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Modeling clinical malaria episodes in different ecological settings in Mali, 2018-2022

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ABSTRACT

Objectives: Following the scaling-up of malaria control strategies in Mali, understanding the changes in age-specific prevalence of infection and risk factors associated with remains necessary to determine new priorities to progress toward disease elimination. This study aimed to estimate the risk of clinical malaria using longitudinal data across three different transmission settings in Mali.

Methods: Cohort-based longitudinal studies were performed from April 2018 to December 2022. Incidence of malaria was measured through community health center-based passive case detection. Generalized estimation equation model was used to assess risk factors for clinical malaria.

Results: A total of 21,453 clinical presentations were reported from 4500 participants, mainly from July to November. Data shows a significant association between malaria episodes, sex, age group, season, and year. Women had lower risk, the risk of clinical episode increased with age up to 14 years then declined, and in both sites, the dry-season risk of clinical episode was significantly lower compared to the rainy season.

Conclusion: Determining factors associated with the occurrence of clinical malaria across different ecological settings across the country could help in the development of new strategies aiming to accelerate malaria elimination in an area where malaria transmission remains intense.

Introduction

Despite considerable malaria control efforts over the past decade, World Health Organization African regions still endure a disproportionate burden of the disease with approximately 94% of all cases and deaths observed in the world in 2022 [1–3]. According to statistics from the national health system information of Mali, malaria is the leading cause of health-seeking behavior in the community (32%) with 33.7% of malaria cases among children under 5 years, and 4.77% in pregnant women [4].

Since 2000, most malaria-endemic countries in sub-Saharan Africa, including Mali, have progressively implemented effective malaria control strategies such as (1) improved access to healthcare with early diagnosis and prompt treatment (rapid diagnostic test [RDT] + Artemisinin-based combination therapies [ACTs]), (2) Intermittent preventive treatment for pregnant women with sulfadoxine-pyrimethamine, (3) universal coverage with long-lasting insecticidal nets (LLINs), (4) Seasonal malaria chemoprevention (SMC) for children less than 5 years old, and (5) indoor residual spraying (IRS) in targeted geographical areas [5–7].

Several factors contribute differently to the presence or absence of clinical symptoms among malaria parasite-infected individuals. Among them are parasite species, exposure to infection, nutritional status, immune status, and genetic factors. Other factors that may affect malaria transmission are environmental: temperature, rainfall, and altitude. These factors have been well described and characterized over the last decade. Nevertheless, the current observed age-specific shift in malaria prevalence of infection requires an in-depth assessment of the disease's epidemiology to identify additional risk factors associated with these changes [8,9].

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Different models have been used to predict malaria transmission dynamics in Africa. The majority were population-based models and such models are based on the assumption that individuals living together have a similar risk of malaria. However, it is well established that such a model will not take into account individual risk factors that may present significant variation within a small geographical area. These factors include premunition, behavioral changes, exposure to malaria vectors, vector abundance, and finally parasite genetic diversity levels [10–12]. Numerous studies have already emphasized the need to adopt standardized longitudinal statistical methods to analyze prospective cohort studies of malaria infection [13]. Neglecting to include these risk factors and their variation over time and space may decrease the accuracy of any model aiming to determine the risk of symptomatic malaria among the population living in endemic areas.

In this study, we utilized a generalized estimating equation (GEE) to assess risk factors associated with symptomatic malaria episodes in three distinct ecological settings in Mali.

Methods

Study sites

This study was conducted in the Malian rural villages of Dangassa, Koïla Bamanan, and Sirakorola (Figure 1) from April 2018 to December 2022. Each site presents a specific ecological setting related to malaria transmission intensity. Dangassa is located 75 km south of Bamako, within the health district of Ouelessebougou, Koulikoro region (8° 12′ 37.253″ W and 12° 8′ 46.279″ N). The specificity of Dangassa is its proximity to the Niger River (about 3 km from) ensuring the persistence of mosquito breeding site during the long dry season while the presence of gardening plains flooded by rain inside and around the village contributes to the high vector density during the rainy season (June to November). Malaria transmission is highly seasonal with an extended transmission season (5-6 months a year). Koïla Bamanan (5° 45′ 32.18″ W and 13° 38′ 24.026″ N) is a village in the Dioro health district, region of Segou, about 385 km northeast of Bamako. The village has a semi-controlled irrigation system rice cultivation area contributing to the permanent presence of mosquito breeding sites (with a considerable decrease in number from March to May). The rainy season lasts from July to October, (with an average of 250–500 mm per year) followed by a long dry season from November to May. Finally, Sirakorola (7° 34′ 00″ N and 13° 17′ 00″ W) 115 km east of Bamako, is in the Koulikoro health district, region of Koulikoro. The climate is Sudan-Sahelian, characterized by a long dry season from November to May and a short rainy season from June to October. The average monthly temperature during the rainy season varies from 29°C to 33°C. Malaria transmission occurs mainly during the rainy season (June to October) picking up between September – October each year.

