



Factors Associated with Malaria Infection Among Febrile Patients Admitted to Emergency Units in Three Hospitals in Southern Benin: A Cross-Sectional Study

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Abstract

Background: Despite the scale-up of vector control interventions, malaria remains a leading cause of morbidity and mortality in Sub-Saharan Africa. In Benin, hospital-based data regarding the profile of severe malaria and the factors associated with infection in the context of widespread bed net coverage are crucial for evaluating control strategies. This study aimed to determine the prevalence of malaria, describe its clinical severity, and identify factors associated with infection among febrile patients admitted to three referral hospitals in Southern Benin.

Methods: We conducted a multicenter, prospective, cross-sectional study from October 9, 2023, to January 15, 2024. The study sites included the National Hospital University Center (CNHU-HKM), the Abomey-Calavi/Sô-Ava Zone Hospital (CHUZ-AS), and the Ouidah Zone Hospital (HZOD). The study population comprised febrile patients (temperature $\geq 38^{\circ}\text{C}$ for children, $\geq 37.6^{\circ}\text{C}$ for adults) aged over one year admitted to emergency wards. Malaria diagnosis was confirmed by Rapid Diagnostic Test (RDT) and/or thick blood smear. Multivariate logistic regression was used to identify independent risk factors. Avec quel logiciel et quelle est la taille d'échantillon ?

Results: A total of 366 febrile patients were enrolled. The overall prevalence of confirmed malaria was 38.3% (140/366). Among confirmed cases, 76.4% were classified as severe malaria according to WHO criteria. The most common signs of severity were severe anemia (57.0%), prostration (43.9%), and incoercible vomiting (33.6%). Age under 15 years was significantly associated with malaria (adjusted Odds Ratio [aOR]: 3.48; 95% CI: 1.32–14.2; $p=0.02$). Conversely, the reported use of Long-Lasting Insecticidal Nets (LLINs) was a significant protective factor (aOR: 0.26; 95% CI: 0.11–0.63; $p=0.03$).

Conclusion: Malaria remains a high-burden disease in emergency settings in Southern Benin, characterized by a predominance of severe forms, particularly severe anemia in children. The protective effect of LLINs highlights the continued need for vector control, while the age-related risk underscores the necessity for targeted pediatric interventions.

Keywords: Malaria; Age under 15; LLINs; Benin.

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Article reçu : 26-11-2025

Accepté : 10-02-2026 **Publié :** 17-03-2026



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Pour citer cet article : Sètondji Géraud R.P. et al. Factors Associated with Malaria Infection Among Febrile Patients Admitted to Emergency Units in Three Hospitals in Southern Benin: A Cross-Sectional Study. 2026; 9(1): 89 - 104

1. Introduction

Malaria remains one of the most complex and persistent global health challenges, despite two decades of massive investment and therapeutic innovation. Although the disease is preventable and curable, the momentum of control efforts has stalled in recent years, giving way to a worrying stagnation in morbidity. According to the World Health Organization (WHO) World Malaria Report 2023, there were an estimated 249 million malaria cases globally in 2022, an increase from 244 million in 2021 [1]. This burden weighs disproportionately on the African Region, which accounts for approximately 94% of cases and 95% of deaths, perpetuating a cycle of disease and poverty that hinders the continent's economic development [1, 2].

Benin presents an epidemiological profile of holo-endemicity, characterized by intense and perennial transmission of *Plasmodium falciparum*. Located in the West African tropical belt, the country offers climatic and ecological conditions ideal for the proliferation of *Anopheles* vectors [3]. National data corroborate the severity of the situation: malaria is the leading cause of healthcare utilization, hospitalization, and mortality, particularly among biologically vulnerable groups such as children under five and pregnant women [4]. Beyond direct mortality, indirect consequences, such as school absenteeism and lost productivity among adults, heavily burden the economy of Beninese households [5].

