GeoHealth

RESEARCH ARTICLE

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Key Points:

- In Sub-Saharan Africa, seasonal malaria transmission is sustained at temperatures well above 15°C or below 40°C with maximum monthly rainfall not exceeding 600 mm
- Rainfall and temperature are significant drivers of malaria seasonality in all parts of Sub-Saharan Africa except in west Central Africa
- Malaria transmission onset lags behind rainfall only at markedly seasonal rainfall areas, otherwise, malaria transmission is year-round

Supporting Information:

Supporting Information may be found in the online version of this article.

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Climate Drivers of Malaria Transmission Seasonality and Their Relative Importance in Sub-Saharan Africa

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Abstract A new database of the Entomological Inoculation Rate (EIR) was used to directly link the risk of infectious mosquito bites to climate in Sub-Saharan Africa. Applying a statistical mixed model framework to high-quality monthly EIR measurements collected from field campaigns in Sub-Saharan Africa, we analyzed the impact of rainfall and temperature seasonality on EIR seasonality and determined important climate drivers of malaria seasonality across varied climate settings in the region. We observed that seasonal malaria transmission was within a temperature window of 15°C–40°C and was sustained if average temperature was well above 15°C or below 40°C. Monthly maximum rainfall for seasonal malaria transmission did not exceed 600 in west Central Africa, and 400 mm in the Sahel, Guinea Savannah, and East Africa. Based on a multi-regression model approach, rainfall and temperature seasonality were found to be significantly associated with malaria seasonality in all parts of Sub-Saharan Africa except in west Central Africa. Topography was found to have significant influence on which climate variable is an important determinant of malaria seasonality in East Africa. Seasonal malaria transmission onset lags behind rainfall only at markedly seasonal rainfall areas such as Sahel and East Africa; elsewhere, malaria transmission is year-round. High-quality EIR measurements can usefully supplement established metrics for seasonal malaria. The study's outcome is important for the improvement and validation of weather-driven dynamical mathematical malaria models that directly simulate EIR. Our results can contribute to the development of fit-for-purpose weather-driven malaria models to support health decision-making in the fight to control or eliminate malaria in Sub-Saharan Africa.

Plain Language Summary In this study, we provide evidence of the direct link between climate variables and the risk of humans to infectious mosquito bites. The study informs our understanding of the connection between climate variables and both the malaria vector and parasite biology and how that translates into malaria seasonality in Sub-Saharan Africa. Information from this study is key for the improvement and validation of weather-driven dynamical malaria models that directly simulates metrics that connects climate to malaria transmission. Our findings provide an understanding of geographical heterogeneous malaria risk from climate effect and support future malaria modeling and forecasting efforts. The study also supplements previous works describing clinical patterns of malaria infection and morbidity. Taking into account the seasonality of malaria management, findings in this study could lead to significant public health advantages by assisting in determining when, where, and how to use vector and parasite control strategies. It can, therefore, help stakeholders establish a robust framework for monitoring, forecasting and control of malaria.

1. Introduction

Sub-Saharan Africa remains the world's region with the greatest malaria burden despite massive efforts over the past decades to lower or eliminate malaria (WHO, 2020). Though poor health care systems and low socio-economic status (Degarege et al., 2019; Yadav et al., 2014) are contributing factors, the climate suitability of the region for malaria transmission has a major influence (Caminade et al., 2014). Generally, climate variables such as temperature, rainfall and relative humidity are known to have a significant influence on the development and survival of both the malaria parasites and their vectors. Malaria parasite development is not possible at temperatures below 16°C and temperatures above 40°C have adverse effects on mosquito population turnover (Blanford et al., 2013; Mordecai et al., 2013; Parham & Michael, 2010; Shapiro et al., 2017). Rainfall provides the environment for

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vector breeding (Ermert et al., 2011; Kar et al., 2014; Tompkins & Ermert, 2013) and relative humidity of at least 60% appears necessary for vector survival (Thompson et al., 2005). Rainfall, therefore, affects the availability, persistence and dimensions of Anopheles vectors and their larval habitats (Afrane et al., 2012; Asare, Tompkins, Amekudzi, & Ermert, 2016; Boyce et al., 2016; Fournet et al., 2010). Previous work studying the relationship between sporozoite development and the survival of infectious mosquitoes found optimal temperatures for efficient malaria transmission between 25°C and 27°C (Bayoh, 2001; Lunde, Bayoh, & Lindtjørn, 2013; Lunde, Korecha, et al., 2013). In Sub-Saharan Africa, most countries have annual mean temperatures between 20°C and 28°C (Lunde, Bayoh, & Lindtjørn, 2013). Given Sub-Saharan Africa's warm tropical climate, a plethora of efficient and effective malaria parasite and vectors thrive in this setting (Murray et al., 2012; Sinka et al., 2010). Understanding the relative importance of climate drivers of malaria seasonality is crucial for describing the geographic patterns of the heterogeneous risk and burden of malaria across the sub-region (Gething et al., 2011; Reiner et al., 2015). This could translate to substantial public health gains, taking into account the seasonality in malaria control and prevention interventions, by helping to determine when, where and how to apply vector and parasite control measures.