Study population and sampling

From an updated population enumeration list of each study village done by the research team, we randomly selected 240 households. All members of selected households were asked to participate. Individuals who voluntarily consented were included. Thus, each site had 1400 children and adults at baseline However, since the cohort was dynamic (all new members of the households were automatically included if all inclusion criteria were met), this size changed progressively from one site to another. Each site had a community health center where the study clinician was based. Each participant received an individual identifier (ID), and a photo ID was taken to produce an individual participant card. Consequently, they were invited to seek medical care if they experienced symptoms relating to malaria. For each visit, the clinician used a well-designed questionnaire to collect information on symptoms, malaria RDT and smear for microscopy were prepared and free antimalarial was given for all malaria-confirmed cases according to the Mali National malaria treatment policy. The follow-up was conducted from April 2018 to December 2022.

Operational definitions

- Malaria episode: A malaria episode was defined as a patient with fever or a history of fever within the past 48 hours with a laboratory-confirmed malaria diagnosis (by microscopy and/or RDT).
- Season: With respect to malaria seasonality, a qualitative dichotomous “season” variable (0 = dry season and 1 = rainy season) was created. A month was considered the rainy season when a minimum cumulative rainfall of 20 mm was observed in 3 days with no consecutive dry sequence of more than 10 days in the following 30 days [14]. A month was considered drier when less than a minimum cu-

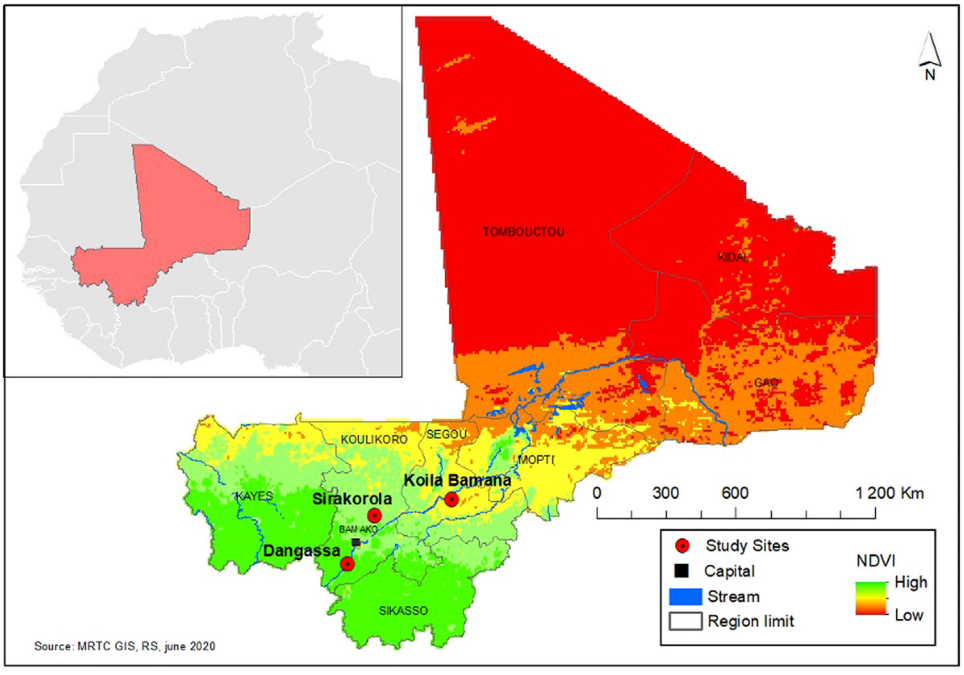

Figure 1. Map showing the three study sites Dangassa, Koïla Bamanan, Sirakorola.

mulative rainfall of 20 mm was observed in 3 days with a consecutive dry sequence of more than 10 days in the following 30 days.

