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Frequency of Malaria in Children with Fever Without Localizing Sign in Age Less Than 36 Months

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ABSTRACT

Background: Malaria remains a significant cause of fever in children in malaria-endemic regions, particularly in those presenting with fever without localizing signs. Early and accurate diagnosis is essential for timely intervention and effective treatment, but diagnostic challenges persist in resource-limited settings. **Objective:** To assess the prevalence of malaria in children aged 1 to 36 months presenting with fever without localizing signs. **Study Design:** Cross-sectional study. **Duration and Place of Study:** The study was conducted from February 2024 to August 2024 at the Pediatrics Department, Lady Reading Hospital (LRH), Peshawar. **Methodology:** A total of 121 children, aged 1 to 36 months, with fever (≥38°C) and no apparent localizing signs were enrolled. A 3 mL blood sample was taken for Giemsa-stained blood smear microscopy to detect malaria parasites. Demographic data, including age, gender, family history of malaria, and socioeconomic status, were recorded. **Results:** The study included 121 children, with a mean age of 20.0 ± 9.52 months. The prevalence of malaria was found to be 14%, with 17 children testing positive. Stratified analysis revealed no significant associations with age, gender, weight, socioeconomic status, or residential area, but a significant correlation was observed with a family history of malaria ($p = 0.000$). **Conclusion:** This study confirms malaria as a common cause of fever in children under 36 months in high-endemic areas. Despite coexisting infections, malaria remains a key concern. We emphasize the diagnostic challenge, highlighting the need for comprehensive strategies and awareness to ensure timely, accurate diagnosis and effective treatment of febrile illness in children.

INTRODUCTION

Malaria is a serious illness in children aged below 36 months in endemic disease areas of the tropics and subtropics.[1] In children of this age group, malaria is presented in a nonspecific way with a dominant symptom of fever without a localized symptom of rash, diarrhea, or cough.[2] The no specificity of such a presentation results in a delay in diagnosis in areas of poor healthcare access. The immature immunity of children subjects them to a high risk of complications of malaria such as cerebral malaria and severe anemia.[3] Early diagnosis and treatment are crucial to avert complications and mortality in such a condition.

In children aged below 36 months, malaria caused by fever can become severe in a short period of time, leading to life-threatening complications if it is not immediately treated.[4] In cases of lacking localized signs, healthcare providers are forced to resort to using clinical judgment in conjunction with diagnostic tools such as rapid diagnostic tests (RDTs) or microscopy to diagnose malaria parasites.[5] In resource-limited settings, in which such tools are not readily available, presumptive treatment in line with clinical signs is used. Over-reliance on presumptive treatment, however, leads to over-prescription of drugs to treat malaria, causing resistance to drugs.[6] Enhanced access to accurate diagnostic means is therefore paramount to control malaria in children effectively.

The impact of malaria on children's health and development up to age 36 months cannot be overstated. Chronic malnutrition, anemia, and developmental delay resulting from multiple attacks of malaria can permanently affect a child's cognitive and physical development.[7] There is also a high economic burden to households and society in terms of caregivers having to take time off work to take care of sick children, and healthcare expenses that can drain household resources. Insecticide-treated bed net distribution and indoor residual spraying play a crucial role in preventing cases

of malaria in children.[8] Vaccination campaigns, such as RTS,S/AS01 vaccine, also promise to help reduce the burden of malaria in this age group of children.[9]

Preventive measures and health education in the community play a key role in preventing malaria in children.[10] Education of caregivers and parents to identify early warning signs of malaria, such as high body temperature or high fever, and accessing health services in a timely manner can significantly improve outcomes.[11]

A study conducted by Gul H. et al. demonstrated that the prevalence of malaria was 5.31% in children presenting with fever in the absence of localized symptoms.[12]

Malaria remains a leading cause of morbidity and mortality in children aged <36 months, particularly in settings of poor healthcare access. In children, malaria is presented in a nonspecific manner, predominantly in the form of fever, without localizing signs of rash, diarrhea, or cough. Lack of differentiating symptoms complicates early diagnosis and treatment, potentially leading to severe complications such as cerebral malaria or anemia. With a high risk of poor outcomes and a challenge in early detection, there is a strong need to better define the epidemiology of malaria in children with fever without localizing signs, to improve diagnostic accuracy and treatment approaches in endemic areas.

