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Modelling the Linear and Nonlinear Effects of Malaria Risk Factors on Child Mortality

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Abstract

Generalized additive model was used to analyse data from Nigeria standard demographic and health survey (NDHS) 2018. The sample consists of 10609 children aged 6-59 months who were tested for malaria parasitemia through the rapid diagnostic test (RDT). Child mortality data was obtained by calculating the difference between the number of children ever born and the proportion of children alive during the survey. The analysis was carried out in R version 4.1.1 via mgcv package. The results obtained indicated linear and nonlinear effects of malaria risk factors on child mortality. The findings also revealed mosquito bed net usage, wealth index, maternal education, type of place of residence and malaria test outcome as significant predictors of child malaria mortality.

Keywords: Malaria risk factors; child mortality; mortality rate; nonlinear effects.

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1 Introduction

Researchers made efforts to elucidate the link between malaria transmission and child mortality [1–8]. Ahmad et al. [9] observed that it is very difficult to determine whether the decline in the infant mortality rate is attributable to the success of a particular health intervention program, change in reproduction patterns, socio-economic development, or the combination of two or more of these factors. This is due to the scarcity of reliable data on the causes of infant death in developing countries. However, they opined that provided major health threats such as malaria and HIV/AIDS do not increase over the next few years in Africa particularly, child mortality might be reduced to half by 2030.

Regardless of age, everyone is liable to malaria infection. However, under five children and pregnant women account for highest burden of malaria infection. It is also observed that younger children under five years stand to be more vulnerable due to under developed immunity against mild forms of the disease [10,11,12,13]. Child mortality in high malaria endemic regions is high [14,5].

It was suggested that 'all cause child mortality' (ACCM) can be proportionately reduced if malaria mortality decreases through scaling up of malaria intervention programs [6,7]. A strong positive association between infant mortality rate and entomological inoculation rate was revealed in Africa [5]. On the other hand, Rowe et al., [15] cautioned the use of malaria burden research results to estimate number of deaths that would be prevented if malaria transmission were reduced or eradicated. However, they further explained that such estimate would lead to under estimation due to the fact that it would not include the large burden of indirect malaria mortality. They found a historical decline in all-cause infant mortality rates due to drastic reduction of malaria transmission.

Significant difference in child mortality rates between areas with insecticide treated nets interventions and the areas without interventions in Western Kenya was not observed [6]. In a similar effort to find out clear and reliable association that may exist between malaria and child mortality rate, Gemperli [16] linked Demographic and Health Surveys (DHS) and Mapping Malaria Risk in Africa (MARA) databases but no clear relationship was observed. Considering the research results and findings cited it is extremely difficult to conclude in generic terms the direct link between malaria transmission and child mortality. Also most of the researches were aimed at assessing and evaluation the effectiveness of the intervention programs rather than the relationship between malaria transmission and child mortality [17].

Several factors are attributable to child (under five) mortality in various countries. The factors include; sanitary conditions, access to health facilities, breast feeding, maternal, environmental, wealth index, age at first birth of the mother, place of residence, education, climate and so on. Saroj et al., [18] identified socio-economic, demographic, educational level, mother's age, size of the child, play a very important role in the under-five child mortality using Cox regression model. Poisson regression model was used to identify number of health facilities as the most significant variable in under-five mortality estimation [19]. In another regression model, sanitation facilities were found to be a determinant factor in child mortality [20]. Adetoro and Amoo [21] identified maternal education as indicator for child mortality rate. Bourne [22] observed log poverty and gross domestic product (GDP) per capita account for ninety percent (90%) of the explanation of changes in child mortality rate. Considering the foregoing, one can observe a direct interlink between malaria and child mortality risk factors.

Dansu and Asiribo [23] attempted to investigate spatial association between malaria pandemic and mortality. Contrary to the title of their work, no data analysis or results were provided for valid association between malaria risk factors and mortality. Moreover, the data collected was historical, small and aggregated without a specified sample.

