



Research Article

# Thrombocytopenia in Malaria in Children

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## I N F O

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## A B S T R A C T

**Introduction:** Malaria is a cause of high mortality and morbidity. In 2022 during August-September, there was a sudden increment in malaria cases among children in our hospital. We evaluated the role of platelet count to diagnose malarial infection in children.

**Methodology:** This study included paediatric patients seen in August-September of 2022 in BCM Hospital, Khairabad, Sitapur for fever who had thrombocytopenia in their first complete blood count report. This research comprised 230 children with fever and thrombocytopenia.

**Results:** It was found that a moderate to severe platelet count decline was 86.21 per cent sensitive and 56.14 per cent specific for malaria with high negative and positive predictive values.

**Conclusion:** In conclusion, moderate to severe thrombocytopenia is a key indicator of malaria, hence all children with fever and thrombocytopenia should be tested for malaria. If moderate to severe thrombocytopenia is seen, further specialised tests such as repeated peripheral blood smears, ELISA for parasite-specific antigens, etc. should be done.

**Keywords:** Malaria, Thrombocytopenia, Platelet, Blood Smears, ELISA

## Introduction

Malignant malaria is a tropical killer. According to WHO, in 2017, there were 219 million cases of malaria worldwide. Malaria is an infectious haematological disease that affects almost all blood components. Malaria usually causes anaemia and thrombocytopenia.<sup>1</sup> These problems have a significant mortality rate, hence scientific literature has focused on them. In contrast, thrombocytopenia is poorly understood and linked with a low fatality rate.

Any illness, particularly endemic ones like malaria, may change haematological parameters. Haematological changes are the main effects of malaria and contribute to its pathogenesis. Red blood cells, white blood cells, and thrombocytes are affected by these alterations. Malaria patients have increased monocyte and neutrophil counts and reduced counts of platelets, white blood cells,

lymphocytes, eosinophils, red blood cells, and haemoglobin. Malaria is most often related to thrombocytopenia. Platelet counts below 150,000/uL increase malaria risk by 12-15 times.<sup>2</sup> This elevated risk was seen in both children and adults of both genders. Over time, the ratio of monocytes to lymphocytes predicted clinical malaria.<sup>3</sup>

### Life Cycle of *Plasmodium vivax*

The *P. vivax* lifecycle is intricate as shown in Figure 1, involving at least four different cell types inside two separate hosts and more than ten phases of cellular differentiation.

### Mosquito to Human Transmission

- Malaria-infected female *Anopheles* mosquitoes inject sporozoites into humans during blood meals.
- In the liver, mosquito sporozoites become schizonts that split and release merozoites.



- The hypnozoite, a malaria parasite stage, may remain latent in the liver for months.

### Hypnozoites

Hypnozoites in the liver may reawaken weeks or months after infection without being recognised by current diagnostic methods, causing repeated clinical exacerbations and transmission.

The number of hypnozoite carriers in regions where *P. vivax* malaria is endemic is unclear. As a result, hypnozoites are a quiet transmission reservoir.

### Asexual Blood Stage Infection

Merozoites infect reticulocytes, which become schizonts and rupture after entering the circulation. The asexual erythrocytic stage (or blood stage) causes malaria 48 hours after infection. During the blood stage, both infected and healthy red cells are removed, which might result in a condition known as anaemia, which can be potentially fatal.

### Sexual Stage Infection

Infectious gametocytes are developed from merozoites during the sexual cycle. Malaria caused by *P. vivax* can be transmitted before the host experiences symptoms or seeks treatment because gametocytes can be created before the host becomes ill.

Malaria is one of the biggest causes of mortality and sickness in developing countries.<sup>4</sup> Malaria amongst children increased in the months of August and September 2022 in our hospital. It may be diagnosed in feverish children

by using their first platelet count values. Peripheral blood smears are the best diagnostic test for malaria, but they take time and need a technician. This research examined how platelet count, a routine test, may diagnose malaria in children. Thrombocytopenia is associated with malaria, with prevalence ranging from 40.5-85%,<sup>5,6</sup> with some studies suggesting a lower incidence in vivax malaria than falciparum malaria.<sup>7</sup> Splenic sequestration, immune-mediated apoptosis, and reduced platelet survival may cause thrombocytopenia.<sup>8</sup>

There is not a single report of a patient who died due to malaria-associated thrombocytopenia alone in the literature.