Data collection and statistical analysis

The data were collected using REDCap (Research Electronic Data Capture) on a tablet and transferred to the server. The R software version 4.3.1 was used for the data analysis.

- Malaria incidence: The malaria incidence rate was calculated by dividing new malaria episodes over the sum of person-time of the population at-risk in the cohort.

$$Incidence\ rate = \frac{Number\ of\ new\ cases}{Follow-up\ time * total\ for\ all\ participants} \times 100$$

- The generalized estimation equation model: The risk factors associated with malaria episodes were estimated using marginal logistic regression models. Among them, we chose a GEE model [15] with an exchangeable correlation structure because of its simplicity and our assumptions. Moreover, in this model, we assume that a malaria episode is not necessarily related to the previous episode. Therefore, the exchangeable correlation structure assumes the following hypothesis: repeated measurements of malaria status in different individuals can be made unevenly at different spaced times. In addition to its assumption, the choice of this correlation structure was also consolidated by a sensitivity analysis test comparing the exchangeable correlation structure to the independent autoregressive and unstructured correlation structures.

To better estimate the risk of malaria, we used “Malaria episodes” as a response variable with gender, age group, season of visit, year of visit, and study site as covariates. A final model was built by incorporating the interaction terms between covariates. The Wald test and Quasi Information Criterion were performed for the best model fit selection.

Regarding the regression analysis of correlated observations, the GEE model can be described as follows: We first estimated the vector of regression coefficients β by assuming that the random variables within a vector Yi are probably independent. Consider a sample of $\boldsymbol{i = 1,\ldots, K}$ independent multivariate observations of subjects $\boldsymbol{Yi = (Y_{i1},\ldots, Y_{it},\ldots, Y_{ini})}$. Here, i may represent a cluster with $\boldsymbol{ni}$ observations and $\boldsymbol{Yit}$ a binary outcome (Malaria visit with Blood smear or RDT positive. The expectations $\boldsymbol{E(Yit) = \mu it}$ are related to the p dimensional regressor vector $\boldsymbol{xit}$ by the mean-link function g. $\boldsymbol{g(\mu_{it}) = x_{it}{}^{T}\beta}$. Let $\boldsymbol{VAR(Y_{it}) = \theta\ ait}$, where θ is a common scale parameter and $\boldsymbol{a_{it} = a(\mu_{it})}$ is a known variance function. Let Ri( ) be a working correlation matrix completely described by the parameter vector of length m. Let $\boldsymbol{Vi = \theta A_i^{1/2} R_i (á) A_i^{1/2}}$

With $\boldsymbol{Ai}$ and where $\boldsymbol{Ri}$ is the correlation matrix of the elements of the vector Yi, which in this case is equal to the identity matrix of dimension $\boldsymbol{ni \times ni}$. We called this matrix the “working” correlation structure for Yi. We obtain the estimator of $\boldsymbol{\beta}$, $\hat{\boldsymbol{\beta}}$, by maximizing the likelihood function of the parameter $\boldsymbol{\beta}$.

The mathematical model formulas

○ Initial model:

$$E(((negative = 0\ ou\ Positive = 1)) = g\left(\mu_{id.visitit}\right) \approx \alpha + \beta_1.sex_{id} + \beta_2.Agegroup_{id} + \beta_3.Study\ site_{id} + \beta_4.Season_{id} + \beta_5.Year\ of\ visit_{id}$$

Binomial distribution family « Logit »
Link function: $g(\mu_{id.visitit}) = log\left(\frac{\mu}{1-\mu}\right); V(\mu) = \mu(1-\mu).\ \mu \in (0.1)$
Exchangeable correlation matrix:

$$R(\alpha) = Corr\left(Malaria_{id.visit}.\ Malaria_{id'.visit'}\right) = \alpha.\ \forall visit \neq visit'.\ |\alpha| < 1$$

