

## Original Research Article

# Haematological profile and its outcome in different species of malaria: a two year study

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## ABSTRACT

**Background:** Malaria is a major health problem in many parts of India and some parts of Andhra Pradesh, which is also one of the endemic areas for malaria. Several factors have been attributed to increased morbidity and mortality in malaria especially with altered hematological and coagulation parameters playing an important role. The aim of present study was to study the hematological and coagulation abnormalities that correspond to severity and the final outcome.

**Methods:** The present study was carried out on 100 patients admitted during the period of November 2016 to October 2018 at Narayana Medical College and hospital, Nellore. All of these patients were confirmed by Peripheral Smear or MPQBC or Antigen Assay followed by detailed clinical history, physical examination and investigated with hematological and coagulation parameters. Then subsequently required routine and special investigation which was followed by monitoring the outcome of the patients with respect to morbidity and mortality.

**Results:** Out of 100 patients 20 patients had severe anemia (Hb% <7 gm%) and most of them patients were falciparum and mixed infection cases. Thrombocytopenia was observed in 63% of the patients and severe thrombocytopenia (<50,000 mm<sup>3</sup>) was seen in 12% of the patients. PT and APTT were increased in 18% and 13% of the cases respectively. BT was increased in 5% of the cases. None of the patients expired in this study.

**Conclusions:** severe anemia is a poor prognostic factor and has adverse outcome. Thrombocytopenia, increased PT, APTT does not have any correlation to mortality.

**Keywords:** Different species, Hematological profile, Malaria, Outcome, Severe anemia, Thrombocytopenia

## INTRODUCTION

Malaria is a protozoan disease transmitted by the bite of infected female Anopheles mosquitoes. The most important of the parasitic diseases of humans, malaria is transmitted in 91 countries containing 3 billion people and causes ~1200 deaths each day. Six species of the genus plasmodium cause nearly all malarial infections in humans. These are *P. falciparum*, *P. vivax*, two morphologically identical sympatric species of *P. ovale* (as suggested by recent evidence), *P. malariae*, and in

Southeast Asia- the Malaria monkey malaria parasite *P. knowlesi*.<sup>1</sup> India harbors both *P. vivax* (50% to 55%) and *P. falciparum* (45% to 50%) and contributes 70% of malarial cases in the South East Asian region hematological changes, which are the most common systemic complications, play a significant role in these serious complications.<sup>2</sup> The hematological abnormalities that have been reported to consistently companion which comprise anemia, thrombocytopenia, atypical lymphocytosis and infrequently disseminated intravascular coagulation.<sup>3</sup> Leucopenia, leucocytosis,

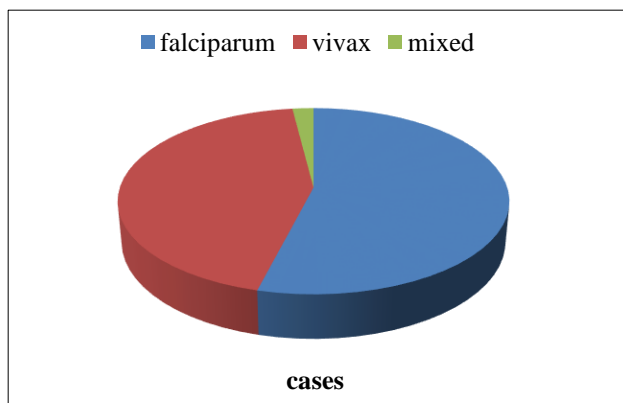
Neutropenia, Neutrophilia, Eosinophilia and monocytosis also have been reported.<sup>4,5</sup> Anemia is a particular problem in children, where profound anemia may lead to sudden death. These complications are particularly likely with haemoglobin concentrations below 5 g/dL (15% haematocrit) and the risk rises steeply below 4 g/dL.<sup>6</sup> Slight coagulation abnormalities are common in falciparum malaria, and mild thrombocytopenia is usual. The aim of present study was to study the hematological and coagulation abnormalities of malaria and its correlation with severity.

**METHODS**

The present study was carried out on 100 patients admitted during the period of November 2016 - October 2018 in Narayana medical college and hospital, Nellore. A detailed history was taken followed by a thorough clinical examination to assess clinical severity and complications. All the patients in this study were proved to be cases of malaria either by Peripheral smear examination (both thick and thin smear) or MPQBC or by Malarial antigen Assay. To study the haematological and coagulation parameters, Complete Blood Picture, Platelet Count, Erythrocyte Sedimentation Rate (ESR), Packed Cell Volume(PCV), Bleeding Time(BT), Clotting Time(CT), Prothrombin Time(PT), Activated Partial Thromboplastin Time(APTT) were carried out in all these patients. Age of less than 18 years, Patients with Chronic Liver Disease, pregnant and Febrile thrombocytopenia of other causes were excluded. Once the patient was diagnosed to have malaria they were started on anti-malarial drugs according to the new WHO guidelines for treatment of Malaria. Other supportive treatment was given according to the patients conditions.

