

Assessing Disease Severity in Children 0 - 2 Years Infected by *P. Falciparum* Post Sulfadoxine-Pyrimethamine in 3 Tertiary Hospitals in Sierra Leone

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ABSTRACT

Background: Malaria is the most important parasitic disease affecting humans in Africa. It is a major cause of anemia in endemic areas such as Sierra Leone. It is one of the indications for blood transfusion. An estimated 90% of deaths as a result of malaria occur in Africa, with more than two-thirds of these being in children aged under 5 years. Most cases were infected with *Plasmodium falciparum*. The aim of this study was to correlate *Plasmodium* parasite density against hemoglobin level in children 0-2 prior administration of S-P.

Methods: This was a cross sectional study conducted across three hospitals in Sierra Leone; Ola During Children Hospital, Kingharman Maternal and Children's Hospital, and Rokupa Government Hospital. The demographic and clinical history of children 0-2 years were collected between September – November 2024 with a total sample of One Hundred and Fifty-Five (155) samples. The participants presented with signs of febrile illness, and blood sample was collected for RDT. Those with positive RDT were followed up for microscopy for malaria parasite and hemoglobin estimation.

Result: There were negative correlations between malaria parasite density and Haemoglobin concentration across the study centers; ODCH ($r=-0.120$, $p=0.346$), KGH ($r=-0.344$, $p=0.022$), RGH ($r=-0.413$, $p=0.004$). These correlations were significant in KGH and RGH centers.

Conclusion: The study highlights that malaria severity in children aged 0–2 years is strongly linked to high parasite density. Early detection and prompt treatment are crucial in reducing anemia and other complications. These findings emphasize the need for improved diagnostic practices and timely interventions to better manage malaria in young children.

KEYWORDS

Malaria, *Plasmodium*, Anemia, Disease severity, Parasite density.

Introduction

Malaria is a life-threatening infectious disease caused by parasites of the genus *Plasmodium*, which are transmitted to humans through the bites of infected female *Anopheles* mosquitoes [1]. Despite significant progress in control and prevention, malaria remains a major global public health challenge where it contributes substantially to morbidity and mortality, particularly in tropical and subtropical regions [2]. An estimated 263 million cases of malaria and 597 000 malaria-related fatalities occurred worldwide in 83 countries in 2023. Furthermore, outside of Africa, the majority of cases are caused by *P. vivax* with the differing distribution relying on a multitude of factors [3].

The burden of malaria worldwide is disproportionately high in the WHO African Region. However, 94% of malaria cases (246 million) and 95% (569 000) of malaria deaths occurred in the WHO African Region in 2023 and approximately 76% of all malaria deaths in the region occurred in children under the age of five particularly in Sierra Leone (health, 2024). Malaria is endemic in Sierra Leone the entire population is at risk of exposure because Sierra Leone is an area of stable malarial endemicity, and most cases were infected with *Plasmodium falciparum* [4]. It's a major threat to the socioeconomic development of Sierra Leoneans with an estimated 7-12 days lost on the average per episode of malaria. It imposes substantial costs on individuals, households and the government.

Sierra Leone, malaria is the leading cause of morbidity, with 95% of the population (6.7 million people) at risk, and it contributes to approximately 14% (131,383) of under-five mortality.

It is estimated that an average of one person (usually a child under 5 years of age) dies every 12 seconds from malaria in Sierra Leone [5]. However, approximately 76% of all malaria deaths in the region occurred in children under the age of five. *Plasmodium falciparum* malaria is a major contributor to childhood anemia in endemic regions due to its destructive impact on red blood cells and suppression of bone marrow function. Children between the ages of 6 and 24 months frequently experience a rapid drop in hemoglobin levels, which can be attributed to both increased transmission of malaria and dietary changes that can result in iron and folate deficits [6]. Around six months of age, when weaning and increased exposure to mosquitoes occur, these barriers start to diminish, making newborns more vulnerable to malaria infections and their sequelae [7]. Incomplete parasite clearance, co-infections (such as helminths), or underlying malnutrition may all have an impact on persistent anaemia in this age range after malaria treatment. These elements raise the chance of death, impair immunity, and cause developmental delays [8].