To our knowledge, there are insufficient field studies using Entomological Inoculation Rate (EIR, defined as the number of infectious mosquito bites a person receives per time) data to relate climate to malaria seasonality in Sub-Saharan Africa. M. L. H. Mabaso et al. (2007) assessed the relationship between EIR seasonality and environmental variables in Africa using a rainfall seasonality index (Markham, 1970). However, this index used in their study has an inherent problem in that it is unable to accurately capture seasonality in regions with bimodal rainfall regimes. Furthermore, their study did not take into consideration the impact of diverse climatic conditions on seasonality outcomes but aggregated data from sites of different climate and environmental settings into a single study, which has the potential to skew the results. Other research has examined the link between malaria and climate variables but primarily relied on clinical data or malaria suitability indices (Komen et al., 2015; Lowe et al., 2013; Midekisa et al., 2015). Both malaria indices and case data have drawbacks to studying malaria seasonality.

Malaria indices are derived using statistical relationships between weather and malaria measures and their out-of-sample generalization over space and time for seasonality studies is subject to significant uncertainties. Clinical case data are also subject to significant uncertainties due to inaccurate diagnostics (often counts of suspected cases, with temporal inconsistency in the use of Rapid Diagnostic Test [RDT] or slide analysis) and under-counting due to varying health-seeking behavior and health policies (Afrane et al., 2012). Given that the biology of the malaria parasite and its vector mosquito are temperature and rainfall dependent (Ermert et al., 2011), and that EIR can directly quantify parasite-infected mosquitoes and their propensity to transmit the parasites to humans (MARA, 1998; Shaukat et al., 2010) or estimate the seasonality of the exposure of a population to malaria parasite inoculations (Beier et al., 1999; Takken & Lindsay, 2003), then EIR should be able to usefully relate climate to malaria seasonality better than malaria cases.

In this study, we investigated the impact of climate variables on EIR seasonality in diverse climate settings across Sub-Saharan Africa with the goal of identifying significant climate determinants of malaria seasonality, their relative importance and variability across the region. To our knowledge, this is the first study to use EIR_m to explore the impact of climatic variables on malaria seasonality in Sub-Saharan Africa on this wider scale. We applied a mixed model statistical framework to a high-quality malaria EIR data (Yamba et al., 2018, 2020) gathered from publicly available field campaigns of sufficient duration and determined the climate effect that explained significant variations in EIR seasonality. Our findings are intended to provide an understanding of geographically heterogeneous malaria risk from climate effect and support future malaria modeling and forecasting efforts. It will contribute to the development of malaria models especially weather-driven dynamical malaria models fit-for-purpose to support health decision-making in the fight to control or eliminate malaria in Sub-Saharan Africa.

2. Data and Methods

2.1. Study Area

The study area includes locations in Sub-Saharan Africa (as shown in Figure 1), where mosquitoes have previously been collected for malariometrics such as Human Biting Rate, CircumSporozoite Protein Rates, and EIR.

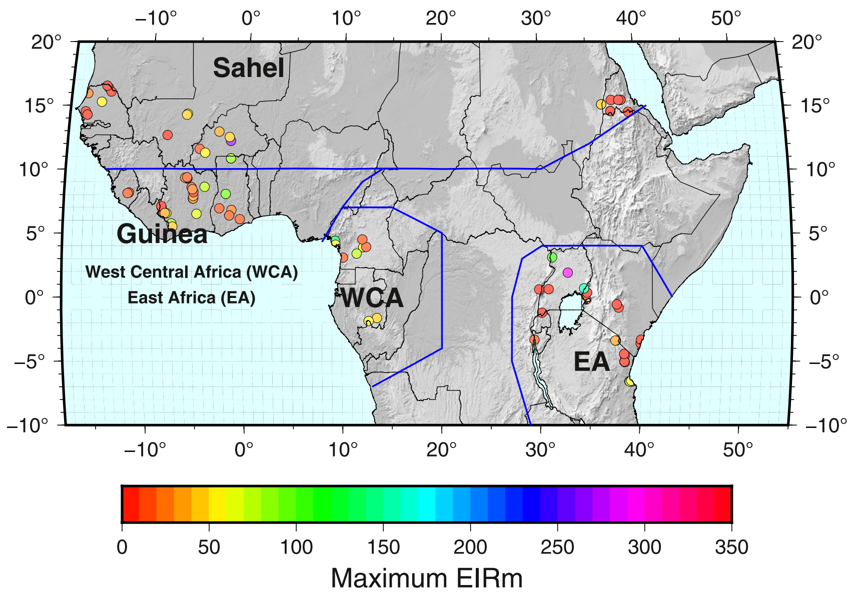

Figure 1. The map of the Sub-Saharan Africa showing field survey sites for Entomological Inoculation Rate (EIR). The color gradient of each site show the maximum EIR available. The blue lines delineate the region into climate zones of Sahel, Guinea, WCA and EA.

The geographical coordinates and elevation of each location are detailed in Tables S1–S4 in Supporting Information S1. The study locations are grouped into four distinct climate zones namely Sahel, Guinea, WCA, and EA (see Figure 1). Each zone has unique climate conditions from others (see Figure S1 in Supporting Information S1) and therefore has different climate implications on malaria seasonality (Yamba, 2016). The division into zones is, therefore, to ensure that malaria transmission patterns are consistent across geographical areas with similar climate characteristics. The seasonal distribution of rainfall and temperature for each zone is shown in Figure S1 in Supporting Information S1. In the Sahel, rainfall is markedly seasonal, with a single wet season (usually June–October) and a protracted dry season (November–May). Seasonal temperature ranges between a minimum value of 20°C during the harmattan season and to a maximum of about 40°C during the pre-monsoon season. In general, temperatures are higher in the Sahel and colder in EA due to the fact that most areas are characterized by higher altitudes.

