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Research Article

Parasitemia Threshold for Hypoglycemia Risk in Pediatric Uncomplicated Malaria: A Cross-sectional Study in Ivory Coast

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Abstract

Background: Malaria remains a significant global health challenge, particularly in children in endemic regions. This study aimed to examine the prevalence, risk factors, and predictive indicators of hypoglycemia in children with uncomplicated Plasmodium falciparum malaria. *Methods:* A cross-sectional study was conducted at the Urban Community Health Center of Anonkoua-Koutéin Abidjan, Ivory Coast. Thirty-eight Black African children aged 3-14 years with uncomplicated P. falciparum malaria were included. Parasitemia, leukocyte count, blood hemoglobin concentration, and glycemia were also evaluated. The Spearman coefficient was used to analyze non-parametric distributions. A receiver operating characteristic (ROC) curve was used to determine the parasitemia threshold for optimal prediction of hypoglycemia risk. *Results:* The prevalence of hypoglycemia was 34.2%, with a mean blood glucose level of 4.17 mmol/l. An inverse correlation was observed between glycemia and parasitemia. ROC curve analysis demonstrated an optimal hypoglycemic risk with a sensitivity of 85% and specificity of 68% for a parasitemia threshold of 3,725/µL. No statistically significant associations were identified between glycemia and leukocyte count, hemoglobin level, or patient age. *Conclusion:* This study revealed a high prevalence of hypoglycemia in children with uncomplicated malaria, which was associated with elevated parasitemia levels. The importance of this factor in clinical settings arises from its potential impact on patient management and development of treatment strategies. The identified parasitemia threshold may serve as a critical indicator for evaluating treatment efficacy and assessing potential complications of malaria. Further research is warranted to validate these findings in larger multisite studies and to explore additional confounding factors.

Keywords

Malaria, Hypoglycemia, Parasitemia, Plasmodium Falciparum, Uncomplicated Malaria, Children

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1. Introduction

Malaria, a parasitic disease caused by Plasmodium species, remains a significant global health challenge in endemic regions such as Côte d'Ivoire. Children are the most vulnerable group, accounting for approximately two-thirds of all malaria deaths worldwide [1, 2]. They experience multiple episodes of malaria annually, leading to impaired cognitive development and increased susceptibility to other infections [3]. The pathophysiology of malaria involves a complex interplay between the parasite's life cycle and the host's immune response, leading to characteristic symptoms such as fever, chills, anemia, and occasionally hypoglycemia. The risk of hypoglycemia in uncomplicated malaria is generally lower; however, it remains likely to lead to complications as serious as those in severe malaria [4]. Hypoglycemia is a significant medical prognostic indicator. Its importance is derived from several key factors, including its role as a predictor of mortality, indicator of underlying conditions, neurological impact, association with cardiovascular risk, and influence on treatment decisions [5, 6]. Several gaps exist in the current understanding of hypoglycemia in the context of uncomplicated malaria. Specifically, there is a scarcity of data regarding the prevalence of hypoglycemia in patients with uncomplicated malaria. Furthermore, the physiological mechanisms underlying hypoglycemia in such cases have not yet been fully elucidated. Additionally, there is a deficiency of comprehensive information concerning the specific factors that may predispose certain individuals to develop hypoglycemia during episodes of uncomplicated malaria.

Therefore, the following research hypotheses were formulated: the prevalence of hypoglycemia in patients with uncomplicated malaria is significantly higher than that in the general population. Hypoglycemia in uncomplicated malaria is primarily attributed to increased glucose consumption induced by parasites. Factors such as age, sex, anemia, and parasite density were significantly associated with the risk of developing hypoglycemia in patients with uncomplicated malaria.

This study aimed to examine the prevalence, risk factors, and predictive indicators of hypoglycemia in children with uncomplicated malaria. Consequently, the objectives of this research were to ascertain the prevalence of hypoglycemia in children diagnosed with uncomplicated malaria and to identify and analyze the key risk factors associated with the occurrence of hypoglycemia in these patients.

2. Materials and Methods

To address these objectives, we conducted a cross-sectional study, as detailed in the following section, focusing on specific diagnostic criteria and statistical analyses to identify and analyze the risk factors for hypoglycemia.

2.1. Study Design, Participants and Ethical Considerations

This cross-sectional study was conducted at the Urban Community Health Center (FSUCOM) of Anonkoua-Kouté and the Health Diagnostic and Research Center (CeDReS) in the University Hospital of Treichville, both in Abidjan, Ivory Coast, West Africa. The study was approved by the Medical Board of FSUCOM and cleared by the Ivorian National Ethics and Research Committee. A total of 38 Black African children, aged 3-14 years were selected after obtaining informed consent from their parents or legal guardians.