Benin's national malaria control strategy aligns with global and regional guidelines [6]. It relies on an arsenal combining vector control—primarily through the mass distribution of Long-Lasting Insecticidal Nets (LLINs) and Indoor Residual Spraying (IRS) in targeted areas—and case management with Artemisinin-based Combination Therapies (ACTs) [7]. Notable progress has been made, particularly with the introduction of Seasonal Malaria Chemoprevention (SMC) in the northern regions [7]. However, the transition from the control phase to pre-elimination faces major obstacles. Despite high theoretical LLIN coverage following mass renewal campaigns, hospital facilities continue to record a constant flow of admissions for severe malaria [8]. This paradox of persistent severe morbidity in a context of high preventive coverage raises critical questions. It suggests potential gaps in intervention effectiveness, which could be linked to the emergence of vector resistance to pyrethroids, changes in mosquito behavior (early biting or exophily), or inadequate use of protective measures by populations [9]. Furthermore, the epidemiological landscape appears to be evolving, with recent studies in sub-Saharan Africa suggesting a shift in the disease burden from very young children to school-aged children and adolescents, a phenomenon that requires precise local documentation [10].

Hospital-based epidemiological surveillance is indispensable for deciphering these dynamics [11]. The hospital, as a convergence point offers a unique window into the clinical presentation of severe forms, such as cerebral malaria and severe anemia, which threaten vital prognosis. Moreover, in overcrowded emergency departments, accurate

identification of factors associated with malaria infection in febrile patients is crucial for differential diagnosis [12]. In endemic zones, the adage "all fever is malaria until proven otherwise" is being challenged by declining transmission in certain urban areas and the emergence of other febrile etiologies (arboviruses, bacterial infections). Excessive presumptive diagnosis leads not only to the overuse of expensive antimalarials, promoting parasite resistance [13], but also delays the management of other potentially life-threatening pathologies.

Yet, few recent studies in Benin have simultaneously assessed the clinical profile of severe malaria and sociodemographic determinants of infection across multiple levels of the healthcare system (national, zonal, and district levels) in the southern part of the country [14]. The southern zone, densely populated and characterized by a lagoon environment, deserves particular attention during seasonal transition periods when transmission risk remains poorly defined.

The present multicenter study was designed to bridge this gap. Its main objective is to determine the prevalence of confirmed malaria among febrile patients admitted to emergency units, to describe clinical severity profiles according to new WHO criteria, and to identify independent risk and protective factors associated with infection.

2. Material and Methods

2.1. Study Design and Setting

This was a multicenter, prospective, cross-sectional descriptive and analytical study. The study was conducted over a period of three months, from October 9, 2023, to January 15, 2024. This period coincides with the transition from the short rainy season to the dry season, a time when malaria transmission remains significant in the coastal zone.

The study was carried out in three referral hospitals in Southern Benin:

- National Hospital University Center Hubert Koutoukou MAGA (CNHU-HKM): Located in Cotonou (Littoral Department), it is the referral hospital for the entire country, handling the most critical cases.
- Abomey-Calavi/Sô-Ava Zone Hospital (CHUZ-AS): Located in the Atlantique Department, serving a dense peri-urban population and lakeside communities.
- Ouidah Zone Hospital (HZOD): Also in the Atlantique Department, serving a mixed urban and rural population.

2.2. Study Population and sampling

The study population consisted of patients admitted to the emergency, internal medicine, or pediatric departments of the selected hospitals.

- Inclusion Criteria: Patients were eligible if they were aged at least one year (12 months), admitted for hospitalization during the study period, and presented with fever (defined as axillary temperature $\geq 38^{\circ}\text{C}$ for children <15 years, or $\geq 37.6^{\circ}\text{C}$ for adults ≥ 15 years).
- Exclusion Criteria: We excluded patients who refused to provide consent or whose clinical condition prevented safe biological sampling.

A non-probability sampling method with exhaustive recruitment was used. All patients meeting the inclusion criteria presenting during the study period were invited to participate. This approach was chosen to capture the true flow of febrile admissions and minimize selection bias associated with specific days or times.