2.2. Data

2.2.1. Monthly EIR Data

Monthly malaria EIR data (hereafter referred to as EIR_m) were obtained from a newly compiled and published monthly malaria EIR database (Yamba et al., 2018, 2020) for each study location shown in Figure 1. The years and months for which the EIR_m data were available for each study location is shown in Table S1–S4 in Supporting Information S1. Generally, most locations had 12 months of data while other locations had data varying between 24 and 36 months. The data also spanned the period 1983–2013 for all locations. The temporal duration of the data is mostly limited to 1 year because sampling mosquitoes for EIR is extremely capital and labor intensive (Badu et al., 2013; Kilama et al., 2014; Tusting et al., 2014). The EIR database from which data were extracted for use in this work is a comprehensive one. It was constructed through an all-inclusive literature review using Google scholar and PubMed search facilities. All data in that database was generated from publicly available field campaigns of adequate duration and is freely available for public usage in the PANGAEA repository (Yamba et al., 2018). Details of how this database was constructed including compilation, sources, recording, spatial coverage, and temporal resolutions are clearly described in Yamba et al. (2020).

2.2.2. Meteorological Data

Monthly rainfall (RR) and temperature (minimum (T_{min}), mean (T_{mean}), and maximum (T_{max})) data for each study location were gathered. Rainfall data were obtained from the Global Precipitation Climatology Centre (GPCC) product, version 2018 (Schneider et al., 2018). The GPCC data are a gridded gauge-analysis product and available globally from 1891 to 2016 at a spatial resolution of 0.25°. GPCC was chosen because it is a rain gauge-analysis product built from quality-controlled rainfall data from ground-based weather stations. Previous validation studies (Atiah et al., 2020; Manzanas et al., 2014) have also found it to be reliable and consistent with ground-based weather observations. The temperature data were obtained from the European Centre for Medium-Range Weather Forecasts (ECMWF) Re-Analysis, 5th generation (ERA5) (Hersbach et al., 2020). ERA5 is also a gridded re-analysis product and available globally on an hourly time scale from 1979 to present at a high spatial resolution of 0.25° by 0.25°. ERA5 was chosen because previous evaluation studies of the product (Gleixner et al., 2020; Oses et al., 2020; Tarek et al., 2020) have widely recommended it for meteorological research. RR, T_{min}, and T_{max} were extracted from the respective database for each study location using the nearest grid point of the location's geographical coordinates. T_{mean} values were estimated by averaging the T_{min} and T_{max} values for the location. The extracted temperature and rainfall data had to also conform with the exact years and months at which $\mathrm{EIR_m}$ data were available for each location. The study relied on GPCC and ERA5 because ground-based local weather stations from which these data could be gathered were mostly not available at the EIR sites or, if present, often have sparse data.

2.3. Data Analysis

The analysis was conducted for each classified zone as shown in Figure 1. EIR data from locations characterized by the presence of permanent water bodies and/or irrigation activities were exempted. Irrigation and permanent water bodies (such as damps, rivers, streams, swamps etc.) have a significant influence on the intensity and length of seasonal malaria transmission (Asare & Amekudzi, 2017; Asare, Tompkins, & Bomblies, 2016; Ermert et al., 2011; Tompkins & Ermert, 2013). Their exclusion was, therefore, a means to dissociate the influence of these hydrological parameters on malaria seasonality and reducing the impact to climate factors alone.

2.3.1. Pair-Wise Comparison

The study examined the ranges of RR, T_{min}, T_{mean}, and T_{max} at which $\mathrm{EIR_m}$ occurred using a simple pair-wise comparison approach. This was done by first aggregating the $\mathrm{EIR_m}$ data from all locations within each zone into a single time series of 12 months irrespective of the year of availability. Similarly, the corresponding RR, T_{min}, T_{mean}, and T_{max} data were also aggregated. The aggregated monthly timeseries of RR, T_{min}, T_{mean}, T_{max}, and $\mathrm{EIR_m}$ were then matched head-to-head as shown in Figure 2. The ranges of RR, T_{min}, T_{mean}, and T_{max} at which EIR occurred were then determined for each zone.

2.3.2. Relative Importance of Climate Predictors

The relative importance of RR, T_{min}, T_{mean}, and T_{max} in predicting $\mathrm{EIR_m}$ for each climate zone was analyzed using a multiple regression model of the form:

$$EIR_{\mathrm{m}} \sim RR + T_{\mathrm{max}} + T_{\mathrm{min}} + T_{\mathrm{mean}} \quad (1)$$

where $\mathrm{EIR_m}$ is the response variable and RR, T_{min}, T_{mean}, and T_{max} are the predictors. The contribution of each predictor to $\mathrm{EIR_m}$ outcome was then quantified (see Tables 1 and 2). Each regressor's contribution was considered as the R^2 from univariate regression, and all univariate R^2 values add up to the full model R^2 (Grömping, 2007). The *R* package "relaimpo" (Grömping, 2007) was utilized for the calculation of the contribution of the regressors in the model. It implements six different metrics for assessing relative importance of regressors namely: first, last, pratt, betasg, lmg, and pmvd. Among these, lmg and pmvd are computer intensive and have an advantage over others in the sense that they decompose R^2 into non-negative contributions that automatically sum to the total R^2 (Grömping, 2007). In this study, lmg was invoked since pmvd is patent protected. The lmg calculates the relative contribution of each predictor to the R^2 with the consideration of the sequence of predictors appearing in the model. It intuitively decomposes the total R^2 by adding the predictors to the regression model sequentially. Then, the increased R^2 is considered as the contribution by the predictor just added. The following are mathematical descriptions of lmg metric referenced from Grömping (2007):

