Hematological changes in patients with malaria in a tertiary care hospital, Multan, Punjab, Pakistan

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ABSTRACT

Background: Malaria is one of the most common human infections and continues to cause significant morbidity and mortality all over the world. To assess and compare the hematological changes in common types of malaria in our patients.

Methods: This observational study included 100 diagnosed malaria patients of Multan Medical and Dental college, Multan both from out patient department (OPD) and in-patient department, between March 2020 and March 2021. The diagnosis of malaria was confirmed by thick and thin film stained with Geimsa’s staining for malaria parasite and plasmodium species and the parasite index (MPI) in some cases. Complete blood counts (CBCs) were performed and WBC differential was done on all cases.

Results: The most common type of malarial parasite was Plasmodium vivax followed by Plasmodium falciparum and 89% of the patient had thrombocytopenia, 70% anemia, 23% had leukopenia and 10% had raised WBC count. The mean parasite load was 1.275±0.629%, 20% of the cases showed neutropenia, 40% had lymphopenia and 40% showed monocytopenia. Of all the cases 15% had neutrophilia, 8% had lymphocytosis and 5% had eosinophilia. Thrombocytopenia was slightly more in P. falciparum (58.69%) than P. vivax (30.18%) cases, p>0.05, whereas there was no significant difference in the incidence of anemia in two groups (34.68% vs 33.82%) with p>0.05.

Conclusions: P. vivax is the common malarial parasite in our population. Both P. vivax and P. falciparum can cause marked hematological changes including thrombocytopenia, anemia, lymphopenia and monocytopenia.

Keywords: Malaria, Thrombocytopenia, Plasmodium vivax

INTRODUCTION

Malaria has often been considered to fall in the grey zone between parasitology and hematology. A European Textbook of hematology published in the 1930s, defined malaria as a “typical blood disease” with anemia, fever and splenomegaly. Despite global efforts for reducing its transmission, malaria still continues to be a serious and widespread protozoal infection of humans. It is endemic in 107 countries including Pakistan. Globally, around 3.3 billion people are exposed to the risk of malaria, with maximum disease burden in sub-Saharan Africa. More than 40% of the world’s population and around 60% of Pakistan’s population, lives in malaria endemic regions. In Pakistan malaria is mostly found in the provinces of Sindh, Balochistan, Khyber Pakhtunkhwa, and the
In malaria changes in haematological parameters have been reported earlier. These include anemia, thrombocytopenia and leukopenia or leukocytosis.9 Splenomegaly, mild-to-moderate atypical lymphocytosis and rarely disseminated intravascular coagulation (DIC) have also been seen.10 Other hematological reactions to malaria that have been reported are neutropenia, eosinophilia, neutrophilia and monocytosis.11

Anemia is one of the most common complications in malaria infection especially in younger children and pregnant women.12 The pathogenesis of anemia in malaria is multifactorial and includes mechanisms such as destruction of parasitized as well as non-parasitized red blood cells, splenic pooling of red blood cells, oxidative stress induced hemolysis, suppression of marrow hemopoeisis, dyserythropoisis and ineffective erythropoiesis.13,14 Besides anemia, a reduction in the number of platelets is another one of the more well-known hematologic changes observed in patients with malaria.15 The pathogenesis of thrombocytopenia is mediated through peripheral destruction, excessive removal of platelets by spleen pooling as well as platelet consumption by the process of disseminated intravascular coagulopathy.16

The white blood cell counts and neutrophil counts are usually within normal limits. However on differential count both neutrophilia and neutropenia has been observed in malaria.17 Alterations in hematological parameters vary with the level of malarial endemcity, background hemoglobinopathy, nutritional status, demographic factors, and also malaria immunity.18 As malaria is a common parasitic infection in our country, so the purpose of current study was to assess the frequency of hematological complications among malaria cases and its impact on the health of effected patient. We also aimed to see if blood indices can be helpful to support suspicion of malaria in the absence of other more suggestive diagnostic facilities.

RESULTS

A total of 100 patients fulfilled the inclusion criteria for diagnosis of malaria. The mean age was 25.1±14.8 with minimum of 10 days and maximum 70 years. The majority were males 64% and 36% were females with a male to female ratio of 1.7:1. The most common type of malarial parasite was Plasmodium vivax followed by Plasmodium falciparum. Mixed infection was 3% and 1% of the cases was due to plasmodium malaria (Figure 1).