Snow et al. [24] made a comprehensive research on paediatric mortality in Africa with emphasis on malaria as mortality risk. The data and information were drawn from the burden of malaria in Africa (BOMA), unpublished ministry of health and conference materials and other archives in some African countries [24]. Publications from the United Kingdom were used in addition to direct contact with the authors of published materials in order to clarify issues that were not clear in their original reports. Mortality reports were based on the definition of demographic surveillance system (DSS). The DSS data was used to provide estimate of annual mortality risk from birth to five years of life. The use of DSS data was borne out of the fact that the DSS restrict areas of definable malaria risk which allows the exploration of malaria transmission dynamics [24]. Other

technical and specialist definitions and medical parameters were extensively explained and the sources of information were provided.

The statistical methods used were descriptive using medians and interquartile ranges. Weighted least square regression was applied to model contiguous relationship between mortality and malaria prevalence. The model considered square of prevalence as a variable that allowed for the possibility of saturating or decreasing mortality risk at the highest prevalence level [24]. Also, the stratified study site locations were considered as categorical variables. No regional influence was taken into consideration. They also revealed that the removal of infection risk might reduce the mortality by more than two folds.

In the second part of their work, causal relationship was considered. Because mortality rate might be due to interactions of malaria and other factors such as poverty that were capable of determining both malaria and mortality. To examine this effect, Snow et al. [24] attempted to investigate the malaria program effectiveness. In other words, how reduction in malaria risk might affect under-five mortality.

As in the case of logistic regression, ordinary regression model assumes linearity between response and explanatory variables. The model does not account for possible nonlinear relationship between dependent variable and independent variables.

1.1 Objective of the Study

The following are the objectives of the study;

i. To identify the malaria risk factors and related child mortality rate,
ii. To assess linear and nonlinear effects of malaria risk factors on child mortality,
iii. To assess the effects of categorical variables on malaria mortality risk,
iv. To assess the effects of continuous covariates on malaria mortality risk.

2 Methodology

2.1 Data source

The data used for the analysis in this study was obtained from the 2018 Nigeria standard demographic and health survey.

2.2 The sample

A sample of 10609 children aged 6-59 months was collected, tested for malaria parasitemia and used for data analysis.

2.3 Variables of malaria risk factors

Eleven (11) variables were selected for analysis. These are;

Age in Months, cluster altitude, Child weight, sleeping inside mosquito net by children, wealth index, mother's educational level, Mortality rate, place of residence, region, number of children and results of malaria test.

2.4 Child mortality data

The multiple indicator survey serves as reliable alternative for vital statistics data in Nigeria. The data was obtained from the information on the number of children ever born and the proportion of children alive during the survey. The difference gives the number of the dead children. That is, Number of dead children = Number of children ever born – Number of children alive during the survey. The difference is then aggregated into the children personal record data in the survey for the analysis in the model. The mortality rate was calculated using equation (9).

2.5 The structured additive regression model

The variable of interest (the dependent variable) y_i is the survival status of a child for malaria infection. Let y_i be the mortality status of a child *i*. Let the status "child is alive" (survived malaria) be 0 and 1 otherwise. That is;

$$y_i = \begin{cases} 0 \text{ if the child is alive (with probability } \pi) \\ \\ 1 \text{ otherwise (with probability } 1-\pi) \end{cases} \tag{1}$$

y_i is exponential family distribution. That is, $y_i \sim \text{EF}(\mu_i, \phi)$ with mean μ_i and scale parameter ϕ. That is, binary response data follows a Bernoulli distribution.

$$y_i \sim Bernoulli(\pi_i) \tag{2}$$

Where π_i is the probability that the child is alive. And $\pi_i = \phi_i(\eta_i)$ where $\phi(.)$ is the cumulative distribution function for the standard normal distribution and η_i is the predictor modelling the dependence of y_i on the covariates [25]. Now let

$$W_i^{'} = \left(w_{i1}, w_{i2}, ..., w_{ip}\right)^{'} \tag{3}$$

be a matrix of explanatory variables. Assuming linear predictor, we obtain

$$\eta_i = W^{'}\beta \tag{4}$$

Since y_i has binary response, we use a logit regression model. Therefore the ordinary logistic regression with log link function is written as:

$$\text{A: } \eta_i = \log\left(\frac{\pi_i}{1-\pi_i}\right) = \beta_0 + \beta_i W_i^{'} \tag{5}$$

where β_0 is the intercept, β_i is a vector of regression coefficients and $W_i^{'}$ is a categorical covariate vector. In generalized structured additive regression model, we replace the linear predictor by additive predictor [26], [25]. Therefore,

$$\log it(\pi) = \log\left(\frac{\pi}{1-\pi}\right) = f_0 + \sum_{i=1}^{q} f_i(x_{ik}) \tag{6}$$