○ Final model:

$$E(((negative = 0\ ou\ Positive = 1)) = g\left(\mu_{id.visitit}\right) \approx \alpha + \beta_1.sex_{id} + \beta_2.Agegroup_{id} + \beta_3.Study\ site_{id} + \beta_4.Season_{id} + \beta_5.Year\ of\ visit_{id} + \beta_5.Agegroup_{id} \times Season_{id.visit} + \beta_6.Study\ site_{id} \times Season_{id.visit}$$

Binomial distribution family « Logit »
Link function: $g(\mu_{id.visitit}) = log\left(\frac{\mu}{1-\mu}\right); V(\mu) = \mu(1-\mu).\ \mu \in (0.1)$
Exchangeable correlation matrix:

$$R(\alpha) = Corr\left(Malaria_{id.visit}.\ Malaria_{id'.visit'}\right) = \alpha.\ \forall visit \neq visit'.\ |\alpha| < 1$$

Management of missing data

Data for this study were meticulously gathered as part of a clinical research investigation, adhering to rigorous data collection protocols established by our data management team to ensure high-quality data. A continuous validation process for data completeness was implemented by the data management team on the server, allowing us to maintain the proportion of missing clinical data below 2%. These missing data, primarily resulting from unintentional omissions during data entry, can be categorically defined as Missing Completely At Random (MCAR). The variable “malaria episode” exhibited a minimal proportion of missing data (<5%), predominantly due to instances of broken or misidentified microscope slides or inaccurately recorded RDT results. Again, these occurrences typify MCAR data. Given the nature (MCAR) and the extremely low proportion of these missing data, there was no need for imputation.

Results

Characteristics of the participants and visit patterns

During the study period from April 2018 to December 2022, a total of 21,453 visits were recorded across the three study sites. Of these, Dangassa had the highest number of visits (10,252), followed by Koïla Bamanan (6374), and Sirakorola (4827) (Table 1). In terms of participant demographics, there was a near-equal representation of sexes, with men constituting around 44-47% and women 53-57% across the study sites. When assessing visits by age group, the highest number of visits were by children aged 5-9 years, which accounted for a significant proportion of visits across all sites, particularly in Dangassa with 13 visits per patient. Conversely, participants in the less than 5 years age group showed fewer visits per patient, with the lowest in Sirakorola at 2.1 visits per patient. Looking at the distribution of visits over the years, there was a noticeable increase in visits in Dangassa and Dioro through 2022. However, a different trend was observed in Sirakorola where a decrease in visits started in 2021. In the analysis of visits by season, the rainy season was associated with a higher number of visits compared to the dry season across all sites, with a particularly stark contrast in Sirakorola where dry-season visits represented only 0.1 visit per patient vs 3.4 visits per patient in the rainy season.

Malaria incidence

Seasonal variation in the incidence rate at all sites is shown in Figure 2. The highest rates were observed between June and November, corresponding to the rainy season in all three study sites. The village of Dangassa had the highest incidence rates during the rainy season (June-December), with a maximum of 4 per 100 person-months, compared to 2 and 3.2 per 100 person-months respectively in Koïla Bamanan and Sirakorola. We observed incident malaria cases in Dangassa and Koïla Bamanan starting from the 2020 dry season.

Table 1
Sociodemographic characteristics of participants and visit distribution across different factors in the three study sites from 2018 to 2022.

A) Sociodemographic characteristics of participants.[a]			
	Dangassa N = 1430	Koila Bamanan N = 1391	Sirakorola N = 1393
Sex			
Male	669 (46.8%)	603 (43.4%)	615 (44.1%)
Female	761 (53.2%)	788 (56.6%)	778 (55.9%)
Age Group			
<5 years	364 (25.5%)	270 (19.4%)	316 (22.7%)
5-9 years	283 (19.8%)	379 (27.2%)	302 (21.7%)
10-14 years	241 (16.9%)	245 (17.6%)	241 (17.3%)
15-20 years	147 (10.3%)	77 (5.5%)	139 (10%)
>20 years	395 (27.6%)	420 (30.2%)	395 (28.4%)
B) Distribution of number of visits by gender, age, season, and year from 2018 to 2022 "Number of Visit (Average Visits per Patient)"[b]			
Overall	10252 (7.2)	6374 (4.6)	4827 (3.5)
Sex			
Male	5231 (7.8)	3245 (5.4)	2620 (4.3)
Female	5021 (6.6)	3129 (3.9)	2207 (2.8)
Age Group			
<5 years	1609 (4.4)	985 (3.6)	670 (2.1)
5-9 years	3665 (13)	1622 (4.3)	1486 (4.9)
10-14 years	2065 (8.6)	1565 (6.4)	1322 (5.5)
15-20 years	766 (5.2)	467 (6.1)	591 (4.3)
>20 years	2147 (5.4)	1735 (4.1)	758 (1.9)
Season			
Dry	1038 (0.7)	638 (0.5)	86 (0.1)
Rainy	9214 (6.4)	5736 (4.1)	4741 (3.4)
Year of Visit			
2018	1115 (0.8)	892 (0.6)	737 (0.5)
2019	990 (0.7)	952 (0.7)	1019 (0.7)
2020	2791 (2)	1154 (0.8)	1359 (1)
2021	2529 (1.8)	1784 (1.3)	772 (0.6)
2022	2827 (2)	1592 (1.1)	940 (0.7)

