

RISK FACTORS IN MALARIA MORTALITY AMONG CHILDREN IN NORTHERN GHANA: A CASE STUDY AT THE TAMALE TEACHING HOSPITAL

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ABSTRACT

Malaria is hyper-endemic in Ghana, accounting for 44% of outpatient attendance, 13% of all hospital deaths, and 22% of mortality among children less than five years of age. The paper analyzed the risk factors of malaria mortality among children using a logistic regression model and also assessed the interaction effect between age and treatment of malaria patient. Secondary data was obtained from the inpatient morbidity and mortality returns register at Tamale Teaching Hospital, from 1st January 2008 to 31st December 2010. The results showed that risk factors such as referral status, age, distance, treatment and length of stay on admission were important predictors of malaria mortality. However, it was found that the risk factors; sex and season were not good predictors of malaria mortality. Finally, the interaction effect between age and treatment was found to be significant. It was recommended, among other things, that the government should provide more assessable roads and expand ambulance services to the various Districts/communities in and around the Tamale metropolis to facilitate referral cases.

Keywords: Malaria, Mortality, Risk factors, Children, Odds ratio

1. Introduction

Malaria threatens the lives of 3.2 billion people globally and leads to over one million deaths annually (WHO 2005). In Ghana, malaria is a significant cause of adult morbidity and the leading cause of workdays lost to illness. Malaria is hyper-endemic in Ghana, accounting for 44% of outpatient attendance, 13% of all hospital deaths, and 22% of mortality among children less than five years of age. Malaria presents a serious health problem in Ghana; it is hyper-endemic with a crude parasite rate ranging from 10 – 70% and plasmodium falciparum the major malaria parasite, dominating (WHO 2005 and Abuaku et al., 2005). Though malaria is responsible for 9% of overall mortality in Ghana, at least 40% of malaria deaths occur among infants and children under the age of five (Asenso-Okyere, 1997). From the United Nations (UN) classification of childhood diseases it ranks third in Africa (Ministry of Health, 2002).

It is also the leading cause of workday loss due to illness in the country. For instance, it accounts for 3.6 ill days in a month, 1.3 workdays absent and 6.4% of potential income loss to Ghana for 1998/99.

The disease is again responsible for 10.2% of all healthy life lost from other diseases making it the chief cause of lost days of healthy life in Ghana it concluded.

As part of measures to eradicate the disease, WHO initiated a "Roll Back Malaria" (RBM) project, of which Ghana is benefiting, to expand availability and coverage of insecticide-treated mosquito nets which includes forecasting and procurement of these nets by Non Governmental Organizations (NGOs). As a result of this effort, the Ministry of Health has drafted a policy on insecticide treated bed nets, and is adopting these nets as an additional control measure to back the RBM project (Chinbuah et al., 1999). The Volta Region, a beneficiary of the project, has so far shown no significant improvement in combating malaria. This is reflected in the 2003 Ghana Demographic Health Survey report (Ghana Statistical Service, 2003), which shows that Northern Region has one of the highest prevalent cases of malaria in the country.

In Tamale, despite many years of prevention and control measures, malaria still remains a public health problem in low lying and water logged areas. In some areas across the metropolis, the transmission persistently occurs throughout the year. It is interesting to note that Tamale Teaching Hospital (TTH) possesses large amount of data on diseases, in particular malaria, on its hospital register. These data is usually compiled and submitted to the district and the regional Ghana Health Service directorate for preparation of quarterly and annual reports. Though records on malaria disease and its risk factors are usually not studied, yet it serves as a rich source of information for the stakeholders in the field.