2.2. Variables and Laboratory Methods

Participants were diagnosed with uncomplicated malaria according to the criteria established by the World Health Organization [7]. Only *Plasmodium falciparum* infections were included in the study. The presence of malaria parasites was confirmed by positive results from both thick and thin blood smears. Individuals with other evident causes of infection or anemia were excluded from the study. Before initiating antimalarial or anti-anemic therapy, the following variables were evaluated in all children: parasitemia, leukocyte count, blood hemoglobin concentration, and glycemia levels.

Parasitemia densities were determined using optical microscopy following differential Giemsa staining and were calculated based on automated leukocyte counts obtained through flow cytometry. Hemoglobin levels were measured using spectrophotometry according to the Drabkin method [8]. Anemia was defined as a hemoglobin level below 11 g/dL for individuals aged 2-12 years, and as a hemoglobin level below 12 g/dL for those aged above 12 years [9, 10]. Glycemic levels were assessed using the spectrophotometric hexokinase enzymatic method, with hypoglycemia defined as values below 3.9 mmol/l [11].

3. Data Analysis

Statistical analyses were performed using SPSS™ (version 25, IBM Corp., Armonk, USA). The Shapiro-Wilk test was used to assess the normality of the distributions. Due to skewed distributions, non-parametric tests were used for data analysis. The frequency of events was calculated for qualitative variables, and means were determined for quantitative variables. The Spearman ρ coefficient and receiver operating characteristic (ROC) curve were used to determine the relationships between variables. All statistical analyses were conducted using a significance threshold of 5%.

4. Results

Participants Characteristics

The mean age of the entire population was 7.8 ± 2.9 years

old. The overall population was predominantly male, accounting for 57.9% of the total. There were no significant biological differences between the male and female participants (Table 1). Therefore, participant sex was not a confounding factor in our study.

Table 1. *Participant Characteristics (n=38).*

	Male (Mean ± SD)	**Female (Mean ± SD)**	***p-value***
Leukocytes (10^3 cells/µL)	8.3 ± 4.0	7.3 ± 1.74	*0.303*
Hemoglobin[#] (g/dl)	8.68 ± 1.95	8.78 ± 1.61	*0.865*
Parasitemia[&] (cells/µl)	8.073 ± 11.380	22.781 ± 26.553	*0.051*
Glycemia* (mmol/L)	4.0 ± 1.35	4.38 ± 1.09	*0.351*

[%]Counted by flow cytometry; [#]Measured by spectrophotometric Drabkin method; [&]Determined by optical microscopy following Giemsa staining and reported to leukocyte count; * Postprandial glycemia (fasting 4 to 8 hours)

Distribution of parasitemia levels

The mean value of parasitemia was 14,266 /µl, with a minimum of 792 /µl and a maximum of 63,800 /µl. The distribution of parasitemia was not normal according to the Shapiro-Wilk test (p <0.001) (Figure 1).

