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FREQUENCY OF RELAPSE OF MALARIA IN CHILDREN PRESENTING WITHPLASMODIUM VIVAX AT GHULAM MUHAMMAD MAHAR MEDICALCOLLEGE HOSPITAL SUKKUR

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Abstract

Objective: *To determine the frequency of relapse of malaria in children presenting with Plasmodium Vivax malaria, Sukkur.*

Methods: *This was a cross-sectional study conducted at the Department of Pediatric Medicine, Ghulam Muhammad Mahar Medical College (GMC), Sukkur, from September 1st, 2024, to February 28th, 2025, using a non-probability consecutive sampling technique. Children aged 2 to 16 years of either sex with confirmed Plasmodium vivax malaria were included. Exclusion criteria were respiratory infections (cough, runny nose, fever >100°F), gastroenteritis (more than three loose stools or vomiting over five episodes daily), enteric fever (fever >7 days or positive culture), and measles (cough, coryza, conjunctivitis, and rash starting on face). After approval from the College of Physicians and Surgeons Pakistan, informed consent was obtained from parents. Demographic data (age, gender, residence) were collected. Confirmed cases received chloroquine 25 mg/kg orally once daily for three days. Patients were followed to identify relapse per operational definition. Clinical, sociodemographic, geographic, and socioeconomic data were recorded using a standardized proforma. Strict exclusion criteria helped minimize bias.*

Results: *Out of 130 children presenting with Plasmodium vivax malaria, 87 (66.9%) were male and 43 (33.1%) were female, indicating a higher prevalence among males. The mean age was 8.63 ± 4.18 years, with mean weight 26.12 ± 10.52 kg, height 117.12 ± 19.12 cm, and BMI 18.01 ± 1.85 kg/m². Most children, 107 (82.3%), were from rural areas, highlighting a higher burden in these regions. The relapse frequency was 25 cases (19.2%), with 105 children (80.8%) not experiencing relapse. Clinically, chills and shivering were most common (90.8%), followed by headache (49.2%) and vomiting (15.4%). Maternal education levels varied, with 24.6% primary, 30.8% secondary, 17.7% matriculation, 14.6% intermediate, and 12.3% graduates. A significant*

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association was found between gender and relapse (p=0.025), with females relapsing more (30.2%) than males (13.8%). Relapse was also significantly linked to rural residence (p=0.046), with 24 of 25 relapses in rural children. Maternal education showed a non-significant trend toward higher relapse in lower education levels (p=0.176; linear trend p=0.042). No association was found between age and relapse (p=0.484). Mean illness duration was 4.09 ± 1.56 days.

Conclusion: *The study emphasizes the complexity of interactions between gender, geography, and sociodemographic variables when considering the so-called malaria relapse in children with P. vivax. The findings claim the need for gender-specific studies, rural-based intervention, and community education in order to enhance the prevention and control of relapse and ultimately have better malaria control in the endemic regions.*

INTRODUCTION

Plasmodium vivax is a malaria parasite that still poses a grave threat to the health of children in most of the endemic regions in the world. As opposed to P. falciparum, the P. vivax can remain in the liver as hypnozoites, which are reactivated by weeks or months below the initial infection (1). The dormant forms result in clinical relapses, which not only contribute to the increased burden of disease but also perpetuate disease cycles within communities. It is particularly problematic in children, who have less developed immune systems and are more susceptible to recurrent infections and the chronic problems that may be a result of repeated malaria episodes (2).

The rate of relapse in P. vivax malaria depends upon a number of factors, such as geographic location, parasite strain, host immunity, and treatment practice. In tropical areas with the most frequent-relapsing strains, children can develop a relapse within three to four weeks of the initial infection, and they can also have more than one relapse unless the dormant liver stages are properly eliminated (3). Childhood re-occurrences are particularly due to a biological tendency, and increased exposure. Children in malaria endemics are likely to form a massive proportion of the infected group and may undergo recurring clinical episodes that significantly hamper their physical growth, mental functioning, and quality of life (4).

The percentage of P. vivax infections, not responding to radical treatment (no cure) and thus relapsing, has an estimated global distribution with a large variability of values, ranging between 20-80%, depending on local transmission patterns and access to healthcare (5). These statistics underline the severe risk of relapses to malaria control measures, particularly in low-resource contexts in which a lack or uneven access to full treatment courses, including primaquine or tafenoquine, is an issue (6). A dormant liver-stage infection may result in recurrent symptomatic disease even when initial treatment eliminates the infection in the bloodstream. In the case of children, it implies that a single bite by a mosquito can lead to many instances of illness in months, which in turn leads to severe anemia, school absenteeism, malnutrition, and higher healthcare expenses among the families (7).

