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Assessment of Risk Determinants in the Regularity of Malaria Using the Binary Logistic Approach

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ABSTRACT Malaria is a deadly sickness caused by parasitic organisms and it is transmitted to humans through the bite from an infected female anopheles mosquitoes. The spread of the mosquito parasites responsible for malaria infection is often traceable to living in an unhygienic condition such as poor environmental sanitations. Binary logistic regression was applied to verify the determinants influencing malaria patients' relapse after treatment and the cloglog model was found to fit the data well (log-likelihood = 31.6994; AIC = 63.607). Indicative threat factors were diagnosed utilizing the likelihood statistical ratio tests and the Wald. It was found that patients residing in poor types of dwelling were more predominantly hit by treatment relapse of malaria (Wald = 6.85; *p-value* <0.05). For the evaluation of the adequacy of the chosen mathematical model, different tests such as Lemeshow and Hosmer test, deviance goodness of fit and Pearson were utilized.

INTRODUCTION

Malaria is a vector-borne disease and estimated to be a leading cause of the most number of deaths globally (Parham et al. 2015). It is among the diseases of the highest mortality in the Democratic Republic of Congo (DRC) (Gemperli et al. 2006; Van Herp et al. 2003; World Health Organization Global Health Observatory 2014). The majority of people in DRC are living in high epidemic areas where there is high intensity of malaria transmission through the year (Roll Back Malaria 2005). Approximately estimated that ninety-five percent of the total population are pre-exposed to the risk of malaria (Adeya 2004), it is responsible for more than sixty-eight percent of malaria outpatient visits and thirty percent of patients' admissions in the hospital (Roll Back Malaria 2005). The morbidity and mortality of malaria burden have affected lots of lives and human productivity (Bhutta et al. 2014). The climatic conditions in central African countries like DR Congo, Rwanda and Uganda are suitably stable for malaria transmission with seasonality fluctuations (Colón-González et al. 2016). Malaria new cases was estimated to be more than 212 million worldwide in 2015, lower in 2000 by twenty-two percent and fourteen percent in 2010 (World Malaria Report 2016). Africa countries were estimated to have the highest malaria cases globally (90%), southeast Asia region estimated to be seven percent and the eastern Mediterranean region was two percent (World Malaria Report 2016). There were an estimated 429,000 deaths due to malaria ranging from 235,000 to 639,000 worldwide, which was recorded in 2015, a decrease of fifty percent since 2000 and twenty-two percent since 2010, and the highest number of these deaths were found in Africa (92%), southeast Asia region (6%) and the eastern Mediterranean region (2%) (World Malaria Report 2016). Besides, the death from malaria diseases from tens of millions of people sometimes come with a persistent symptoms like severe anemia (Adewoyin 2015). In DR Congo, malaria accounted for almost forty percent of public health expenditure and thirty percent to fifty percent of hospital admissions (World Malaria Report 2014; Bourtzis et al. 2016). The occurrence of drug-resistant parasites has generated the necessity for preventive measures, which will be remarkably decrease the transmission of malaria and mortality in various places across sub-Saharan Africa (Sturrock et al. 2015; Zelman et al. 2016; Newby et al. 2016).

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In countries with extreme malaria infections, such as the DR Congo, coherent involvement and pre-emptive attempts must be made by understanding the geographic specimens of regularity and the determinants of these regularities. Moreover, malaria frequency differs over any given place, and malaria-frequency records are required to pinpoint interventions strategies in areas where they are needed most.

Statement of the Problem

DR Congo is one of the countries with highest rates of malaria-related deaths in the world. It is second only to Nigeria, which leads with twenty-six percent (World Malaria Report 2016). Due to lack of sanitation, poor hygiene practices, and contaminated water, which all favor the reproduction of mosquito, malaria is the second highest cause of deaths in the DR Congo (Pan American Health Organization 2012; World Malaria Report 2014; Messina et al. 2011). Malaria infection in human beings may be amassed by suffering a bite from a female mosquito that developed in deteriorated hygienic conditions amid many other factors (Chaturvedi et al. 2014; Carter et al. 2015; Diouf et al. 2014). In Lubumbashi, most of the people are living in deteriorated hygienic environments, which leaves the population vulnerable to malaria. However, the authors focus on prevention and the determinants that increase the chances of patients relapsing after treatment for malaria, with the awareness to medications administered to patients to fight the disease.

