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Frequency ofthrombocytopenia in various species of malaria in patients presenting to Lady Reading Hospital, Peshawar

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Abstract:
Background:
A number of observational studies have confirmed the association of thrombocytopenia to malaria. Both non-immunological as well as immunological destruction of platelets have been implicated in causing thrombocytopenia.
Objective:
To determine the frequency of thrombocytopenia in various species of malaria in patients presenting to Lady Reading Hospital, Peshawar.
Material and Methods:
This Cross Sectional Study was conducted in the Department of Medicine, Lady Reading Hospital, Peshawarfrom 1st March 2021 to 30th August 2021.A total of 194 patients of both gender with malaria (Plasmodium falciparum and Plasmodium vivax species)were included in the study. Two milliliters of EDTA (ethylene diamine tetra-acetic acid) anticoagulated blood was collected and immediately sent to hospital laboratory. Data regarding thrombocytopenia was noted.
Results:
Age range in this study was from 18 to 60 years with mean age of 36.716±8.21 years, mean duration of malaria 6.329±1.46 days and mean weight was 80.427±7.14 Kg. Plasmodium falciparum was observed in 54.6% patients, Plasmodium vivax 39.7% and mixed was 5.7%. Thrombocytopenia was seen in 67% patients. Thrombocytopenia was seen in 61.3% patients with Plasmodium falciparum, with Plasmodium vivax it was 71.4% and in mixed it was 90.9%.
Conclusion:
Higher frequency of thrombocytopenia was observed in-patients suffering from malaria and more significant thrombocytopenia were seen in P. vivax malaria.
Keywords: *Malaria, Thrombocytopenia, P. vivax*

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I. Introduction

The five protozoa that cause malaria—Plasmodium falciparum, P. vivax, P. malariae, P. ovale, and most recently P. knowlesi—are spread by mosquitoes. [1] More than 90% of malaria-related deaths worldwide are attributed to P. falciparum infection, which means that the disease still poses a serious threat to public health on a global scale. [2] According to the World Health Organization's (WHO) 2019 World Malaria Report, there were 228 million cases of malaria worldwide in 2018, which resulted in 405 000 deaths, many of them children under the age of 5. More than 90 nations have an ongoing malaria epidemic that affects 40% of the global population.[2]In non-malarial nations like North America and Europe, there are a considerable number of instances of imported malaria and local transmission following importation. 3 Travelers to endemic areas are more likely to contract malaria, and the rising incidence of imported malaria necessitates knowledge of the sometimes vague symptoms, challenges in malarial diagnosis, and available treatments.[2]

Before the blood stage begins, sporozoites travel through the peripheral bloodstream and are taken up by hepatocytes, where they go through an asexual pre-erythrocytic liver stage as liver schizonts that can last up to two weeks. [3] They produce motile merozoites as they multiply within hepatocytes, which are then discharged into the bloodstream where they invade red blood cells (RBC). [4]Merozoites replicate asexually in serial cycles,

going through the ring, trophozoite, and schizont stages before producing and releasing new, invasive daughter merozoites that subsequently infect fresh RBC and increase the parasite population.[5]

The link between thrombocytopenia and malaria has been confirmed by a number of observational studies. [6] Thrombocytopenia has been linked to both non-immunological and immunological degradation of platelets. [7] Sequestration in the spleen, antibody-mediated platelet destruction, oxidative stress, and the role of platelets as cofactors in causing severe malaria are some of the hypothesised causes. Malaria has been linked to abnormalities in platelet shape and function, and in certain rare cases, the parasites themselves have been seen to infiltrate platelets.[7]

The prevalence of thrombocytopenia was found to be 77.7% in Plasmodium falciparum species, 76.9% in Plasmodium vivax species, and 90% in mixed Plasmodium falciparum and Plasmodium vivax species, according to a study by Gupta NK, et al. [8] Another study by Nadeem A, et al. revealed that 55.9% of Plasmodium vivax species exhibited thrombocytopenia.[9]

This study will attempt to highlight the frequency of thrombocytopenia in various species of malaria. There is not much literature to emphasize on this subject in our general population. Malaria is mostly caused in KPK by two types of species (Plasmodium vivaxand Plasmodium falciparum), and P. vivaxinfection is higher as compare to the P. falciparum infection.10 Therefore it's a dire need to get local evidence which will be helpful for practitioners.