Methodology

Study Design

This research employs a comparative cross-sectional study in children 0-2 years of age at Ola During Children Hospital (ODCH), King Harman Maternal and Child Health Hospital (KHMCH), and Rokupa Government Hospital (RGH) to examine the disease

severity in positive cases of malaria infestation. The study was conducted during the from July to November 2024.

Study population

The targeted population for this research were Children under the age of two years who visited the ODCH, KHMCH and RGH in the Metropolitan District of Sierra Leone post S-P. A total of One-Hundred and Fifty-Five (155) children were enrolled in this study after doctors' visits. The Inclusion and exclusion criteria were done to eliminate bias by imploring it in this format Children 0-2 years old who have received S-P with clinical manifestations of malaria infestation and have received any form of malaria vaccine. The children attending **ODCH**, **KHMCH**, and **RGH** for postnatal care and disease manifestation of febrile illness. Exclusion criteria: Children 0-2 with complicated illnesses, have had multiple malaria episodes and have been treated with multiple antimalarial drugs.

Parents who failed to give consent for their minors to partake in the study. Participants demographics were sorted out using questionnaire which were answered by either their parents or guardian during the course of this research.

Sampling Strategy and Representativeness

Participants were recruited consecutively from children aged 0 to 2 years attending the three hospitals (ODCH, KHMCH, and RGH) for postnatal care or febrile illness during the study period from July to November 2024.

The study employed purposive sampling to include children who had received Sulfadoxine-Pyrimethamine (S-P) prophylaxis and met the inclusion criteria, ensuring a focus on those at risk for malaria infection in this age group.

To ensure that the sample of 155 children was representative of the under-two population served by each hospital, the selection reflected the proportionate patient load at each facility based on hospital attendance records for children in this age range during the study period. Additionally, demographic characteristics such as age distribution, sex, and clinical presentation were compared with hospital records to confirm similarity with the broader population of children under two years attending these hospitals. This approach minimized selection bias and allowed findings to be generalized to the local under-two population receiving care at the participating hospitals.

Justification of Sample Size

This study included One Hundred and Fifty-Five (155) 0-2 years in total. A precision-based method was used to select the sample size, with the goal of estimating the percentage of children with moderate to severe malaria with a 95% confidence level and a $\pm 8\%$ margin of error. A minimal sample size of about 150 individuals was shown to be adequate to generate accurate estimates, assuming an estimated prevalence of moderate-to-severe malaria of roughly 50% (to allow for maximum variability). This figure also took into consideration the possibility of data loss as a result of incomplete

records or withdrawals. Therefore, it was decided that the final sample of 155 kids was sufficient to achieve the goals of the study.

Sample Collection

Clinical Assessment: Upon enrollment, a detailed clinical examination was conducted, including an assessment of fever, pallor, dizziness, and other signs of malaria and anemia severity.

Venipuncture techniques: A suitable vein was identified, usually in the infant's arm (antecubital vein), hand, or scalp (in very young infants). 2mls of blood was drawn into the collection tubes.

Sample Collection Timing in Connection with S-P Dosing

Blood samples for malaria and hemoglobin testing were taken from children between 0 and 2 years old who came to the hospital with symptoms of fever. All children included in the study had already received at least one dose of Sulfadoxine-Pyrimethamine (S-P) through the national immunization program, which gives S-P at 10 weeks, 14 weeks, and 9 months of age. Because S-P is given based on age, the number of doses each child received depended on how old they were at the time they visited the hospital.

Samples were not taken at a specific number of days after S-P was given instead, the children were tested when they showed signs of illness. The goal was to check how severe the malaria was in children who had previously received S-P. Information about S-P doses was confirmed using the child's health card or by asking their caregiver.

Sample collection and analysis

Sample was collected with the aid of a standard operating procedure (SOP) by trained and qualified phlebotomists using two methods which are the Venipuncture technique and Finger pricking techniques (capillary). Rapid diagnostic testing was carried out on children with clinical symptoms of febrile illness as confirmed prior by clinician. For every positive RDT sample, venous blood sample was implored for thick smear. Additionally, the aim for thick smear was made for parasite density count. Each smear was put to air dry, followed directly by staining using a 15% Giemsa working solution.