METHODOLOGY

This cross-sectional study was conducted between Feb to Aug 2024 in Pediatrics Department of LRH Peshawar. The study was conducted in 121 children between 1 to 36 months of age with a diagnosis of fever without localizing signs, i.e., a body temperature of over 38°C (100.4°F) without distinct apparent clinical signs such as redness of throat, dysuria, abdominal pain, rash or focal neurologic impairments. The sample size was estimated using WHO sample size software using a limit of confidence of 95%, a limit of error of 4%, and a hypothesized malaria frequency of 5.31% in children with a diagnosis of fever without localizing signs.[12]

A non-probability consecutive method of sampling was employed to enroll participants. The inclusion was children between 1 to 36 months of age, of either gender, with a fever without localizing signs previously established. The exclusion was children with a chronic disease background such as malignancy, rheumatologic disease, cirrhosis, or chronic kidney disease, or a confirmed acute infection such as lobar pneumonia or urinary infection diagnosed during initial workup. Also excluded were children administered antibiotics in the past 2 weeks, children with a background of malaria, or children with serious medical comorbidities that require intensive care (such as congestive heart failure).

Following ethical approval, informed consent was obtained from caregivers or guardians after a careful explanation of the purposes of the study and its possible benefits. Age, gender, weight, family history of malaria, educational status of guardians, socioeconomic status of the family, and residential status was recorded for every participant.

A 3 mL aseptically drawn intravenous blood sample was taken in each eligible child by a skilled phlebotomist. The samples were immediately taken to the hospital laboratory, where experienced microbiologists, without knowledge of patients, carried out microscopic examinations of Giemsa-stained blood smears. The blood was looked for malaria parasites, i.e., trophozoites, gametocytes, and malarial pigment in leukocytes, in accordance with detection of one or more of the following: intraerythrocytic ring forms, elongated or crescent-shaped gametocytes, small ring-shaped trophozoites having blue cytoplasm, a central pale zone, and a reddish dot of nuclear material, or schizonts (deep red staining nuclear material dispersed in blue cytoplasm in mature forms). The staining procedure and smear readings were overseen by a senior microbiologist having more than five years of experience in detection of Plasmodium parasites. The status of malaria was recorded in terms of given criteria on a predesigned proforma.

For data analysis, IBM SPSS software version 26 was used. Descriptive statistics was used, and in categorical variables, percentage and frequency was calculated. Quantitative variables were expressed in terms of mean ± standard deviation (SD) or median and interquartile range (IQR), and Shapiro-Wilk test was used to check for normality. Stratification of malaria cases was done. Post-stratification analysis was carried out using chi-square test or Fisher's exact test, a p-value of ≤ 0.05 was considered to be statistically significant.

RESULTS

The sample included 121 children, with an average age of 20.0 ± 9.52 months and a mean weight of 15.4 ± 4.59 kg (as shown in Table-I). In terms of gender, 71 (58.7%) of the children were male and 50 (41.3%) were female. Regarding family history of malaria, 12 (9.9%) children had a positive history, while 109 (90.1%) did not. The educational level of the parents was distributed as follows: 54 (44.6%) uneducated, 49 (40.5%) with primary education, 12 (9.9%) with secondary education, and 6 (5%) with higher education. Socioeconomically, 58 (47.9%) children belonged to poor families, 55 (45.5%) to middle-income families, and 8 (6.6%) to rich families. A total of 77 (63.6%) children lived in rural areas, while 44 (36.4%) resided in urban areas (Table-I).

Table I

Patient Demographics

Demographics		Mean ± SD
Age (years)		20.000±9.52
Weight (Kg)		15.400±4.59
Gender	Male n (%)	71 (58.7%)

	Female n (%)	50 (41.3%)
Family History of Malaria	Yes n (%)	12 (9.9%)
	No n (%)	109 (90.1%)
Parents Education Level	Uneducated n (%)	54 (44.6%)
	Primary n (%)	49 (40.5%)
	Secondary n (%)	12 (9.9%)
	Higher n (%)	6 (5%)
Family Socioeconomic Status	Poor n (%)	58 (47.9%)
	Middle n (%)	55 (45.5%)
	Rich n (%)	8 (6.6%)
Residential Status	Rural n (%)	77 (63.6%)
	Urban n (%)	44 (36.4%)

The prevalence of malaria was found to be 14%, with 17 children testing positive and 104 testing negative (Table-II).