For a model with regressors in set *S*, the R^2 is given as:

$$R^2(S) = \frac{ModelSS(modelwithregressorsinS)}{TotalSS} \quad (2)$$

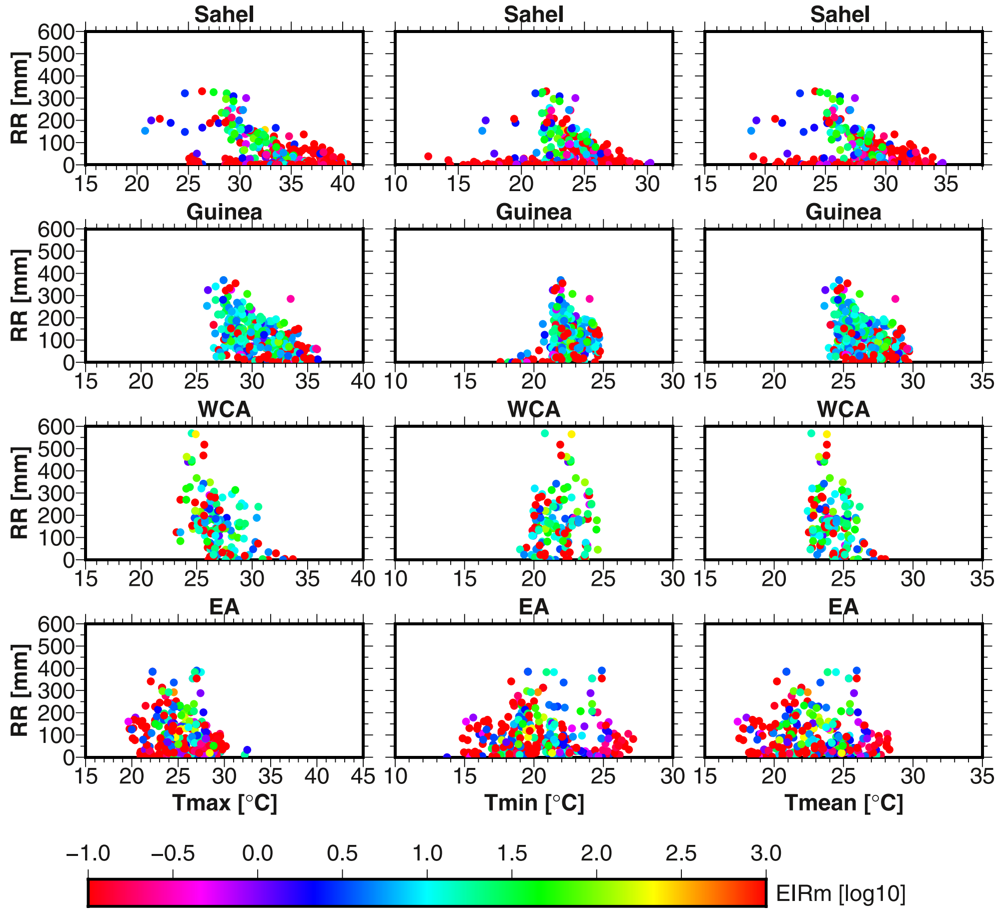

Figure 2. A pair-wise comparison showing the ranges of RR, T_{min}, T_{mean}, and T_{max} at which EIR_m occurs. The colored circles show log-transformed EIR_m values.

To add regressors in set M to a model with the regressors in set S, the additional R^2 is given as:

$$seqR^2(M|S) = R^2(MUS) - R^2(S) \tag{3}$$

where the order of the regressors is a permutation of the available regressors $x_1, \ldots, x_p$ denoted by the tuple of indices $r = (r_1, \ldots, r_p)$. Let $S_k(r)$ denote the set of regressors entered into the model before regressor x_k in the order r. Then the portion of R^2 allocated to regressor x_k in the order r can be written as:

$$seqR^2(\{x_k\}|S_k(r)) = R^2(\{x_k\}U S_k(r)) - R^2(S_k(r)) \tag{4}$$

With Equation 4, the metric lmg (in formulas denoted as LMG) can be written as:

$$LMG(x_k) = \frac{1}{P!} \sum_{r permutation} seqR^2(\{x_k\}|r) \tag{5}$$

Orders with the same $S_k(r) = S$ can be summarized into one summand, which simplifies the formula into:

$$LMG(x_k) = \frac{1}{p!} \sum_{S \subseteq \{x_1, \ldots, x_p\} \setminus \{x_k\}} seqR^2(\{x_k\}|S) \tag{6}$$

The analysis also assessed the relative importance of each regressor (in Equation 1) by looking at what each regressor alone can explain (i.e., comparing the R^2 value of regression model with one regressor only without considering the dependence of others as is the case of the metric *lmg*). The metric *first* in the "relaimpo" package was invoked for this purpose because, unlike *lmg*, it is completely ignorant of the other regressors in the model

Table 1
The Relative Contribution of RR, T_{min}, T_{mean}, and T_{max} in Predicting EIR_m Bootstrapped at a Confidence Interval of 95% for Locations With Elevations ≤500 m