The model can be extended to include parametric and non-parametric terms. Therefore we can write (5) and (6) as

$$\text{B: } \eta_i = \beta_0 + \beta_i W_i^{'} + \sum_{k=1}^{q} f_k(x_{ik}) \tag{7}$$

Where $\sum_{k=1}^{q} f_k(x_{ik})$ are nonlinear smooth effects of the continuous covariates. β_0 is the intercept, β_i is the parameter corresponding to the categorical fixed variables $W_i^{'} = \left(w_{i1}, w_{i2}, ..., w_{ip}\right)^{'}$.

The model can be further extended to include spatially unstructured random effect ϕ_i, spatially structured random effects υ_i [27] and mortality rate ψ_i. Therefore we obtain:

$$\text{C: } \eta_i = \beta_0 + \beta_i W_i^{'} + \sum_{k=1}^{q} f_k\left(x_{ik}\right) + \phi_i + \upsilon_i + \psi_i \tag{8}$$

Where ψ_i represents mortality rates due to malaria at time *t*. Mortality rate can be obtained through the Standard Mortality Rate (SMR) given by:

$$\psi_i = SMR = \frac{\text{Observed child deaths due to malaria}}{\text{Expected number of child deaths}} \times 100\% \tag{9}$$

2.6 Variable description

Dependent variable: The response variable for this study was the mortality status of a child aged 6-59 months. The response was dichotomous as dead (1) or alive (0).

2.7 Independent variables

The explanatory variables used for this study were classified into two groups: Categorical variables such as; sleeping inside insecticide treated nets, wealth index, mother's educational level, type of place of residence, region and result of malaria test. Region was categorized into six geo-political zones as North East, North West, North Central, South South, South East and South West. Type of place of residence is categorical (Rural/Urban), Result of malaria test (positive or negative), sleeping inside bed net (all, none, some and no net), wealth index (poorest, poorer, middle, richer and richest), mother's educational level (no education, primary, secondary and higher). Continuous variables include; Cluster altitude (meters), number of children, age (months), child weight (kg) and mortality rate (%) [28].

3 Results

Structured additive regression analysis was carried out using R version 4.1.1 to determine the effects of each of the malaria risk factors on child mortality. Estimation of parameters was done through the restricted maximum likelihood (REML) in mgcv package.

Table 1. Output summary of the parametric component

Predictor		Estimate	Std. Error	p-value
Intercept		–5.6414	0.4101	2.0×10^{-16}
Sleeping under bed net	All children	–0.5256	0.1100	1.77×10^{-6}
	Some Children	–0.6383	0.1527	2.92×10^{-5}
	No net	–0.5530	0.1194	3.62×10^{-6}
	None of the children	1.00		
Wealth Index	Poorer	–0.3173	0.1023	0.0019
	Middle	–0.4454	0.1168	0.0001
	Richer	–0.8266	0.1538	7.60×10^{-8}
	Richest	–1.1335	0.2459	4.02×10^{-6}
	Poorest	1.0		
Mother's level of Education				
	Primary	0.1218	0.1202	0.3109
	Secondary	0.1529	0.1225	0.2121
	Higher	0.5512	0.2636	0.0365
	Don't know	0.1585	0.1515	0.2955
	No Education	1.0		
Malaria test results	Positive	4.9465	0.3443	$< 2.0\times10^{-16}$
	Negative	1.0		

Region	North East	- 0.0361	0.1355	0.7899
	North West	0.1050	0.1321	0.4268
	South East	- 0.2277	0.1781	0.2010
	South South	- 0.2297	0.1930	0.2340
	South West	0.3607	0.1477	0.0146
	North Central	1.0		
Place of Residence	Rural	0.3682	0.1125	0.0011
	Urban	1.0		

Table 1 shows the results for the parametric component of the model. It gives the parametric coefficients as in the usual logistic regression model (linear model). The intercept gives the value of the child mortality when all numerical predictors equal to zero and the factor (categorical) variables were at their reference level. For instance, if the malaria test is negative, it means the average child mortality for malaria negative child is –5.64. That is, the probability of child mortality for malaria negative child is 0.003. The effects of sleeping under mosquito bed net, wealth index of the households, results of malaria rapid diagnostic test and place of residence were highly significant. Effect of mother's educational at higher level and the South West region were also significant.