Parasite load was also noted among patients. The mean parasite load was 1.3±0.63% with maximum 2.4% and minimum 0.2%. 70 patients were anemic, out of which 58(83%) normocytic, 11(16%) microcytic and only 1(1%) had macrocytic type of anemia. Among these patients 40% had mild, 25% had moderate and 5% had severe anemia. Red blood cell (RBC) count was normal in majority (70%), only 28% patients had low RBC count. The majority of the patients (89%) were thrombocytopenic. The median platelet count was 66.0 (35.3-110.1) ×10^9/ul, with range of 0 to 432×10^9/ul. Of these 37%, 24%, 12% and 11% had moderate, severe,
very severe thrombocytopenia and normal platelet count respectively. The mean platelet volume was within normal limits in 95% patients, high in 4% and low in 1%. The difference of MPV among different parasite infection was found to be statistically insignificant with a p value of 0.986. The white blood cell (WBC) within normal limits in 63% while 23% had leukopenia and 10% had raised WBC count. The median WBC count was 5.2 (3.7-6.9) x10⁹/ul with range of 0.81-28.06 x10⁹/ul.

### Table 1: Hb and RBC comparison among type of parasite.

| Parameter | Plasmodium vivax | Plasmodium falciparum | Plasmodium malariae | Mixed infection | P value |
|-----------|------------------|-----------------------|---------------------|----------------|---------|
| Hb        | Mean±SD          |                       |                     |                |         |
| RBC       | 11.1±2.3         | 10.5±2.5              | 15.8                | 14±2.8         | 0.033   |
| RBC       | 4.1±0.8          | 4.1±0.9               | 6.9                 | 5±0.4          | 0.006   |

Mean values of different parameters in different malarial type infection were as follow: hemoglobin 11.08±2.34 g/dl in vivax and 10.56±253 in falciparum, WBC count 6.17±4.64x10⁹/ul and 8.61±5.27x10⁹/ul, platelet count 93.96±83.18x10⁹/ul and 44.92±41.36x10⁹/ul, RBC count 4.099±0.88 and 4.08±0.9 x 10⁹/ul in P. vivax and P. falciparum respectively. When different parameters were assessed among different species of malarial parasite infection by using one-way ANOVA, differences in hemoglobin and red cell count were significant with p value of 0.033 and 0.006 respectively. (Table 1) No difference of TLC as well as platelet count was found between parasite types.

### Table 2: Parasite type and anemia grade.

| Parasite type | Anemia grade | Total |
|---------------|--------------|-------|
|               | Mild anemia  | Moderate anemia | Severe anemia | No anemia |   |
| Vivax         | N 34         | 22     | 4      | 24        | 84   |
|               | % 85.0       | 88.0   | 80.0   | 80.0      | 84.0 |
| Falciparum    | N 5          | 3      | 10.0   | 12.0      |      |
|               | % 12.5       | 12.0   |        |           |      |
| Malaria       | N 0          | 0      | 0      | 3.3       | 1.0  |
|               | % 0          | 0      | 0      | 3.3       |      |
| Mix           | N 1          | 0      | 0      | 2         | 3    |
|               | % 2.5        | 0      | 0      | 6.7       | 3.0  |
| Total         | N 40         | 25     | 5      | 100       |      |
|               | % 100.0      | 100.0  | 100.0  | 100.0     | 100.0|

Pearson Chi-Square value 5.105, P value 0.825

### Table 3: Absolute counts of different white blood cells.

| Parameter | Mean (x10⁹/ul) | SD | Minimum | Maximum |
|-----------|----------------|----|---------|---------|
| AbsNeut   | 5.0            | 7.33| 0.5     | 56.0    |
| AbsLym    | 1.4            | 1.03| 0.04    | 4.87    |
| AbsMono   | 0.2            | 0.18| 0.04    | 1.02    |
| AbsEosin  | 0.1            | 0.16| 0.01    | 1.00    |

The severity of anemia when compared among various parasite types showed that among patients with mild anemia 34 (85 %) had P. vivax infection, 1 (20 %) had P. falciparum and only 1 (2.5 %) had mix infection. Among patients with severe anemia, 4 (80 %) had P. vivax infection, and only 1(20%) had P. falciparum infection. (Table 2). The absolute white cell counts are given in (Table 3). When the differential white cell counts were analyzed it was found that 20% of malaria patients had neutropenia, 40% had lymphopenia, 40% had monocytopenia and only 2% has eosinopenia. Moreover, neutrophilia was seen in 15% of cases, lymphocytosis in 8% of cases, monocytopenia in 1% of the cases and eosinophilia was seen in 5% of the cases.