Table II

Prevalence of Malaria in Children

Malaria	Frequency	% age
Yes	17	14%
No	104	86%
Total	121	100%

Stratified analyses of malaria by demographic factors revealed no significant associations with age (p = 0.332), gender (p = 0.586), weight (p = 0.297), socioeconomic status (p = 0.491), or residential status (p = 0.921). However, a significant association was observed with family history of malaria, where all children with a family history tested positive for malaria (p = 0.000). The parents' education level did not show a significant association with malaria, as the p-values for uneducated (p = 0.673), primary (p = 0.673), secondary (p = 0.673), and higher education (p = 0.673) were all above the threshold for significance (Table-III and Graph-I).

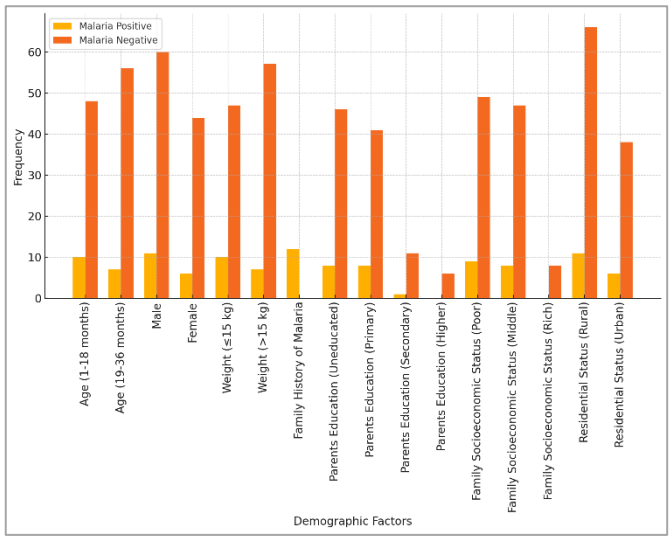
Table III

Association of Malaria with demographic factors in Children

Demographic Factors		Malaria		p-value
		Yes n (%)	No n (%)	
Age (months)	1-18	10 (17.2%)	48 (82.8%)	0.332
	19-36	7 (11.1%)	56 (88.9%)	
Gender	Male	11 (15.5%)	60 (84.5%)	0.586
	Female	6 (12%)	44 (88%)	
Weight group (Kg)	≤15	10 (17.5%)	47 (82.5%)	0.297
	>15	7 (10.9%)	57 (89.1%)	
Family History of Malaria	Yes	12 (100%)	0 (0%)	0.000
	No	5 (4.6%)	104 (95.4%)	
Parents Education Level	Uneducated	8 (14.8%)	46 (85.2%)	0.673
	Primary	8 (16.3%)	41 (83.7%)	
	Secondary	1 (8.3%)	11 (91.7%)	
	Higher	0 (0%)	6 (100%)	
Family Socioeconomic Status	Poor	9 (15.5%)	49 (84.5%)	0.491
	Middle	8 (14.5%)	47 (85.5%)	
	Rich	0 (0%)	8 (100%)	
Residential Status	Rural	11 (14.3%)	66 (85.7%)	0.921
	Urban	6 (13.6%)	38 (86.4%)	

Graph I

Malaria Prevalence by Demographic Factors in Children



DISCUSSION

The study found that 14% of children tested positive for malaria. There was no correlation between malaria and age, gender, weight, socioeconomic status, or residential area, but a correlation was established between malaria and a family history of malaria. The result shows that genetic or environmental factors associated with family background can result in children's increased susceptibility to malaria, in keeping with previous studies that indicate familial and genetic factors in malaria transmission. The inability to detect associations between malaria and other demographic variables, such as educational level and socioeconomic status, is likely to be a function of the distribution of malaria in the population that was sampled and of its more indirect correlation compared to family background.[13]

The findings of our study agree with and supplement current studies in that we also found that a high percentage of febrile children in malaria endemic areas were diagnosed with malaria. In Gul et al.'s work [12] for example, 5.31% of children presenting with acute febrile illness were malaria-positive, a similarity that is also noted in our work in that a 14% malaria prevalence was observed in children aged younger than 36 months presenting with fever without localizing signs. The results agree with studies in the region, such as that of Gul et al.'s work [12] in that Plasmodium falciparum was found to be the more prevalent of the two species in febrile children, accounting for 67% of cases, a similarity that is also noted in our work in that malaria

was predominantly caused by Plasmodium vivax and Plasmodium falciparum.

