

## Original Research Article

# Changes in bone marrow in malaria-a prospective study of 47 cases

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### ABSTRACT

**Background:** Bone marrow aspiration done in cases of repeated fever, fever of unknown origin, pancytopenia to detect Malaria parasite in bone marrow. The study was undertaken to evaluate the role of bone marrow aspiration in establishing the etiology of Plasmodium vivax in cases of pancytopenia or thrombocytopenia in recurrent fever or fever of unknown origin.

**Methods:** Patients of different age groups presenting with recurrent fever or fever of unknown origin with pancytopenia or thrombocytopenia from Jan 2015 to Oct 2017. Out of the 108 bone marrow aspirations abiding the above criteria 47 showed presence of Plasmodium vivax trophozoites in bone marrow.

**Results:** The age of patients varied from 8 months to 65 years. 47 cases showed presence of Plasmodium vivax trophozoites, mainly with hyperplastic marrow showing normoblastic and megaloblastic hyperplasia, presence of hemophagocytosis in 6 cases and also 2 cases showing increase in plasma cells.

**Conclusions:** Bone marrow aspiration studies are of vital importance in diagnosing malarial infection in endemic areas as being one of the cause of pancytopenia or thrombocytopenia.

**Keywords:** Bone marrow aspiration, Hemophagocytosis, Malaria, Pancytopenia

### INTRODUCTION

*Plasmodium vivax* is the most widely distributed human malaria parasite and responsible for large amounts of disease burden.<sup>1</sup> The presence of *P. vivax* was first noticed in the late 19<sup>th</sup> century and examination of sternal bone marrow aspirates were performed as an accessory to examination of peripheral blood in malaria, including *P. vivax*.<sup>2,3</sup> Since then, little progress has been made in studying *P. vivax* infections in the tissue. One report explored accumulation of dyserythropoetic cells in anemia.<sup>4</sup> In addition, two case studies reported *P. vivax* infections after autologous bone marrow transplantation and a third one documented an accidental *P. vivax* infection due to bone marrow transplantation between a malaria infected donor and a malaria free recipient.<sup>5-7</sup> In Brazil, one patient with persistent thrombocytopenia and an enlarged spleen was diagnosed with chronic *P. vivax*

malaria after the finding of schizonts in the bone marrow aspirate.<sup>8</sup> The hematological changes seen in patients with malaria include anemia, neutropenia, reactive lymphocytosis, monocytosis, eosinopenia, neutrophil leukocytosis and thrombocytopenia. Of these abnormalities, the most important is anemia as this is often associated with considerable morbidity particularly in areas with sustained year-round infection.<sup>9</sup>

### METHODS

During the period from Jan 2015 to October 2017, out of 108 cases of pancytopenia and thrombocytopenia in patients with repeated fever or fever of unknown origin, 47 cases were reported as *Plasmodium vivax* positive in Bone marrow. The red cell indices, including hemoglobin, red blood cell count, total white blood cell count and platelet count were measured by automated cell

counter and manual method. Thick and thin blood films for peripheral blood and bone marrow aspirate slides were made and stained with Giemsa stain. Cases with pancytopenia on peripheral smear or thrombocytopenia or pyrexia of unknown origin or history of repeated fever were subjected for bone marrow aspiration. The bone marrow was aspirated from posterior superior iliac spine or sternum in adults and medial aspect of tibial tuberosity in children. The bone marrow cellularity was reported as hypercellular, hypocellular and normocellular. The erythropoiesis was expressed as normoblastic, micronormoblastic and megaloblastic. The bone marrow slides were reviewed by two competent pathologists. Bone marrow smears were examined for presence or absence of hemophagocytosis and plasma cells.

**RESULTS**

Out of the total 108 bone marrow cases of pancytopenia and thrombocytopenia in repeated fever or fever of unknown origin studied during Jan 2015 to Oct 2017, 47 patients were found to have *Plasmodium vivax* trophozoites in bone marrow. Age distribution is shown in Table 1. The patients belonged to the age group 8 months to 65 years with majority in age group of 11-20-years. There was clustering of cases in young and old (>40years) age groups. Among these patients 22 (46.80%) were males and 25 (53.19%) females. Male:Female ratio was 0.8:1. Among the 47 positive cases, 41 cases presented with pancytopenia on peripheral smear and 06 cases with thrombocytopenia. Results of the morphological changes in bone marrow is shown in Table 2.

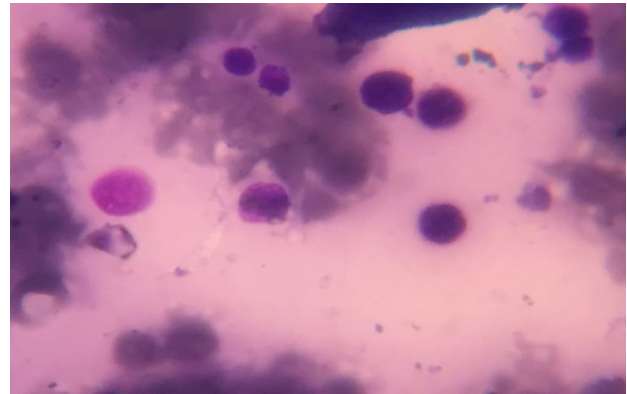
**Table 1: Age distribution of patients (2015 to oct 2017).**

Age group	Male	Female	Total
0-10 years	02	08	10
11-20 years	10	11	21
21-30 years	05	02	07
31-40 years	01	00	01
41-50 years	02	00	02
51-60 years	00	02	02
61-70 years	02	02	04
Total	22	25	47