### Literature Review

In endemic locations, the conventional diagnostic test (the thick blood smear) has excellent specificity, but only when executed by professional laboratory technicians. This has posed a major challenge to malaria detection as the number of people trying to travel to tropical places has increased dramatically. This has added a great challenge to the field of travel medicine, which is currently facing a great deal of competition. According to the research done by D'Acromont et al. in 2002,<sup>9</sup> thrombocytopenia with acute fever in patients who have recently returned from tropical locations is a very sensitive clinical indicator of malaria. In another study, the diagnosis of malaria in acutely ill febrile patients was found to have a sensitivity of 60% and a specificity of 88% when thrombocytopenia was present.<sup>10</sup>

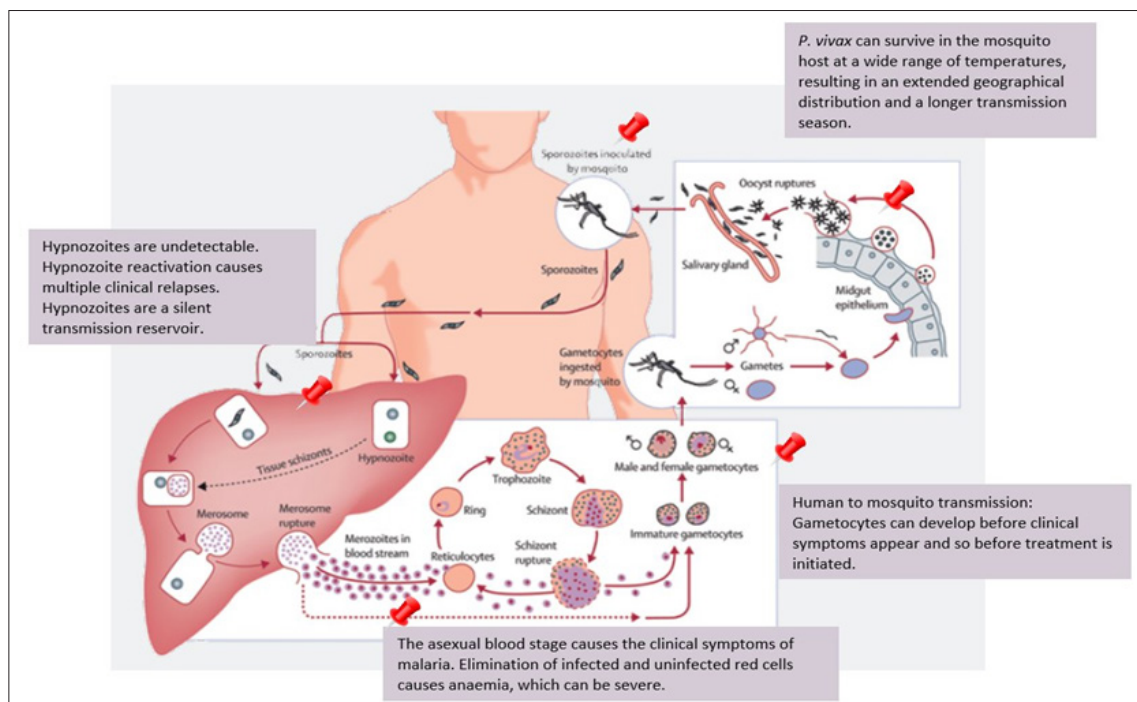


Figure 1. Life Cycle of *Plasmodium Vivax*

According to the study conducted by Patel et al.,<sup>11</sup> malaria was diagnosed in a patient with combined thrombocytopenia and acute febrile syndrome with a sensitivity of 100%, specificity of 70%, positive predictive value of 86%, and negative predictive value of 100%.