2.3. Data Collection

Data collection was performed by trained medical doctors using a structured digital questionnaire (KoboCollect). Clinical and Sociodemographic Data: Information was collected on age, sex, residence, use of LLINs (bed nets), history of fever, self-medication prior to admission, and clinical signs. Physical Examination: A thorough physical examination was conducted to identify signs of severity according to WHO guidelines (e.g., consciousness level, respiratory distress, pallor, jaundice). Laboratory Diagnosis: Peripheral venous blood samples were collected. Malaria diagnosis was performed using Rapid Diagnostic Tests (RDT) targeting HRP2/pLDH antigens and/or thick blood smears stained with Giemsa for parasite quantification. A Complete Blood Count (CBC) was performed to assess hemoglobin levels and other hematological parameters.

2.4. Variables

- Dependent Variable: Malaria infection status (Positive/Negative), defined by a positive RDT or positive thick smear.
- Independent Variables:
 - Sociodemographic: Age (categorized as <15 years and ≥ 15 years), sex, study site.
 - Behavioral: Use of LLINs (Yes/No), use of herbal medicine, self-medication.
 - Clinical: WHO severity signs (severe anemia [$\text{Hb} < 5\text{g/dL}$], convulsions, coma, prostration, shock, renal failure, etc.).

2.5. Statistical Analysis

Data were analyzed using Stata® version?. Descriptive Analysis: Categorical variables were summarized as frequencies and percentages. Continuous variables were summarized as means \pm standard deviation (SD) or medians. Univariate Analysis: association between potential risk factors and malaria infection was assessed using the Chi-square test or

Fisher's exact test. Multivariate Analysis: Factors with a p-value ≤ 0.20 in the univariate analysis were included in a multivariate logistic regression model. A stepwise backward selection method was used to identify independent predictors. Results are reported as adjusted Odds Ratios (aOR) with 95% Confidence Intervals (CI). A p-value < 0.05 was considered statistically significant.

2.6. Ethical Considerations

The study protocol was approved by the institutional ethics authorities of the participating hospitals. Written informed consent was obtained from all adult participants and from parents or legal guardians of minors. The confidentiality of patient data was strictly maintained. insérer le numéro éthique

3. Results

3.1. Study Flow and Participant Characteristics

During the study period, a total of 6,412 patients were hospitalized across the three sites. Of these, 366 patients met the inclusion criteria (febrile and aged >1 year) and consented to participate. The mean age of the participants was 26.6 ± 1.6 years, with a median of 26 years (range: 1–90 years). The sex ratio (Male/Female) was 1.27.

3.2. Prevalence of Malaria Infection

Among the 366 febrile patients, 140 tested positive for malaria, yielding an overall hospital-based prevalence of 38.3%.

The distribution of cases varied by site, with a significant burden observed across all three hospitals.

3.3. Characteristics of Malaria Cases

Among the 140 confirmed malaria cases, 52.1% were male. The mean age was 19.9 ± 22.9 years. Notably, children under 5 years of age accounted for 31.4% of all malaria cases, highlighting the continued vulnerability of this age group (figure 1).

