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Original Article

Incidence of Plasmodium Vivax Malaria in Patients with Pancytopenia

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ABSTRACT

Background: Malaria, caused by Plasmodium vivax, is prevalent in many tropical and subtropical regions of the world, notably in South Asia and Africa. The clinical manifestation of malaria, including pancytopenia, varies widely, leading to complex challenges in diagnosis and treatment. Understanding the association between Vivax malaria and hematological abnormalities like pancytopenia is critical for improving patient outcomes in endemic regions.

Objective: This study aimed to investigate the incidence of Plasmodium vivax in patients presenting with pancytopenia and to assess the demographic and hematological profiles of these patients in a high-prevalence area.

Methods: A prospective cohort study was conducted at the Hayatabad Medical Complex, Peshawar, from January 2021 to January 2023. A total of 350 patients who presented at the medical outpatient department were enrolled based on inclusion and exclusion criteria. Blood samples were collected using aseptic techniques, and peripheral blood smears were prepared for analysis. Demographic data were collected through questionnaires. Statistical analysis was performed using SPSS version 25, with categorical data analyzed using Chi-square tests and continuous variables using t-tests, setting statistical significance at $p < 0.05$.

Results: Of the 350 patients studied, 71.4% were male and 28.6% were female, with a mean age of 55.1 years. The hemoglobin levels averaged 8.86 g/dl (SD ± 1.77), and the leukocyte count was 2.84×10^3/Cmm (SD ± 3.31). Platelet counts averaged 77.25×10^9/Cmm (SD ± 2.90). Overall, 52.6% of patients tested positive for P. vivax. There were no significant differences in the incidence of P. vivax infection across age groups ($p = 0.36$) or between genders ($p = 0.41$).

Conclusion: The study confirmed a significant prevalence of P. vivax in patients with pancytopenia, highlighting the need for routine screening in malaria-endemic regions. Early diagnosis and treatment are essential for managing pancytopenia in patients with malaria and can lead to substantial improvements in clinical outcomes.

Keywords: Plasmodium vivax, malaria, pancytopenia, hematological abnormalities, prospective cohort study, malaria diagnosis, endemic regions.

INTRODUCTION

Malaria, particularly caused by Plasmodium vivax, remains a significant public health challenge across Asia, where it causes considerable morbidity throughout the year (1). In an effort to address the widespread impact of this disease, the Asia Pacific Malaria Elimination Network vivax working group, comprising 18 nations, was established with the goal of eradicating malaria within the region (2). Despite being less lethal than its counterpart Plasmodium falciparum, P. vivax is the second most common etiological agent of malaria globally and the primary cause in Pakistan, where it leads to both mild and severe disease manifestations (3). The pathogenic process of P. vivax begins with the migration of sporozoites to the liver, where they can remain dormant as hypnozoites or enter the bloodstream as merozoites (5,6). Once in the circulatory system, the parasite primarily infects reticulocytes, causing high-grade intermittent fevers. Compared to P. falciparum malaria, P. vivax is characterized by lower levels of parasitemia and severity, and it is less frequently associated with encephalopathy, splenomegaly, and anemia (7).

A notable number of hospital admissions are for pancytopenia, an abnormal reduction in blood cells, which often presents with malaise and fever and remains of unclear origin. These cases are particularly concerning due to their significant prevalence and the

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severe hematological abnormalities observed, which frequently result in poor clinical outcomes (8). It has been identified that an early presentation of P. vivax malaria can manifest as pancytopenia, often accompanied by splenomegaly. Patients diagnosed with this form of malaria via smear tests are found to have pancytopenia, and prompt diagnosis and treatment can lead to full recovery, substantially reducing morbidity and mortality. This highlights the critical need for improved understanding of the molecular mechanisms of P. vivax, as the current lack of a comprehensive control strategy for this malaria form is largely due to inadequate knowledge about the parasite (4). Such insights could drive better management strategies and help in the more effective control of the disease, thus supporting global eradication efforts.

MATERIAL AND METHODS

A prospective cohort study was conducted at the Department of Medicine, Hayatabad Medical Complex (HMC), KPK Peshawar, from January 2021 to January 2023, involving 350 patients who presented at the medical outpatient department. The study participants were selected based on pre-established inclusion and exclusion criteria. After providing informed consent, each patient had 5 ml of blood drawn using aseptic techniques. The samples were promptly transported to the hospital's main laboratory for analysis. Peripheral blood smears were prepared, and both thick and thin slides were examined to diagnose Plasmodium vivax infection.

