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STUDY OF CNS MANIFESTATIONS IN PEDIATRIC PATIENTS WITH PLASMODIUM VIVAX MALARIA AND THEIR CORRELATION WITH DEGREE OF PARASITEMIA

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ABSTRACT

Background: Plasmodium vivax malaria, traditionally considered a benign form of malaria, has increasingly been associated with severe manifestations, including central nervous system (CNS) involvement in pediatric patients. Understanding the relationship between parasitemia levels and CNS manifestations is crucial for early diagnosis and management.

Materials and Methods: This prospective observational study was conducted at C. U. Shah Medical College, Surendranagar, involving 100 pediatric patients aged 1–13 years diagnosed with P. vivax malaria. Malaria diagnosis was confirmed through microscopic examination of Giemsa-stained thick and thin blood films and HRP2 antigen testing. A complete blood count was performed, and parasitemia was quantified by calculating the parasitic index (percentage of infected erythrocytes). Clinical evaluation focused on CNS manifestations, including seizures, altered consciousness, and other neurological signs. Data analysis was performed using SPSS version 17, employing descriptive statistics, Chi-square test, and Pearson correlation coefficient.

Results: The study cohort comprised 69% children aged 5–13 years and 62% males. Parasitic index distribution was as follows: <1% (71%), 1–1.5% (20%), 1.5–2% (4%), and >2% (5%). CNS manifestations were observed in 8% of patients, with 75% of these cases having a parasitic index >1.5%. Statistical analysis revealed a significant association between higher parasitic index and CNS involvement (Chi-square = 47.2, P = 0.00001).

Conclusion: The study demonstrates a significant correlation between elevated parasitemia and the occurrence of CNS manifestations in pediatric P. vivax malaria. These findings underscore the importance of considering parasitemia levels in the clinical assessment and management of pediatric malaria cases.

Keywords: Plasmodium vivax, pediatric malaria, parasitic index, neurological manifestations.

INTRODUCTION

Malaria remains a significant global health concern, with Plasmodium vivax being the most prevalent malaria parasite outside sub-Saharan Africa. Traditionally considered a benign form of malaria, recent studies have highlighted the potential severity of P. vivax infections, including neurological complications such as cerebral malaria (CM). Although CM is predominantly associated with P. falciparum, emerging evidence suggests that P. vivax can also lead to severe neurological manifestations in pediatric patients.[1,2]

In regions like India, where both P. vivax and P. falciparum are endemic, there has been a noticeable increase in cases of severe malaria due to P. vivax. A study from Rohtak, India, reported that over half of the severe malaria cases in children were attributed to P. vivax monoinfection, with clinical presentations including CM, severe anemia, thrombocytopenia, and acute respiratory distress syndrome. Notably, two fatalities were observed in this cohort,

underscoring the potential severity of P. vivax infections in children.[3]

The pathophysiology of P. vivax-induced CM remains under investigation. Unlike P. falciparum, P. vivax does not exhibit cytoadherence of infected erythrocytes to endothelial cells, a hallmark of cerebral sequestration. However, studies have suggested that P. vivax-infected red blood cells may sequester in organs such as the lung, potentially contributing to severe pathology.[4]

The degree of parasitemia has been identified as a potential factor influencing the severity of P. vivax infections. Research indicates that higher parasitemia levels are associated with increased risk of severe manifestations, including neurological complications. Understanding this correlation is crucial for early identification and management of severe cases.[5,6]

Given the increasing recognition of P. vivax as a cause of severe malaria in children, it is imperative to investigate the clinical and parasitological characteristics of these infections. This study aims to examine the central nervous system (CNS) manifestations in pediatric patients with P. vivax malaria and assess their correlation with the degree of parasitemia, thereby contributing to the understanding and management of severe P. vivax infections in children.[3]

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of Paediatrics, C. U. Shah Medical College, Surendranagar. The study included 100 paediatric patients admitted with *Plasmodium vivax* malaria who provided written informed consent for participation.

Study Design and Diagnostic Criteria: The diagnosis of malaria was confirmed through microscopic examination of thick and thin blood films stained with Giemsa stain for malaria parasites, along with Histidine-Rich Protein 2 (HRP2) antigen testing. Once malaria was confirmed, complete blood count (CBC) analysis was performed using an automated cell counter. All malaria-positive smears were reviewed to confirm *P. vivax* infection and to record platelet counts and other haematological parameters, including anaemia. The parasitic load was determined by calculating the "parasitic index," defined as the percentage of infected erythrocytes on a stained thin blood film (e.g., 1% parasitaemia).

Clinical Evaluation: In addition to history-taking, each patient underwent a thorough clinical examination with particular attention to symptoms and signs suggestive of central nervous system (CNS) involvement. These included:

- Seizures
- Altered level of consciousness
- Cranial nerve involvement
- Speech disturbances
- Movement disorders
- Meningeal signs
- Cerebellar signs
- Signs of raised intracranial pressure
- Abnormal posturing
- Abnormal reflexes

All patients exhibiting CNS manifestations were evaluated for parasitic load to assess the association between CNS involvement and severity of parasitaemia.

Inclusion Criteria

1. Paediatric patients aged 1–13 years with *P. vivax* positive in blood investigation reports.
2. Paediatric patients aged 1–13 years with both *P. vivax* and *P. falciparum* positive in blood investigation reports.

Exclusion Criteria

1. Paediatric patients with CNS manifestations and *P. falciparum* positivity in blood investigation reports.
2. Paediatric patients with haematological abnormalities and *P. falciparum* positivity in blood investigation reports.