In sub-Saharan Africa, malaria is a leading cause of morbidity and mortality among young children. Spatial variation of malaria incidence in young children from a geographically homogeneous area with high endemicity was studied. In their methods, the spatial variation of malaria incidences and socioeconomic factors were assessed over 21 months, from January 2003 to September 2005, in 535 children from 9 villages of a small rural area with high *Plasmodium falciparum* transmission in Ghana. They observed that malaria incidence was surprisingly heterogeneous between villages, yet malaria risk was affected by a number of socioeconomic factors (Kreuels et al., 2008). Child mortality is highest in Sub-Saharan Africa, although causes of mortality in this region are not well documented. Malaria is the single largest cause of death, accounting for 21.8% of cases in Manhica, Mozambique (Sacarlal et al., 2007). The patterns of malaria-related hospital admissions and mortality among Malawian children were examined using hospital register. It was found that; rates of malaria hospitalization and in-hospital mortality decreased with age, case fatality rate was associated with distance, age, wet season and increased if the patient was referred to the hospital. Furthermore, death rate was high on first day, followed by relatively low rate as length of hospital stay increased. Improved prognosis as the length of hospital stay increased suggests that appropriate care when available can save lives (Kazembe et al., 2006).

The averaged population-adjusted parasitaemia risk was 20.0% in children less than five years with the highest risk predicted in the northern (38.3%) province. The odds of parasitaemia in children living in a household with at least one bed net decreases by 40% (CI: 12%, 61%) compared to those without bed nets, in a survey carried out by the Zambian Ministry of Health and partners (Riedel et al., 2010). A spatial analysis carried out to identify factors related to geographic differences in infant mortality risk in Mali by linking data from two spatially structured databases showed that, mother's education, birth order and interval, infant's sex, residence, and mother's age at infant's birth had a strong impact on infant mortality risk in Mali. The residual spatial pattern of infant mortality showed a clear relation to well-known foci of malaria transmission, especially the inland delta of the Niger River (Gemperli et al., 2004). The generalized linear mixed models in the spatial analysis of small-area malaria incidence rates in KwaZulu Natal, South Africa revealed that malaria incidence was significantly positively associated with higher winter rainfall and a higher average maximum temperature and was significantly negatively associated with increasing distance from water bodies (Kleinschmidt et al.,

2001). Risk of self-diagnosed malaria in urban informal settlements of Nairobi using self-reported morbidity survey was assessed. The aim was to explore the risk of perceived malaria and some associated factors in Nairobi informal settlements using self-reported morbidity survey. Their logistic model included variables such as site of residence, age, ethnicity and number of reported symptoms. Participants reported 165 illnesses among which malaria was the leading cause (28.1%). The risk of perceived-malaria was significantly higher in Viwandani compared to Korogocho (OR 1.61, 95%CI: 1.10–2.26). Participants in age group 25–39 years had significantly higher odds of perceived-malaria compared to those under-five years (OR 2.07, 95%CI: 1.43–2.98). The Kikuyu had reduced odds of perceived-malaria compared to other ethnic groups. Malaria was the leading cause of illness as perceived by the residents in the two informal settlements (Yé et al., 2007).

This study, therefore, seeks to analyze the risk factors affecting malaria mortality among children, using inpatient morbidity and mortality returns register, from the TTH in the Northern Region of Ghana. The paper would also assess the interaction effect between age and treatment of malaria patient.

2. Methods

2.1 Study Area and Source of Data

Tamale metropolis, one of the 20 districts located in Northern Region, is generally classified as malaria endemic, although the highland zones in the central parts of the district are of low transmission and may be prone to epidemic malaria. Tamale has a total population of 2,468,557 people as per the last census (Statistical Service, 2011). The Tamale Teaching Hospital is a state run teaching and referral hospital built in 1974. The hospital, with about 380 patient beds is the largest facility in the metropolis which serves both as the first consultation point for patients within its catchment, and as a referral centre for about other 20 primary health centers. These facilities are managed by the Ministry of Health and the Ghana Health Service with support from other some partners. It has a capacity of about 380 patient beds; a four -storey structure that houses four wards, the general purpose theatre and an X-ray Unit. The obstetric/gynecology ward; and antenatal Units (Gunu, 2009).

