

ORIGINAL ARTICLE**CO-EXISTENCE OF MALARIA WITH THROMBOCYTOPENIA**

¹Shahzad Ali Jiskani, ²Dolat Singh, ³Sikandar Ali Bhand, ¹Qandeel Abbas Soomro, ¹Ghulam Abbas Soomro, ²Khadim Hussain

¹*Department of Pathology, Indus Medical College Tando Muhammad Khan*

²*Department of Medicine, Indus Medical College Hospital Tando Muhammad Khan*

³*Department of Paediatrics, Indus Medical College Hospital Tando Muhammad Khan*

Corresponding Author:**Shahzad Ali Jiskani,**

MBBS, M. Phil (Haematology)

Senior Lecturer, Department of Pathology

Indus Medical College, Tando Muhammad Khan

Corresponding Author Email:

shahzadbaloach289@gmail.com

Co-Author:**Dolat Singh,**

MBBS, MD (General Medicine)

Assist. Professor, Department of Medicine

Indus Medical College, Tando Muhammad Khan

Sikandar Ali Bhand, MBBS, FCPS (Paediatrics)

Assoc. Professor, Department of Paediatrics

Indus Medical College, Tando Muhammad Khan

Qandeel Abbas Soomro,

MBBS, M.Sc.(Medical Molecular Microbiology)

Senior Lecturer, Department of Pathology

Indus Medical College Hospital

Ghulam Abbas Soomro,

MBBS, M. Phil (Microbiology)

Senior Lecturer, Department of Pathology

Indus Medical College, Tando Muhammad Khan

Khadim Hussain, MBBS, FCPS (Medicine)

Senior Registrar, Department of Medicine

Indus Medical College, Tando Muhammad Khan

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ABSTRACT

BACKGROUND: Malaria, especially in developing countries, is an important health problem. It is significant cause of mortality and morbidity, particularly in tropics. In this specific disorder, there are many haematological changes, including thrombocytopenia, anaemia, atypical lymphocytosis as well as rare intravascular coagulation.

OBJECTIVE: Purpose of this study is to identify and evaluate the extent of different haematological variations, particularly additional findings of thrombocytopenia in a specific form of malaria.

METHODS AND MATERIALS: This was an observational study carried out at Department of Pathology, Indus Medical College Hospital Tando Muhammad Khan, on patients attending the clinically suspected malaria outpatient and inpatient departments. Thin and thick peripheral smear slides for malarial parasites were developed and were stained with Leishman's stain, followed by antigen tests were also incorporated where possible. Total blood counts were used in other studies.

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RESULTS: 238 (28%) patients showed malaria parasites on peripheral blood film among the 850 patients with suspected malaria included. Male superiority of 2.01:1 was observed as compared to females. A total of 196 out of 238 patients had thrombocytopenia. Higher levels of thrombocytopenia were observed in *P. Vivax* (62.26%) is accompanied with Mixed-type Infection (21.42%) and *Plasmodium falciparum* (15.81%).

CONCLUSION:

The anaemia specifically with decreased count of platelets (thrombocytopenia) was observed specifically in *Plasmodium vivax*, accompanied with *Plasmodium falciparum*. Given that thrombocytopenia is linked with patients of malaria, as shown in current research, in patients having low platelet count and fever, the care of doctors should preserve malaria as one of the differential diagnoses.

KEYWORDS: Malaria, Thrombocytopenia, *Plasmodium falciparum*, *Plasmodium vivax*.

INTRODUCTION

In particular, in Asian and African developing countries, malaria is important health concern. It is significant reason of mortality and morbidity, particularly in the tropical regions. Despite advances in technical expertise, this appears as major issue among majority of inhabited countries, placing financial strain on countries troubled. ⁽¹⁾ Approximately, more than 40 percent of population of the world is estimated to live in areas in which malaria is endemic and 300-500 million patient cases and 1.5-2.7 million fatalities are expected to happen yearly. ⁽²⁾ In extreme malarial types, the fatality ratio is augmented by 20% (parasitaemia > 5%) ⁽³⁾. As the haematological system is key target for malaria, a range of malaria-related complications are seen, and such problems play an important role in causing severe complications. They play an important role in contributing to severe