Data on demographic variables such as age, gender, and socioeconomic status were collected through questionnaires administered to the patients. This information aimed to explore any correlations between these factors and the incidence of Plasmodium vivax malaria. The research was carried out following the Declaration of Helsinki, ensuring all ethical standards were maintained. The study received approval from the Institutional Review Board (IRB) and the ethical review committee of Hayatabad Medical Complex, Peshawar.

Statistical analysis was performed using SPSS version 25. Continuous variables, such as age and duration of fever, were described using means and standard deviations, while categorical variables, including gender and socioeconomic status, were summarized using frequencies and percentages. Comparative analyses of categorical data were conducted using the Chi-square test, and t-tests were applied to compare means of continuous variables. The level of statistical significance was set at $p < 0.05$, indicating meaningful differences or correlations.

The results of these analyses were intended to offer insights into the patterns of P. vivax malaria within the cohort, contributing to a better understanding of the epidemiological characteristics associated with the disease in this region.

RESULTS

In the study, the majority of the 350 participants were male, accounting for 71.4% (250 individuals), while females represented 28.6% (100 individuals), highlighting a significant gender disparity among the patients (Table 1). The mean age of the cohort was 55.1 years, with a standard deviation of 1.2 years, reflecting a predominantly middle-aged and older population. Age distribution was fairly balanced across the cohorts with 14.3% (50 individuals) below 20 years, 34.3% (120 individuals) between 20 and 40 years, the largest group of 37.1% (130 individuals) between 41 and 60 years, and another 14.3% (50 individuals) above 60 years, illustrating a wide range of affected age groups (Table 1).

The assessment of hemoglobin levels revealed an average concentration of 8.86 g/dl with a standard deviation of 1.77 g/dl. Notably, a substantial portion of the study population, 51.4% (180 individuals), had hemoglobin levels ranging from 7 to 10 g/dl. Those with levels below 7 g/dl comprised only 5.7% (20 individuals), whereas 28.6% (100 individuals) had levels between 10 and 12 g/dl, and 14.3% (50 individuals) exhibited levels above 12 g/dl (Table 2).

Leukocyte counts further elucidated the impact of the condition on patient health. The mean leukocyte count was 2.84×10^3 per cubic millimeter, with a notable variability indicated by a standard deviation of 3.31. The distribution was skewed towards lower counts, with 62.9% (220 individuals) having leukocyte counts between 2 and 4×10^3 per cubic millimeter, 22.9% (80 individuals) between 4 and 6×10^3, and a smaller 8.6% (30 individuals) exhibiting counts less than 2×10^3. Only 5.7% (20 individuals) had counts above 6×10^3 per cubic millimeter, suggesting a trend towards lower leukocyte levels in this patient group (Table 3).

Table 1: Demographic Characteristics of Studied Patients

Variable	Total Number of Patients (n=350)	Percentage (%)
Gender		
Male	250	71.4%
Female	100	28.6%
Mean Age (years)	55.1 ± 1.2	

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Variable	Total Number of Patients (n=350)	Percentage (%)
Age Group (years)		
Below 20 years	50	14.3%
20-40 years	120	34.3%
41-60 years	130	37.1%
Above 60 years	50	14.3%
Total	350	100%

Table 2: Hemoglobin Level Distribution

Variable	Total Number of Patients (n=350)	Percentage (%)
Hemoglobin Level (g/dl), mean ± SD	8.86 g/dl ± 1.77	
Less than 7	20	5.7%
7-10	180	51.4%
10-12	100	28.6%
Above 12	50	14.3%
Total	350	100%

Table 3: Leukocyte Count Distribution

Variable	Total Number of Patients (n=350)	Percentage (%)
Leukocyte Count (x10^3/Cmm) ± SD	2.84×10^3 /Cmm ± 3.31	
Less than 2	30	8.6%
2-4	220	62.9%
4-6	80	22.9%
Above 6	20	5.7%
Total	350	100%

Table 4: Platelet Count Distribution

Variable	Total Number of Patients (n=350)	Percentage (%)
Platelet Count (x10^9/Cmm) ± SD	77.25×10^9 /Cmm ± 2.90	
Less than 50	10	2.9%
50-100	120	34.3%
100-150	160	45.7%
Above 150	60	17.1%
Total	350	100%