Significance of the Study

This investigation will provide an analytical procedure effective when discerning threat determinants related to relapsing from malaria. The investigation lay out the statistical significant threat determinants; it will encourage persuasive strategies and organizations convenient in forestallment, care policies and countenance of relapsing from malaria that will be of benefit to health professionals, academics, researchers and the general public. Moreover, findings will serve as motivation of supplementary surveys of malaria remission in which the studied population must have alike characteristics compared to the one who participated to this investigation.

Aims of the Study

Through this investigation, the aim of the study is aim to determine the risk determinants that are related to relapse from malaria, pinpoint the pre-eminent dichotomous logistic mathematical model related to malaria's statistics utilizing the probit (normit), the complementary log log (cloglog) and logit, link functions, and, finally, evaluate the mathematical model for adequately utilizing existing assessment materials.

MATERIAL AND METHODS

Data

This study was based on the records of the 109 outpatients who were diagnosed with uncomplicated falciparum malaria before being taken into the study. After being treated positively, the patients were monitored till the time they started experiencing the malaria sickness again. Patients' demographic information, as well as the time of relapse, was retrieved from the medical records. Patients' relapse to malaria was used as response variable with the binary option of X_j yes = 1 and no = 0, and thirteen other covariates were considered as independent variables, presumed to influence the prediction of patients' relapse status.

Methodology

Since the response is a binary variable that consists of various explanatory variables, multiple logistic model was used to analyze the data collected. Besides being friendly to manoeuver and mathematically adaptable, the logistic model emanates in a categorically significant explaination (Al-Bajalan et al. 2015; Kudakwashe and Yesuf 2014). Throughout this sub-section, authors explore the logistic modeling concept related to the Logit, Probit and the complementary log log link functions.

Logit Model

The Logit model is outlined below:

$$Logit\left(P(Y=1)\right)=\beta_0+\beta_{1X_{i1}}+\sum_{k=1}^{3}\beta_{2k}X_{2ki}+\beta_3X_3+...+\sum_{k=1}^{14}\beta_{13k}X_{13ki} \quad (1)$$

Where, is the j^{th} threat determinant, K is the k^{th} category of the determinant, β_0 is the intercept of the Logit model, β_j is the approximated coefficient for individual threat determinant j for the logit model and $p\ (Y=1)$ is the likelihood of the i^{th} patient's relapse.

Probit (Normi) Model

Utilizing the Probit link function, the binary logistic model is outlined as a normal distribution that is inversed.

$$\text{Probit}\left(P(Y=1)\right) = \Phi^{-1}\left(P(Y_i=1)\right) \quad (2)$$

Complementary Log-Log (cloglog) Model

The cloglog link function emerges in a mathematical model outlined below:

$$Log\left(-\log\left(1-P(Y=1)\right)\right) = \beta_0 + \beta_{1X_{i1}} + \sum_{k=1}^{3}\beta_{2k}X_{2ki} + \beta_3X_3 + \ldots + \sum_{k=1}^{14}\beta_{13k}X_{13ki} \quad (3)$$

Model Structuring Procedures

The technique was utilized in the building of a point model only (null model), and thereafter a model with additional parameters was built (built model). The postulates $H_0: \beta_j$ for each of j against $H_1: \beta_j \neq 0$ at a minimum of one j was thereafter checked for statistical significance and the likelihood ratio test χ^2_{LR} =-2 log (L_0/L_1) was used, where L_0 stands for the maximized value of the null model and L_1 standing for the maximized value of the built model. If a test leads to the rejection of H_0 then this will mean one parameter or more is significant in the model. Once is rejected to the favor of the statistical significance of parameters was done using Wald test. When using a bivariate approach the unique issue could be that the concept overlooks a possibility of having covariates that are imperfectly associated to the results might emerge as controlling prognosticator of the final result. When utilizing the Statistical Analysis System (SAS) package, the logistic modeling procedure is a stepwise technic, which commences by selecting the sturdy contestant prognosticator and then analyzing additional contestant threat determinants (prognosticators) one by one for implication in the model. Founded on the Akaike Information (AIC), the best threat determinants to be considered in the model will be determined using various stepwise selection techniques that are provided by the logistic modeling procedures.