complications. Anaemia, atypical lymphocytes, thrombocytopenia and, to a slighter extent, disseminated intravascular coagulation (DIC) are all anomalies. ⁽⁴⁾ Leucopaenia, leukocytosis, eosinophilia and monocytosis are other observed findings. In patients suffering from malaria, thrombocytopenia comprises 70%, extreme anaemia 25%, cell count in the blood may be high, low or normal i.e. elevated count of the blood cells constitutes <5%, which is taken as a weak factors in prognosis. ⁽⁵⁾ Thrombocytopenia is most frequent among the reported haematological complications and is observed in *Plasmodium falciparum* as well as *vivax*. Whilst thrombocytopenia is found in peripheral film, that in patients with fever lacks the usual amount, it is an indicator that patient is infected from malaria. ⁽⁴⁾ As the accurate mechanism of thrombocytopenia is not completely known, it is believed that immune-mediated breakdown of the cells, spleen sequestration, and dyserythropoietic processes in bone marrow with reduced development of platelets take part in the mechanism. ⁽⁵⁾ Purpose of the research was to identify and evaluate the extent of different haematological variations, particularly in case of thrombocytopenia in a specific form of malaria.

PATIENTS AND METHODS

It was a cross-sectional observational research was carried out from December 2018 to June 2019 at Department of Pathology, Indus Medical College Hospital Tando Muhammad Khan. Research included clinically suspected malaria cases in patients presenting with fever. Patients with bleeding problems, drugs, thrombocytopenia, chronic liver disease attributes were excluded. Using the automated Mindray BC5000 Haematology Analyzer unit, blood parameters were computed. Two slides were used to make thick and thin blood films, stained with Leishman's dye, and the malarial parasites were recognized and confirmed for

diagnosis of malaria. Peripheral smear slides that were malaria positive were reviewed for further validation from pathologists, defining the particular type of organisms. Among slides studied, including ring form, schizonts form and trophozoites form, all stages of haemoparasite were recognized. In *Plasmodium vivax* species and gametocyte form in *Plasmodium falciparum* species, ring forms and trophozoites were primarily observed. Final re-evaluation has been carried out for platelet counts. SPSS 21.0 was used for statistical analysis.

RESULTS

196 (23.05%) patients showed malaria parasites on peripheral blood film among the 850 patients with suspected malaria included. The overall males included were 131 (66.83%), while females were 65 (33.16%). The predominance of male was observed (ratio of 2.01:1). Groups for age were classified in 7 groups and average

age was 18.2 years, ranging from 1-70 years. The highest number of cases reported was between 21 and 30 years of age and less than 10 years in the least common age group (Table 1).

Of total of 196 individuals, 122 (62.26%) had *Plasmodium vivax* infection and 42 patients (21.42%) had a mixed-type infection with *Plasmodium vivax* and *Plasmodium falciparum* (Table 2). Of the total, 196 were having thrombocytopenia (82.35%). In both types of malarial species, thrombocytopenia has been identified (Table 3). Individuals with *Plasmodium vivax* infection and mixed-type infection had a substantial reduction in grade III platelet counts, consisting of 65.55% of *P. vivax* cases and 31.11% of mixed infection cases 238 cases showed smear-related malaria infection and 196 patients had thrombocytopenia. Sensitivity and precision were 89.9% and 87.5%, respectively.

Table 1: Allocation of Patients by Age Groups (n=196)

| Age Group (in Years) | No. of Patients | Percentage (%) |
|----------------------|-----------------|----------------|
| <10 | 6 | 3.06 |
| 11-20 | 26 | 13.26 |
| 21-30 | 74 | 37.75 |
| 31-40 | 59 | 30.10 |
| 41-50 | 21 | 10.71 |
| 51-60 | 4 | 2.04 |
| >60 | 5 | 2.55 |

Table 2: Distribution of Malaria Species (n=196)

| Species of Malaria | Frequency (No.) | Percentage (%) |
|-------------------------------------|-----------------|----------------|
| <i>Plasmodium Vivax</i> specie | 122 | 62.26 |
| <i>Plasmodium Falciparum</i> specie | 31 | 15.81 |
| Mixed <i>Plasmodium</i> Infection | 42 | 21.42 |