II. Material and Methods:

ThisCross Sectional Study was conducted Department of Medicine, Lady Reading Hospital,Peshawarfrom 1st March 2021 to 30th August 2021.Sample size of 194 was calculated using WHO sample size software with 95% confidence interval, 7% margin of error and prevalence of thrombocytopenia by 55.9% in mixed Plasmodium falciparum/ Plasmodium vivax species.[9]Non-probability consecutive sampling was used.

All patients of both genders with age ranging from 18 to 60 year diagnosed with Malaria (It was defined as when patient presented with fever (>100°F, chills, sweats) and blood smear stained with Leishman's, showing inside red blood cell one or more red chromatin dots with blue cytoplasm by laboratory test.(Plasmodium falciparum and Plasmodium vivax) species) for duration > 3 days were included in the study while patients with history of leukemia, dengue fever and enteric fever were excluded from the study, dengue fever and enteric fever were excluded from the study

194 patients from the medical department at Lady Reading Hospital in Peshawar who met the inclusion criteria were included in the study after receiving approval from the hospital's ethics council. The patient received a thorough explanation of the benefits of participating in the trial, and their informed consent was acquired. Basic demographic information like age, gender, malaria duration, species type, and weight (as measured by a weighing machine) was recorded. Blood with the anticoagulant EDTA (ethylene diaminetetraacetic acid) was drawn and transmitted right away to the hospital laboratory. The researcher took note of the operational definition of thrombocytopenia and documented the information on a specifically created proforma.(Annexure-I).

Data was entered and analyzed with statistical analysis program (SPSS version 23). Frequencies and percentages were computed for categorical variables like gender, type of species and thrombocytopenia. Mean±SD was used to calculate quantitative variables like age, duration of malaria and weight. Thrombocytopenia was stratified for age, gender, type of species, duration of malaria and weight. Post stratification chi square test was applied, $p \leq 0.05$ was considered statistically significant.

III. Results:

Age range in current study was from 18 to 60 years with mean age of 36.716±8.21 years, mean duration of malaria 6.329±1.46 days and mean weight was 80.427±7.14 Kg. Male patients were 58.8% and females were 41.2%.Plasmodium falciparum was observed in 54.6% patients, Plasmodium vivax 39.7% and mixed was 5.7%.Thrombocytopenia was seen in 67% patients as shown in Table-1.Stratification of thrombocytopenia with respect to age, gender, type of species, duration of malaria and weight are shown in Table 2-6 respectively.Thrombocytopenia was seen in 61.3% patients with Plasmodium falciparum, with Plasmodium vivax it was 71.4% and in mixed it was 90.9% as shown in Table-VII.

Table- 1: Frequency of thrombocytopenian=194

Thrombocytopenia	Frequency	%age
Yes	130	67%
No	64	33%
Total	194	100%

Table-2: Stratification of thrombocytopenia with respect to age.

Age (years)	**Thrombocytopenia**		**p-value**
	Yes	No	
18-40	87(66.9%)	43(33.1%)	0.971
41-60	43(67.2%)	21(32.8%)	
Total	130(67%)	64(33%)	

Table-3: Stratification of thrombocytopenia with respect to gender.

Gender	**Thrombocytopenia**		**p-value**
	Yes	No	
Male	70(61.4%)	44(38.6%)	0.047
Female	60(75%)	20(25%)	
Total	130(67%)	64(33%)	

Table-4: Stratification of thrombocytopenia with respect to type of species.

Type of Species		**Thrombocytopenia**		**Total**	**p-value**
		Yes	**No**		
Plasmodium falciparum	Yes	65(61.3%)	41(38.7%)	106 (100%)	0.064
	No	65(73.8%)	23(26.1%)	88 (100%)	
	Total	130(67%)	64(33%)	194 (100%)	
Plasmodium vivax	Yes	55(71.4%)	22(28.6%)	77(100%)	0.288
	No	75(64%)	42(36%)	117(100%)	
	Total	130(67%)	64(33%)	194 (100%)	
Mixed	Yes	10(90.9%)	1(9.1%)	11(100%)	0.082
	No	120(65.6%)	63(34.4%)	183(100%)	
	Total	130(67%)	64(33%)	194 (100%)	

Table-5: Stratification of thrombocytopenia with respect to duration of malaria.