Table 2. Output summary of the nonparametric component

Predictor	**edf**	**Ref.df**	**Chi. Sq.**	**p-value**
Cluster altitude	4.2693	4.9896	17.653	0.0032
Child weight	1.0031	1.0060	7.422	0.0065
Mortality rate	1.0002	1.0003	4.868	0.0274
Age	1.8957	2.3328	2.708	0.2894
Number of children	1.0001	1.0002	1.563	0.2113

The results in Table 2 shows that the cluster altitude has a statistically significant nonlinear effect (edf = 4.2693, p = 0.0032). the effects of child weight and mortality rate were linearly significant with edf 1.0 each, p-values 0.0065 and 0.0274 respectively. The effect of age was nonsignificant and nonlinear (edf =1.8957, p = 0.2894). Number of children has nonsignificant linear effect (edf = 1.0001, p = 0.2113).

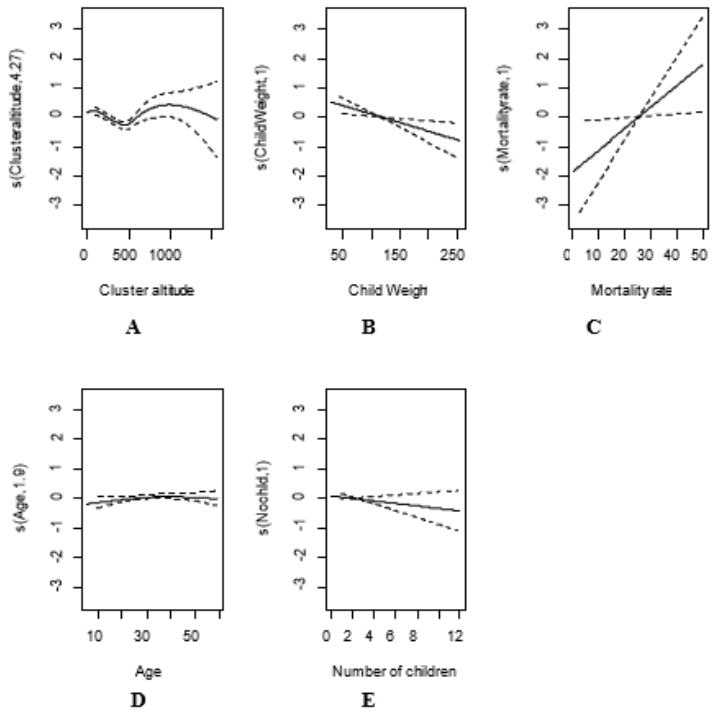

Fig. 1. Smooth effect of the continuous covariates

Fig. 1 shows the graph of nonlinear effect of the continuous covariates included in the modified model. The *x*-axis contains the values of cluster altitude (in meters), child weight (in kilogram), mortality rate (percent), age (in months) and number of children (in units) for respective graphs. The *y*-axis contains the partial effects of the covariates on the response (child mortality). The curvy shapes on the graphs for cluster altitude and age resulted from smoothing splines that models the nonlinearity in the data. The dotted lines around the main (bold) line signify the 95% confidence region.

Fig. 1A indicates a nonlinear effect of cluster altitude on malaria related child mortality. The effect of malaria mortality was lowest at 500 meters and highest at 1000 meters above sea level. Fig. 1B shows inverse linear relationship between child weight and its effects on malaria related mortality. The effect on child malaria mortality sharply decreases with increase in child weight. Fig. 1C revealed a linear increase in the effect of mortality rate on child malaria mortality with increase in mortality rate with very wide confidence limits. Nonlinear partial effect of child's age on malaria mortality was observed in Fig. 1D. The highest effect of malaria related mortality was indicated in children of 35 months old and lowest in children aged less than 10 months. The effect of number of children was linear and decrease with increase in the number of children.