Microscopic Examination of blood smears

Microscopic examination of blood film was carried out using the times 100 oil immersion lens for parasite density count. Parasite density count was done by utilizing WHO standard for parasite density count with white cells against the parasite using the following:

Parasite density = number of parasites counted x 8000 white cells/ μL \ number of white cells counted. **We assessed the distribution of parasite density using the Shapiro-Wilk test; because the data were skewed, we applied a log transformation to meet the assumptions of parametric tests.**

Data Analysis

Malaria Diagnosis

Confirmation of malaria infection via blood using RDT and further

malaria test thick and thin smear microscopy.

Hemoglobin Level: Hemoglobin concentration was measured using hemocue to assess Anaemia. Anaemia severity was assessed according to WHO criteria (mild, moderate, severe) according to the varying hemoglobin concentration.

Rationale for Microscopy and Hemoglobin Estimation

Microscopy was performed only on RDT-positive cases to confirm malaria infection and determine parasite density.

This selective approach was chosen to optimize laboratory resources and reduce unnecessary workload, as RDTs serve as a reliable initial screening method for malaria in clinical settings. However, we acknowledge that relying on RDTs alone may miss sub-microscopic infections or non-falciparum species, which is addressed as a study limitation.

Hemoglobin estimation was included to assess the severity of anemia in children with confirmed malaria infection. Since malaria is a known contributor to anemia in young children, measuring hemoglobin levels helped evaluate the clinical impact of infection and classify anemia severity according to WHO criteria (mild, moderate, or severe). This provided a clearer picture of the disease burden beyond parasite presence alone. The results were analyzed using SPSS statistical package.

Ethical clearance

Ethical clearance was obtained for the commencement of this research through the Sierra Leone Ethic Board.

Results

In this chapter, we discuss into the analysis of data collected through cross sectional methods to explore the research questions outlined in earlier chapter. This analysis provides insights into correlations and significant outcome related to malaria and hemoglobin level. The results are discussed in relation to the study objectives and the existing literature on the topic. These results are presented systematically, with quantitative data illustrated through charts and tables.

The result presented indicates a Pearson correlation analysis between hemoglobin levels and parasite density across a sample of 155 individuals from a general population. The result presented indicates a Pearson correlation analysis between hemoglobin levels and parasite density across a sample of 155 individuals from a general population.

Table 1: Demographics of participants.

SEX	AGE (Months)				
	0-6	7-12	13-18	19-24	Total
Female	9	49	7	34	99
Male	4	24	4	24	56
TOTAL	13	73	11	58	155

Table 1 shows demographic data of participants in varying age and sex distribution.

Female participants are most common in the 7-12 age group (49), followed by 19-24 (34). A smaller number is present in the 0-6 (9) and 13-18 (7) age groups.

Male participants are most common in the 7-12 (24) and 19-24 (24) age groups. Fewer males are in the 0-6 (4) and 13-18 (4) age groups.

Table 2: Parasite density and hemoglobin.

		Hemoglobin	Parasite density
Hemoglobin	Pearson Correlation	1	-.141
	Sig. (2-tailed)		.081
	N	155	155
Parasite density	Pearson Correlation	-.141	1
	Sig. (2-tailed)	.081	
	N	155	155

Table 2 Shows distribution table and correlation analysis of patient with parasite and hemoglobin density

- The result presented indicates a Pearson correlation analysis between hemoglobin levels and parasite density across a sample of 155 individuals from a general population.
- The correlation coefficient between hemoglobin and parasite density is -0.141 . This value suggests a weak negative correlation, meaning that as parasite density increases, hemoglobin levels tend to decrease slightly. However, this relationship is weak because the coefficient is close to zero rather than -1 .
- The p-value associated with this correlation is 0.081 . Typically, in hypothesis testing, a p-value below 0.05 is considered statistically significant. Since the p-value here is greater than 0.05 , this correlation is not statistically significant at the standard level.
- Therefore, while there is a slight negative trend, it is not strong enough to conclude a meaningful relationship between hemoglobin and parasite density in this sample. Larger or more targeted samples may reveal stronger relationships, but within this dataset, the correlation is minimal and statistically weak.