**RESULTS**

Among the 100 cases of malaria, most commonly observed species was falciparum seen in more than half of patients which contributes to about 54% i.e 54 cases and vivax contributes to 44% i.e 44 cases and mixed infection with falciparum and vivax was observed in 2% i.e 2 patients (Figure 1).



**Figure 1: Incidence of different species of malaria.**

Among the 100 patients 76% (76) of patients had haemoglobin less than 11gm/dl, 33% (33) of patients had haemoglobin between 9-11 gm/dl (mild anemia), 23% (23) of patients had Hb between 7-9 gm/dl (moderate anemia) and 20% (20) of patients had haemoglobin less than 7gm/dl (severe anemia). Anemia was frequently observed in patients infected with falciparum Malaria.

Anaemia was present in 76% of patients and among them 40 patients had splenomegaly i.e. 52.6% of the patients with anaemia had splenomegaly. And 60.5% of patients who had splenomegaly were found to have anemia. It has a P value which is significant (p=0.018) (Table 1).

**Table 1: Association of anaemia with splenomegaly.**

Anaemia	Splenomegaly		Total
	Present	Absent	
Present	40	36	76
Absent	6	18	24
Total	46	54	100

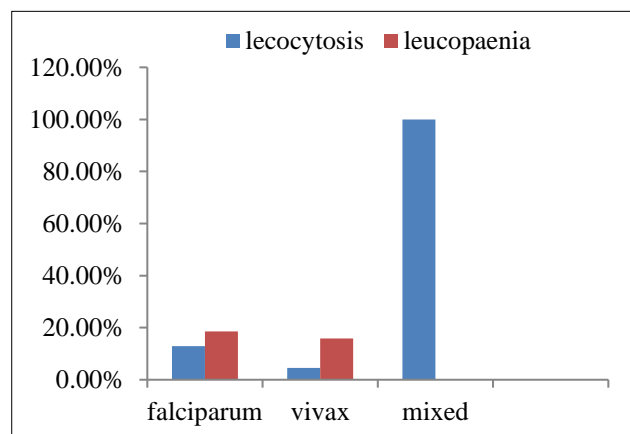
Chi-Square Value = 5.61, p value = 0.018 (Significant)

Of the total 100 cases 63 patients had thrombocytopenia and 52.3% of the patients with thrombocytopenia had splenomegaly. 73.01% of the patients with splenomegaly had thrombocytopenia (Table 2).

**Table 2: The Association of thrombocytopenia with splenomegaly.**

Thrombocytopenia	Splenomegaly		Total
	Present	Absent	
Present	33	30	63
Absent	13	24	37
Total	46	54	100

Chi-Square value = 2.79, p value = 0.0948 (Not Significant)



**Figure 2: Leucocytes abnormalities.**

Leucocytosis (above 11000/cumm) was observed in 11% (11) patients, among falciparum infected 12.9% (7) of patients had leucocytosis and 4.5% (2) of vivax infected patients had leucocytosis and 100% (2) of patients of

mixed species had leucocytosis. Leucopaenia was observed in 17% (17) of total patients among which falciparum were 18.5% (10) patients and in 15.9% (7) of vivax had leucopenia (Figure 2).

Neutrophilia was observed in 23% (23) of total patients. It was observed in 25.9%(14) of falciparum , 18.1%(8) of vivax and 50%(1) of patients mixed infection. Neutropenia was observed in 17% (17) of total patients. It was observed that 20.3% (11) of falciparum, 11.6% (6) with vivax. Lymphocytosis occurred in 36% (36) of total patients of which falciparum were 42.5% (23) and vivax

malaria patients were 25% (11) and in mixed infection 100% (2). Lymphopaenia was observed in 13% (13) of total patients. Among which in 16.6% (9) of falciparum and 9% (4) of vivax infected patients. Eosinophilia was observed in 5% (5) of total patients. Among this vivax were 6.8%(3) and falciparum were 3.6%(2). Monocytosis was observed in 15% (15) of total patients. Species wise monocytosis was found in 18.1% (8) of vivax, 12.9% (7) in falciparum and 50% (1) of mixed infection patients. Neutropenia, Lymphopenia and Eosinophilia were not present in the mixed infections (Table 3).