4 Discussion

The model was used to analyse data from the Nigeria national demographic and health survey (NDHS) [29]. The results of the analysis showed that the effects of sleeping under mosquito bed net, wealth index and results of malaria rapid diagnostic tests were highly significant while educational level of the mother was not. This contradicts the work of Ernst et al., [30] and Seyum [31] that reported significant effect of maternal level of education. A significant association was observed between the mortality status of children and risk factors such as wealth index, sleeping inside mosquito bed net, regional location of children, place of residence and results of malaria test. The probability of malaria related mortality in children aged 6-59 months was highest in the South West (0.0175) and lowest in the South East (0.012). Use of mosquito bed net for sleeping significantly reduces the probability of malaria infection and consequently reduces the risk of malaria child mortality. Likelihood of child malaria mortality declined in the households where all children sleep inside mosquito bed net than in the households where none of the children sleep inside the bed net. This is in agreement with the work of [32,33 and 34]. This however, contradicts the findings of [35 and 36] that the use of mosquito bed net has nonsignificant effect on malaria positivity in children.

Economic status of the household plays a key role in determining the probability of child malaria mortality. Direct measurement of household of household income seems to be extremely difficult due to a number of reasons. For instance, many respondents tend to conceal their income to interviewers. In addition, most of household income was persistently varied on daily, weekly or seasonal basis. Therefore, household wealth index serves as alternative variable that measure economic status of the households. Wealth index is a composite measure of a household cumulative living standard. This entails the ownership of some easy to measure household assets such as television sets, radio, mobile phone, car, bicycle, material used for building the house, sanitation facilities and so on. The indices were generated using principal component analysis.

Probability of malaria child mortality decreases significantly with increase in household wealth quantile. In other words, children from the poorest household were more likely to die of malaria infection than children from the richer households. This confirms the findings of [37,22 and 18]. Type of place of residence showed a significant effect on the probability of malaria risk of child mortality. The probability of malaria mortality risk was higher in the households living in the rural areas than those from the urban centres. This supports the research finding of [34].

Continuous covariates were modelled with smoothing splines to take care of possible nonlinear effects. The results showed that the cluster altitude and age of the subjects had nonlinear effect on the response variable. The effect of the cluster altitude was statistically significant while the effect of age was not. The risk of child malaria mortality was highest at 1000 meters above sea level and lowest at 500 above sea level. Similar finding was reported in [38 and 39]. However, this contradicts the findings of [40 and 41]. The nonlinear effect of age on child malaria mortality was parabolic indicating maximum value at 35 months. The risk of malaria child mortality was lower for younger children and stepwise increases with age. This supports the findings of [42] that claimed significant association exists between child's age and mortality. This result was also supported by the

research finding of Desai et al., [43] that reported decline in malaria related mortality in children of less than 36 months old and increase among children aged between three to five years.

The effects of child's weight, mortality rate and number of children in the household were linear. The likelihood of child malaria mortality decreases with increase in child weight. In other words, child weight had inverse negative effect on child mortality. The risk of malaria mortality declines with increase in child's weight. This confirms the findings of [44,45 and 46]. The size of the households has not shown nonlinear effect on the child malaria mortality. However Guerra et al. [47] reported significant association between household size and malaria risk. The partial effect of mortality rate on child malaria mortality was linear and directly proportional. This means as the mortality rate increases the child malaria mortality also increases. This finding was contrary to the findings of [48] who reported lack of evidence to link mortality rates to malaria specific mortality. However recent researches confirm a strong link between malaria child mortality and mortality rate [49,50]. The random effects of regional location and type of place of residence on child malaria mortality were statistically significant. This confirms the work of Chirombo et al. [40].

5 Conclusion

The findings in this study showed that there was both linear and nonlinear relationship between the child malaria mortality and the predictors. Linear relations were indicated by categorical variables such as sleeping under mosquito bed net, wealth index, maternal education, results of malaria RDT test, regional location and place of residence. The continuous predictors that showed linear effects were; child weight, mortality rate and number of children in the household. The findings also revealed nonlinear relationship between child malaria mortality and smooth effects of cluster altitude and age. This study also revealed that the variables; sleeping under mosquito bed net, wealth index, mother's level of education, malaria test results, cluster altitude, child weight, mortality rate and type of place of residence were relevant predictors in modelling malaria risk factors of child mortality. Therefore, it can be concluded that structured additive regression model can be effectively used to model malaria risk factors of child mortality.

Competing Interests

Authors have declared that no competing interests exist.

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