Duration of malaria (days)	**Thrombocytopenia**		**p-value**
	Yes	No	
4-7	89(66.9%)	44(33.1%)	0.968
>7	41(67.2%)	20(32.8%)	
Total	130(67%)	64(33%)	

Table-6: Stratification of thrombocytopenia with respect to weight.

Weight (Kg)	**Thrombocytopenia**		**p-value**
	Yes	No	
≤80	66(66.7%)	33(33.3%)	0.917
>80	64(67.4%)	31(32.6%)	
Total	130(67%)	64(33%)	

IV. Discussion:

In several regions of Pakistan, P. vivax and P. falciparum-related malaria are endemic. Malaria is a true haematological illness that affects practically all blood components. The two haematological problems most usually linked to malaria are thrombocytopenia and anaemia. Malaria has been identified as the main factor contributing to decreased platelet counts in endemic regions. This is so typical of malaria that it is sometimes used to diagnose the disease in those who have fever. Malaria risk is 12–15 times higher when platelet count is less than 150,000/cumm.[10-12]

The most prevalent species in our study was Plasmodium falciparum (54.6%), however many of the patients who participated also had infections with Plasmodium vivax (39.7%) and mixed infections (5.7%). In

their investigation, Faseela et al. [13] discovered comparable outcomes. In 67% of the individuals in our study, thrombocytopenia was observed. 72% of individuals with malaria infection had thrombocytopenia, according to Colonel et al[14]. In their study of paediatric patients, Jamal et al. [15] found that 72% of those with malaria had low platelet counts. However, a small number of trials, including 40% 10 and 58.97%, indicated a slightly reduced incidence of thrombocytopenia.[16]

The precise cause of malarial thrombocytopenia is uncertain. P. vivax was found inside platelets, as shown by Fajardo and Tallent, who hypothesised that the parasite had a direct lytic effect on the platelets. [17] Recently, it has been discovered that platelet lysis may be caused by both non-immunological destruction and an immune mechanism[18] including particular platelet-associated IgG antibodies that bind to the platelets' malarial antigen. [19] Based on the discovery of low levels of platelet superoxide-dismutase and glutathione peroxidase activity and high levels of platelet lipid peroxidation in malaria patients, when compared to those of healthy subjects, oxidative stress damage to platelets has also been implicated in the etiopathogenesis. [20] Because platelet-forming megakaryocytes in the marrow are typically normal or enhanced, decreased thrombopoiesis has been ruled out.[10,20,21,22]Malaria is widely known for having a high tolerance for low platelet counts. An increased agreeability and platelet activation may be the cause of this. [12] Despite substantial thrombocytopenia, bleeding events are exceedingly uncommon in acute malarial infections because of the hyperactive platelets' potential to promote hemostatic responses.[23]

In our study, P. vivax malaria (71.4%) had more noticeable thrombocytopenia. Thrombocytopenia was observed in 61.3% of Plasmodium falciparum patients and 90.9% of mixed patients. My study's findings are close to those of a study by Gupta NK, et al., which showed that thrombocytopenia was common in 77.7% of Plasmodium falciparum species, 76.9% of Plasmodium vivax species, and 90% of mixed Plasmodium falciparum and Plasmodium vivax species. [8] Another study by Nadeem A, et al. revealed that 55.9% of Plasmodium vivax species exhibited thrombocytopenia.[9]

The emergence of a novel genotype of P. vivax may be responsible for an increase in occurrences of thrombocytopenia in vivax malaria infections. [20] Contrary to the widespread idea that it may be seen in P. falciparum malaria, recent research have demonstrated that thrombocytopenia is equally or even more common in P. vivax malaria. [24-30]In individuals with P. vivax infections, thrombocytopenia was more common and more severe, according to more recent data. [31] Recent researches from the Indian subcontinent indicate that P. vivax malaria patients had substantial thrombocytopenia. [32,33] Studies from Venezuela and Qatar had produced comparable findings..[34,35]

V. Conclusion:

Patients with malaria were more likely to experience mild to severe thrombocytopenia, and P. vivax malaria patients were more likely to experience significant thrombocytopenia. In the context of preventing needless platelet infusion in malaria patients, the aforementioned finding may have therapeutic ramifications. Among the tropics, the likelihood of malaria increases in patients with acute febrile illness who also have thrombocytopenia. To raise the suspicion of this disease and hasten the start of treatment, this may be utilised in addition to the clinical and microscopic characteristics.

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