2.2 Data collection and data management

Data used in this study were obtained as primary data from discharge records of all pediatric hospital admissions at Tamale Teaching Hospital, from 1st January 2008 to 31st December 2010.

For this study, cases with primary diagnosis as malaria, from the hospital wards, were used. Each case was clinically assessed and definitively confirmed as malaria on admission. The registers included patients' age, sex, date of admission and discharge, outcome (i.e. death, discharged home, or absconded), village or location of residence, cost (i.e. for treatment), referral status and treatment given. From the data, the following variables were coded: *outcome* (1 = dead and alive = 0); *season* of the year when admitted (1 = wet season from April to October, 0 = dry season from November to March); *treatment* given (1 = artesunate amodiaquine, 0 = quinine); *distance* to the hospital (1 = distance > 5 km, 0 = distance ≤ 5 km). The distance of 5 km was chosen to reflect travel time of 1 hour on foot. Also, length of hospital stay was used. In addition, the variable *referral* was defined, with children who used the hospital as a first point of consultation given a code 0 and those referred to the district hospital from peripheral health facilities in the metropolis given the code 1.

2.3 Model specification, estimation and tests

The response variable in logistic regression is usually dichotomous, that is, the response variable can take the value 1 with a probability of success p , or the value 0 with probability of failure $1-p$. This type of variable is called a Bernoulli (or binary) variable.

To explain the logistic regression, we show here the logistic function, which describes the mathematical form on which the logistic model is based. Let the function be called $f(z)$, is given by

$$f(z) = \frac{1}{1 + e^{-z}} \quad (1)$$

When the values of this function are plotted, z varies from $-\infty$ to $+\infty$ and its shape is an elongated S shape.

The relationship between the predictor and response variables is not a linear function in logistic regression, instead, the logistic regression function is used, which is the logit transformation of p .

To obtain the logistic model from the logistic function, we write z as the linear sum

$$z = \alpha + \beta_1 x_1 + \beta_2 x_2 + \dots + \beta_k x_k \quad (2)$$

Where the x 's are independent variables of interest and α and the β_i 's are constant terms representing unknown parameters.

Substituting equation 1 into 2 we obtain

$$f(z) = \frac{1}{1 + e^{-(\alpha + \sum \beta_i x_i)}}$$

For notational convenience, we will denote the probability statement as simply $p(x)$ where x is a notation for the collection of variables x_1 through x_k .

Thus, the logistic model may be written as

$$p(x) = \frac{1}{1 + e^{-(\alpha + \sum \beta_i x_i)}}$$

However, since the above logistic model is non-linear, the logit transformation would be used to make it linear, this is given by

$$\text{Logit } p(x) = \ln_e \left[\frac{p(x)}{1 - p(x)} \right] \quad (3)$$

Where

$$p(x) = \frac{1}{1 + e^{-(\alpha + \sum \beta_i x_i)}} \quad (4)$$

This transformation allows us to compute a number, called logit $p(x)$, for an individual with independent variables given by x .

By substituting Equation 4 into Equation 3 and simplifying, we obtain

$$\text{Logit } p(x) = \alpha + \sum \beta_i x_i$$

$$\therefore \text{Logit } p(x) = \alpha + \beta_1 x_1 + \beta_2 x_2 + \dots + \beta_k x_k$$

Thus, the logit of $p(x)$ simplifies to the linear sum.

The quantity $p(x)$ divided by $1-p(x)$, whose log value gives the logit, describes the odds for a malaria patient being dead, with independent variables specified by x .

$$\frac{p(x)}{1-p(x)} = \text{odds for individual } x$$

The goal of logistic regression is to correctly predict the category of outcome for individual cases using the most parsimonious model. To this end, a model is created that includes all predictor variables that are useful in predicting the response variable (Kleinbaum and Klein, 1994).