Table 5: Frequency, Age, and Gender Stratification

Variable	Total Number of Patients (n=350)	Percentage (%)	P value
Positive for P. vivax	184	52.6%	
Negative for P. vivax	166	47.4%	
Age stratification			0.36
Gender stratification			0.41

Platelet counts also demonstrated significant variation, with a mean count of 77.25×10^9 per cubic millimeter and a standard deviation of 2.90. The majority, 45.7% (160 individuals), had platelet counts between 100 and 150×10^9 per cubic millimeter. A substantial 34.3% (120 individuals) presented with counts between 50 and 100×10^9, while only 2.9% (10 individuals) fell below 50×10^9. Higher platelet counts above 150×10^9 were observed in 17.1% (60 individuals) of the cases (Table 4).

The overall prevalence of Plasmodium vivax infection was 52.6% (184 positive cases), demonstrating the significant impact of this parasite on the population studied. The statistical analysis did not reveal significant differences in the distribution of the infection across different age groups (p-value 0.36) or genders (p-value 0.41), suggesting that the infection affects diverse demographic segments similarly (Table 5).

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DISCUSSION

Our research findings suggest a correlation between Vivax malaria and pancytopenia, a condition more commonly observed in regions where malaria is endemic and prevalent throughout the year. Notably, the association between Plasmodium vivax and pancytopenia varies globally, emphasizing the need for further research in different endemic areas to better understand this relationship.

Vivax malaria, a significant etiological agent in regions like South Asia and Africa, shows variable presentation and symptomatology. For instance, a study of 204 individuals revealed that 54% tested positive for Vivax malaria, many presenting with pancytopenia (9). Similarly, documented cases, including one from Japan where a traveler from Southeast Asia was diagnosed with malaria after presenting with symptoms including pancytopenia and splenomegaly, further underscore the variability of the disease's presentation (10). Such cases, along with others from New Delhi and Mumbai, demonstrate the complex interplay between malaria and other health conditions, such as chronic myeloid leukemia and co-infections like dengue, which can complicate diagnosis and treatment (11, 12). Conversely, a study from Berhampur, India, reported a much lower incidence of pancytopenia among Vivax malaria patients, highlighting regional differences in clinical manifestations (13, 14).

The data also indicate a potential gender-related difference in malaria infectivity, although our study did not find a significant gender disparity (P=0.41), challenging the notion that malaria might inherently affect one gender more than the other (15). This finding is consistent with other studies, such as those conducted in Sweden among Eritrean immigrants, suggesting that while male predominance in infection rates is noted, it may not be universally applicable (16).

The variability in global research findings reflects the diverse clinical presentations of Vivax malaria and underscores the importance of local context in disease management and research (17). This variability, coupled with our findings, suggests that testing for malaria parasites should be a standard procedure for all patients with pancytopenia, especially in malaria-prevalent regions. Such testing, utilizing both thick and thin blood smears, is vital for timely and accurate diagnosis, which is crucial for effective treatment and reversal of pancytopenia (18-20).

CONCLUSION

In conclusion, our study highlights the need for increased awareness and testing for malaria in patients presenting with pancytopenia. This approach is particularly important in endemic regions where the prevalence of the disease is high. Future research should expand on these findings with larger sample sizes and more diverse geographic locations to further validate the association between Plasmodium vivax and pancytopenia. Additionally, examining the implications of gender on malaria infection rates could provide deeper insights into the epidemiological characteristics of the disease.