**Table 3: WBC abnormalities in different species.**

Parameter	Falciparum	Vivax	Mixed	Total
Neutrophilia	25.9% (14)	18.1% (8)	50% (1)	23% (23)
Neutropaenia	20.3% (11)	11.6% (6)	0%	17% (17)
Lymphocytosis	42.5% (23)	25% (11)	100% (2)	36% (36)
Lymphopaenia	16.6% (9)	9% (4)	0%	13% (13)
Eosinophilia	3.6% (2)	6.8% (3)	0%	5% (5)
Monocytosis	12.9% (7)	18.1% (8)	50% (1)	15% (15)

**Table 4: Thrombocytopenia in different species of malaria.**

Thrombocytopenia	Falciparum	Vivax	Mixed	Total
Present	68.5% (37)	54.5% (24)	100% (2)	63% (63)
Absent	31.4% (17)	45.5% (20)	0%	37% (37)
Total	54	44	2	100

Chi-Square Value = 3.23, p value = 0.199 (Not Significant)

**Table 5: Percentage of decreased PCV and increased ESR in different species.**

Parameter	Falciparum	Vivax	Mixed	Total
Packed cell volume (PCV) (Decreased)	88.8% (48)	81.8% (36)	100% (2)	86% (86)
Erythrocyte Sedimentation Rate (ESR) (Increased)	74.0% (40)	40.9% (18)	100% (2)	60% (60)

Thrombocytopenia was observed in 63 patients (63%), in falciparum were 37 (68.5%), vivax were 24 (54.4%) and 100% (2) in mixed infections had thrombocytopenia. Severe thrombocytopenia (platelet <50,000/mm<sup>3</sup>) was observed in 12% (12). Out of them, 9 patients (6.6%) were falciparum and 6.8% (3patients) were vivax (Table 4).

Packed cell volume is decreased in 86% (86) of patients. Most of them were in falciparum 88.8% (48) and 81.8% (36) with and 100% (2) of patients with mixed infection. PCV of less than 20 was observed in 13% (13) of patients, among which 8(14.8%) with falciparum and 3(6.8%) patients of vivax and 2(100%) patients of mixed infection. The average haematocrit was 27.9. Elevated ESR which is an indicator of infection was observed in 60% of the patients. It was seen in 74.0%(40) of falciparum and 40.9%(18) of patients with vivax and 100% (2) of patients with mixed infection .Very high

ESR ( above 60) was observed in 11%(11) of patients, out of this falciparum were 14.8%(8) and 4.5%(2) of vivax and in mixed infections 50%(1) had very high ESR (Table 5).

Prothrombin time was increased in 18% (18) of total cases. Among in this 24.0% (13) were falciparum, 6.8% (3) were vivax and 100% (2) of mixed infection. In all these cases prothrombin time was increased by greater than 2 seconds. The mean PT was 13.99 seconds. In the present study, Mean APTT was 29.0. It was increased in 13% (13) of the total cases. It was found to be increased more in falciparum14.8% (8) and 6.8% (3) of the vivax and 100% (2) of the mixed infection patients. Bleeding time was increased in 5% of the total cases in this study. Bleeding time was increased in 7.4% (4) of falciparum cases and 50% (1) of mixed infection cases and bleeding time of all patients' vivax malaria within normal range (Table 6). No patient of group falciparum, vivax or mixed

infection died in our study. All patients recovered and discharged in good health condition.

**Table 6: Percentage of coagulation abnormalities in different species of malaria.**

Coagulation profile	<i>Falciparum</i>	<i>Vivax</i>	Mixed	Total
Prothrombin time (PT)	24.0% (13)	6.8% (3)	100% (2)	18% (18)
Activated Partial Thromboplastin Time (APTT)	14.8% (8)	6.8% (3)	100% (2)	13% (13)
Bleeding time (BT)	7.4% (4)	Zero	50% (1)	5% (5)

## DISCUSSION

In the present study is the incidence of falciparum malaria is higher with 54%, and the incidence of vivax malaria and mixed infections are 44% and 2% respectively. In the study by Alberto Tobin et al, the prevalence of falciparum is 62.6% and whereas vivax was just 35.2% and mixed infection was 2.1%.<sup>7</sup> In another study by Arevalo et al incidence of vivax and falciparum malaria was almost equal, 50.7% by falciparum and 48.9% by vivax malaria and only 0.4% by mixed species.<sup>8</sup> From these observations we can conclude that the incidence of particular species varies with geographical area.