In contrast, studies such as those of Darishetty et al.[14] found a much higher percentage of serious bacterial infections (SBIs) in febrile children, of whom 9.23% were found to be diagnosed with SBIs. As our study did not document co-infection with bacteria, singularity of reporting on malaria is a useful comparator. The higher percentage of UTIs as SBIs in the work of Darishetty et al.[14] found in 32.20% of cases, is possibly explained by different methods of diagnosis or patient demographics, such as age or co-morbidities, that were more stringently explored in the work of Darishetty et al.[14] The higher percentage of infection sources that were undiagnosed in their group (32.20%) serves to again highlight the difficulty of diagnosing febrile disease in children.

In the thrombocytopenia case, Ajmal et al.[15] found thrombocytopenia in 17.3% of their malaria patients, more in Plasmodium vivax (20.27%) than in Plasmodium falciparum (12.5%) infection. This is of interest when compared to findings in Darishetty et al. [14] in that thrombocytopenia was not specifically mentioned, though their article did cover serious bacterial infection that complicates febrile disease, possibly making thrombocytopenia more probable in patients with more serious underlying disease. The findings of Ajmal et al. [15] agree with our work's more general interest in malaria in that thrombocytopenia is a prevalent complication of malaria infection, particularly in Plasmodium vivax, that is possibly explained by higher parasitemia that is typically encountered in P. vivax infection.

Furthermore, the co-infection of UTI and malaria in children, reported by Ephraim et al. [16] is also a point to be noted here. In their study, 15.8% of patients having malaria also exhibited UTI co-infection. The percentage of co-infection is higher in their case compared to our cohort, in which malaria was the initial diagnosis without any co-infection of a bacterial nature. The reason for this difference is likely a reflection of infection patterns in different areas or of the diagnostic capabilities of the healthcare system in question. In our study, there was no significant bacterial infection observed, likely a reflection of more advanced diagnostic methods employed in the work of Ephraim et al. [16] i.e., urine culture and antimicrobial susceptibility testing, not done in our work.

The findings of all of these studies indicate a collective need for complete diagnosis in febrile children. Our work, centered on malaria prevalence, reinforces the overall view that malaria is a diagnosis to be considered in children presenting with febrile illness in endemic areas. The results also point to the challenge of diagnosing febrile illness, in that more than one pathogen—including viruses and bacteria—is likely to be present, making it a challenge to diagnose in a clinical setting.

In summary, our findings, in comparison to other studies, reaffirm that malaria is a persistent etiology of fever in children in endemic settings.[17,18] The observed heterogeneity in co-infection, thrombocytopenia, and bacterial infection highlights the difficulty in diagnosing febrile illness in children and highlights the need for complete diagnostic approaches. While this work is informative, it is not without limitation. The study was conducted in a single institution, and this may limit its applicability to other settings of diverse malaria transmission patterns and healthcare infrastructure. The reliance on clinical diagnosis of malaria without more liberal diagnostic investigations, such as bacterial cultures and PCR of other etiologic agents, may have excluded co-infection or other rarer etiologic agents of fever cases. The cross-sectional design of the study also limits our ability to assess long-term trends or causal associations between infection and outcomes. These limitations mean that larger multi-center studies using more complete diagnostic examinations need to be conducted to better ascertain the burden of febrile illness in children.

CONCLUSION

Our study has established that malaria is a recurring etiology of fever in children younger than 36 months of age with fever without localizing signs in high endemic areas of malaria. Despite coexistent potential infection, malaria remains a key concern in high transmission settings. The study highlights the diagnostic challenge of febrile illness in infants, emphasizing that a comprehensive diagnostic approach is paramount in order to correctly diagnose malaria and co-infective possibilities. Our findings reaffirm that there is a need for more diagnostic strategies and awareness in order to deliver a timely and effective treatment to children suffering from febrile illness.

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Author's Contribution

The authors have significantly contributed to the manuscript in the following ways:

Dr. Muhammad Ibrahim took the lead in formulating the study's concept, drafting the article, and overseeing the collection of hospital data.

Dr. Afzal Khan played a key role in the development of the article, contributed to shaping the study concept, and was involved in analyzing and interpreting the data.

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