[a] **A)** Sociodemographic characteristics of participants in the three study sites, Dangassa, Koila Bamanan, and Sirakorola. The table shows the number and percentage of participants by sex and age group for each location.

[b] **B)** Distribution of the number of visits by gender, age, season, and year from 2018 to 2022 in the three study sites. The data presented includes the total number of visits (with the average visits per patient in parentheses) across different demographic and temporal factors.

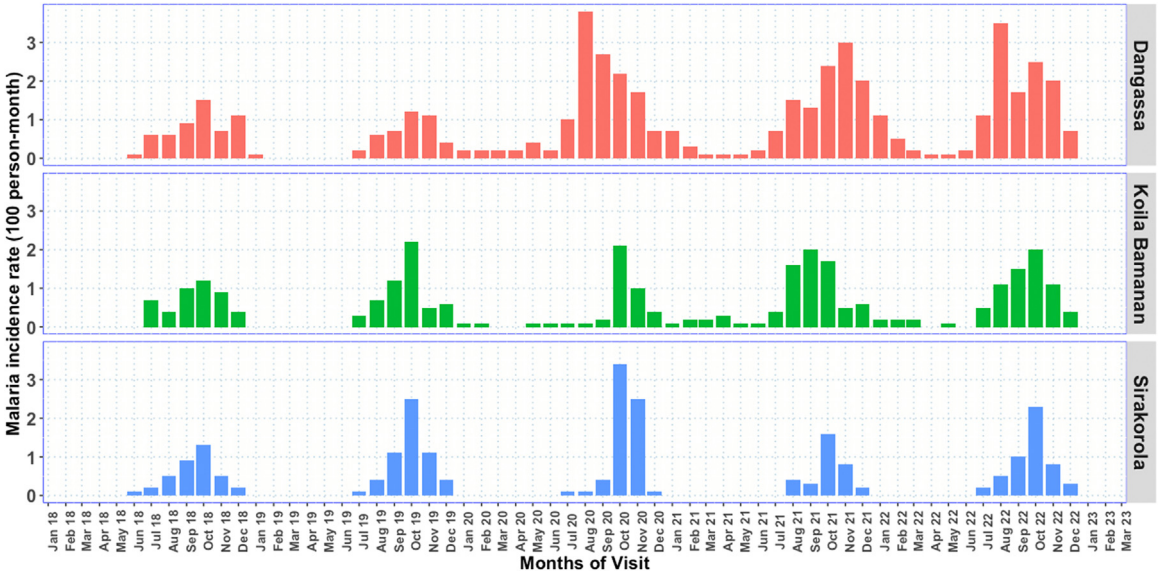

Figure 2. Dynamic of malaria incidence rate for 100 person-month from 2018 and 2022 in Dangassa, Koila Bamanan, and Sirakorola. *Note* – This bar chart illustrates the monthly incidence rate of malaria across different study sites. The incidence rate, represented on the Y-axis, is calculated per 100 person-months and represents the number of new cases occurring during the study period. The X-axis signifies the months during which the study visits took place, and the bars are color-coded by study sites. Each bar's height indicates the malaria incidence rate for a given month at a specific study site.

Table 2
Estimating the risk of a malaria episode from 2018 to 2022 (GEE model).