However, in the case of Pakistan, P. vivax has contributed to most cases of malaria and, as such, it is the dominant species in most provinces. At the national level, data on malaria cases show that about 79% of all reported cases of malaria in the country are caused by the P. vivax form, with the other 21%, made up of P. falciparum and mixed infections (8). The consequences of this P. vivax predominance can be very serious in relation to the pediatric population, as children are typically the most frequently infected group, as well as the most affected by frequent attacks. The burden is huge, especially among the rural and underserved communities where diagnosis, treatment, and follow-up are not timely (9).

Although no specific studies quantify the rate of relapse among Pakistani children, the information on the subject in various regional medical facilities is useful. Some studies have reported relapse rates of around 5-7 % within the short term (i.e., 28-90 days) of children who have undergone a standard regimen (e.g., chloroquine and primaquine) in places such as Punjab and also in Khyber Pakhtunkhwa (10). Nevertheless, these statistics are probably

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underestimated since relapses that take place after the study periods or because of poor adherence to primaquine are not always registered. In addition, other issues like low adherence to the 14-day course of the primaquine regimen, ignorance of the caregivers, and failure to conduct regular glucose-6-phosphate dehydrogenase (G6PD) screening, complex effective radical curing (11).

It is worth mentioning that the relapse rates are cumulative. In short-term studies, the frequency of relapse may be relatively slight; however, when children are studied over a period of six months to one year, the cumulative risk of relapse is higher. According to international data, as many as 50% of all children infected with P. vivax can have at least one relapse in one year unless they receive total and effective treatment. With the high rate of P. vivax in Pakistan, even with liberal estimates, thousands of children are at risk of relapse every year, especially in regions where healthcare access is minimal or where antimalarial drug resistance is developing (12).

Another challenge is the systemic issues, including delays in diagnosis, unsteady regimes of treatment, inadequate community education, and logistical challenges in offering supervised radical cure. Children who live in remote or war-affected regions are more likely to fall through the cracks and are the victims of recurring episodes, yet never receive any definitive treatment. Any untreated relapse not only harms the specific child but also serves as a storage of further transmission into the greater population (13).

METHODOLOGY:

This was a cross-sectional study conducted at the Department of Pediatric Medicine, Ghulam Muhammad Mahar Medical College (GMC), Sukkur, from 1st September 2024 to 28th February 2025, using a non-probability consecutive sampling technique. Children aged 2 to 16 years, of either sex, presenting with confirmed Plasmodium vivax malaria as per the operational definition were included. Children with respiratory tract infections (cough, runny nose, fever >100°F), gastroenteritis (more than three loose watery stools per day or vomiting over five episodes per day), enteric fever (fever lasting more than seven days or culture positive), and measles (cough, coryza, conjunctivitis, and maculopapular rash starting on the face and spreading downward) were excluded. Approval was obtained from the College of Physicians and Surgeons Pakistan before enrollment. All eligible patients presenting to the department were enrolled after informed written consent was taken from their parents. Demographic data including age, gender, and place of residence were collected through a brief history from the parents. Confirmed P. vivax cases were treated with chloroquine therapy for three days at a dose of 25 mg/kg body weight orally once daily. Patients were followed during and after treatment to identify relapse cases according to the operational definition. Clinical, sociodemographic, geographical, and socioeconomic data were recorded using a standardized proforma. Strict adherence to exclusion criteria was maintained to reduce bias and ensure reliability of findings.

RESULTS:

Out of 130 children presenting with Plasmodium vivax malaria, 87 (66.9%) were male and 43 (33.1%) were female, indicating a higher prevalence among male children in the study population. The mean age of the children was **8.63 ± 4.18 years**, with a mean weight of **26.12 ± 10.52 kg** and a mean height of **117.12 ± 19.12 cm**. Additionally, the mean Body Mass Index (BMI) of the children was **18.01 ± 1.85 kg/m^2 (Table 1).**

In terms of place of residence, a majority of the children **107 (82.3%)** were from rural areas, while only **23 (17.7%)** were from urban settings, highlighting a significantly higher burden of P. vivax malaria among children living in rural regions.

In our study, the frequency of relapse of malaria in children presenting with Plasmodium vivax malaria was **25 cases (19.2%),** while **105 children (80.8%)** did not experience a relapse **(Table 1).**

Clinical manifestations were also assessed in this study population. **Chills and shivering** were the most commonly reported symptom, observed in **118 children (90.8%). Headache** was present in **64 children (49.2%)**, while **vomiting** was reported in only **20 children (15.4%)**. These findings suggest that chills and shivering are the predominant presenting symptoms in children with Plasmodium vivax malaria, followed by headache and, to a lesser extent, vomiting.