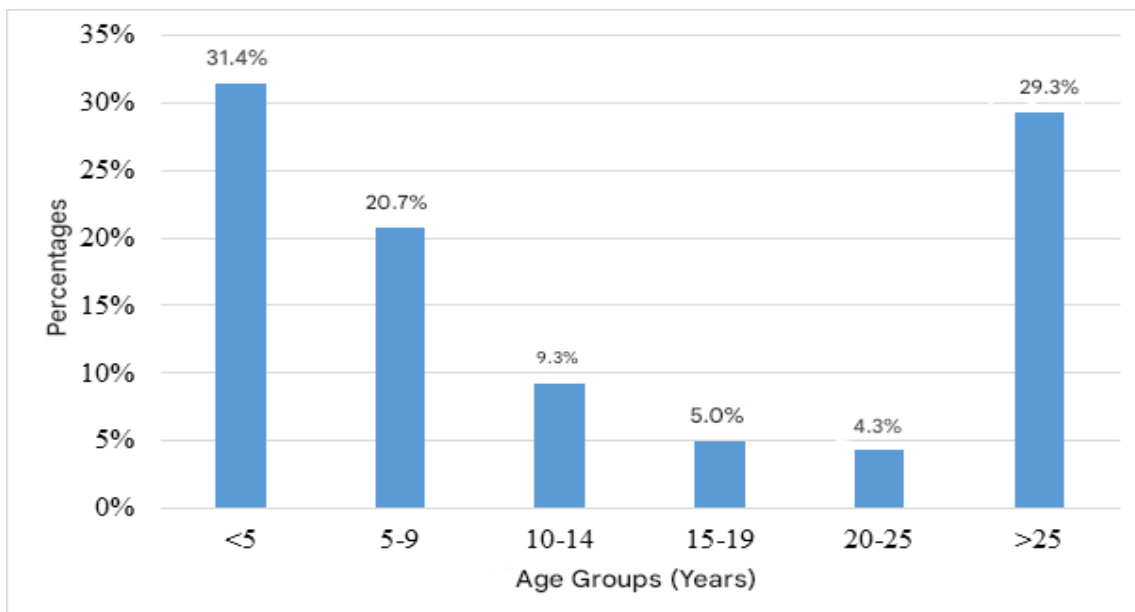


Figure 1 : Age group of participants with malaria infection

Interestingly, 87.9% of malaria-positive patients reported sleeping under an LLIN, suggesting potential issues with net integrity, proper usage, or outdoor transmission. The most common functional symptoms reported were asthenia (59.3%), anorexia (53.6%), and vomiting (36.4%) (figure 2).

