-cytopenia has been emerged as predictor of malaria.[14,17] In our study out of total cases, 49 (83%) cases showed thrombocytopenia

and 10 (17%) were having normal platelet count. In cases having PI <2% platelet count was normal in 19.2%, mild thrombocytopenia in 30.8%, moderate thrombocytopenia in 50% and no severe thrombocytopenia whereas all the cases with PI >2% showed moderate or severe thrombocytopenia. It was observed that at high parasitemia the platelets were found to be significantly lower. Similar finding was observed by study by Solmon Sirak et al.[4]

The pathogenesis of thrombocytopenia consists of a myriad of pathogenetic mechanisms involving splenic pooling of platelets, antibody (IgG) mediated platelet destruction, adenosine diphosphate (ADP) release following the haemolysis of parasitised RBCs, dysmegakaryopoiesis, platelet aggregation and activation, parasite invasion of platelets, platelet phagocytosis, platelet adhesion to erythrocytes, and oxidative stress. Nevertheless, thrombocytopenia in malaria is observed to improve with disease resolution, and a normal platelet count is usually reported within 7 days after the initiation of antimalarial treatment.[5,16]

In our study mean platelet volume (MPV) was increased (>8fl) only in 12 (20.33%) cases and normal in 47(79.66%) cases. Similar finding was observed by Haruna Muwonge et al. [5] Thrombocyto-penia with increased mean platelet volume can serve an indicator for PV malaria[7,16] In an attempt to compensate for the low absolute platelet count, the bone marrow increases the formation of megakaryocytes, which usually escape from the bone marrow as megaplatelets during an acute malaria infection. Evidence to support this hypothesis comes from a study by Kreil et al that found a marked elevation in the level of thrombopoietin, a key platelet growth factor in patients with malaria. Because of an increase in the amount of mega platelets, the mean platelet volume is increased during an acute malaria infection. In contrast, in majority of the patients the mean platelet volume (MPV) of parasitemic patients in the study by Haruna Muwonge et al[5] like ours was normal. According to them these findings may suggest that uncomplicated malaria is associated with mild or nonsignificant changes in the platelet profile. Also majority of our patients were of PV and having low parasitemic index.

In a study by Sudhir Babu Devineni et al[10] it was observed that severe thrombocytopenia is seen in both PF and PV infections but is more common in PF infection and these patients are more prone to develop complications than mild and moderate thrombocytopenia. In a study by Haruna Muwonge et al[5] also observed that acute uncomplicated malaria is not associated with a marked reduction in platelets, as compared to severe malaria.

In "A Study of clinical and laboratory profile of patients having fever with thrombocytopenia and its outcome" by Sujata S. Kumbhar et al[18] observed that thrombocytopenia is associated with large number of cases of febrile illness in which infections formed the largest group (78%) and malaria was the commonest (28.2%).

For continued survival and reproduction, plasmodium parasites need to infect the red blood cells of their human host. Consequently, changes in the red blood cell indices are some of the commonest observations seen in malaria.[5] In endemic areas malaria is the most common cause of severe anaemia.[5,14,16] Although malaria caused by PV is thought to be benign, some studies have shown that it can cause severe anaemia as well. In the study of "Comparison of hematological parameters in various acute febrile illnesses" by Neha Chaudhary et al[19] found that malaria showed maximum number of cases of anemia. Anaemia in malaria is believed to occur due to haemolysis of parasitised and non-parasitised RBCs, peripheral sequestration of RBCs, and ineffective erythropoiesis. In malaria endemic areas, the prevalence and severity of anaemia are usually determined by a number of interacting factors. These include the level of parasitaemia, age of host, host genetic factors (e.g., co-existing RBC

polymorphisms like haemoglobinopathies, G6PD), and non-malarial causes of anaemia (e.g., infections, malnutrition)[5,16]

In our study out of the total 59 cases, 36 (61.0%) cases had anemia. Out of 52 cases with PI<2%, 29 (55.8%) cases had anemia and among these majority of cases-20 (68.96%)] were having mild anemia. All the cases (100%) with PI >2% had anemia and 5/7 (71.42%) cases had moderate or severe anemia. Similarly In a study conducted by Saurabh Srivastava et al[16] on hematological profile of vivax malaria patients, 44.3 % cases had anaemia however severe anaemia was not seen. Although there is extensive documentation of anemia, in this study and another similar study by Laura M. et al[14] observed only mild decreases in hemoglobin in malaria cases and according to them this discrepancy may be related to the multifactorial etiology of anemia. The impact of malaria anemia is greatest in regions of sub-Saharan Africa where underlying anemia and poor nutrition are common. Furthermore, some observers have suggested that malaria-related anemia is more severe in areas of intense malaria transmission and in younger children rather than in older children or adults. Laura et al stated that their study and others in south-eastern or eastern Asia have noted Hb decreases or mild anemia among malaria cases may reflect a lower prevalence of underlying anemia, better nutritional status, and/or better access to treatment. In a similar study by Rajendra Kumar Verma et al[12] observed anemia in 54.3% PV, 50% of PF and 41.6% of mixed infection cases. Thus there is variation in the hemoglobin levels in different studies. According to Rajendra Kumar Verma et al[12] this variation might be due to the severity of infection and the level of immunity against the parasite in patients of falciparum and vivax malaria in different countries having endemic and non-endemic pockets.

In our study only mild decrease in hemoglobin in some cases observed may be because of almost all the cases (98.3%) cases were affected by PV and majority (88.14%) of these cases were having < 2% PI index, as well good nutritional status of the affected cases and early detection and treatment might contribute.