Characteristic	GEE: Initial model vs final model (exchangeable)					
	Initial model			Final model		
	OR	95% CI	*P*-value	OR	95% CI	*P*-value
Sex						
Male	—	—		—	—	
Female	0.89	0.80 - 0.98	0.018	0.88	0.80 - 0.98	0.016
Age group						
<5 years	—	—		—	—	
5-9 years	2.39	2.07 - 2.77	<0.001	2.54	2.18 - 2.96	<0.001
10-14 years	3.18	2.68 - 3.76	<0.001	3.41	2.84 - 4.10	<0.001
15-20 years	1.75	1.41 - 2.16	<0.001	1.83	1.46 - 2.29	<0.001
>20 years	0.73	0.64 - 0.85	<0.001	0.8	0.69 - 0.93	0.003
Study area						
Dangassa	—	—		—	—	
Koila Bamanan	0.79	0.71 - 0.89	<0.001	0.89	0.79 - 1.01	0.071
Sirakorola	0.97	0.84 - 1.13	0.7	1.08	0.93 - 1.25	0.3
Season						
Rainy	—	—		—	—	
Dry	0.27	0.24 - 0.31	<0.001	0.6	0.44 - 0.81	0.001
Year of visit						
2018	—	—		—	—	
2019	1.31	1.11 - 1.54	0.001	1.3	1.11 - 1.53	0.002
2020	0.64	0.55 - 0.75	<0.001	0.64	0.55 - 0.74	<0.001
2021	0.76	0.66 - 0.88	<0.001	0.76	0.66 - 0.88	<0.001
2022	1	0.86 - 1.16	>0.9	0.99	0.85 - 1.15	>0.9
Study area * Season						
Dangassa*Rainy				—	—	
Koila Bamanan * Dry				0.51	0.39 - 0.67	<0.001
Sirakorola * Dry				0.3	0.16 - 0.56	<0.001
Age group * Season						
<5 years*Rainy				—	—	
5-9 years * Dry				0.59	0.41 - 0.85	0.005
10-14 years * Dry				0.55	0.37 - 0.82	0.004
15-20 years * Dry				0.81	0.47 - 1.39	0.4
>20 years * Dry				0.49	0.34 - 0.72	<0.001

CI, confidence interval; OR, odds ratio; GEE, generalized estimating equation.

Estimating the risk of a malaria episode

In both the initial and final models (Table 2), we observed significant associations between the risk of symptomatic malaria episodes and various factors, including sex, age group, season, and year of visit. In the initial model, female participants had a slightly lower risk of symptomatic malaria than men (odds ratio [OR] = 0.89, 95% confidence interval [CI]: 0.80-0.98, $P = 0.018$). This association remained significant in the final model (OR = 0.88, 95% CI: 0.80-0.98, $P = 0.016$).

The risk of symptomatic malaria episodes increased with age in both models, peaking in the 10-14-year-old age group (initial model: OR = 3.18, 95% CI: 2.68-3.76, P <0.001; final model: OR = 3.41, 95% CI: 2.84-4.10, P <0.001) before declining in the older age groups. The risk was significantly lower during the dry season than the rainy season in both models (initial model: OR = 0.27, 95% CI: 0.24-0.31, P <0.001; final model: OR = 0.6, 95% CI: 0.44-0.81, $P = 0.001$).

In the final model, we observed significant associations between the risk of symptomatic malaria episodes and various factors, including sex, age group, season, and year of visit. In terms of the study area, there was no significant difference in risk between Koïla Bamanan and Dangassa (OR = 0.89, 95% CI: 0.79-1.01, $P = 0.071$) or between Sirakorola and Dangassa (OR = 1.08, 95% CI: 0.93-1.25, $P = 0.3$). However, there were pronounced interactions (Figure 3) between the study area and season, as well as age group and season. In Koïla Bamanan and Sirakorola, the risk of symptomatic malaria episodes during the dry season was significantly lower than in Dangassa (OR = 0.51, 95% CI: 0.39-0.67, P <0.001 and OR = 0.3, 95% CI: 0.16-0.56, P <0.001, respectively).