In present study anemia observed in 76% of total patients and it is present in most of the falciparum cases compared to vivax and mixed infections. Some studies like Surve KM et al which had 79% and Yadav RK et al, study had 80% of anemia incidence in their studies both of which are similar to our present study.<sup>9,10</sup> But in other studies had very low incidence of malaria compared to this study. In Vaidya MS et al, study it was about 27.3%.<sup>11</sup> Arevalo Herrera et al had 19.7% and Rathod SN et al, had 27.3% of anemia incidence in their studies.<sup>12</sup>

The percentage of incidence of severe anemia (7gm/dl) in our present study is 20% most of which is due to falciparum infection malaria compared to vivax malaria. Another study which had some similar rate of incidence of severe anemia is Patel GI et al, study which had 25.4% of patients with severe anemia.<sup>13</sup> In Khuraiya P et al, study 36.4% of patients had severe anemia which is much higher rate compared to this study.<sup>14</sup> In Charulata SL al study rate of severe anemia is very low observed in only 7.64%.<sup>15</sup> Out of the 76% patients who had anemia only 40 patients had splenomegaly this indicates that there are other factors other than splenic sequestration which could lead to anemia.

Leucocytosis was observed in 11% of total patients. Most of the patients with falciparum malaria are observed to have higher rates of leucocytosis which 12.9%. A similar observation was made in Surve KM et al, study group where the incidence of malaria was 10%. Neutrophilia was observed in all the patients who had leucocytosis which shows superadded infection. In this study the mean

leukocyte count was 6,753 cells per cubic millimeter. It indicates that majority of patients with normal leukocyte count, 72% of patients had leukocyte counts within normal range. Another two studies which lower rate of incidence of leucocytosis are Reshma GK et al, and Alberto Tobon et al, which had 5% and 3.5% respectively.<sup>16</sup>

Leucopenia is observed in 17% of the total patients in our study. It was observed in 18.5% of patients with falciparum malaria. In Surve KM et al, and Alberto Tobon et al, had similar rates of leucopenia which is 18%. Surve KM et al, and our present study had similar rates of incidence of leucocytosis and leucopenia.

In this study Neutrophilia was observed in 23% (23) of total patients and It was observed in 25.9% (14) of falciparum malaria affected individuals. Present study had higher rate neutrophilia compared to other studies and in other studies it was significantly lower. In Vaidya MS et al, the percentage of patients with neutrophilia was 13% and in other studies mentioned above Alberto Tobon et al, and Surve KM et al, had similar and very lower rates of incidence of Neutrophilia 5.4% and 5% respectively. Incidence of neutropenia observed in our study is 17%. It was observed that 20.3% (11) of falciparum malaria patients and 11.6% (6) of patients with vivax malaria infection had Neutrogena. No patients of mixed infection group had neutropenia. In other studies Percentage of patients of with neutropenia was low compared to our study. In Surve KM et al. it was 12% and in 7.6% in Vaidya MS et al study and it was very low in AlbertoTobon et al. which is 3.4%.The percentage of patients observed with lymphocytosis in our study is 36% of patients of which falciparum malaria-infected patients are 42.5%(23) and vivax malaria patients are 25% (11) and mixed infection patients are 100% (2). But in other Studies it was very low compared to this study. In Alberto Tobon et al, study it was only 2% and in Vaidya MS et alit was only 3.8% of total. Lymphocytosis observed in this study is very high but in other studies it was very low. The percentage of patients with lymphopenia is 13% and it was observed in 16.6% of Patients with falciparum malaria in other studies it is high compared to our study. It was 53.8% in Alberto Tobin et al, which is very high compared to this study and in Vaidya MS et al, it was 44.6% and in Surve KM et

al, it was only 8% which was low compared to our study. It was observed in our study that lymphocytosis is high and Lymphopenia is low. But in other studies it is lymphocytosis is at lower rate of incidence and lymphopenia at higher rate. Monocytosis was observed in 15% of the patients in our study. It was observed by N.K.D.Hakim et al, in their study that monocytosis in patients those on anti-malarial drugs may be an indicative of an anti-malarial effect by monocytes, thus monocytosis may enhance predisposition to a favourable outcome.<sup>17</sup>

Eosinophilia was observed in 5% of the cases in our study. Eosinophilia also noted in few cases in a study conducted by Surve KM et al, which constitutes only 1% of total cases. In another study Alberto Tobon et al, it was 14.8%.

