ORIGINAL ARTICLE

Battle of the Blood: Thrombocytopenia in Children with Vivax Malaria

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ABSTRACT

Objective: The study aimed to determine the incidence of thrombocytopenia in children with plasmodium vivax malaria.

Study Design: This was a descriptive cross-sectional

Place and Duration of Study: After the approval from the institution review board, this study was conducted at the Department of Pediatrics, Combined Military Hospital, Bahawalpur from 01st January 2024 to 31st May 2024.

Material and Methods: A sum of 280 children were recruited for this research. At first, those who had symptoms of sudden onset of high-grade fever without any other symptoms were selected. All the patients were gone through a detailed history and clinical examination. Patients who fulfilled the study's inclusion and exclusion criteria were considered for participation, Samples of 5 CC of blood were obtained from people who were thought to have malaria and were immediately sent to the hospital laboratory, for blood tests thick and thin smear microscopy. The peripheral smear was used to test for thrombocytopenia in patients with vivax malaria.

Result: The male gender patients were 190 and females were 90. Out of which 155 and 58 males and females respectively had thrombocytopenia. 72 patients of age group 2-5 years had thrombocytopenia. The p-value was less than 0.05 using chi square test.

Conclusion: Our study concludes that the frequency of thrombocytopenia was 76.07 % in children presenting with plasmodium vivax malaria.

Key Words: Pediatric, Thrombocytopenia, Children, Plasmodium, Vivax Malaria, Kids

INTRODUCTION

Malaria poses a significant health challenge and remains a leading cause of mortality, especially among children in developing countries. If left untreated, it can lead to severe complications, including hematological issues. Identifying these risk factors is crucial for the effective malaria management.[1] Although vivax malaria has a global impact, it has historically been overlooked and is regarded as a benign disease. However, in the last decade, the medical literature has presented evidence challenging this perception.[2]

Plasmodium vivax infects approximately 7 million people annually. Previously, vivax malaria was considered relatively benign compared to P. falciparum malaria. However, recent reports have highlighted its severe clinical consequences, which have become increasingly evident over the last decade.[3] Malaria is an infectious disease caused by protozoa Plasmodium, transmitted to humans through infected female Anopheline mosquitoes.[4] Patients with acute malaria commonly exhibit hematological abnormalities, such as thrombocytopenia, characterized by a low platelet count. This research investigates how thrombocytopenia can serve as a diagnostic indicator for malaria for individuals with sudden illness with fever.[5] Malarial parasite resides in the blood and can lead to various hematological abnormalities, including anemia, thrombocytopenia, lymphopenia, monocytosis, and eosinopenia. In rare cases, it may cause disseminated intravascular coagulation. These hematological changes can vary based on factors such as the prevalence of malaria in a particular region, underlying hemoglobinopathies, nutritional well-being, various demographic elements, and individual protection against malaria.[7] Plasmodium falciparum is known to cause the most lethal form of malaria.[8] Recently, it has been recognized that Plasmodium vivax can cause severe malaria with clinical manifestations similar in magnitude to those of other forms of the disease.[9]

MATERIAL AND METHODS

This cross-sectional study was conducted after the approval from the institution review board (IRB No. 133/DME/2023), at a tertiary care hospital, combined with the Military hospital, Bahawalpur. Patients were admitted to the ward and visited as outpatients from 01 January 2024 to May 31, 2024. at the very first Permission was obtained from the institutional review board. All patients were aged < 12 years.

Inclusion criteria: All patients were diagnosed with vivax malaria (confirmed using thin and thick films). The results were then cross-checked using thin and thick smears.

Exclusion criteria: The exclusion criteria included cases diagnosed with other strains of malaria, P falciparum (verified by peripheral thick and thin smears), dengue positive cases (by Dengue Day1NS1 Test kit), and leptospirosis (IgM and IgG). The study population was calculated using open epi, keeping the confidence limit at 5%, the anticipated frequency at 23.3%, and the design effect at 1.0. The calculated sample size was 275. The parents of the patient were counseled about the study, and informed consent was obtained. A detailed history was obtained from the parents, and a detailed physical examination was performed. After obtaining consent, samples were collected from patients suspected of having malaria. The samples were then collected. The samples were immediately sent to the laboratory for assessment. The samples were then examined by trained lab technicians and crosschecked by a consultant pathologist on duty. Platelet count and TLC was calculated using an automated cell counter. All patients with a platelet count less than 150×10^9/L were labeled as having thrombocytopenia, and those reports that reported a platelet count less than 100×10^9/L were verified manually. A Google form was created on which the data were collected by a duty doctor. It was then obtained in the form of Excel sheets, which were analyzed using IBM SPSS version 20. Statistical significance was set at $p < 0.05$. Our null hypothesis was that thrombocytopenia would not be present in most cases of vivax malaria. Another hypothesis is that thrombocytopenia is present in vivax malaria cases.