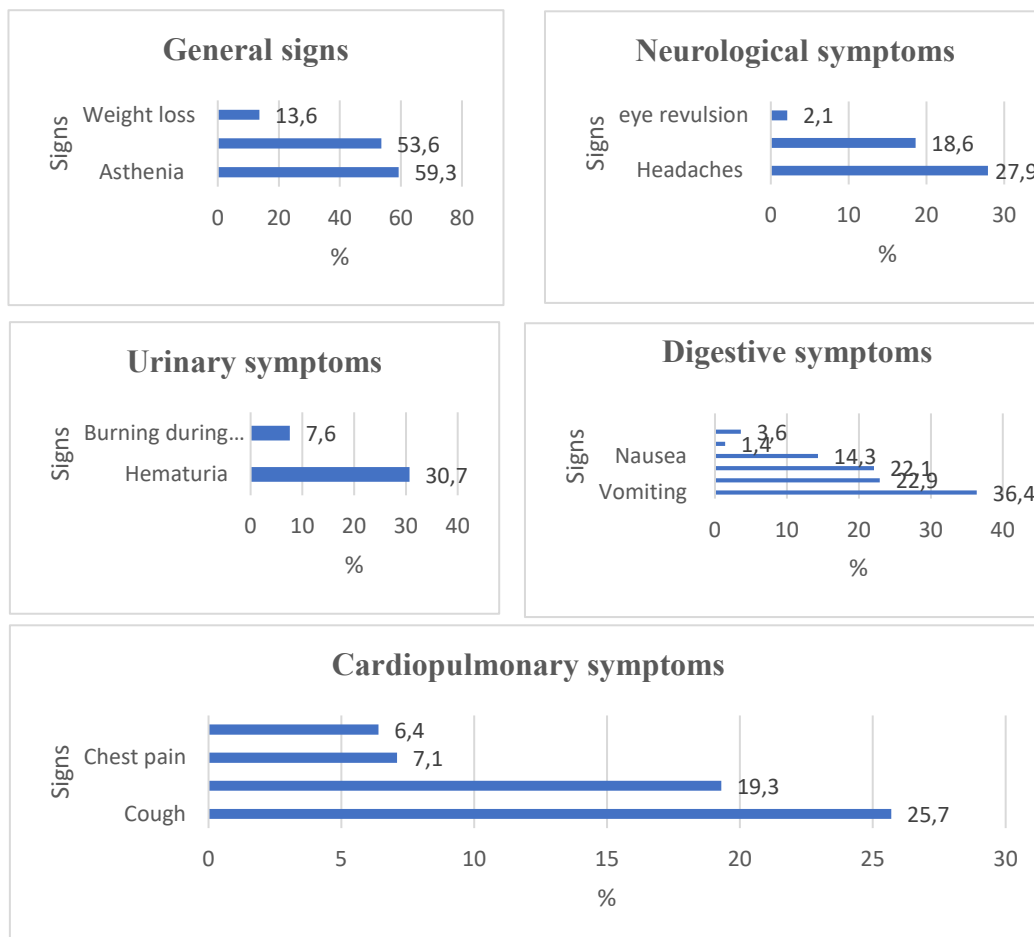


Figure 2 : Functional symptoms

3.4. Criteria of Severity

A striking finding was the high proportion of severe malaria among admitted cases. Of the 140 positive patients, 107 (76.4%) met the WHO criteria for severe malaria.

The breakdown of severity signs was as follows: severe Anemia (Hb < 5 g/dL): 57.0% (The most prevalent sign), prostration: 43.9%, incoercible Vomiting: 33.6%, convulsions: 16.8%, coma (Cerebral Malaria): 15.9%. (figure 3).

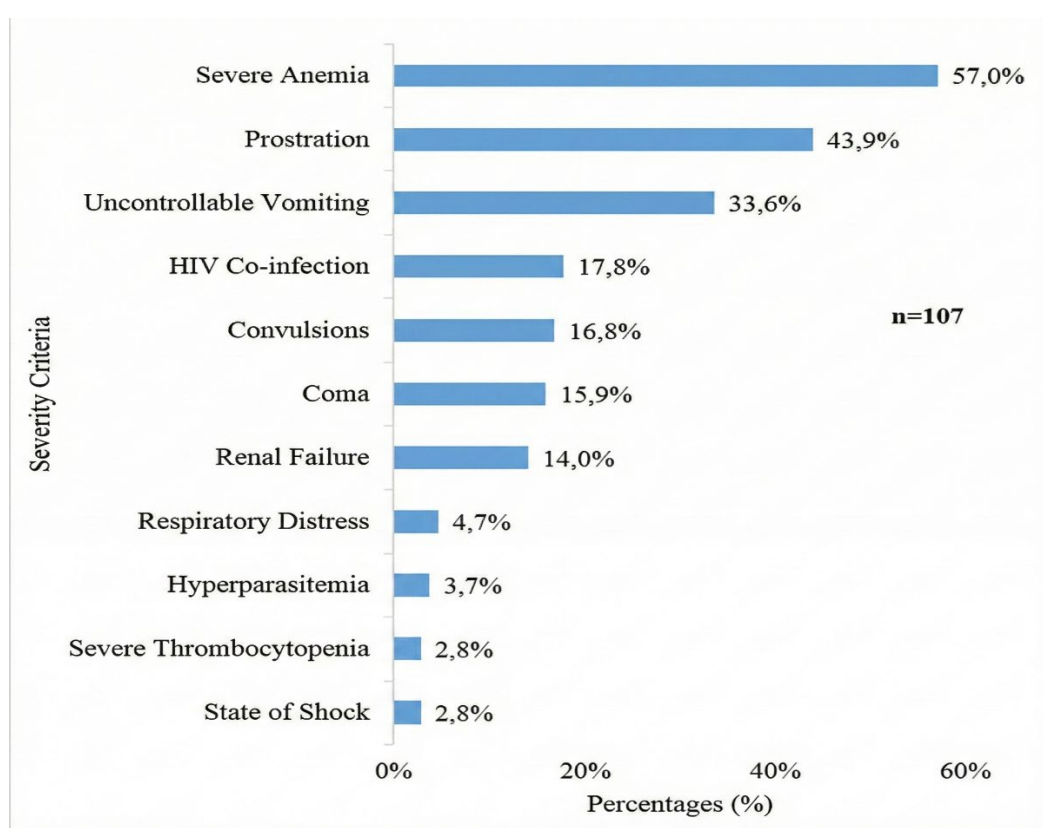


Figure 3 : Severity signs, WHO criteria.