For this study, the malaria patients at risk of death are influenced by predictors such as referral, age, distance, treatment, sex, season, length of stay and the interaction between age and treatment. The following logistic regression model was fitted to the data.

$$\log it(p(y=1)) = \alpha + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \beta_4 x_4 + \beta_5 x_5 + \beta_6 x_6 + \beta_7 x_7 + \beta_8 x_2 x_7 + \varepsilon$$

where p is the probability of dead, the x 's are independent variables of interest, α and the β_i 's are constant term and coefficients respectively representing unknown parameters and ε is the residual term.

The coefficients of the model predictors are tested via the hypothesis as follows

$$H_0 : \beta_j = 0$$

$$H_1 : \beta_j \neq 0 \quad j = 1, 2, 3, 4, 5, 6, 7, 8.$$

Once a logistic regression model has been fit to a given set of data, the adequacy of the model is examined by overall goodness-of-fit tests and examination of influential observations. One concludes a model fits if the differences between the observed and fitted values are small and if there is no systematic contribution of the differences to the error structure of the model. A goodness-of-fit test that is commonly used to assess the fit of logistic regression models is the Hosmer–Lemeshow test (Hosmer and Lemeshow, 1980). Other goodness-of-fit tests for logistic regression models have been proposed (Cox, 1958; Tsatis, 1980; Brown, 1982; Azzalini et al., 1989; le Cessie and van Houwelingen, 1991, 1995; Su and Wei, 1991; Osius and Rojek, 1992; Pigeon and Heyse 1999a, b). These goodness-of-fit tests have been studied under independent and identically distributed random variable assumptions, which we refer to as the ‘iid-based’ setting.

Although appropriate estimation methods which take into account the sampling design in estimating logistic regression model parameters are available in various statistical packages, there is a corresponding absence of design-based goodness-of-fit testing procedures. Due to this noted absence, it has been suggested that goodness-of-fit be examined by first fitting the design-based model, then estimating the probabilities, and subsequently using iid-based tests for goodness-of-fit and applying any findings to the design-based model (Hosmer and Lemeshow, 2000).

The hypothesis for model fitness can be measured by the *Hosmer and Lemeshow test* as follows

$$H_0 : \text{The model fits the data}$$

$$H_1 : \text{The model does not fit the data}$$

3. Results

It was observed that out of 2293 number of administered malaria patients, about 111 (4.8%) were dead upon admission. Moreover, about 2157 (94.1%) children called at the Tamale Teaching Hospital as their first consultation point, although 136 (5.9%) children were referred from other peripheral health facilities in and around the metropolis. It was noticed that there were 946 (41.3%) of female children as against 1347 (58.7%) of their male counterparts. Further, it was observed that, about 1784 (77.8%) of children were residing at homes which are less than 5km to the Tamale Teaching hospital where as about 509 (22.2%) of children were living at homes which are greater or equal to 5km to the Tamale Teaching hospital. Also, out of 2293 administered malaria cases 775 (33.8%) of them were treated with artesunate ammodiaquine whilst 1518 (66.2%) were treated with quinine. The mean age of the children was 3.69 years with about half (50%) of the children having ages below or equal to 3 years and about half (50%) of the children having their ages above or equal to 3 years. The age which was most common among the children was 2 years.