Maternal level of education was also recorded as a sociodemographic factor. Among the mothers, **32 (24.6%)** had received primary education, **40 (30.8%)**

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had secondary education, and **23 (17.7%)** had completed matriculation. Additionally, **19 (14.6%)** had attained intermediate education, while **16 (12.3%)** were graduates **(Table 1).**

Table 1. Socio-demographic characteristics, anthropometric measurements, and clinical features of the study participants (n = 130)

Socio-Demographics	**N (%) / Mean ± SD Total=130**
Gender	
Male	87 (66.9%)
Female	43 (33.1%)
Anthropometric measurements	
Age (in years)	8.63 ± 4.18
Weight (in kg)	26.12 ± 10.52
Height (in cm)	117.12 ± 19.12
BMI (kg/m²)	18.01 ± 1.85
Residential status	
Urban	107 (82.3%)
Rural	23 (17.7%)
Relapse of Malaria	
Yes	25 (19.2%)
No	105 (80.8%)
Clinical Symptoms	
Chills/Shivering	118 (90.8%)
Headache	64 (49.2%)
Vomiting	20 (15.4%)
Parental Education Level	
Primary	32 (24.6%)
Secondary	40 (30.8%)
Matriculation	23 (17.7%)
Intermediate	19 (14.6%)
Graduate	16 (12.3%)

A chi-square test was conducted to examine the association between gender and malaria relapse. The results showed a statistically significant association ($p = 0.025$), with relapse occurring more frequently among female children (30.2%) compared to males (13.8%). Fisher's Exact Test further confirmed this association ($p = 0.034$) **(Table 2).**

Similarly, a significant association was found between place of residence and relapse ($p = 0.046$), with the vast majority of relapse cases (24 out of 25) occurring among children from rural areas. Although the continuity correction and Fisher's Exact Test were slightly above traditional significance thresholds ($p = 0.088$ and $p = 0.076$, respectively), the likelihood ratio and linear-by-linear association supported a meaningful relationship.

When examining the association between maternal level of education and relapse, no statistically significant relationship was found overall ($p = 0.176$). However, a trend was observed through the linear-by-linear association ($p = 0.042$), suggesting that lower levels of maternal education might be associated with higher relapse rates, although this did not reach statistical significance in the full model **(Table 2).**

A chi-square test was conducted to assess the association between age category and malaria relapse.

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The results showed no statistically significant association between age groups and relapse (p = 0.484). This indicates that the likelihood of malaria relapse did not differ significantly across the age Finally, the mean duration of illness among children presenting with Plasmodium vivax malaria in our study was found to be **4.09 ± 1.56 days (Figure 1).**

categories of 2-5 years, 6-12 years, and 13-16 years in this study population **(Table 2).**

Table 2. Association between socio-demographic variables and malaria relapse among study participants (n = 130)

Variables	Categories	Relapse		P-value
		Yes (n = 25)	No (n = 105)	
Gender	Male	12 (48.0%)	75 (71.4%)	0.025 *
	Female	13 (52.0%)	30 (28.6%)	
Place of Residence	Urban	1 (4.0%)	22 (21.0%)	0.046 *
	Rural	24 (96.0%)	83 (79.0%)	
Age Distribution	2–5 years	9 (36.0%)	27 (25.7%)	0.484
	6–12 years	12 (48.0%)	52 (49.5%)	
	13–16 years	4 (16.0%)	26 (24.8%)	
Maternal Education	Primary	4 (16.0%)	28 (26.7%)	0.176
	Secondary	5 (20.0%)	35 (33.3%)	
	Matriculation	5 (20.0%)	18 (17.1%)	
	Intermediate	7 (28.0%)	12 (11.4%)	
	Graduate	4 (16.0%)	12 (11.4%)	