Table 3 analysis reveals a generally negative correlation between hemoglobin levels and parasite density across different subsets of

Table 3: This result shows a Pearson correlation analysis between hemoglobin levels and parasite density in all three study sites.

		Hemoglobin	Parasite Density	Hemoglobin	Parasite Density	Hemoglobin	Parasite Density
		KHMCH	ODCH	RGH			
Hemoglobin	Pearson Correlation	1	-.344*	1	-0.12	1	-.413**
	Sig. (2-tailed)		0.022		0.346		0.004
	N	44	44	64	64	47	47
Parasite density	Pearson Correlation	-.344*	1	-0.12	1	-.413**	1
	Sig. (2-tailed)	0.022		0.346		0.004	
	N	44	44	64	64		

data. Pearson correlation coefficients range from -0.120 to -0.413 , indicating weak to moderate negative relationships. In some cases (e.g., $r = -0.344$, $p = 0.022$; $r = -0.413$, $p = 0.004$), the correlations are statistically significant, suggesting that increased parasite density is associated with decreased hemoglobin levels. However, in one case ($r = -0.120$, $p = 0.346$), the weak correlation is not statistically significant, implying the observed trend could be due to chance.

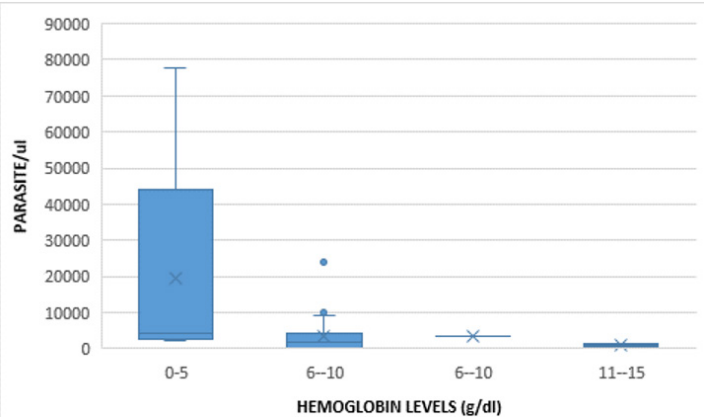


Figure 1: Disease severity for KHMCH.

Median: The central line within the box represents the median parasite count for this hemoglobin level range. It's located at around 20,000 parasites/ μ l.

Interquartile Range (IQR): The box itself shows the range where 50% of the data points lie (from the 25th percentile to the 75th percentile). It spans approximately 5,000 to 45,000 parasites/ μ l.

Outliers: The individual points above the box indicate outliers, suggesting significantly higher parasite counts for some individuals in this hemoglobin range. The highest outlier is around 80,000 parasites/ μ l.

Hemoglobin Level 6-10 g/dl

Median: The central line within the box represents the median parasite count for this hemoglobin level range.

Interquartile Range (IQR): The box itself shows the range where 50% of the data points lie (from the 25th percentile to the 75th percentile).

Outliers: The individual points above the box indicate outliers,

suggesting significantly higher parasite counts for some individuals in this hemoglobin range.

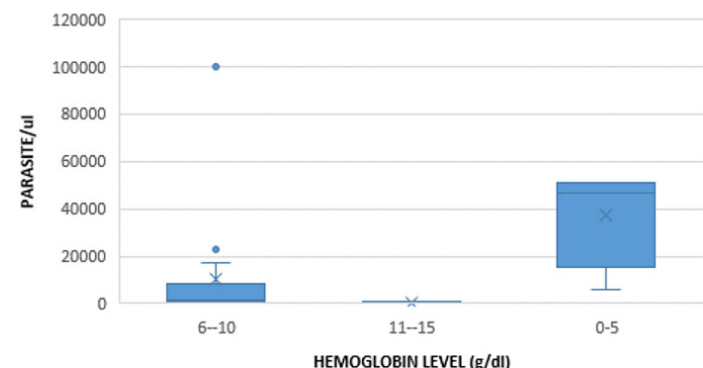


Figure 2: Shows disease severity in *P. falciparum* infected participants for RGH.