Zone	R^2 (%)	Variable	lmg (%)	First (%)	Coefficient (*R*)	*P*-value
Sahel	**30.72**	**RR**	**7.73**	**15.76**	0.3497	**0.0000**
		$\boldsymbol{T_{max}}$	**12.03**	**17.54**	−15.7276	**0.0000**
		T_{min}	4.89	1.79	3.6380	0.0138
		$\boldsymbol{T_{mean}}$	**6.07**	**3.20**	−6.8674	**0.0033**
Guinea	**13.59**	**RR**	**5.85**	**10.22**	0.4848	**0.0000**
		$\boldsymbol{T_{max}}$	**4.09**	**9.65**	−13.3808	**0.0000**
		T_{min}	0.64	0.19	2.7410	0.3760
		$\boldsymbol{T_{mean}}$	**3.01**	**6.38**	−15.7753	**0.0000**
WCA	**1.69**	RR	0.34	0.23	0.0974	0.5550
		T_{max}	0.60	0.95	5.4640	0.3770
		T_{min}	0.42	0.49	−4.5700	0.5810
		T_{mean}	0.33	0.35	6.8450	0.5280
EA	**31.83**	RR	0.62	0.00	−0.0141	0.9360
		$\boldsymbol{T_{max}}$	**10.23**	**26.50**	−23.2210	**0.0000**
		$\boldsymbol{T_{min}}$	**8.84**	**20.10**	−12.1120	**0.0000**
		$\boldsymbol{T_{mean}}$	**12.14**	**26.04**	−18.2160	**0.0000**

Note. Variables with significant *p*-values contributions are boldfaced. R^2 represents the total proportion of variance in EIR explained by all the climate predictors. lmg values show the individual contribution of each predictor to R^2 relative to others. *First* is the contribution of each predictor alone to R^2 with complete ignorance of the others.

and so no adjustment takes place (Grömping, 2007). Since *first* does not decompose R^2 into contributions like *lmg*), the contribution of the individual regressors alone does not naturally add up to the overall R^2. The sum of these individual contributions is often far higher than the overall R^2 of the model with all regressors together.

Whether *lmg* or *first*, each metric's outcome was bootstrapped to ensure that the relative importance of each regressor was clearly defined (i.e., those different and those that are similar in terms of relative importance). Bootstrapping in "relaimpo" was done using the function boot in the package. Prior to calculating the *lmg* and *first* metrics, all data series (i.e., EIR_m, RR, T_{min}, T_{mean}, and T_{max} timeseries) were log-transformed. The essence of the log transformation was to decrease the variabilities in the data pairs and make them conform more closely to a normal distribution with similar variance and standard deviation (Curran-Everett, 2018).

2.3.3. EIR Lag Behind Rainfall

Seasonal malaria transmission onset lags behind rainfall season onset because of the time taken for mosquito breeding and vector population growth after rainfall season onset (Asare & Amekudzi, 2017; Badu et al., 2013; Tompkins & Ermert, 2013). This lag time as influenced by climate and whether it varies from one climate zone to another is not known. In this analysis, we quantified this lag time for each climate zone using a cross-correlation statistics performed between RR and EIR_m data pairs. In this statistic, RR was treated as the predictor variable and the corresponding EIR_m as the response variable. The pairs were then cross-correlated at lags of −5 to 0 months and the correlation co-efficient at each lag was calculated. The lag with the strongest positive correlation coefficients was identified as the optimum period of delay between rainfall onset and the EIR season for the zone.

3. Results

3.1. Pair-Wise Comparison

Figure 2 shows the EIR_m response ranges of pairs of rainfall (RR) and temperature (T_{min}, T_{mean}, and T_{max}). In the Sahel, maximum rainfall (RR) ranges were about 400 mm per month. Temperature ranges generally varied between 20°C–40°C in this zone. T_{max} ranges were clustered between 25°C–40°C, T_{min} within 20°C–30°C, and T_{mean} observed within 25°C–35°C. In Guinea, RR ranges were also centered around 400 mm per month. Temperature response ranges were mostly observed within 25°C–35°C for T_{max}, 20°C–25°C for T_{min}, and 24°C–30°C for T_{mean}. In WCA, maximum RR ranges were centered at about 600 mm per month, which is higher compared to ranges observed in the Sahel, Guinea and EA. Temperature response ranges in this zone were slightly lower than observed in the Sahel and Guinea. These include 24°C–32°C for T_{max}, 20°C–25°C for T_{min}, and 22°C–27°C for T_{mean}. The EA maximum RR ranges were also about 400 mm. Temperature ranges of 20°C–30°C for T_{max}, 15°C–27°C for T_{min}, and 18°C–29°C for T_{mean} were observed.

3.2. Relative Importance of Climate Predictors

In Tables 1 and 2, the relative importance of climate variables in predicting EIR_m is presented for locations with elevations ≤500 m and >1,000 m respectively. The predictors with *p*-value ≤ 0.05 were considered significant and interpreted that the respective climate variable significantly predicted the EIR seasonality in that zone. At lower elevations (≤500 m) in Sahel, rainfall and temperature were all significant drivers of EIR seasonality cumulatively contributing about 30.72% of the variations in EIR seasonality. At these lower elevation areas, important predictors of EIR_m seasonality were RR and T_{max}. At higher elevations (>1,000 m), rainfall and temperature are together responsible for about 40% of the variations in EIR_m with insignificant contribution from T_{min}.