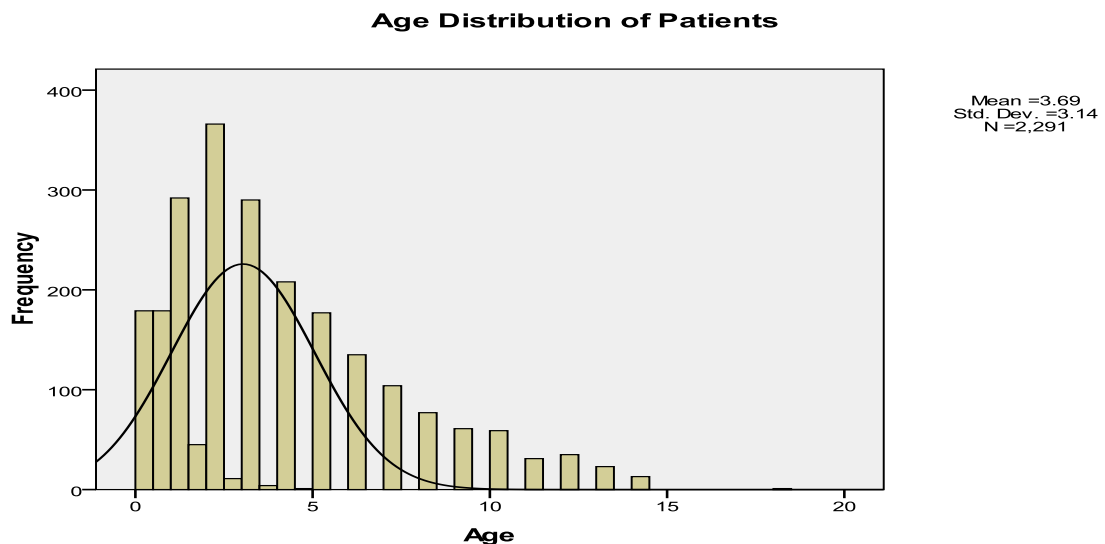


Fig.1 The age distribution of malaria patients

Further, the age distribution of the children administered of malaria was about 1.181 positively skewed with standard error of 0.051. Again, Fig. 1 shows that about 50% of the children were aged from 0-5 years with the remaining 50% further divided into about 25% each for children from 6-10 years and 11-14 years. The most common length of stay on admission among the children was 3 days.

The logistic regression obtained was as follows (see Table 1 below):

$$\log it(p(y=1)) = -2.910 + 2.793 \text{Referral status} - 0.134 \text{Age} - 0.395 \text{Sex} + 0.94 \text{Season} - 0.103 \text{Length} \\ + 1.947 \text{Distance} - 1.454 \text{Treatment} + 0.153 \text{Age} * \text{Treatment}$$

It can be noted that, the risk factors; referral status, age, length of stay, distance, treatment and the interaction between age and treatment are significant at $\alpha = 0.05$ with their respective significance values equal to 0.000, 0.022, 0.003, 0.000, 0.000 and 0.048. Against this backdrop, therefore, these risk factors are relevant in predicting malaria mortality at the Tamale Teaching hospital. From Table 1 below, it is revealing to note that, the risk factors sex and season are not **statistically** significant when the other factors are held constant.

As in Table 1, the strongest risk factors of the mortality of malaria administered patient was *referral status*, recording an odds ratio of 16.329 (95 % C.I. = 9.714 – 27.446). This indicate that administered patients who had been referred were over 16 times as likely to die of malaria as those who were not referred, controlling for all other factors in the model. The odds ratio 0.234 (95% C.I. = 0.113 – 0.482) for *treatment* was less than 1, indicating that there were (23.4%) higher malaria children mortality when the treatment is quinine compared to using artesunate ammodiaquine, controlling for other factors in the model. With respect to *distance*, the odds ratio was 7.010 (95% C.I. = 4.091 – 12.012), meaning that patients from distances greater than or equal to 5km are about 7 times more likely to die from malaria compared to patients coming from a distance less than 5km, holding other factors constant.

It can be observed from the model that, for a unit increase in a child's age mortality will decrease by 0.134 controlling for all other risk factors. This means that mortality diminishes as children's grow.

Table 1: Logistic Regression Predicting Likelihood of Malaria Mortality

Variable	B	S.E.	Wald	P-value	Odds Ratio	Lower C.I.	Upper C.I.
Referral status	2.793	0.265	111.114	0.000	16.329	9.714	27.446
Age	-0.134	0.059	5.224	0.022	0.875	.780	.981
Sex	-0.395	0.236	2.796	0.094	0.674	.424	1.070
Season	0.094	0.239	0.156	0.693	1.099	.688	1.756
Length o f stay	-0.103	0.035	8.921	0.003	0.902	.843	.965
Distance	1.947	0.275	50.211	0.000	7.010	4.091	12.012
Treatment	-1.454	0.371	15.365	0.000	0.234	.113	.483
Age*Treatment	0.153	0.077	3.907	0.048	1.165	1.001	1.357
Constant	-2.910	0.370	61.715	0.000	0.054		

Table 2 below, indicates that the p – value of the Hosmer and Lemeshow test (0.167) is greater than the significance level of 0.05. It can be concluded that there is enough evidence that the hypothesized model fits the data well. This indicates that the risks factors of deaths due to malaria may not be significantly different from those used in the postulated model.