Data Analysis: Data were collected, compiled, and analysed using SPSS version 17. Descriptive statistics, Chi-square test, and Pearson correlation coefficient were applied to study associations between CNS manifestations, haematological abnormalities, and parasitic load.

Treatment Protocol: All admitted patients received routine treatment as indicated, along with anti-malarial therapy in accordance with institutional protocol and classification of P. vivax malaria. Study objectives and procedures were explained to parents/guardians in their local language prior to obtaining written informed consent.

RESULTS

In the present study, the majority of Plasmodium vivax malaria cases occurred in the 5–13-year age group, whereas younger children (<5 years) accounted for a smaller proportion (Table 1). Male patients constituted a higher proportion of the total cases compared to females. [Table 1]

Table 1: Distribution of Plasmodium vivax Malaria Cases by Age Group and Gender

Variable	n	%
Age group		
Under 5 years	31	31%
5–13 years	69	69%
Gender		
Male	62	62%
Female	38	38%
Total	100	100%

Analysis of the parasitic index (PI) distribution revealed that most patients exhibited a PI of less than 1, with progressively fewer cases in the higher severity categories. [Table 2]

Table 2: Parasitic Index Severity Distribution

Parasitic Index severity	< 1	1 to 1.5	1.5 to 2	> 2
Distribution	71(71%)	20(20%)	4(4%)	5(5%)

CNS involvement was observed in a small subset of patients. Among those with CNS manifestations, higher PI values (≥1.5) were more frequent, while patients without CNS involvement predominantly had a PI of less than 1 (Table 3, Figure 1). Out of 100 patients only 8 patients presented with CNS involvement clinical features. Out of them 6 (75%) patients had Parasitic Index more than 1.5. Among them 3(37.5%) patients had High range of P.I., Index which was more than 2. How ever Out of 92 patients with No CNS involvement,3(3%) patients had P.I. more than >1.5. Total 5 patients had higher range P.I. > 2 out of which 3(60%) patients had CNS manifestation which shows strong association. When we have applied statistics we can say that Chi square value is 47.2 and P value is 0.00001 (Significant) which is less than 0.05 showing strong association between CNS Involvement and degree of Parasitic Index.

Table 3: CNS manifestation and Parasitic Index

	Total Cases	< 1	1 to 1.5	1.5 to 2	> 2
CNS involvement	8	1(12.5%)	1(12.5%)	3(37.5%)	3(37.5%)
No CNS Involvement	92	70(76.5%)	19(20.5%)	1(0.9%)	2(2.1%)
Total	100	71(71%)	20(20%)	4(4%)	5(5%)

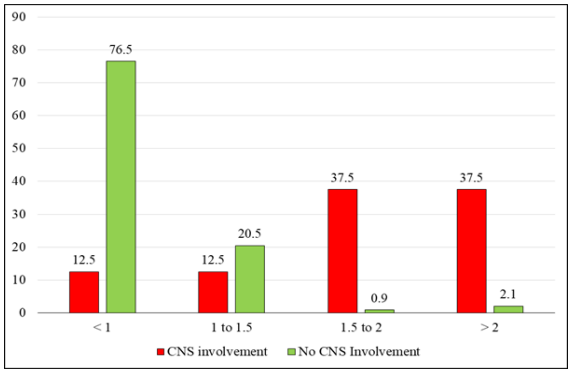

Figure 1: CNS manifestation and Parasitic Index

DISCUSSION

Our study provides compelling evidence of CNS manifestations in pediatric patients with Plasmodium vivax malaria, highlighting a significant association between elevated parasitemia and the occurrence of neurological symptoms. These findings challenge the traditional view of P. vivax as a benign pathogen and underscore the necessity for heightened clinical vigilance in endemic regions.

The observed prevalence of CNS involvement in 8% of our cohort aligns with recent studies indicating that P. vivax can cause severe neurological complications, including seizures, altered consciousness, and movement disorders, particularly in children.[7] Notably, a substantial proportion (75%) of these cases had a parasitic index exceeding 1.5%, suggesting a dose-dependent relationship between parasitemia levels and the severity of CNS manifestations. This association is consistent with findings from other studies that have reported increased severity of P. vivax infections with higher parasitemia levels.[8-10]

The pathophysiology underlying P. vivax-induced CNS involvement remains incompletely understood. Unlike P. falciparum, P. vivax does not typically cause sequestration of infected erythrocytes in the brain. However, recent research suggests that P. vivax may lead to neurological complications through mechanisms such as ischemic strokes and inflammatory responses. Additionally, studies have implicated alterations in neurotransmitter systems, including glutamate and dopamine pathways, in the development of cerebral malaria.[11-14]

Our findings emphasize the importance of considering P. vivax as a potential cause of severe malaria in children, particularly in regions where both P. vivax and P. falciparum co-circulate. Clinicians should maintain a high index of suspicion for CNS involvement in pediatric patients with high parasitemia levels, regardless of the species involved. Further research is warranted to elucidate the precise mechanisms by which P. vivax induces neurological complications and to develop targeted therapeutic strategies.

CONCLUSION

This study demonstrates that Plasmodium vivax malaria in pediatric patients can result in significant CNS manifestations, particularly in those with higher parasitemia levels. The observed strong correlation between elevated parasitic index and CNS involvement highlights the importance of early recognition and close monitoring of children with high parasitemia. These findings challenge the traditional perception of P. vivax as a benign infection and emphasize the need for clinicians to consider the risk of severe neurological complications in pediatric malaria management. Prompt diagnosis, appropriate antimalarial therapy,

and careful neurological assessment are essential to reduce morbidity and improve outcomes in this population.

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