As hemoglobin, the other red blood indices i.e. RBC count, PCV, MCV, MCH, MCHC, RDW not much altered in this study. Similar was the observation by Haruna Muwonge et al[5] According to them this could probably be because uncomplicated malaria is associated with milder biochemical changes, for example, a lower production of cytokines, less endothelial cell activation, milder changes in the coagulation profile, less sequestration, and less hemolysis as opposed to complicated/severe malaria. Smita Chandra and Harish Chandra[7] also observed the similar findings.

Increase in mean corpuscular volume (MCV) in malaria-infected patients might be due to anemia associated with malaria that causes increased rate of RBC production leading to the release of immature RBCs into blood circulation. Furthermore due to abnormalities in the nitric oxide (NO) levels that occur in malarial infection, the mean corpuscular volume might be increased. In addition, NO can inhibit the enzyme methionine synthase, so functional vitamin B12 deficiency state may occur, which can lead to megaloblastic anemia, and studies suggested that NO is associated with the low serum level of vitamin B12.[4]

Anemia in this study was mainly normocytic normochromic. Similar finding was there in the study by Saurabh Srivastava. [16] In the majority of cases, anaemia does not require any treatment and improves gradually; but in a few cases, blood transfusion (packed red blood cells) may be required.[16]

In our study leukopenia was observed in 10 (17%) cases leucocytosis was only in 8 (13.5%) cases and. Similar observation was found in the study by Khuraiya P et al.[11] Whereas in a similar study by Saurabh Srivastava reported leucopenia as commonest abnormality

(21.6%) compared to leucocytosis (2.5%). Smita Chandra and Harish Chandra[7] also found leucopenia as commonest leucocyte abnormality.

No difference was noted in total leucocyte count with respect to parasite index in our study

Leukocyte changes in malaria are variable and depend on many factors such as acuteness of infection, parasitemia, disease severity, state of the host immunity to malaria, and concurrent infections. Leukocytes play a vital role in the defense against malaria.[5,16]

Commonly, majority of patients with acute uncomplicated *P. falciparum* malaria usually have their mean total leukocyte count (TLC) within the normal range. However, in some cases, a mild leucopenia may occur, especially in nonimmune adults or in cases of complicated malaria. In addition, according to previous studies, leucopenia does not appear to be parasite specific.[5]

On the contrary a study by Solmon Sirak et al[4] revealed leucocytosis and neutrophilia as a major feature in malaria infected patients. This is due to increase in the release of WBCs at the initial stage of infection to fight against malaria infection. Further they stated that their study supports that effective immune response to malaria is feature in malaria endemic areas.

Although some discrepancies appear to exist, there have been reports of leukopenia as well as leukocytosis in malarial infection and studies have reported that neutropenia, eosinophilia, neutrophilia, and monocytosis, lymphopenia, are other hematological reactions to malarial infection. This finding is in contrast to previous studies which reported that malaria-induced changes include a reduction in neutrophil counts. In their report, reduction in neutrophil was observed as an important abnormality in patients with severe malaria and associated with a poor prognosis. The reason for this might be the marginalization of neutrophils to the sites of inflammation, splenic localization, and serum lymphotoxic factors.[4]

In our study in majority of cases differential count was normal except neutrophilia in 15.3% cases, neutropenia in 10.1% cases, lymphopenia in 20.3%, lymphocytosis in 1.7% cases and Monocytosis in 6.8%, eosinophilia in 8.47%. Among these parameters lymphopenia was the commonest abnormality. Our findings are supported by the other studies[5,16] according to the literature lymphopenia, sometimes profound but transient, is a common finding in acute malaria in nonimmune adults. The tissue redistribution of lymphocytes, from the free flowing pool to the marginal pool at the endothelial lining is usually responsible for transient malaria lymphopenia, particularly observed in T lymphocytes. Sometimes lymphocyte destruction as a result of Fas-induced apoptosis is also a factor responsible for lymphopenia.[5,16]

Activation of either phagocytes (neutrophils and macrophages) or natural killer (NK) cells is responsible for the innate immune response to blood borne pathogens. Thus reticuloendothelial hyperplasia involving macrophages is one of the most important early pathological hallmarks in malaria. Hence, monocytosis has been one of the most consistent observations reported from prior similar studies.

In the present study elevation of ESR was observed in 78% of cases our finding is in concordance with the study by Akaniwor et al.[3] Elevation of ESR have been reported in acute and chronic infections, chronic inflammatory disorders, malignancies especially Hodgkin's disease tissue necrosis and pregnancy.

ESR is used by some researchers as basis for the diagnosis and monitoring of therapeutic intervention of malaria. They suggested that ESR was elevated during acute malaria infection and declined with recovery. However, measurement of ESR is often used as a non-specific test for acute illness and may reflect the acute process of the disease.[3]

CONCLUSION

PV is predominant species in our region. Because of low parasitemic index in majority of the cases there are no major changes in the hematological parameters, however thrombocytopenia was observed in majority of the cases and all the cases presented with fever. Therefore in every case of fever with thrombocytopenia malaria should be considered in differential diagnosis in malaria endemic regions. Complications do occur in malaria so it is vital to know and perform hematological investigations to detect early complications, also to monitor the case and treat them effectively.

Though the hematological changes in malaria cases in this study are not novel, our findings have added more information in the limited knowledge and sparse reports on clinico-hematological profile of malaria infected patients.

Limitations of the study and recommendation

The limitations of this study were cross sectional nature of the study design, small sample size and confounding factors that may affect hematological parameters, such as nutritional deficiencies and genetic backgrounds of patients, common bacterial, viral, and helminth infections. We have not excluded these confounding factors. We recommend studies on larger sample size and using experimental designs (case control, etc) and with exclusion of the confounding factors.

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Authors' contributions

All authors contributed toward data analysis, drafting and revising the article and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in the article work and its publication.

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