Furthermore, the interaction between age group and season (Figure 3) revealed that the risk of symptomatic malaria episodes during the dry season was significantly lower for 5-9-year-olds (OR = 0.59, 95% CI: 0.41-0.85, $P = 0.005$), 10-14-year-olds (OR = 0.55, 95% CI: 0.37-0.82, $P = 0.004$), and those aged over 20 years (OR = 0.49, 95% CI: 0.34-0.72, P <0.001) compared to the reference age group of under 5 years. In summary, our findings indicate that sex, age group, season, and year of visit are significantly associated with the risk of symptomatic malaria episodes. The interaction between study area and season, as well as age group and season, further highlights the complex interplay of factors affecting malaria risk in Mali's different ecological settings.

Discussion

This study used a GEE to assess risk factors associated with malaria clinical episodes in a multi-site cohort study involving participants from three different ecological settings in Mali. Among the three sites, Dangassa had the highest number of patients visiting health centers and the highest number of confirmed malaria cases. Despite the differences in malaria seasonal pattern across sites, Dangassa experienced a longer and higher transmission period than the other sites. These observations may be attributed to Dangassa's proximity to the river, as reported by Ateba et al. [16]. Previous studies have also indicated that rivers provide favorable breeding conditions for Anopheles mosquitoes during the dry season, extending the transmission season beyond the rainy period [17,18].

The overall risk of malaria episodes in children under 5 years old was lower than in the 5-9, 10-14, and 15-20-year-old age groups. This shift in malaria risk from younger to older children has been reported in previous studies conducted in Mali [19,20]. The primary focus of control interventions on children under 5 years old may have delayed the immune responses in older age groups. This may increase their risk of malaria infection and disease. Other studies have suggested that school-aged children and adults with less exposure to antimalarial interventions could represent an alternative reservoir of malaria infection for children

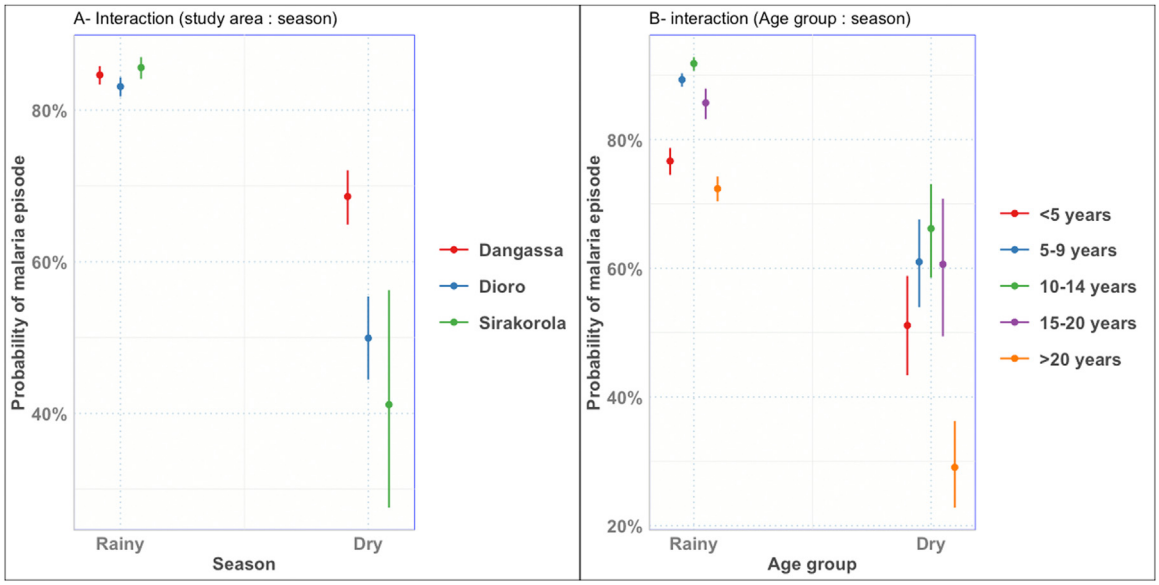

Figure 3. The effect plots from the generalized estimating equation model, illustrate the impact of interaction effects on the probability of experiencing a malaria episode. *Note* – Panel a represents the interaction effect between the study areas and the seasons on the likelihood of a malaria episode. Panel b illustrates the interaction effect between different age groups and seasons on the probability of a malaria episode.

under 5 years old [21,22]. This study revealed that the relatively low risk of malaria episodes in children under 5 is not constant throughout the year. Specifically, during the dry season following the end of the yearly SMC campaign (which ends in October each year), the risk becomes higher compared to older age groups, indicating that while children aged 5-9 and 10-14 years are presented as the main parasite reservoirs there is an increase in the risk of malaria among children less than 5 years after the last round of SMC corresponding to the start of the dry season.