This profile indicates that severe anemia remains the predominant clinical manifestation of severe malaria in this population, particularly among children.

3.5. Factors Associated with Malaria Infection

Several factors were significantly associated with malaria infection in the bivariate analysis. Age: Patients <15 years were significantly more likely to have malaria compared to those ≥ 15 years ($p < 0.0001$). LLIN Use: Those who reported sleeping under an LLIN were less

likely to be infected ($p = 0.001$). Clinical Signs: Severe anemia, incoercible vomiting, and convulsions were strongly associated with a positive malaria diagnosis ($p < 0.001$) (table 1).

Table 1: Factors associated with malaria infection. Univariate analysis.

Variables	Malaria Infection (Yes)	Malaria Infection (No)	p-value
Study Site			0.4
CNHU	30	148	
HZAC	15	55	
HZOD	25	93	
Age (years)			< 0.0001
≥ 15	42	152	
< 15	98	74	
Sex			0.35
Male	73	129	
Female	67	97	
Sleeping under LLIN*			0.001
No	17	8	
Yes	123	218	
Severe Anemia			< 0.0001
No	17	141	
Yes	123	85	
Intravascular Hemolysis			0.4
No	108	193	
Yes	32	33	
Uncontrollable Vomiting			0.001
No	79	164	
Yes	61	62	
Convulsions			< 0.0001
No	92	207	
Yes	48	13	
Coma			0.8
No	130	198	
Yes	30	28	
Renal Failure			0.64
No	119	196	

Yes	21	30	
Respiratory Distress			0.44
No	135	214	
Yes	5	12	
Severe Thrombocytopenia			0.96
No	137	221	
Yes	3	5	
State of Shock			0.58
No	137	219	
Yes	3	7	

In the logistic regression model adjusting for potential confounders, two factors remained independent predictors of malaria infection (Table 1): young Age: Age <15 years was a significant risk factor, with an adjusted Odds Ratio (aOR) of 3.48 (95% CI: 1.32 – 14.2; p = 0.02). LLIN Use: The use of Long-Lasting Insecticidal Nets was a significant protective factor. Patients not using LLINs had a higher risk, or conversely, LLIN use was associated with reduced odds of infection (aOR: 0.26; 95% CI: 0.11 – 0.63; p = 0.03) (table 2).

Table 2: Factors Associated with Malaria Infection (multivariate logistic regression).

Explanatory Variables	Adjusted OR [95% CI]	p-value
Age (years)		0.02
≥ 15	1	
< 15	3.48 [1.32 - 14.20]	
Sleeping under LLIN		0.03
No	1	
Yes	0.26 [0.11 – 0.63]	
Severe Anemia		0.1
No	1	
Yes	3.12 [0.25 - 9.50]	
Convulsions		0.1
No	1	
Yes	3.50 [0.23 - 8.12]	

4. Discussion

This study provides a detailed clinical and epidemiological snapshot of malaria in referral hospitals in Southern Benin during the transition period between the short rainy season and the dry season. Our results confirm that malaria remains a major health emergency, characterized by high prevalence and an alarming predominance of severe anemic forms in children.

The overall prevalence of 38.3% observed among febrile admissions confirms that *Plasmodium falciparum* remains the dominant etiology of fevers requiring hospitalization in our context. This rate is consistent with those reported in other stable endemic areas in Sub-Saharan Africa. For instance, Otu et al. in Nigeria reported a prevalence of 55.0% in secondary care settings [15], while studies in Cameroon place this prevalence around 33.8%. These inter-regional variations reflect the heterogeneity of transmission, influenced by rainfall and urbanization [16].

It is important to emphasize that our study took place during a seasonal transition period. The maintenance of such high prevalence outside the traditional peak rainfall suggests that transmission has become quasi-perennial in the coastal zone of Southern Benin, likely favored by the presence of permanent breeding sites in lagoon and poorly drained peri-urban areas. This challenges the notion of strict seasonality for clinical vigilance; practitioners must maintain a high index of suspicion for malaria throughout the year.