### DISCUSSION

Malaria is one of the most common infections worldwide and is one of the leading causes of febrile illnesses in our part of world. The most frequent manifestation and complication of malaria are changes in hematological parameters. These are changes in red blood cells, platelets and leukocytes and have significant role in malarial pathology.

In our study we found that most common type of malarial parasite was plasmodium P. vivax (84%) followed by P. falciparum (12%) which was in concordance with the report of National malarial control programme. Mehdi Nateghpouret al in iran reported similar results whereas a
study conducted by Ameekumari Patel in India found more cases of Plasmodium falciparum as compared to Plasmodium vivax.\textsuperscript{19,20} However Zeba Shamim et al reported results similar to our study with 146 out of 172 patients having Plasmodium vivax infection as compared to only 8 patients having Plasmodium falciparum infection.\textsuperscript{14}

Among the peripheral blood changes anemia is a common presentation as in our case we found that 70% of study subjects had anemia. Anemia was normocytic normochromic in 83% cases while 16% had microcytic hypochromic anemia. Previous studies also showed same results with Latif et al reporting that 97.3% of their malaria patients were anemic and mostly normocytic normochromic anemia has been reported.\textsuperscript{20} The pathogenesis of anemia in malaria is multifactorial and is not fully understood. The main mechanisms are destruction of parasitized red blood cells as well as non-parasitized, splenic pooling of red blood cells, oxidative stress induced hemolysis, suppression of marrow hemopoisis, dyserythropoiesis and ineffective erythropoiesis.\textsuperscript{2,9,10}

The parasitized and non-parasitized red cells are less deformable and are removed in high shear rates of spleen.\textsuperscript{21} Increased level of tumor necrosis factor alpha (TNF-α), interleukin 4 (IL-4) and interferon gamma (IFN-γ) are proposed to cause bone marrow suppression and ineffective erythropoiesis. Anemia of chronic disorder due to failure of marrow to utilize the iron due to raised level of IL-6 and TNF-α. Another proposed mechanism is imbalance in red cell surface marker such as chemokine receptor-1.\textsuperscript{22} All these mechanisms lead to the development of anemia.\textsuperscript{23} In our study most common hematological abnormality was thrombocytopenia (89%). Previous studies had shown that thrombocytopenia is a characteristic finding of malarial infection and is more common than anemia.\textsuperscript{15} We observed that thrombocytopenia is more frequent finding in P. vivax infection. Saravu et al reported that the prevalence of thrombocytopenia was similar amongst both infection of vivax and falciparum malaria, but patients with severe falciparum malaria had a significantly lower platelet count compared to the non-severe falciparum malarial patients.\textsuperscript{24} Other studies have reported lower platelet counts among patients infected with P. falciparum in comparison to those of P. vivax.\textsuperscript{25}

The pathogenesis of thrombocytopenia is multifactorial. Demonstration of P. vivax within platelets and a direct lytic effect of the parasite on the platelets has been suggested by some.\textsuperscript{26} Another mechanism may be the generation of immune complexes by malaria antigen which might lead to sequestration of the injured platelets by macrophages in the spleen,\textsuperscript{27} Platelet consumption by the process of disseminated intravascular coagulation (DIC) as well as antibody mediated platelet destruction is another mechanism causing thrombocytopenia.\textsuperscript{28} WBC count was within normal limits in majority of cases (63%) in our study and same finding was reported in many previous studies.\textsuperscript{29} Differential leucocyte count showed neutropenia in 20% cases, neutrophilia in 15%, lymphopenia in 40% and lymphocytosis in 8% cases. Differential leucocyte count is also usually reported to be within normal limits, however both neutrophilia and neutropenia has been observed in malaria.\textsuperscript{15,30} In this study 40% cases showed monocytopenia on differential leucocyte count. This is in agreement with a study published by Prasad et al who found neutrophilia and monocytopenia in malaria patients.\textsuperscript{31}

**CONCLUSION**

Present study concludes that significant hematological changes occur in malaria infection constituting mainly anemia and thrombocytopenia. Changes in the white blood cell are less pronounced with the total count being normal mostly but differential count showing lymphocytopenia and monocytopenia in 40% cases. It would be worthwhile to carry out prospective studies on other hematological variables such as coagulation parameters, bone marrow changes and the direct coomb’s test to further improve our understanding of the anemia in malaria.

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