Table 2: Assessing Model Fit by Hosmer and Lemeshow Test

Chi-square	df	P-value
11.662	8	0.167

4. Discussion

The study provides evidence of the risk factors which influence in-hospital malaria mortality among children, from 0 – 14 years, at Tamale Teaching hospital in the northern region of Ghana. The model indicates that distance contributes more, among other factors, in terms of influencing malaria in-hospital deaths. Distant villages or areas with ill resourced health centers or none at all suggest problems of access to health care, which does translate into high mortality rate in. Thus the further the village is from the health centre, the more disadvantaged the households are in terms of getting early health care. The study showed that patients within 5 km of hospital were less likely to die in hospital than those beyond 5 km, and does reflect the fact that nearness to the hospital improved early access to care, thus reduced the risk of mortality.

It was also observed that *referral* children were at higher chance of dying in hospital, after adjusting for distance and other risk factors. This seems to suggest that delayed effective treatment, in the process of being transferred to the Tamale Teaching hospital, increased the severity of the disease. This could be because most referring health facilities may often be faced with stock-out of effective drugs or may not have prompt access to ambulatory support when needed. This also suggests inadequate care being available at primary facilities, regardless of whether they are distant from the hospital or not. It is also possible that referring hospitals are referring the more severe cases which are expected to have higher mortality case. This challenge is agreed in a previous study⁹. With regard to the *length of hospital stay*, there was inverse relationship with malaria mortality. Hence, as days of stay increased the risk reduced. This suggests that by and large the care that is provided in the hospital is effective and saves lives as day of stay go by.

Although, there is the perception that malaria transmission is more intense in the wet season than the dry season, yet the study showed that there were 1306 (57%) cases in dry season and 987 (43%) cases in wet season. At least, in Tamale, *season* surprisingly was not even significant predictor in the model. This could due to the fact that all 3 years were combined in this analysis, implying that an interaction between year and season could improve the understanding of the 'season' effect. Also, the predictor *sex* was not significant in the model, which suggests that it does not contribute significantly to predicting deaths, though the converse was shown in Malawi. This study provides evidence that mortality for malaria among children, in and around, Tamale metropolis could be describe as high.

One major shortcoming of using this data is that they only represent those patients who visited the Tamale Teaching hospital. Meanwhile, some malaria treatments occur outside the formal hospital, and only do so if the illness is perceived to be near fatal.

5. Conclusion

The study indicated that many more children used the Tamale Teaching hospital as their first call for consultation. Most of the children were aged between 0 – 5 years and just few were above 10 years.

The findings showed risk factors such as referral status, age, distance, treatment type and length of stay on admission were significantly contributing to mortality of children administered as malaria patients at the Tamale Teaching hospital. However, risk factors such as sex and season were not significantly contributing to malaria mortality. Finally, the interaction effect between age and treatment was found to be significant, which may imply that the ACT treatment is more effective at certain age group compared to another age group. Three policies are urgent: a strategic plan to build poly-clinics in every district capital and cheap-compound health facilities, at least in every community.

This could help curb the long distance villagers staying around the metropolis have to travel to access health care; other stake holders such as the World Health Organization (WHO), should step up effective campaign to discourage, if not ban entirely, the use of quinine in treating malaria and rather strengthen the use of ACTs drugs in the fight to reduce malaria mortality; and the expansion of ambulance services as well as improving more assessable roads in and around the Tamale metropolis to facilitate timely transportation of referral cases.

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