*Plasmodium vivax* malaria is associated with a number of complications, one of the most common of which is thrombocytopenia. In one study, the platelet count returned to normal following therapy, and among the patients, only one patient had purpuric lesions on the lower limbs at the same time as they had the lowest platelet count.<sup>12</sup>

Malaria-related thrombocytopenia has been linked to both *Plasmodium vivax* as well as *Plasmodium falciparum* infections since the beginning of the 1970s when data began to suggest that the two types of malaria are relatively comparable in this regard.<sup>5</sup> On the other hand, more recent research carried out in India has demonstrated that patients suffering from *P. vivax* infection are more likely to experience severe cases of thrombocytopenia.<sup>13</sup>

Platelet counts in children and adults from Malawi with acute *P. falciparum* malaria were studied in two separate trials before and after therapy.<sup>14</sup> The author provided evidence that thrombocytopenia is a common symptom of severe *P. falciparum* malaria across a range of ages and genders in regions where the disease is prevalent. It occurs during acute falciparum malaria in Malawians of different ages but fades during convalescence a month after treatment.

Jiero & Pasaribu<sup>15</sup> examined the haematological changes associated with malaria infection in kids who had developed symptoms of malaria. Anaemia, low platelet count, low white blood cell count, and high lymphocyte count are shown to be the most significant indicators of malaria infection in the research area. The author came to the conclusion that several haematological indices showed abnormalities in malaria-infected children. Children who live in high-endemic regions may show signs of malaria based on these indicators.

Patients with malaria with volatile malaria epidemiology were analysed for their levels of thrombocytopenia and its associations with different species of malaria in a study conducted by Bansal et al.<sup>16</sup> Between August 2017 and October 2018, all patients with microbiologically confirmed malaria and a reported platelet count were included in a retrospective analysis. Rapid diagnostic tests and analysis of blood films helped establish the microbiological diagnosis.

The severity of thrombocytopenia was determined by measuring platelet count. For the sake of reducing the spread of transfusion-transmitted illnesses, the author concluded that those who have been diagnosed with malaria and are febrile thrombocytopenic should forego receiving unnecessary transfusions.

## Aims and Objectives

The primary objective of this research was to determine whether or not platelet count was useful in the diagnosis of malaria in children.

## Objectives

- To evaluate the role of platelet count as a marker in diagnosing malaria in children.
- To conduct more specific tests like multiple peripheral blood smears and ELISA for parasite-specific antigen.

## Material and Method

This retrospective research was conducted in BCM Hospital's Paediatric Department in Khairabad, Sitapur, Uttar Pradesh, India. Microsoft excel was used for analysis. The study plan was approved by hospital research committee and a written consent by first-degree relative was mandatory. This research comprised children in the age group of 1-18 years. 230 children with fever and thrombocytopenia in their first complete blood count report were studied in the time period of August-September 2022. The analysis was done through excel. Peripheral blood smears for the malaria parasite divided patients into malaria and non-malaria groups. To detect nonsexual forms of malarial parasite on the peripheral blood smear, geimsa stain was used for thick smears and wright stain was used for thin smears. A patient was considered to be in the non-malaria group if three consecutive blood smears were negative. The diagnosis of thrombocytopenia was made if the platelet count was less than 150,000 cells/cmm. Based on platelet counts, patients were divided into three groups. Severe thrombocytopenia was defined as < 50,000 cells/cmm, moderate as 50,000-99,999 cells/cmm, and mild as 100,000-150,000 cells/cmm. The group that did not experience malaria was used as a comparison.

## Results

230 patients were studied (164 males, and 66 females). Malaria was found in 116 people - 87 males and 29 females with a mean age of 9.3 years (range: 1 month-17 years). 114 patients - 77 males and 37 females averaged. 10.1 years in the control group (range: 3 months - 17 years).