Explanation of Parameters

The model is monotonous and controlled by the sign of β. If increases by a unit the value of will increase or decrease depending on the sign of , which can be positive or negative. For the logit model, the odds are an exponential function of. Hence, stands as odds of relapsing from malaria for the subjects. An increase of related to odds will be observed when increases by a unit. When using a Probit and cloglog models an approximate of the odds ratio will not be given.

Evaluating the Fit of the Model

For assessing the equality of the suited mathematical model, the authors used Pearson's chi-square statistic and the likelihood ratio statistics (G^2). A variable is considered as significant in the model if its X^2 value is statistically significant. The Hosmer-Lemeshow test was also used. The Likelihood ratio test statistic X^2_{LR}= 2log(L_0-L_1) = -2(log L_0-Log L_1) was utilized with L_0 standing for the optimized value of the null model and L_1 standing for the optimized value of the likelihood function for the suited model.

RESULTS

Demographic Characteristics and Health Factors

From the 109 patients who participated in the study, 98 (89.9%) relapsed from malaria, 59.2 percent of them were female and the remaining respondents were male (40.8%). More than one-third (39.8%) were in the age group of 18-35 and 36-59 for female and male respectively, and were found to be the most relapsing age group, while 20.4 percent of the patients were aged 60 years and above as displayed in Table 1. More than half (57.1%) of the treated patients were living in unhygienic conditions while 42.9 percent of the patients were living in hygienic places. This could be the reason for having a record of almost ninety percent for relapse from malaria cases, as an unhygienic environment favors the multiplication of mosquitoes, which are the source of malaria. About 69.7 percent patients were using protected dug wells as source of water, and all of them experienced a relapse from malaria at the end of the study. The majority of patients (57.1%) living in an area surrounded by dumping sites experienced a re-infection as exposure to dumping sites increases the chances of getting bitten by malaria-carrying mosquitoes.

Patients who were residing in a poorly covered house (shack) had a higher risk of relaps-

Table 1: Demographic information of the re-infected malaria patients

Variables	*Frequency (%)*
Gender	
Male	40 (40.8)
Female	58 (59.2)
Age Group	
18-35 years	39 (39.8)
36-59 years	39 (39.8)
60 years and above	20 (20.4)
Marital Status	
Single	34 (34.7)
Married	49 (50.0)
Divorced	6 (6.1)
Widowed/Widower	9 (9.2)
Level of Education	
Completed primary school	18 (18.4)
Primary school not completed	10 (10.2)
Completed secondary school	13 (13.3)
Secondary school not completed	42 (42.9)
Completed College/University	7 (7.1)
College education not completed	8 (8.2)
Surrounding Area	
Hygienic place	42 (42.9)
Unhygienic place	56 (57.1)
Source of Drinking Water	
Unprotected dug well	30 (30.3)
Protected dug well	68 (69.7)

ing from malaria, with 68.8 percent of patients from the study confirmed to relapse from the disease as they were exposed to the bites of mosquitoes. Patients who were living in a poorly covered type of dwelling and were exposed to dumping sites were the most vulnerable with almost ninety percent of them relapsing from malaria.

Determination of Risk Factors for Malaria Relapse among Patients

Taken one by one all explanatory variables were checked for correlation with relapsing from malaria or not. Moreover, a test of correlation such as Pearson Chi-square (χ^2) and likelihood ratio (G^2) were utilized. In Table 2 the results indicate that the following variables influence the relapse of malaria patients in a significant way, namely, type of dwelling, source of drinking water, kind of toilet, maintenance of toilet, waste disposal, presence of stagnant water in the compound, crop cultivation in the compound, type of mosquito spray used, type of mosquito net used, treatment of mosquito net, and main cause of malaria.

Outcome from Multiple Logistic Modeling Evaluation

Identification of Variables by Gradual Assortment

In this investigation the logit, probit and cloglog link functions were used to identify the variables and the results are displayed in Table 3.