RESULTS

In this study we collected the data of 280 patients. demographic factors and clinical factors related to past medical history are mentioned in the table 1.

TABLE 1: Demographic and clinical factors

Parameters	Number (%)
Age (mean ± SD)	5 ± 5.5
2-5	131 (46.7)
5-12	149 (53.2)
Gender	
Male	190 (67.8)
Female	90 (32.2)
Previous history of malaria	
Yes	31 (11.1)
No	249 (88.9)
Gestational age	
Term	141 (50.4)
Preterm	139 (49.6)
Thrombocytopenia	
Yes	213 (76.07)
No	67 (23.93)

Age was 5 ± 5.5 years the study population was 190 (67.8%) males and females were 90 (32.2%). The mean fever duration was 4 Days. 95 (33.9%)

people were having less than 4 days and 185 (66.1%) Patients had greater than 4 days. The 31 (11.1%) population had the known history of the malaria. The mean gestational age was 37.1 weeks. The percentage of thrombocytopenia was: 76.07 %. The division of thrombocytopenia with respect to sex, age, past history, gestational age is given as in table 2.

TABLE 2: Demographic factors with respect to thrombocytopenia

Parameters	Thrombocytopenia		p value
	Yes (%)	No (%)	
Age (mean ± SD)			
2-5	72 (54.7)	59 (45.3)	0.028
5-12	101 (67.8)	48 (32.2)	
Gender			0.002
Male	155 (81.6)	35 (18.4)	
Female	58 (64.4)	32 (35.6)	
Previous history of malaria			0.001
Yes	17 (54.8)	14 (45.2)	
No	199 (79.9)	50 (20.1)	
Gestational age			0.18
Term	99 (70.2)	42 (29.8)	
Preterm	87 (66.4)	52 (37.4)	

As calculated by the chi square test applied on IBM SPSS version 23 the p value for thrombocytopenia is less than the 0.05 thus the null hypothesis is rejected and the hypothesis stating that the thrombocytopenia is present in most of the cases diagnosed as vivax malaria.

DISCUSSION

Malaria is a significant health issue and a major cause of mortality, especially among pediatric populations in developing countries. If left untreated, it can lead to various hematological complications.[10] Studies on malaria induced in one of the U.S. servicemen returning from non-endemic areas provided initial detailed descriptions of signs and symptoms and other information regarding vivax malaria. In a case series of 195 non-immune individuals, adult prison volunteers were infected with the Chesson strain of P. vivax by researchers in the 1940s. Common symptoms were observed, aside from fever, including anorexia, headache, asthenia, nausea, eye pain, and myalgia. Chest pain, abdominal pain, dizziness, and cough .[11] Vivax infections are associated with a significant global burden, estimated at approximately 7-14 million per annum. This impact is particularly pronounced in pregnant women and children.[12] For more than a decade, there has been a need to present a better version of the definition of severe vivax malaria. However, inconsistent reporting by various groups has hindered reliable data collection and guidelines. Another study searching for the red flags of intensive care unit (ICU) admission in patients with vivax malaria suggested that several points mentioned in the definition of severe falciparum malaria infection were predictive, except for hyperbilirubinemia.[13] The significance of thrombocytopenia as a diagnostic indicator in cases of severe vivax malaria is a topic of importance.[14] When it enters, the plasmodium affects various organs in the body, including the liver, brain, spleen, gastrointestinal tract, pancreas, gall bladder, placenta, and blood vessels. As a result, the clinical presentation can vary widely, from mild malaise to life-threatening central nervous system symptoms, such as coma. Hematological abnormalities, particularly anemia and thrombocytopenia, are commonly observed in malaria patients. In Papua, Indonesia, Lampah et al. reported that the mortality risk of P. vivax infections in patients presenting to a referral hospital with severe thrombocytopenia was 1.5% (25 of 1650) when platelet counts were below 50 × 10^^{9}/L. Additionally, the risk was 3.6% (6 of 168) when the platelet count was < 20 × 10^^{9}/L. They proposed the latter threshold as the severity criterion.[15] The practical utility of incorporating platelet counts into routine malaria diagnosis and treatment requires further investigation, especially in outpatient settings where complete blood counts are often unavailable. Conversely, a