In present study percentage of patients with thrombocytopaenia is 63% out of which 37% are due to falciparum. Thrombocytopenia was present in 68.5% of the cases with falciparum malaria in our study. In study by Horstmann et al, the incidence of thrombocytopenia was 85%.<sup>18</sup> Kuch et al, observed that 85% of patients with falciparum malaria had thrombocytopenia.<sup>19</sup> In this study 54.5% of the patients with vivax malaria had Thrombocytopenia. It was comparable to the study by Horstmann et al, where the incidence of thrombocytopenia in vivax malaria was 72%. In present study 100% of the patients with the mixed infection had thrombocytopenia. A study conducted Yadav RK et al, also had 87% of Thrombocytopenia in their cases. Other studies Patel GI et al, and Charulatha SL et al, had near similar rate of incidence of thrombocytopenia with our study which is 68.8% and 55.8% respectively. Only 33 patients (52.8%) out of 63 had splenomegaly. So here by one can conclude that thrombocytopenia is not only caused by splenic sequestration other causes like immune mediated platelet destruction also play a role.

In this study there are 12% of patients with severe thrombocytopenia. There was no big difference between the percentage of cases of thrombocytopenia with falciparum and vivax malaria. In Yadav RK et al, study it was about 45%, which had more incidence of falciparum malaria in their cases. In Shailaja VR et al (20) it was 60%. Vaidya MS et al, study group had higher rate of incidence of severe thrombocytopenia which is 65% and this study group contains more of vivax malaria incidence compared to falciparum and mixed group.

Packed cell volume was decreased in about 86% of patients in our study. PCV was decreased in 88.8% of the patients with falciparum malaria. This could be due to the decreased red cell mass in cases of falciparum. Haematocrit of less than 20 was seen in 13% of the patients. The percentage of patients with PCV <20 was 14.8% among falciparum malaria, this indicates the degree of anaemia and its higher rate of destruction associated with falciparum malaria. In study was done by Surve KM et al, percentage of patients with packed cell

volume less than 20 was about 9% which is lesser compared to this study.

Elevated ESR which is an indicator of infection was observed in 60% of the patients. It was seen in 74.0% (40) of falciparum malaria patients This was comparable to the study by Bhakshi et al, who had an incidence of 75% cases with elevated ESR in their study of falciparum cases it signifies exaggerated immune response which occurs with severe disease.<sup>21</sup>

In present study prothrombin time increased in 18% of total patients and it increased in 24% of falciparum cases. In a study conducted by Jayashankar CA et al, PT increased in about 34% of total cases.<sup>22</sup> The increase was noted in 73.3% of the patients with falciparum malaria. In another study conducted by Mohan. Kashinkunti et al, PT increased by 21% which had a comparatively similar rate with present study.<sup>23</sup> In a study conducted which was by S.Roy et al, PT increased in 11.6% of cases.<sup>24</sup> In a study which includes only severe falciparum malaria cases by R. Clemens et al, PT was prolonged in 22.7% of the cases.<sup>25</sup>

Mean aPTT was 29.0. It was increased in 13% (13) of the total cases. It was found to be increased in 14.8% (8%) of patients with falciparum malaria. In a study which is conducted by Mohan. Kashinkunti et al, had similar rates of altered aPTT which is 13%. Another study which was conducted by Jayashankar CA et al also had almost similar rates of altered aPTT which was 12% and it was found in be Increased in 20% of the patients with falciparum malaria. In a study conducted by S. Roy et al, APTT was increased in 16.6% of the patients.

In present study about five patients had an increase in bleeding time and all these cases were falciparum and mixed infection. Bleeding time was increased in 7.4% (4) of falciparum malaria cases and 50% (1) of mixed infection cases and bleeding time of all patients of vivax malaria were within normal range. Three out of these five patients had bleeding manifestations. In a study by Sharma et al, 6.7% of patients had increased bleeding time.<sup>26</sup> In a study by S Roy et al on-falciparum malaria cases 5% of the patients had increased bleeding time. Authors observations were comparable to both these studies.

In present study 57% of the patients had normocytic normochromic blood picture. It was comparable to a study which was conducted by Sen et al, which showed about half the patients had normocytic normochromic blood picture.<sup>27</sup> In present study 25% of the patients had microcytic hypochromic blood picture. This might be due to the prevalence of iron deficiency anemia in our country. Sen et al, in their study also had microcytic hypochromic picture in about 20% of cases. Prevalence of dimorphic anemia was seen in 18% of the cases similar results were also observed by Sen et al, where the prevalence of dimorphic anemia was 20% in their study.



## CONCLUSION

Severe anaemia is a poor prognostic factor and has adverse outcome. Thrombocytopenia, increased PT, APTT does not have any correlation to mortality. Early diagnosis and treatment can decrease the mortality and morbidity.

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