Parameter Estimates

The results as illustrated in Table 4 indicate that the determinant type of dwelling plays a

Table 2: Test of dependence between remission of malaria and each of explanatory variables

Variables	*Chi-square value*	*p-value*	*Likelihood ratio test value*	*p-value*
Treatment	0.9724	0.3241	0.9828	0.3215
Gender	2.1393	0.1436	2.3578	0.1247
Age group	2.8445	0.2412	4.8093	0.0903
Marital status	1.3102	0.7267	1.4167	0.7016
Level of education	7.0456	0.2173	7.0636	0.216
Type of dwelling	7.999	0.0047*	7.051	0.0079*
Source of drinking water	5.3124	0.0212*	8.4591	0.0036**
Type of toilet	6.3591	0.0117*	7.4761	0.0063**
Having well maintained toilet	4.2293	0.0397*	6.9488	0.0084**
Dumping places in the leaving area	6.0299	0.0141*	6.3752	0.0116*
Pit toilet covered	4.6461	0.0311*	7.5405	0.0060**
Water dummy in the compound	6.3671	0.0116*	6.6982	0.0097**
Cultivating in the compound	4.4351	0.0352*	7.2426	0.0071**
Type of mosquito spray used	6.5481	0.0105*	10.081	0.0015**
Type of net being used	5.2311	0.0222*	6.2405	0.0125*
Main cause of malaria	6.719	0.0095*	7.0312	0.0080**

Key: * = $p<0.05$ ** = $p<0.01$ *** = $p<0.001$

Table 3: Variables identified using the logit link function

Variables	*Logit link function*		*Probit link function*		*Clog log link function*	
	AIC	*Intercept*	*AIC*	*Intercept*	*AIC*	*Intercept*
Type of dwelling	73.307	68.256	73.307	68.256	73.307	68.256
Source of drinking water	73.307	66.847	73.307	66.847	73.307	66.847
Type of toilet	73.307	67.83	73.307	67.83	73.307	67.83
Having well maintained toilet	73.307	68.358	73.307	68.358	73.307	68.358
Dumping places in the leaving area	73.307	68.931	73.307	68.931	73.307	68.931
Pit toilet covered	73.307	67.766	73.307	67.766	73.307	67.766
Water dummy in the compound	73.307	68.608	73.307	68.608	73.307	68.608
Cultivating in the compound	73.307	68.064	73.307	68.064	73.307	68.064
Type of mosquito spray used	73.307	65.226	73.307	65.226	73.307	65.226
Type of net being used	73.307	69.066	73.307	69.066	73.307	69.066
Main cause of malaria	73.307	68.275	73.307	68.275	73.307	68.275

major role in remission from malaria using the logit link function, the probit link function or the cloglog link function with *p-value* equal to 0.009, 0.007 or 0.010, respectively.

Ultimate Chosen Model

In the process of choosing the prime model, the collection basis required selecting the distribution and link function, and furthermore, the predictive variables to incorporate in the model. The choice of the prime model will be based on the value of Akaike information criteria (AIC). The prime model must have a smallest value of Akaike information criteria (AIC).

Table 5: Significance of the goodness of the models' parameters

Model	*Log-likelihood*	*No. of parameters*	*AIC*
Logit	30.6825	12	64.624
Probit	31.0347	12	64.272
Cloglog	31.6994	12	63.607

The cloglog model was selected since it has the smallest Akaike information criterion (AIC) (See Table 5).

Model Suitability Inspection

To examine the general strength of the chosen cloglog model the authors used the goodness of suitability test (G^2), which is the chi-square difference between the null model (with intercept only) and the model comprising one or more prognosticators. For the chosen cloglog model, χ^2_{LR} is equal to 7.8145 with degrees of freedom of 11 and a *p-value* of 0.7298, indicating an insignificant growth in the likelihood, therewith indicating a good suitability of the model. The residue between the deviance of the null (M1) and full (M2) models gives $\chi^2_{LR}=DM_1-DM_2\sim\chi^2_{(P-1)}$. A better suitability to the data will be reached when using the Pearson and Deviance tests only when the *p-value* is large. The results indicated the deviance test values and Pearson being respectively equal to 6.0632 and 5.2908 with their corresponding *p-values* as 0.9999 and 0.9997, and hence the population from where the data was selected is following a logistic regression model.

DISCUSSION

This study showed 89.9 percent relapse for malaria from 109 sufferers at outpatient departments who participated to this investigation. This is higher than the reinfection rate of malaria in a peri-urban area of Bamako, Mali (80.7%) (Sagara et al. 2002). It is also higher than the 33.6 percent of malaria cases and 66.6 percent of malaria control group among patients in Blantyre, Malawi (Kazembe and Mathanga, 2016) but lower than malaria threat determinants in the Butajira area of South Central Ethiopia (70.1%) (Woyessa et al. 2013). Women were more affected with higher rates of malaria relapse (59.2%), which corresponds to findings in Ethiopia (Kazembe and Mathanga 2016).