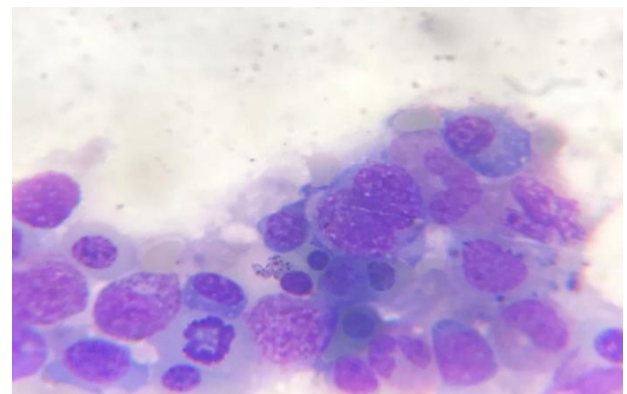
**Table 2: Morphological changes in bone marrow due to malaria (Jan 2015 to oct 2017).**

Diagnosis	No. of cases
Hyperplasia with micronormoblast	01
Hyperplasia with normoblastic and megaloblastic change	42
Bone marrow suppression with megaloblastic change	04
Hemophagocytosis	06
Plasma cells	02

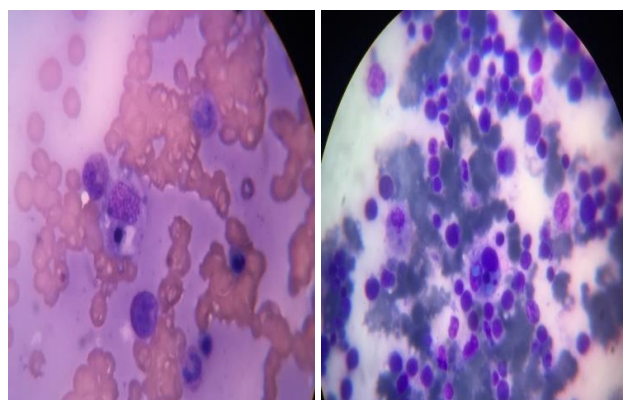
43 cases showed hyperplastic marrow compared to 04 showing hypoplastic marrow. Hypoplastic marrow also showed megaloblastic change. Erythroid hyperplasia showing normoblastic and megaloblastic changes was seen in 42 cases and micronormoblastic hyperplasia in 01 cases (Figure 1, 2). 02 Cases showed increase in plasma cells and 06 showed presence of hemophagocytosis (Figure 3, 4).



**Figure 1: Plasmodium vivax trophozoite in bone marrow, 100 X, Giemsa stain.**



**Figure 2: Schizont of Plasmodium vivax seen in centre 100X, Giemsa stain.**



**Figure 3: Bone marrow showing hemophagocytosis in Plasmodium vivax infection, 40X, Giemsa stain.**

Majority of bone marrow cases are dimorphic with normoblastic and megaloblastic hyperplasia.

## DISCUSSION

The commonly used laboratory method for diagnosis of malaria is microscopic examination of Romanowsky's stained thin and thick peripheral blood film. However, its sensitivity is directly proportional to the microscopic skill, screening time and staining. However, diagnostic bone marrow examination is often performed when a patient with suspected infection has persistent fever. Malaria surveys based on microscopic examination of the blood film do not always detect chronic, low grade infection due to either scanty parasitemia or the patient's immunity. The free malarial parasite phagocytosed plasmodia, free hemozoin pigments and pigmented leukocytes are commonly seen in Bone marrow aspirated as compared to blood film.<sup>10</sup>

In acute falciparum malaria the bone marrow may be hypercellular, normocellular or mildly hypercellular. Immature gametocytes, which are not usually seen in the peripheral blood, may be detected in the bone marrow. In chronic falciparum malaria there is hypercellularity with erythroid hyperplasia. Other features include dyserythropoiesis, giant metamyelocytes and increased eosinophils, lymphocytes, plasma cells and macrophages, sometimes with hemophagocytosis.<sup>11-13</sup>

The bone marrow in *P. vivax* malaria is also characterized by dyserythropoiesis, increased macrophages (some showing hemophagocytosis), increased plasma cells and sometimes increased eosinophils.<sup>11</sup> In hyper-reactive malarial splenomegaly there may be a marked increase in bone marrow lymphocytes.

Routine diagnostic use of bone marrow for the diagnosis of malaria has till date not received complete consensus due to its limitations. But still bone marrow examination is a valuable tool in the investigation of patients with suspected malaria.<sup>14</sup> Macrophages are increased and may be associated with hemophagocytosis.<sup>15</sup> Human studies of *Plasmodium vivax* in the bone marrow are scarce, even though its presence in this tissue was first noticed more than a century ago.<sup>16</sup>

## CONCLUSION

Concluding our study, Majority of bone marrow infected with *Plasmodium vivax* show normoblastic and megaloblastic hyperplasia, 06 cases showing hemophagocytosis and even 2 cases showing increase in plasma cells. Majority of patients clustering is in young and old age group. Sex has no special predilection as the Male:female ratio is almost equal. Henceforth, all cases of pancytopenia with repeated fever or unexplained fever should be subjected for bone marrow aspiration to rule out Malaria infection, thus emphasising the importance of *Plasmodium vivax* infection in bone marrow as one of the

major cause of pancytopenia or thrombocytopenia in endemic areas for malaria.

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