We observed a significant overall decrease in malaria episodes risk by up to 40% during the dry seasons, with an even stronger effect in Koïla Bamanan, and Sirakorola, where the risk decreased by about 60%. Although malaria transmission decreased overall, transmission persisted in Dangassa, which could be explained by the heterogeneous nature of malaria transmission and the lag phenomenon between malaria incidence and the combination of meteorological factors such as rainfall, temperature, and evaporation. Several studies have reported a 3-month lag between weather factors and malaria incidence [16,19,23–27]. In Dangassa, rainy seasons are longer, affecting the duration of suitable conditions for vector development, and the spread of disease through riverbeds that persist throughout the drying season. Accurately estimating malaria risk and identifying factors associated with its variation in these areas is crucial for optimizing the allocation of malaria control resources. This is also crucial for developing strategies adapted to each context in Mali [19,28–31]. We have also noted a marked reduction in malaria episode risk over time. This be attributed to the implementation of various malaria control interventions, such as SMC, LLINs, and IRS, which have been widely adopted in these areas in recent years [28].

In summary, this study highlights the importance of understanding malaria transmission risk factors and dynamics in different ecological settings. Our findings reveal variations in malaria risk across age groups, seasons, and study areas, emphasizing the need for tailored interventions and resource allocation strategies. The persistence of malaria transmission in certain areas, such as Dangassa, and the shifting risk of infection among age groups underscore the necessity of continuous surveillance and adaptive management of malaria control efforts. To further improve malaria prevention and control strategies, future research should focus on evaluating the effectiveness of existing interventions. It should also explore innovative approaches that target infection reservoirs and areas of persistent transmission.

Limitations of the study

This study, while illuminating in its findings, has a few noteworthy limitations. One significant constraint is that the GEE models used in this study do not account for the effects of various malaria interventions that have been implemented in the study areas. Consequently, the observed patterns and associations might be confounded by unmeasured interventions. For instance, the reduced risk of malaria over time could be influenced by the implementation of interventions like SMC, LLINs, and IRS, which were not incorporated into our models. Additionally, our study focused on elucidating the associations between various factors and malaria incidence, rather than predicting future patterns of malaria transmission. Predictive modeling is of utmost importance in malaria control, as it allows for proactive planning of interventions and resources. Therefore, future research should strive to incorporate intervention variables and prediction-based approaches to provide a more comprehensive picture of malaria dynamics and enable effective planning for malaria control and elimination strategies.

Conclusion

This study shows evidence of the factors associated with clinical malaria episodes in three distinct ecological settings in Mali. By performing a generalized estimation equation, we have identified key differences in malaria risk among age groups, seasons, and study areas. The findings underscore the necessity for context-specific and adaptive malaria control strategies, which take into account the unique dynamic of transmission in each setting. This knowledge will allow policymakers and public health practitioners to optimize resource allocation and tailor interventions to effectively address malaria challenges. Moving forward, continuous surveillance and innovative approaches targeting identified reservoirs of infection and areas with persistent transmission are crucial to achieving significant progress in the ongoing fight against this pervasive disease.

Declarations of competing interest

The authors have no competing interests to declare.

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Ethical considerations

The protocol of the ICEMR project was approved by the ethics committee of the University of Sciences, Techniques, and Technologies of Bamako (USTTB) (*2011/77/FMPOS*). The community consent was obtained before the occurrence of any study activities. Individual informed consent and/or assent forms were obtained for each cohort participant. We carried out research activities according to good clinical research practices on humans and good laboratory practices as stated in international conventions (Helsinki Declaration International Conference on Harmonization of Good Practices in Biomedical Research).

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Author contributions

FK: has worked on the research hypothesis and collecting the data analysis and manuscript writing. MT, NS: has worked on the research hypothesis and manuscript writing. BT, DS, DK, SID, SK, MK, IS: has worked on collecting the data and manuscript writing. AC: has worked on collecting and management of the data. SMT, IC: has worked on the administrative and coordination aspects. AB, JGS, MD, and SD: have worked on the research hypothesis and corrected and approved the latest version before submission. All authors read and approved the final manuscript.

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