Table 3: Grading of Thrombocytopenia According to Plasmodium Species (n=196)

| Platelets (in cumm) | Grading of Thrombocytopenia | Plasmodium Vivax specie | Plasmodium Falciparum specie | Mixed Plasmodium Infection |
|------------------------|--------------------------------|----------------------------|------------------------------------|----------------------------------|
| 75,000 – 150,000 | Grade I | 12 | 2 | 3 |
| 50,000 – 75,000 | Grade II | 31 | 4 | 8 |
| 5,000 – 50,000 | Grade III | 57 | 3 | 28 |
| <25,000 | Grade IV | 21 | 22 | 5 |

DISCUSSION

In most parts of the world, malaria seems to be a big health burden, primarily by *Plasmodium vivax* and *falciparum* that is endemic among several countries in Africa, Asia, and Nepal. Characteristic leading to diagnosis may be malaria that causes many haematological anomalies, such as thrombocytopenia and anaemia. ⁽⁶⁾ In comparison to the previous studies that recorded a average age of 38 years, out-of-patient numbers in current study were among ages of 21-30 years of age. Age and gender information is limited, but few researches have revealed an increased involvement of male gender in comparison to the female gender, and the current research has revealed similar results. ^(1, 7) Dhungat et al revealed a male-female fraction of 68% and 32% respectively that is about in near alignment with current research (Males-66.33% and Females-33.16%). One of main variables for superior hazard in males is outdoor activity and less mosquito bite protection. ⁽⁸⁾

P. vivax has been confirmed to be the primary malaria parasite for the disease process in the subcontinents. ⁽⁹⁾ Various studies have reported *Plasmodium vivax* to be prevailing specie, though the percentage of positive cases varies (56.5%; 69% and 51.6%). In the current analysis, similar results were obtained. In the north-

eastern areas of Asia, though, an increased prevalence of *Plasmodium falciparum* has been identified. ⁽⁸⁻¹³⁾

Decrease in platelet count (thrombocytopenia) is a typical characteristic of acute malaria, as found in our research. It can occur irrespective of severity in *Plasmodium vivax* as well as *Plasmodium falciparum*. ⁽⁴⁾ Conflicting amount of decrease in platelet count in circulating is consistently observed in various malaria species. A drop in the usual amount of platelets relies on peripheral film followed by fever that in the case of malarial infection is a diagnostic clue. ⁽¹⁴⁾ It is used in patients suffering from fever of unknown origin as an indication of malaria. ⁽¹⁵⁾ Patients with malaria who acquire thrombocytopenia rarely bleed, regardless of the degree of reduction in count of platelet ⁽¹⁶⁾, however, on the divergent; no bleeding deaths were observed in the current study.

Several observational studies have been carried out and have also established the correlation of thrombocytopenia with malaria; however the accurate reason of thrombocytopenia is still hard to identify. Reason and correlation of thrombocytopenia with disturbances in coagulation profile, splenomegaly, oxidative stress, alteration in the bone marrow, and antibody-mediated destruction of platelet have been identified

as several causes.⁽¹⁷⁻¹⁸⁾ As also observed in our research, increased tolerance to decreased count of platelets is seen in malaria. No bleeding trends and losses were found in the patients, despite the much decreased count in platelets (up to 20,000/cumm). In many trials, thrombocytopenia has not been linked with any fatality or complications by bleeding, including the present one.⁽¹⁹⁾ The tolerance of low platelet counts in malaria has been clarified by increased platelet activation and aggregation.⁽⁷⁾ Increased haemostatic reactions due to hyperactive platelets, despite a substantial reduction in the count of platelets, have been clarified as explanation for uncommon bleeding manifestations in acute malaria.⁽¹⁹⁾ Several studies were performed on thrombocytopenia scoring that was actually dependant on the amount of reduced count of platelets comparable to current research.⁽²⁰⁻²²⁾ Khan et al performed research in which highest frequency of individuals in grade I was 21%, whilst the major category in the current research was among group III, consisting of 37.75%.⁽²⁰⁾

CONCLUSION

Anaemia specifically with decreased platelet count (thrombocytopenia) was observed specifically in *Plasmodium vivax*, followed by *Plasmodium falciparum* infection. As thrombocytopenia is correlated with malaria, as shown in current research, among patients with reduced platelets and fever, the care of doctors should preserve malarial infection among differential diagnosis.

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