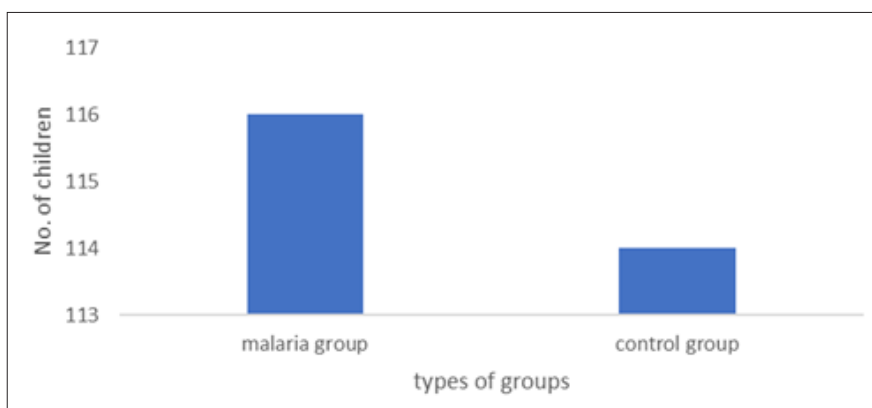


Figure 2.Groups of Children based on the Occurrence of Malaria

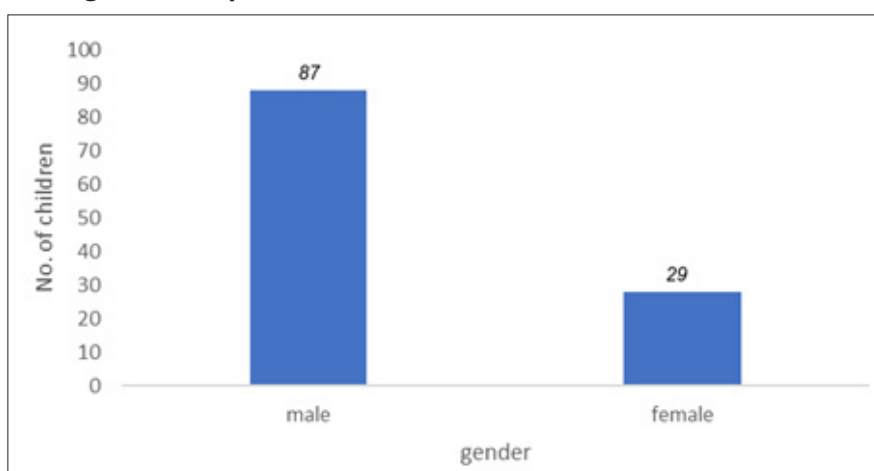


Figure 3.Gender Distribution in Malaria Group

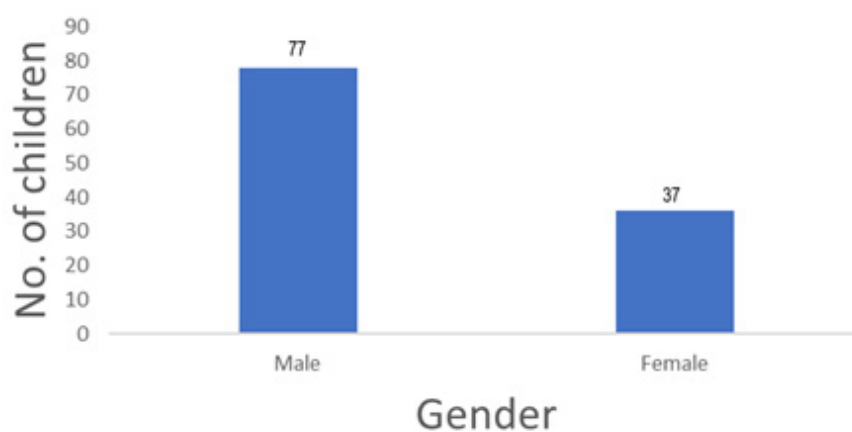


Figure 4.Gender Distribution in Control Group

Figure 2 shows the distribution of children on the basis of occurrence of malaria.

Figures 3 and 4 show the gender distribution in malaria and control groups respectively.

### Presence of Thrombocytopenia

Out of 230 children, 80 (59 males, 21 females) had mild thrombocytopenia, 56 (37 males, 19 females) had moderate thrombocytopenia, and 94 (68 males, 26 females) had

severe thrombocytopenia as shown in the Figure 5.