Table 2
Same as Table 1 but for Locations With Elevation >1,000 m

Zone	R^2 (%)	Variable	Img (%)	First (%)	Coefficient (R)	P-value
Sahel	40.47	**RR**	7.43	**14.83**	0.3745	**0.0780**
		$\boldsymbol{T_{max}}$	**17.66**	**35.91**	−10.8070	**0.0036**
		T_{min}	3.69	4.17	−1.4543	0.5950
		$\boldsymbol{T_{mean}}$	**11.69**	**23.40**	−7.7660	**0.0513**
Guinea	–	RR	–	–	–	–
		T_{max}	–	–	–	–
		T_{min}	–	–	–	–
		T_{mean}	–	–	–	–
WCA	16.55	RR	1.41	1.25	−0.0844	0.7653
		T_{max}	6.70	0.23	6.1700	0.6620
		T_{min}	1.53	0.39	14.1000	0.5970
		T_{mean}	6.91	1.32	12.2800	0.5300
EA	18.22	**RR**	**10.44**	**13.37**	0.5510	**0.0000**
		$\boldsymbol{T_{max}}$	**1.82**	**3.94**	8.1570	**0.0289**
		$\boldsymbol{T_{min}}$	**2.88**	**7.77**	10.2080	**0.0011**
		$\boldsymbol{T_{mean}}$	**3.08**	**6.95**	11.0460	**0.0026**

Note. In Guinea, EIR data were unavailable for locations at this elevation hence represented as dashed lines. The boldfaced values show the corresponding climate variables (RR, T_{max}, T_{min}, and T_{mean}) that are significant drivers or determinants of malaria seasonality in Sub-Saharan Africa.

Like the Sahel, temperature and rainfall were also significant determinants of EIR_m at lower elevations (≤500 m) in Guinea just that their contribution to EIR_m variations is small (about 13.59%) compared to that of Sahel (about 30.72%). In Guinea, also, EIR_m data were unavailable for locations >1,000 m for further analysis in this regard. In WCA, rainfall and temperature were insignificantly associated with EIR_m seasonality whether at lower or higher elevations. Their percentage explanation of the variation in EIR_m were also low (extremely low at lower elevation areas and slightly higher for higher elevation areas) compared to other climate zones. In EA, temperature variables (T_{min}, T_{mean}, and T_{max}) were the significant drivers of EIR seasonality at locations ≤500 m. It explained about 31% of the seasonality in EIR_m in these areas with extremely insignificant contribution from rainfall. But at areas >1,000 m, all the climate variables were significant contributors with rainfall showing higher contribution to EIR_m variation than temperature.

3.3. EIR Lag Behind Rainfall

In Figure 3 the monthly distribution of rainfall and EIR is displayed. It is observed that EIR_m distribution positively correlated with rainfall at all locations. Both rainfall and EIR showed significant peaks at Sahel and EA with EIR peaks lagging behind rainfall for about 1 month. However, at Guinea and WCA EIR peaks showed no lag behind rainfall. The cross-correlation statistics determining the lag between the onset of the rainy season and the start of the EIR season are shown in Figure 4. It was observed that the lag at which EIR_m seasonality strongly and positively correlated with rainfall was 1 month in the Sahel and EA but 0 months in Guinea and WCA.

4. Discussion

Our study first examined the seasonal ranges of rainfall and temperature at which EIR_m occurred in a pair-wise comparison study. In general, temperature ranges of EIR_m response were mostly clustered between a minimum of

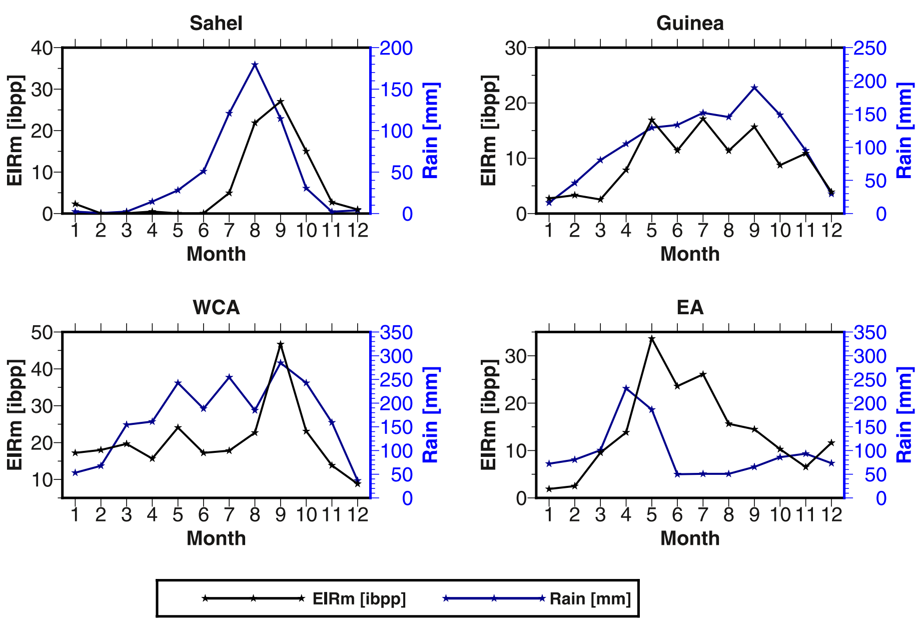

Figure 3. Average monthly time series of EIR_m and rainfall.