Hemoglobin Level 11-15 g/dl

Median: The central line is close to the bottom of the box, suggesting a lower median parasite count compared to the 6-10 g/dl range.

IQR: The box is relatively short, indicating a smaller spread of parasite counts within this hemoglobin range.

Outliers: There are no visible outliers in this group.

Hemoglobin Level 0-5 g/dl

Median: The central line is towards the top of the box, indicating a higher median parasite count compared to the other two ranges.

IQR: The box is wider, suggesting a larger spread of parasite counts within this hemoglobin range.

Outliers: The individual points above the box indicate outliers, suggesting significantly higher parasite counts for some individuals in this hemoglobin range.

Interpreting the Data

Hemoglobin Level 6-10 g/dl

Median: The central line within the box represents the median parasite count for this hemoglobin level range.

Interquartile Range (IQR): The box itself shows the range where 50% of the data points lie (from the 25th percentile to the 75th percentile).

Outliers: The individual points above the box indicate outliers, suggesting significantly higher parasite counts for some individuals in this hemoglobin range.

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Outliers: There are no visible outliers in this group.

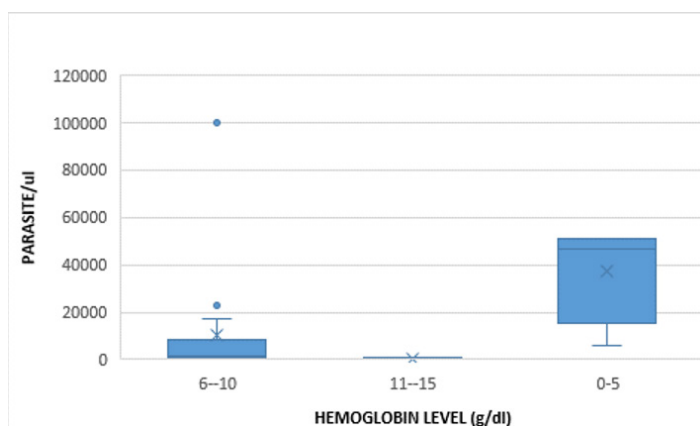


Figure 3: Show Disease severity for RGH.

Hemoglobin Level 0-5 g/dl

Median: The central line is towards the top of the box, indicating a higher median parasite count compared to the other two ranges.

IQR: The box is wider, suggesting a larger spread of parasite counts within this hemoglobin range.

Outliers: The individual points above the box indicate outliers, suggesting significantly higher parasite counts for some individuals in this hemoglobin range.

Overall Observations

Hemoglobin Level and Parasite Count

There appears to be a negative correlation between hemoglobin levels and parasite counts. Lower hemoglobin levels are associated with higher parasite counts, and vice versa.

Outliers: The presence of outliers in the 6-10 g/dl and 0-5 g/dl ranges suggests that some individuals within these groups may have significantly higher parasite loads compared to others with similar hemoglobin levels. This could be due to various factors such as individual susceptibility, exposure to parasites, or other health conditions.

Discussion

This study found a significant prevalence of anemia (Hb <11 g/dL) among children aged 0–2 years following *P. falciparum* infection, even after administration of S-P as compared to study done by [9]. Hemoglobin levels were notably lower in infants aged 6–12 months compared to older toddlers (12–24 months), highlighting a critical vulnerability in early infancy with severe malaria as compared to studies on in Burundi [6]. This aligns with previous studies indicating that the youngest children suffer the most severe hematologic consequences due to immature immunity and high

parasitemia rates [6].

Anaemia that persists after treatment could indicate a number of issues, including delayed haematologic healing or insufficient parasite clearance. co-infections (such as helminths or bacterial infections), pre-existing nutritional deficits (such as iron or folate), and potential emergence of resistance to S-P, albeit this study was not designed to identify definite resistance markers [10].