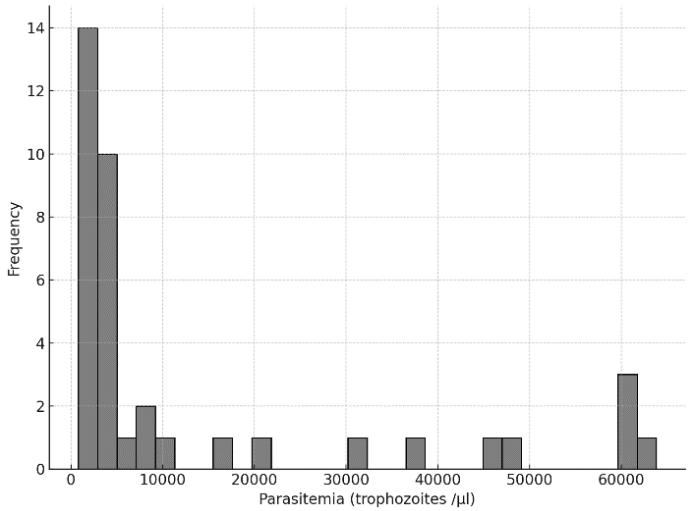

Figure 1. *Distribution of parasitemia (n=38).*

Prevalence of Anemia and Hypoglycemia

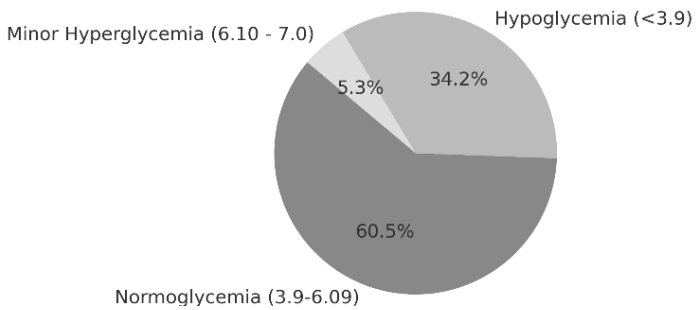

Figure 2. *Distribution of glycemia (n=38).*

The prevalence rates of anemia and hypoglycemia were 91.9% and 34.2%, respectively, in this study. The mean blood glucose level was 4.17 mmol/l, with observed values ranging from a minimum of 1.78 mmol/l to a maximum of 7.01 mmol/l. Furthermore, two instances of mild hyperglycemia were recorded, with glucose levels of 6.11 mmol/L and 6.70 mmol/l (Figure 2).

Relationships Between Variables

An inverse correlation was observed between glycemia levels and parasitemia. However, no statistically significant correlations were identified between glycemia and leukocyte count, hemoglobin levels, or patient age (Table 2).

Table 2. *Correlation between glycemia and different variables (n=38).*

Variable	Spearman ρ	*p-value*	Interpretation
Age	-0.07	*0.679*	Not significant
Parasitemia	-0.37	*0.027*	Significant
Hemoglobin	-0.022	*0.897*	Not significant
Leukocytes	-0.012	*0.944*	Not significant

ROC Curve Analysis

The association between hypoglycemia risk and parasitemia was demonstrated by the significant area under the ROC curve for hypoglycemic risk based on parasitemia, which was 0.751 (p = 0.012). The ROC curve demonstrated an optimal hypoglycemic risk with a sensitivity of 85% and specificity of 68% for a parasitemia threshold of 3,725/µL (Figure 3).

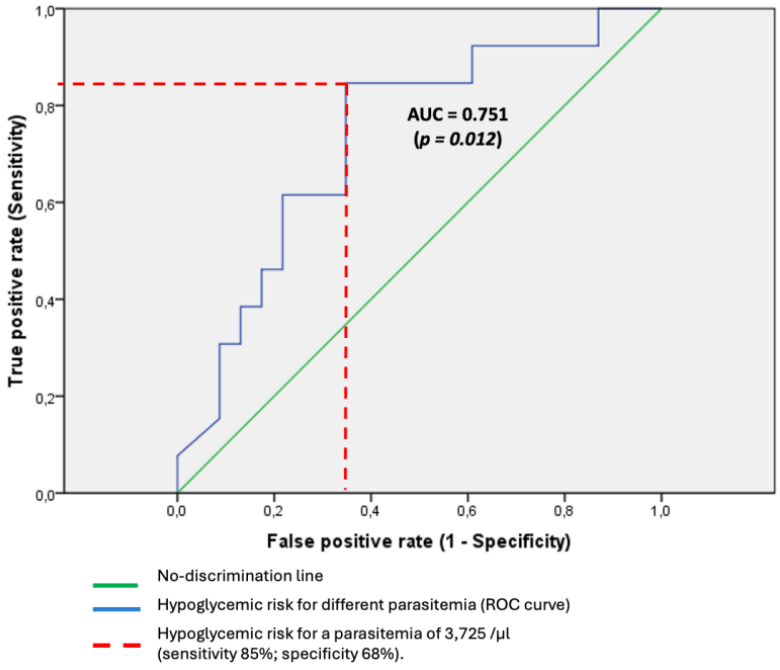

Figure 3. *ROC curve of hypoglycemic risk according to parasitemia.*

5. Discussion

In critically ill nondiabetic children, the prevalence of hypoglycemia is approximately 2.2% to 7.5% of cases, with the rate depending on the blood glucose threshold used to define hypoglycemia [12-14]. Our study identified a significantly higher prevalence of hypoglycemia (34.2%) than that in the non-diabetic pediatric population. The prevalence of hypoglycemia observed in our study fell within the range of hypogly-

cemia reported in type 1 and type 2 diabetes mellitus, which varies from 10% to 53%. All the participants had a parasitemia under 200,000 /µl, which is considered the threshold for complicated malaria. However, hypoglycemia, a biological sign of complicated malaria, was observed in our population [15]. These findings highlight the frequent occurrence and often unrecognized presence of hypoglycemia in patients, underscoring the necessity for vigilant monitoring and management to avert adverse outcomes [16-18]. Comprehending and monitoring hypoglycemia as a prognostic indicator is essential for healthcare providers to optimize patient care, adjust treatment plans, and enhance overall outcomes in diverse medical conditions.