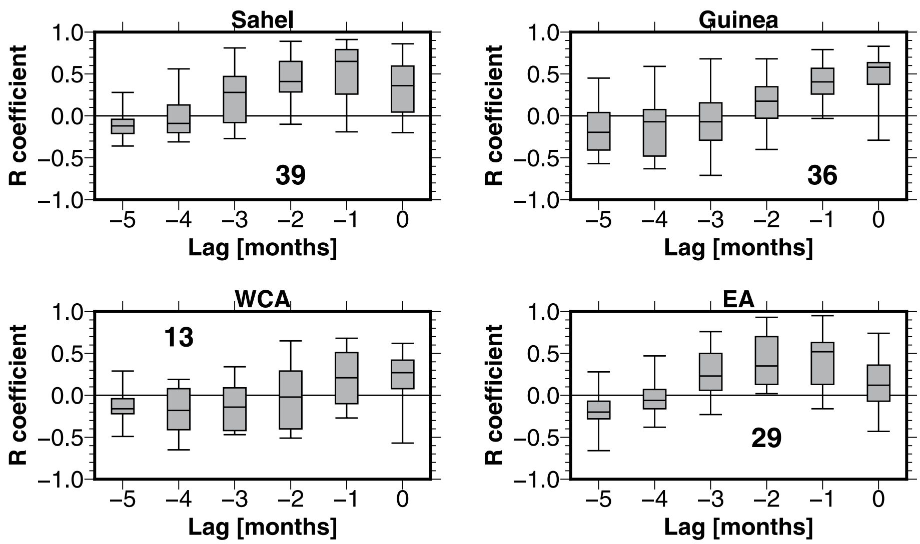

Figure 4. The cross-correlation between Rainfall and EIR_m at different lags. The numbers 39, 36, 13, and 29 show the number of location observations contributing to the box-and-whisker for each lag.

15°C and a maximum of 40°C. This outcome suggests that seasonal malaria transmission is barely impossible below 15°C or above 40°C. Previous studies (Lunde, Bayoh, & Lindtjørn, 2013; Mordecai et al., 2013; Parham & Michael, 2010; Shapiro et al., 2017) have indicated that malaria parasite development is not possible at temperatures below 16°C and that temperatures above 40°C have adverse effect on mosquito population turnover. The outcome of our study using EIR_m corroborates these previous findings. It provides an additional justification that the number of infectious mosquito bites a person receives per time is associated with temperature changes. While T_{min} may be below 16°C as observed in the Sahel and EA (see Figure 2), the daily T_{mean} must be greater than 16°C particularly for the Anopheles mosquitoes for transmission to occur. It should also be significantly less than 40°C for Anopheles mosquitoes to survive thermal stress and possible death if seasonal transmission has to take place. Similarly, maximum monthly rainfall value for EIR_m occurrence was 600 mm in WCA but 400 m in the Sahel, Guinea, and EA. The higher monthly maximum rainfall in WCA is due to the fact that annual total rainfall is mostly higher in this region than in others (Froidurot & Diedhiou, 2017; Nicholson, 2013). Previous works (Craig et al., 1999; Ermert et al., 2011) have demonstrated that the least monthly amount of rainfall required for malaria transmission is about 80 mm. Our findings suggest that the monthly maximum limit required for seasonal malaria transmission should be about 600 in WCA but 400 mm in Sahel, Guinea and EA. Excess of these thresholds could result in flooding of breeding grounds and flushing out and killing the water-bound stage vectors (Ermert et al., 2011; Paaijmans et al., 2010).

The evaluation of the relative importance of RR, T_{min}, T_{mean}, and T_{max} in predicting EIR seasonality (see details in Tables 1 and 2) revealed climate variables that were significantly associated with EIR seasonality in Sub-Saharan Africa. These climate variables are observed as the drivers of malaria seasonality in those zones of the sub-region. The climate variables with the highest contribution to EIR variance in each zone are attributed as the most significant drivers. This means that any changes in these significant drivers can result in a substantial changes in malaria seasonality in those areas. Elevation or topography was also observed to play a significant role in determining the important climate drivers of seasonal malaria transmission. In EA for instance, temperature was the important determinant of EIR seasonality at lower elevated areas (≤500 m). On the contrary, both rainfall and temperature significantly influenced EIR_m seasonality at higher elevated areas (>1,000 m). Though temperature and rainfall are important factors in malaria transmission, our study does not find them to have any significant association with EIR seasonality in WCA. This suggest that malaria seasonality in this zone is importantly driven by other factors other than climate. This requires additional studies to unravel these factors driving malaria seasonality in this zone. M. L. H. Mabaso et al. (2007) predicted EIR seasonality from environmental data and found that seasonality in rainfall, minimum temperature, and irrigation were important determinants of seasonality in EIR in Sub-Saharan Africa. Though this study outcome is important, it is not climate specific as it does not justify the implications of diverse climate conditions on EIR seasonality as demonstrated in this study. Other studies (M.

L. Mabaso et al., 2006; Simple et al., 2018) have used malaria case records from hospitals and found significant correlation between rainfall and temperature. As stated in the introduction, malaria case records have drawbacks for studying malaria seasonality as they are subject to significant uncertainties due to the inaccurate diagnostics and under counting due to varying health-seeking behavior and health policies (Afrane et al., 2012).

The cross-correlation statistics showed the lag(s) at which rainfall strongly correlated with EIR_m in each zone. The lag period suggest the time taken for malaria season to start after rainfall season has started. The lag of 1 month in Sahel and EA signifies that malaria transmission season delays 1 month after the start of rainfall season at these zones. In Guinea and WCA, this lag period was 0 months suggesting that there is no delay between rainfall season onset and the start of the malaria season. Hence malaria transmission in these zones is year-round. In markedly seasonal rainfall zones such as the Sahel and EA, the delay between rainfall onset and the start of the malaria season is expected. Rainfall in the Sahel is markedly seasonal, lasting from June to October, followed by about 6–8 months of dry period (Froidurot & Diedhiou, 2017; Nicholson, 2013). Hence, mosquitoes are barely present during the dry and long hot season. Even if present, they are inactive due to low humidity and high temperature and only recover within the rainy season when rainfall and temperature requirements are suitable. The absence of delay between rainfall season onset and the start of malaria season at Guinea and WCA is also expected. These zones are highly humid with shorter dry seasons (Froidurot & Diedhiou, 2017; Nicholson, 2013). For this reason, vectors are able to persist all year round at these zones resulting in year-round transmission at these areas. Previous studies (Ikeda et al., 2017; Reiner et al., 2015; Simple et al., 2018; Tompkins & Di Giuseppe, 2015) have reported malaria lagging behind rainfall at about 1–2 months but our study has further demonstrated that malaria season onset may lag behind rainfall only at markedly seasonal rainfall areas in Sub-Saharan Africa.