mathematical modeling study proposed using platelet counts (>200,000 per µL) to enhance the specificity of severe falciparum malaria case definitions.[16] This approach aimed to reduce misdiagnoses; however, few articles have explored platelet counts in association with severe malaria syndromes. Thrombocytopenia and anemia are common hematological complications associated with malaria. Malaria is a major cause of low platelet counts in endemic areas. Some places use platelet counts below 150,000/cumm as an indicator of malaria in patients with fever. A platelet count below this threshold increases the likelihood of malaria by 12-15 times.[17] In our study, P. vivax was the predominant species, although a significant proportion of patients also had P. falciparum infections (25%) or mixed infections (12%). Faseela et al. observed similar results.[18] In this study, 172 (61.7%) patients had thrombocytopenia. In another study by Colonel et al.,[19] 72% of patients with malarial infection had thrombocytopenia. Another study by Jamal et al.[20] on pediatric patients highlighted decreased platelet counts in approximately 72% of individuals with malaria. On the contrary, few studies documented lower incidences of thrombocytopenia, such as 40%[21] and 58.97%.[22] Recent studies have highlighted the significance of thrombocytopenia as being equally or more prevalent in P. vivax malaria, against the common belief that it is found in P. falciparum malaria.[23] Shaikh et al. reported a significantly higher incidence of thrombocytopenia in patients infected with P. vivax. Thrombocytopenia in malaria may result from increased platelet consumption or destruction, the suppression of thrombopoiesis, or a combination of both. Proposed mechanisms include disseminated intravascular coagulation (DIC), immune-mediated destruction, reticuloendothelial system pooling, microcirculation sequestration, and malaria-induced apoptosis [24] Unlike our study, Patel et al. reported a significantly higher incidence of thrombocytopenia in P. falciparum compared to P. vivax.[25]

CONCLUSION

Our study found that 75.7% of the patients presented with vivax malaria and had thrombocytopenia. Vivax was thus found to be the cause of the decrease in platelet count in these patients. Thus, it can serve as a valuable tool for diagnosing malaria. This can be beneficial as it may reduce the patient burden and unnecessary tests for patients who present with fever. It can be done that all the patients presenting with febrile illness and having thrombocytopenia may be confirmed for malarial testing for prompt detection.

Conflict of interest: The authors who have contributed claim that they have no conflict of interest with any other organization or with any other.

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REFERENCES

1. Shah F, Said S, Khan A. Hussain U. Frequency of thrombocytopenia in children with vivax malaria in a tertiary care center. September-December, 2018, Vol. 11, No. 3.
2. O'Brien AT, Ramírez JF, Martínez SP. A descriptive study of 16 severe Plasmodium vivax cases from three municipalities of Colombia between 2009 and 2013. Malar J. 2014 Oct 15; 13:404.
3. Phyo AP, Dahal P, Mayxay M, Ashley EA. Clinical impact of vivax malaria: A collection review. PLoS Med. 2022 Jan 18;19(1): e1003890.
4. Gupta NK, Bansal SB, Jain UC, Sahare K. Study of thrombocytopenia in patients of malaria. Trop Parasitol. 2013 Jan;3(1):58-61.
5. Angesom Gebreweld, Yonas Erkihun, Daniel Getacher Feleke, Gebru Hailu, Temesgen Fiseha, "Thrombocytopenia as a Diagnostic Marker for Malaria in Patients with Acute Febrile Illness", Journal of Tropical Medicine, vol. 2021, Article ID 5585272, 6 pages, 2021.