Furthermore, the risk of hypoglycemia correlates with elevated parasitemia in Plasmodium falciparum infections. This finding highlights the potential contribution of increased glucose consumption by parasites to the onset of hypoglycemia, as assumed in previous studies [15, 19]. The significance of the inverse association between parasitemia and glycemia can be attributed to the increased glucose consumption induced by the parasite load. Its clinical importance lies in its potential impact on patient management and treatment strategy. Understanding this relationship can help healthcare providers anticipate and prevent dangerous decreases in blood glucose levels, especially in patients with high parasite loads. Moreover, this association may provide insights into the metabolic interactions between malaria parasites and their human hosts, potentially leading to new therapeutic approaches. Further research into the mechanisms underlying this inverse relationship could reveal novel targets for antimalarial drugs and strategies to mitigate the metabolic disturbances caused by the infection.

The threshold of parasitemia associated with a significant risk of hypoglycemia was identified as a moderate parasitemia level of 3,725/µL, in comparison to the WHO guidelines [20]. It can serve as a critical indicator for evaluating the efficacy of treatment and assessing the potential risk of malaria complications that may lead to poor prognosis. This could be a standard way to compare outcome results from different studies and treatments in research and clinical trials and in clinical decision-making.

Regarding the other risk factors, patient age did not appear to be a significant factor in determining the risk of hypoglycemia in this population (Table 2). This suggests that both younger and older patients in the pediatric age range may have similar risks of experiencing hypoglycemic events. Similarly, the data analysis indicated that there was no significant correlation between a patient's sex and the likelihood of developing hypoglycemia (Table 2). This finding implies that both male and female patients may have an equal propensity to experience hypoglycemic episodes. Consistent with several other investigations into hypoglycemia across various pathologies, these studies suggest that although there are some variations in hypoglycemic risk, broader demographic factors such as age and sex may not significantly impact this risk [9, 21].

The hemoglobin level in the blood, anemia status, and white blood cell count did not seem to be associated with an increased or decreased risk of hypoglycemia (Table 2). This implies that malaria patients with varying hemoglobin levels or varying white blood cell counts may have similar risks of experiencing low blood sugar events.

These findings indicate that clinicians should not rely solely on these specific variables (age, sex, hemoglobin concentration, and leukocyte count) when assessing a patient's risk of hypoglycemia. Other factors not mentioned in this study may play a more significant role in determining the risk of hypoglycemia. Healthcare providers should consider a broader range of clinical parameters and individual patient characteristics when evaluating and managing the risk of hypoglycemia in patients with malaria.

The prevalence of anemia observed in our study (91.2%) exceeded the rates reported in previous studies conducted among pregnant women in Malawi (57.2%) and children in Kenya (71.8%) [22, 23]. However, no association was found between hemoglobin levels and hypoglycemia. This finding does not strengthen the expected relationship between increased destruction of parasitized blood cells and enhanced anaerobic glycolysis, as well as the relationship between impaired hepatic gluconeogenesis and elevated hepatic parasite load [24-26].

Some limitations of our study should be noted. Despite the use of appropriate statistical tools, the small sample size of children limits the generalizability of the conclusions. The cross-sectional design precluded the determination of causality but allowed the assessment of multiple relevant variables. Potential confounding factors such as nutritional status, type 1 diabetes mellitus, or genetic diseases associated with hypoglycemia were not assessed [16-18]. Furthermore, the single study location limits the external validity. Despite these limitations, this study provides insights into the relationship between parasitemia and hypoglycemia risk in pediatric uncomplicated malaria that warrants further investigation in larger, multi-site studies with more potential confounding factors.

6. Conclusions

The study reveals a high prevalence of hypoglycemia in children with uncomplicated malaria, with a strong inverse correlation between glycemia and parasitemia. A relative moderate parasitemia threshold (3,725/µL) was established for assessing hypoglycemia risk, showing a good sensitivity and a moderate specificity (68%). No significant associations were found between hypoglycemia risk and factors like age, sex, hemoglobin concentration, and leukocyte count. The findings emphasize the importance of vigilant blood glucose monitoring in managing uncomplicated malaria in children and suggest potential use of the identified parasitemia threshold for risk assessment and treatment decisions. Further research is recommended to explore additional factors and mechanisms of hypoglycemia in malaria.

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Abbreviations

µL	Microliter
g/dL	Gram per deciliter
mmol/L	Millimole per Liter
AUC	Area Under the Curve
BMI	Body Mass Index
CeDReS	Health Diagnostic and Research Center
ROC	Receiver Operating CHARACTERISTIC
SD	Standard Deviation
FSUCOM	Urban Community Health Center

Author Contributions

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Jo ëlle Akissi Koffi: Conceptualization, Methodology, Investigation, Writing – review & editing

B énédicte Kon é-Dakouri: Investigation, Formal analysis, Writing – review & editing

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Data Availability Statement

The data is available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have influenced the work reported in this study.

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Research Field

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