A striking finding of our study is the massive proportion of severe malaria (76.4%) among infected patients. This figure, while biased by recruitment in referral hospital settings (where complicated cases end up), testifies to the severity of the disease. Specific analysis of severity signs reveals that severe anemia ($Hb < 5$ g/dL) is by far the most frequent complication (57.0%), surpassing prostration and coma. This clinical profile is typical of intense transmission zones (holo-endemic) [17, 18]. In these regions, young children undergo repeated and poorly treated infections that lead to chronic hemolysis and dyserythropoiesis, progressively resulting in profound anemia. This result contrasts with profiles observed in low or unstable transmission zones, where cerebral malaria (coma) often predominates due to a lack of acquired immunity. Our results align with those of Mabilia-Babela in Congo and Eleke in the DRC, who also identified anemia as the predominant silent killer in children [21]. The clinical implication is direct: the management of severe malaria in Southern Benin cannot be dissociated from anemia management. This requires not only the immediate availability of labile blood products, often in shortage, but also prevention strategies integrating iron supplementation and systematic deworming, as co-infection with helminths and malnutrition often aggravate the clinical picture [22, 23].

In a West African context marked by alarming reports of vector resistance to pyrethroids, our study provides reassuring evidence of the continued effectiveness of LLINs. Reported

net use was associated with a 74% reduction in the risk of malaria infection (aOR = 0.26) [24]. This result is crucial for public health advocacy. It suggests that even if the chemical lethal effect of the net is potentially reduced by mosquito resistance, the physical barrier effect remains highly protective against nocturnal bites [25]. Yé et al. had already demonstrated the positive impact of mass distribution campaigns in Benin [26]. Our data reinforce the idea that abandoning nets under the pretext of resistance would be a major strategic error. However, as protection is not total, there is an urgent need to accelerate the deployment of next-generation nets (PBO-impregnated or dual-active ingredient) to maximize impact [27, 28].

The strong association between age under 15 years and malaria (aOR = 3.48) reaffirms the central role of acquired immunity. Doolan et al. have described that antimalarial immunity is a slow cumulative process: one first acquires protection against death, then against severe disease, and finally partial tolerance to parasitemia [29].

It is pertinent to note that our study identified a high risk in children up to 15 years old, not just in those under 5. This potential shift of morbidity toward older children and adolescents is a phenomenon observed elsewhere in Africa [30-32]. These school-aged children often sleep less under nets than infants and do not always benefit from free healthcare, delaying their treatment. Future control strategies, including vaccination (RTS, S or R21), must account for this dynamic to avoid leaving pockets of transmission among adolescents.

This study has certain limitations inherent to its cross-sectional and hospital-based design. Recruitment in emergency units induces a selection bias toward the most severe cases, not reflecting community prevalence [33-35]. Furthermore, LLIN use was measured by self-reporting, exposing the data to social desirability bias [36-40]. Finally, the absence of molecular characterization of parasites prevents us from discussing antimalarial resistance in our cohort.

5. Conclusion

Malaria remains a major pathology in Southern Benin's hospitals, primarily striking children in a severe anemic form. However, the use of LLINs remains an effective bulwark. To reduce mortality, we recommend strengthening vector control: maintain universal LLIN coverage and introduce next-generation nets, managing anemia: integrate systematic anemia screening into primary healthcare to prevent decompensation, expanding targeting: extend prevention and free care actions to school-aged children (> 5 years) who remain highly vulnerable. Differential Diagnosis: Strengthen laboratory capacities to identify non-malarial fevers and rationalize the use of antibiotics and antimalarials.

Competing Interests: the authors declare that they have no competing interests.

Authors' Contributions: SGRP, CA, BGD conceived the study. SGRP, CA, BGD, CA, AA, AO, OA, EH, JO supervised data collection. SGRP, CA, BGD, CA, AA, AO, OA, EH, JO, BA, analyzed the data. SGRP, CA, BGD wrote the manuscript. All authors read and approved the final manuscript.

Acknowledgements: We thank the staff of CNHU-HKM, CHUZ-AS, and HZOD for their cooperation, and all patients who participated in the study.

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