### Severity of Thrombocytopenia in Malaria and Control Group

Out of all malaria patients, 67 had severe thrombocytopenia, 33 had moderate thrombocytopenia, and 16 had mild thrombocytopenia. In the non-malaria group, 27, 23, and 64 had severe, moderate, and mild thrombocytopenia respectively as shown in Figures 6 and 7.

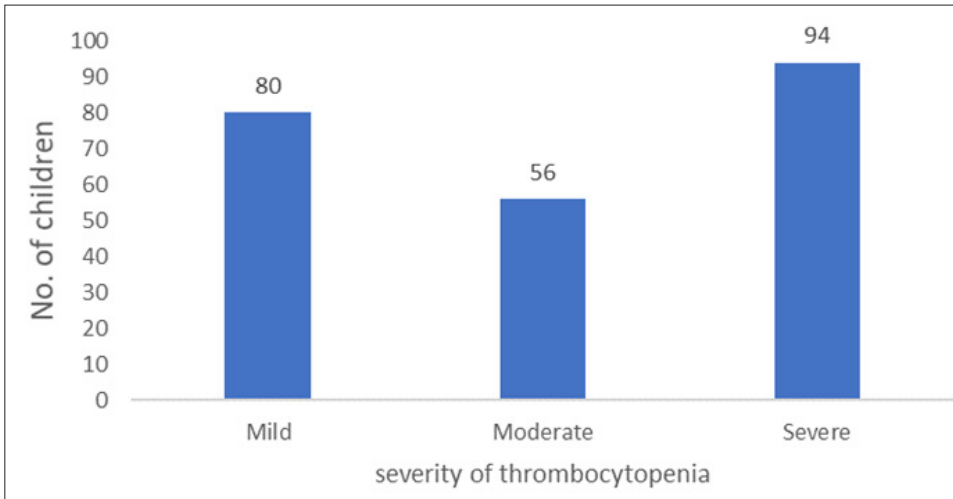


Figure 5. Presence of Thrombocytopenia in Children

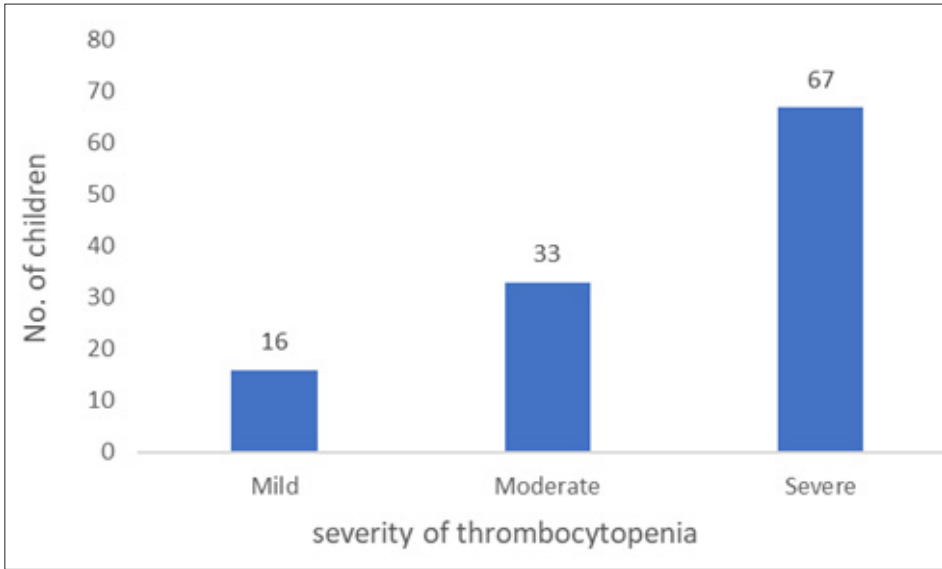


Figure 6. Severity of Thrombocytopenia in Malaria Group Children

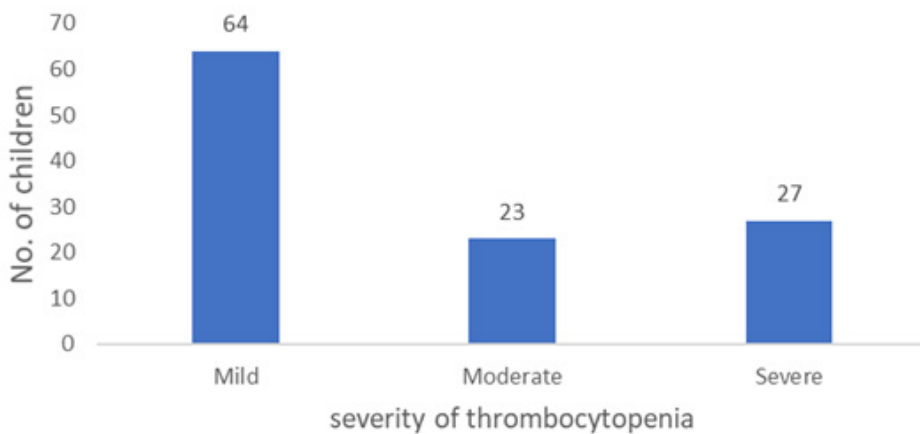


Figure 7. Severity of Thrombocytopenia in Control Group Children

The difference in moderate to severe thrombocytopenia between the two groups was statistically significant ( $p < 0.00001$ ).

The presence of moderate to severe thrombocytopenia in malaria was analysed as shown in Table 1.

**Table I. Presence and Absence of Moderate to Severe Thrombocytopenia in Malaria**

Moderate to Severe Thrombocytopenia	MALARIA		Total
	Present	Absent	
Present	100	50	150
Absent	16	64	80
	116	114	230

In our hospital, moderate to severe thrombocytopenia diagnosed malaria in children with 86.21% sensitivity, 56.14% specificity, 66.67% positive predictive value, and 80% negative predictive value.

### Discussion

This study looked at thrombocytopenia in children who had malaria. We investigated if platelet count might detect malaria in children. Multiple peripheral blood smears diagnosed malaria in youngsters. We conducted a retrospective meta-analysis of 230 children with fever and thrombocytopenia in August and September 2022. Moderate to severe thrombocytopenia diagnosed malaria in children with 86.21% sensitivity, 56.14% specificity, 66.67% positive predictive value, and 80% negative predictive value. It was discovered that children with fever and moderate to severe thrombocytopenia in their initial complete blood count report had a high