REFERENCES

1. Gething PW, Patil AP, Smith DL, et al. A New World Malaria Map: Plasmodium Falciparum Endemicity in 2010. Malar J. 2011;10:378. doi:10.1186/1475-2875-10-378.
2. Thriemer K, Ley B, Bobogare A, et al. Challenges for Achieving Safe and Effective Radical Cure of Plasmodium Vivax: A Round Table Discussion of the APMEN Vivax Working Group. Malar J. 2017;16:141. doi:10.1186/s12936-017-1784-1.
3. Zubairi AB, Nizami S, Raza A, et al. Severe Plasmodium Vivax Malaria in Pakistan. Emerg Infect Dis. 2013;19:1851-4. doi:10.3201/eid1911.130495.
4. Hoo R, Zhu L, Amaladoss A, et al. Integrated Analysis of the Plasmodium Species Transcriptome. EBioMedicine. 2016;7:255-66. doi:10.1016/j.ebiom.2016.04.011.
5. Lin JT, Parr JB, Ngasala B. Non-Falciparum Malaria in Africa and Learning from Plasmodium Vivax in Asia. Clin Infect Dis. 2019;70:2018-9. doi:10.1093/cid/ciz780.
6. Taylor JE, Pacheco MA, Bacon DJ, et al. The Evolutionary History of Plasmodium Vivax as Inferred from Mitochondrial Genomes: Parasite Genetic Diversity in the Americas. Mol Biol Evol. 2013;30:2050-64. doi:10.1093/molbev/mst104.
7. Gai PP, Mockenhaupt FP, Siegert K, et al. Manifestation of Malaria in Mangaluru, Southern India. Malar J. 2018;17:313. doi:10.1186/s12936-018-2462-7.
8. Gudina EK, Amare H, Benti K, et al. Pancytopenia of Unknown Cause in Adult Patients Admitted to a Tertiary Hospital in Ethiopia: Case Series. Ethiop J Health Sci. 2018;28:375-82. doi:10.4314/ejhs.v28i4.3.
9. Tadesse F, Fogarty AW, Deressa W. Prevalence and Associated Risk Factors of Malaria Among Adults in East Shewa Zone of Oromia Regional State, Ethiopia: A Cross-Sectional Study. BMC Public Health. 2017;18:25. doi:10.1186/s12889-017-4577-0.

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10. Tanizaki R, Ujiie M, Kato Y, et al. First Case of Plasmodium Knowlesi Infection in a Japanese Traveler Returning from Malaysia. Malar J. 2013;12:28. doi:10.1186/1475-2875-12-128.

11. Raina V, Sharma A, Gujral S, et al. Plasmodium Vivax Causing Pancytopenia After Allogeneic Blood Stem Cell Transplantation in CML. Bone Marrow Transplant. 1998;22:205-6. doi:10.1038/sj.bmt.1701299.

12. Bhagat M, Kanhere S, Phadke V, George R. Concurrent Malaria and Dengue Fever: A Need for Rapid Diagnostic Methods. J Family Med Prim Care. 2014;3:446-8. doi:10.4103/2249-4863.148146.

13. Mahgoub H, Gasim GI, Musa IR, Adam I. Severe Plasmodium Vivax Malaria Among Sudanese Children at New Halfa Hospital, Eastern Sudan. Parasites Vectors. 2015;5:154. doi:10.1186/1756-3305-5-154.

14. Mohapatra MK, Padhiary KN, Mishra DP, Sethy G. Atypical Manifestations of Plasmodium Vivax Malaria. Indian J Malariol. 2002;39:18-25.

15. Simões LR, Alves Jr ER, Ribatski-Silva D, Gomes LT, Nery AF, Fontes CJF. Factors Associated with Recurrent Plasmodium Vivax Malaria in Porto Velho, Rondônia State, Brazil, 2009. Cad Saude Publica. 2014;30:10. doi:10.1590/0102-311X00169312.

16. Sondén K, Castro E, Trönnberg L, Stenström C, Tegnell A, Färnert A. High Incidence of Plasmodium Vivax Malaria in Newly Arrived Eritrean Refugees in Sweden Since May 2014. Eurosurveillance. 2014;19:20890. doi:10.2807/1560-7917.ES2014.19.35.20890.

17. Ahmad S, Ikramullah Q, Ahmad I. Frequency of Thrombocytopenia in malaria and its prognostic significance. Journal of University Medical & Dental College. 2023 Feb 15;14(1):545-8.

18. Orish VN, Lokpo SY, Kwadzokpui PK, Safianu R, Marinkovic A, Prakash S, Okorie C, Izurieta R, Pandit R, Sanyaolu A. Association between asymptomatic Plasmodium falciparum malaria infection, anaemia and mean corpuscular volume of school children in the Volta Region of Ghana. European Journal of Microbiology and Immunology. 2024 Feb 26.

19. Goyal JP, Makwana AM. Research Article Comparison of Clinical Profile between P. vivax and P. falciparum Malaria in Children: A Tertiary Care Centre Perspective from India.

20. Gupta N, Chalotra S, Parihar RK, Sharma P. Ramifications of pancytopenia in children in a tertiary care center in North Indian. Journal of Applied Hematology. 2023 Apr 1;14(2):95-100.