6. N. Awoke and A. Arota, “Profiles of hematological parameters in plasmodium falciparum and plasmodium vivax malaria patients attending tercha general hospital, Dawuro zone, south Ethiopia,” Infection and Drug Resistance, vol. 12, p. 521, 2019.
7. P. Patel, M. Patel, B. Gamit, J. Modi, S. Kevadiya, and S. Padsala, “Thrombocytopenia in malaria: correlation with various prevalent species,” International Journal of Medical Science and Public Health, vol. 2, no. 4, pp. 946–950, 2013.
8. Bansal Y, Maurya V, Aggarwal N, Tak V, Nag VL, Purohit A, Goel AD, Bohra GK, Singh K. Thrombocytopenia in malaria patients from an arid region of Western Rajasthan (India). Trop Parasitol. 2020 Jul-Dec;10(2):95-101.
9. WHO. Management of Severe Malaria – A Practical Handbook. 3rd ed. Geneva, Switzerland: WHO; 2013.
10. Latif I, Jamal A. Hematological changes in complete blood picture pediatric patients of malaria caused by plasmodium vivax and falciparum. J Ayub Med. 2015;27(2):351-5.
11. Whorton CM, Yount E Jr, Jones R Jr, Alving AS, Pullman TN, Craige B. Jr et al. The Chesson strain of Plasmodium vivax malaria; clinical aspects. J Infect Dis. 1947;80(3):237–49.
12. Howes RE, Battle KE, Mendis KN, Smith DL, Cibulskis RE, Baird JK, et al. Global Epidemiology of Plasmodium vivax. Am J Trop Med Hyg. 2016;95(6 Suppl):15–34.
13. Lança EF, Magalhães BM, Vitor–Silva S, Siqueira AM, Benzecry SG, Alexandre MA, et al. Risk factors and characterization of Plasmodium vivax–associated admissions to pediatric intensive care units in the Brazilian Amazon. PLoS ONE. 2012;7(4): e35406.
14. Lacerda MV, Mourão MP, Coelho HC, Santos JB. Thrombocytopenia in malaria: who cares? Mem Inst Oswaldo Cruz. 2011;106(Suppl 1):52–63.
15. Lampah DA, Yeo TW, Malloy M, Kenangalem E, Douglas NM, Ronaldo D, et al. Severe malarial thrombocytopenia: a risk factor for mortality in Papua. Indonesia J Infect Dis 2015;211(4):623–34.
16. Watson JA, Ndila CM, Uyoga S, Macharia A, Nyutu G, Mohammed S, et al. Improving statistical power in severe malaria genetic association studies by augmenting phenotypic precision. Elife. 2021;10.
17. Maina RN, Walsh D, Gaddy C, Hongo G, Waitumbi J, Otieno L, et al. Impact of Plasmodium falciparum infection on haematological parameters in children living in Western Kenya. Malar J. 2010;9(suppl 3): S4.
18. Faseela TS, Roche, Anita KB, Malli CS, Rai Y. Diagnostic value of platelet count in malaria. J Clin Diagn Res. 2011; 5:464–6.
19. Colonel KM, Bhika RD, Khalid S, Khalique-ur-Rehman S, Syes ZA. Severe thrombocytopenia and prolonged bleeding time in patients with malaria (a clinical study of 162 malaria cases) World Appl Sci J. 2010; 9:484–8.
20. Jamal A, Memon IA, Latif F. The association of Plasmodium vivax malaria with thrombocytopenia in febrile children. Pak Paediatr J. 2007; 31:85–9.
21. Harish R, Gupta S. Plasmodium vivax malaria presenting with severe thrombocytopenia, cerebral complications and hydrocephalus. Indian J Pediatr. 2009; 76:551–2.
22. Kakar A, Bhoi S, Prakash V, Kakar S. Profound thrombocytopenia in Plasmodium vivax malaria. Diagn Microbiol Infect Dis. 1999; 35:243–4.
23. Aggarwal A, Rath S, Shashiraj Plasmodium vivax malaria presenting with severe thrombocytopenia. J Trop Pediatr. 2005; 51:120–1.
24. K. Srivastava, M. Sharma, and W. B. Mitchell, “Malaria and thrombopoiesis: a possible mechanism for the malarial thrombocytopenia,” Journal of Immunology, Infection & Inflammatory Diseases, vol. 6, p. 2, 2017.
25. B. J. McMorran, “Immune role of platelets in malaria,” ISBT Science Series, vol. 14, no. 1, pp. 67–76, 2019.