Despite being part of national malaria treatment guidelines in many regions, S-P's efficacy has been under scrutiny due to rising resistance. In our study, although clinical symptoms resolved in most children within 72 hours of treatment, the sustained low hemoglobin levels suggest that parasitological and hematological recovery may not be synchronous. S-P may still offer initial parasite suppression, but its role in preventing malaria-related anemia may be diminishing. This observation raises questions about the continued use of S-P in high-transmission settings, especially where *dhfr* and *dhps* mutations are prevalent. Our study's findings on disease severity post-S-P treatment should therefore be interpreted within this context of emerging resistance, underscoring the urgent need for continuous molecular surveillance and possibly re-evaluating current prophylactic treatment policies to ensure optimal malaria control in children under two years of age. Recent data from Nigeria reveal increasing prevalence of S-P resistance mutations, including *dhps*-431V, in *Plasmodium falciparum*, raising concerns of potential spread to Sierra Leone [11].

The slow hematological response further supports the argument for integrating iron supplementation and nutritional interventions in post-treatment protocols. Age appeared to be a critical factor influencing hemoglobin recovery. Children aged 0–6 months had higher Hb levels, potentially due to the protective effect of maternal antibodies and fetal hemoglobin [12]. However, from 6 months onwards, there was a sharp decline in Hb, corresponding with weaning, nutritional transitions, and increased exposure to mosquito vectors [13]. This finding reinforces the need for age-specific interventions and intensified monitoring of infants' post-malaria treatment. Our findings corroborate existing studies which emphasize that malaria-induced anemia is multifactorial, involving red blood cell destruction, bone marrow suppression, and nutritional deficiencies.

The persistent anemia post-S-P treatment echoes similar reports from Sub-Saharan Africa where resistance to antifolate drugs is increasing. Several studies have demonstrated that S-P, while still effective in IPTp (intermittent preventive treatment in pregnancy), has limited utility in children under five due to suboptimal cure rates and poor hematologic outcomes. This study strengthens the case for transitioning to artemisinin-based combination therapies (ACTs) in these settings, supplemented by post-treatment monitoring of hemoglobin.

Conclusion

To assess disease severity and the impact of malaria on hemoglobin level in children 0-2 years post S-P administration. The study found

that disease severity in children aged 0-2 years was closely associated with the presence of high parasite density, delayed treatment, and nutritional status. Children with severe malaria symptoms often required hospitalization and intensive care, underscoring the importance of early detection and timely intervention. Overall, this study provides critical insights into malaria diagnosis and treatment in children aged 0-2 years. The findings highlight the importance of choosing the appropriate diagnostic method (capillary vs. venous) for accurate parasite density measurement.

Recommendations

The high prevalence of post-treatment anemia in children under two years of age underscores an urgent need for integrated malaria management strategies that go beyond parasite clearance. These could include:

- **Routine Hemoglobin Monitoring:** Introducing Hb estimation as part of the post-treatment follow-up protocol for all pediatric malaria cases.
- **Nutritional Support:** Incorporating iron and micronutrient supplementation, particularly in children under 2 years, as a standard part of recovery protocols.
- **Treatment Policy Review:** Revisiting the use of SP in first-line treatment for children under five, especially in regions with documented resistance.
- **Community Education:** Enhancing caregiver awareness about signs of anemia and the importance of follow-up care.

Limitations

This study has several limitations. First, microscopy was performed only on children with positive RDT results, which may have missed sub-microscopic malaria cases and non-falciparum species not detected by RDTs. Second, molecular diagnostic tools such as PCR were not used to confirm *Plasmodium* species or identify antifolate drug resistance markers, limiting our ability to evaluate emerging resistance to S-P. Third, because this was a cross-sectional study, we were unable to conduct follow-up assessments to evaluate long-term hematologic recovery or reinfection rates. Additionally, factors like nutritional status and co-infections (e.g., helminths) were not fully investigated, even though they may contribute to persistent anemia. These limitations should be considered when interpreting the findings and planning future research.

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