possibility of having malaria infection. Thus, we can use moderate to severe thrombocytopenia as a screening tool to diagnose malaria in a child with fever in peripheral centres where the skill and manpower for making a definitive diagnosis of malaria are not available. In this way, early treatment can be provided to the patient without much delay. However, whenever in doubt, we need to go for definitive diagnostic tests. Moderate to severe thrombocytopenia can be useful to prioritise feverish children for peripheral blood smears. Thus, in increased incidence situations, moderate to severe thrombocytopenia can reduce the burden of technicians and laboratories of doing multiple peripheral blood smears.

### Limitation

The limitation of our study is less specificity. Thus, a child with fever but no moderate to severe thrombocytopenia does not exclude the diagnosis of malaria.

### Conclusion

The definitive test for malaria is a peripheral blood smear, which involves the detection of malarial parasites.<sup>11</sup> It takes time and expertise, especially in cases of low parasitic infection. This research indicates that a platelet count of less than 100000 cells/cmm, which is considered moderate to severe thrombocytopenia, is a very sensitive test for malaria in children, with a strong negative predictive value.

Therefore, we contend that any kid with fever and moderate to severe thrombocytopenia in their first complete blood count report may need a malaria diagnosis, and the platelet count may be a key indicator. Moderate to severe thrombocytopenia suggests malaria, hence many peripheral blood smears or the most sensitive parasite-specific antigen test, such as ELISA, should be done. Other causes of fever may be considered if the platelet count is normal.

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**Conflict of Interest:** None

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