5. Conclusion

Clinical malaria case data is commonly utilized as a malariometric in examining the relationship between climate and seasonal malaria transmission in Sub-Saharan Africa. This data, on the other hand, is fraught with uncertainty due to out-of-sample generalization over geography and time, erroneous diagnosis, and under-counting due to varying health-seeking behavior and policy. As a result, in this work, we explored the applicability of high-quality EIR measurements to link rainfall and temperature seasonality to seasonal malaria outcomes in Sub-Saharan Africa. The main goal was to determine the climate variables that significantly drive malaria seasonality and their relative importance in the sub-region. Sub-Saharan Africa was first divided into four distinct climate zones namely Sahel, Guinea, WCA, and EA. The division was necessary because each zone has a unique climate conditions and therefore will have different climate implications on malaria seasonality. Applying a multi-regression statistics, pair-wise comparison and cross-correlation approaches to a EIR_m database gathered from publicly available field campaigns for each zone, the climate variables that explained significant variations in EIR seasonality were determined.

Findings in this study affirmed previous understanding that seasonal malaria transmission is barely impossible below 16°C or above 40°C temperature threshold (Mordecai et al., 2013; Shapiro et al., 2017). Hence, for seasonal malaria transmission to be sustained, average temperature should be well above the minimum or well below maximum threshold. While previous studies (Craig et al., 1999; Ermert et al., 2011) suggest that the monthly minimum rainfall requirement for seasonal transmission is about 80 mm, our study observed monthly maximum rainfall limit should be about 600 in WCA, and 400 mm in the Sahel, Guinea, and EA. While rainfall and temperature were found to be significantly associated with EIR_m seasonality in the Sahel, Guinea and EA, they were not important drivers of malaria seasonality in WCA. Important drivers of malaria seasonality in WCA may be due to other factors other than climate variables. In zones characterized by elevations such as EA, topography has a significant influence on which variable is an important determinant of malaria seasonality. At markedly seasonal rainfall areas such as Sahel and EA, malaria seasonal starts 1 month later after the rainfall season has started. However, for zones where rainfall season is bimodal such as Guinea and WCA, there is no delay between rainfall season onset and malaria season onset.

In this study, we showed that high-quality EIR_m measurements can usefully supplement established metrics for seasonal malaria by demonstrating evidence for the use of EIR to directly link the risk of humans to infectious mosquito bites to climate. The study informs our understanding of the connection between climate variables and both the malaria vector and parasite biology and how that translates into malaria seasonality in Sub-Saharan Africa. This information is key for the improvement and validation of weather-driven dynamical mathematical malaria models that directly simulate EIR. Our findings provide an understanding of geographical heterogeneous malaria risk from climate effect and support future malaria modeling and forecasting efforts. The study also supplements previous works describing clinical patterns of malaria infection and morbidity. Taking into account the seasonality of malaria management, findings in this study could lead to significant public health advantages by assisting in determining when, where, and how to use vector and parasite control strategies. It can, therefore, help stakeholders establish a robust framework for monitoring, forecasting and control of malaria.

This study does not claim to have identified all the EIR_m data available across sub-Saharan Africa. It relied on EIR_m data available in a repository (Yamba et al., 2018) with details explained in (Yamba et al., 2020). The study also acknowledges that the observed EIR_m data were both spatially and temporally limited and thus unavailable for many settings (as shown in Figure 1). This limitation was unavoidable because sampling mosquitoes for the determination of EIR is both labor and cost-intensive. Hence, it is very difficult to have EIR_m data available for many locations and for a long period. Future mosquito sampling should, therefore, focus on areas of unavailable data in order to consolidate the spatial homogeneity of available EIR_m data distribution. However, an important strength of this study is its restricted geographic and climate relevance. To our knowledge, this study is the first of its kind and also that EIR_m data has not been explored on such a wider scale in Sub-Saharan Africa. With the amount of EIR_m utilized for each climate zone, it is not anticipated that the inherent limitations may have any major adverse influence on the outcome of the study.

Conflict of Interest

The authors declare no conflicts of interest relevant to this study.

Data Availability Statement

The monthly Entomological Inoculation Rate (EIR) data used are freely available in an online repository at: https://doi.org/10.1594/PANGAEA.892682. The rainfall data used were obtained from the Global Precipitation Climatology Centre (GPCC) product, version 2018 and are freely available at: https://opendata.dwd.de/climate_environment/GPCC/html/fulldata-monthly_v2018_doi_download.html. The temperature data used were obtained from the European Centre for Medium-Range Weather Forecasts (ECMWF) Re-Analysis, 5th generation (ERA5) and are available at: https://cds.climate.copernicus.eu/cdsapp%23%21/dataset/reanalysis%2Dera5%2Dsingle%2Dlevels%3Ftab%3Doverview.

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