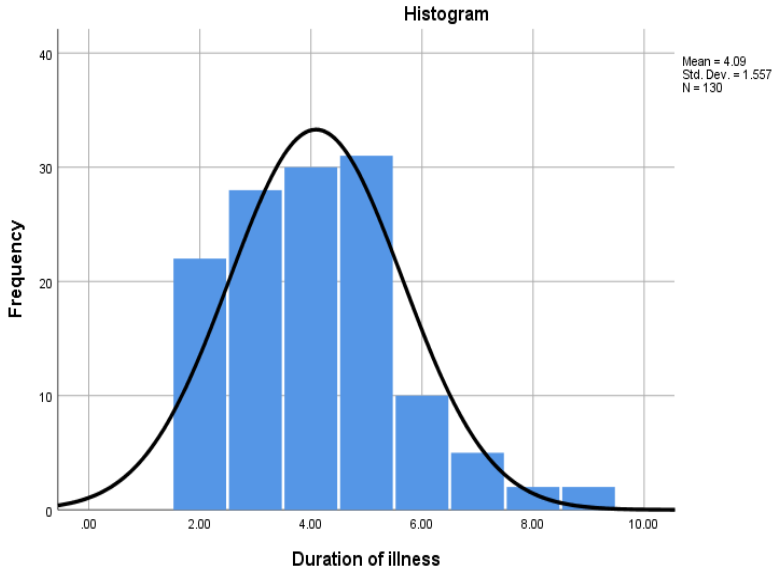


Figure 1. Mean duration of illness children present with Plasmodium Vivax

DISCUSSION:

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This study was an endeavor to determine the relapse of malaria in children who report with Plasmodium vivax infection, which is an extremely crucial component of malaria epidemiology that is challenging to treat and limit its transmission. An understanding of the demographic, clinical, and sociodemographic profile of P. vivax relapse is essential to the development of effective interventions and the reduction of the disease burden in susceptible population groups of children.

Another characteristic of malaria is that P. vivax is more widespread among male children (66.9%), which is in line with the already existing epidemiological after effects that the sex of Males has a high risk of exposure due to their behavioral and environmental characteristics (14). Interestingly, even though males were infected more often, the relapse was significantly more common among females (30.2% vs. 13.8% p=0.025), which is reflective of the fact that the genders had biological or immunological differences regarding the recurrence of the parasite, as postulated by Ye C et al. in 2023 (15). This difference in the prevalence of relapse between the genders should be further studied on the hormonal and immune responses differences between the two sexes.

The average age of the affected children was 8.63 years, which is aligned with age groups that have been identified to be more susceptible to malaria because of the development of immunity (WHO, 2023). It is important to note that the age category did not have any significant effects on relapse (p=0.484), which is consistent with the results of Lee JA et al. study that established parasite biology or host factors as possible contributors to relapse (16).

There were normal average weight, height, and BMI, which indicate generally good nutritional condition, which is a significant factor since malnutrition may affect malaria susceptibility and severity (17). The possible impact of nutrition in the process of relapse is yet to be explained.

The unequal P. vivax malaria burden in the rural setting is reflected in the rural-based cases (82.3% cases) and relapses (24 out of 25 relapses) (p=0.046). The findings are backed up by the existing literature that has identified rural communities as malaria foci due to their environmental and socioeconomic factors, such as poor healthcare services and control of vectors (18). The overall trend is rather clear and, in fact, shows that a set of special malaria control measures among rural populations is needed, except for some marginal p-values.

Chills and shivering (90.8%) were the most frequent, followed by headache and vomiting, which is also a typical P. vivax symptom reported in the literature. The symptoms can be useful in the early diagnosis and therapy, which is important in reducing the complications and the risk of relapse (19).

Mother's education, which is a very crucial social determinant of child health, had no significant direct relationship with malaria relapse (p=0.176). However, the linear trend (p=0.042) shows that reduced maternal education may be a risk factor in the case of relapses indirectly by affecting health literacy and treatment adherence, which is also consistent with Masuda K et al. in the year 2020 (20). Malaria control interventions may thus include increased maternal education.

The observed relapse rate (19.2%) is also in line with the global estimates, reflecting the challenge in dealing with hypnozoites, which is latent in P. vivax malaria. The brief illness of no more than four days indicates the acute clinical burden and the necessity to introduce effective treatment plans as soon as possible to reduce the morbidity and interrupt the transmission (21).

CONCLUSION:

The study highlights the sophistication of interaction between gender, geographic, and sociodemographic factors as regards to malaria relapse among P. vivax children. The findings indicate that gender-specific interventions, rural-based interventions, and community-based education are important to enhance prevention and control of relapse and eventually to achieve better malaria control in the endemic areas. Furthermore, one can also integrate culturally sensitive strategies, which will be inclined to the issues of the local beliefs, differences in access to healthcare, and gender relations, to make these interventions more effective. Perhaps the most important step to lighten the burden of relapse in the context of sustaining long-term malaria control efforts is when health messages and treatment are customized based on the unique vulnerabilities of boys and girls in rural and low-income regions.

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