From the results, there were no significant differences in the three link functions used in variable identification by the selection procedure of patient relapse characteristics. All the variables were incorporated into their corresponding models and then examined for suitability, in which the Akaike information criterion (AIC) for Logit, Probit and cloglog were the same for all the variables used in the selection proce-

Table 4: Approximated coefficients for the predictive variables in the logit, probit and cloglog link functions

Covariates	Logit link function			Probit link function			Cloglog link function		
	Estimate	*Wald*	*P-value*	*Estimate*	*Wald*	*P-value*	*Estimate*	*Wald*	*P-value*
Intercept	-10.376	0.312	0.577	5.648	0.07	0.791	3.702	0.033	0.857
Type of dwelling	1.112	6.85	0.009**	-0.661	7.313	0.007**	-0.68	6.588	0.010*
Source of drinking water	4.622	0.012	0.912	-2.188	0.002	0.964	-1.423	0.001	0.977
Type of toilet	0.723	0.959	0.327	-0.435	1.032	0.31	-0.452	1.255	0.263
Having well maintained toilet	3.388	0.004	0.948	-2.046	0.001	0.972	-1.734	0.001	0.974
Dumping places in the leaving area	0.79	0.284	0.594	-0.469	0.392	0.532	-0.458	0.531	0.466
Pit toilet covered	-5.498	0.007	0.933	2.92	0.002	0.969	2.379	0.001	0.974
Water dummy in the compound	-4.936	0.003	0.956	2.212	0.001	0.983	1.39	0	0.99
Cultivating in the compound	1.778	0.026	0.872	-1.016	0.007	0.933	-0.519	0.002	0.965
Type of mosquito spray used	4.132	0.145	0.704	-2.14	0.029	0.865	-1.611	0.019	0.89
Type of net being used	1.272	1.772	0.183	-0.76	1.873	0.171	-0.75	2.026	0.155
Main cause of malaria	3.374	0.001	0.97	-1.304	0	0.99	-0.546	0	0.996

Key: $^{*}= p<0.05^{**}= p<0.01^{***}= p<0.001$

dure. The results from the parameters estimates showed that only "type of dwelling" was significant among the three link functions used, which showed that "type of dwelling" was a risk factor for malaria relapse probably due to people's continuous contact with contaminated water that serves as a habitat for mosquitoes. About 57.1 percent of the patients living in unhygienic conditions were discovered to relapse back to malaria and this result confirms the finding of Muhammad et al. (2017).

One of the risk factors was patients living in uncovered houses. 68.8 percent of those who lived in uncovered houses were found to relapse with malaria sickness, a figure much higher than the 41.6 percent reported by Fana et al. (2015) but lower than the 91.6 percent reported in Lagos (Agomo and Oyibo 2013) in a study involving malaria infection among pregnant women in Nigeria. Dumping sites located close to where people reside were shown to be a risk factor for malaria relapse with about ninety percent in the study. There was, however, no significant association among the following variables of treatment, gender, age, marital status and level of education.

As the cloglog link function had the lowest AIC (63.607), it was chosen as the prime prognostic model in this investigation. Even though the use of logistic regression was applied, many of the authors have not contrasted the considered three link functions in sequence of formulating an adequate model that might be used to speculate the threat determinants linked to malaria relapse.

CONCLUSION

The dichotomous logistic model with cloglog link function was the prime model for malaria relapse data. The threat determinants that influence the coming back of malaria after being treated were type of dwelling, sources of drinking water, kind of toilet, maintenance of toilet, waste disposal, presence of stagnant water in the compound, crop cultivation in the compound, type of mosquito spray used, type of mosquito net used, and main cause of malaria. The other factors like treatment, gender, age, marital status and level of education were found to be insignificant. Female patients within the age group of 18-59 years were found mostly affected by malaria relapse. The same situation was found for female patients and those within unhygienic environments. The patients who were living in uncovered houses were more likely to have less hygienic conditions, which can pre-expose them to malaria parasites.

RECOMMENDATIONS

The following recommendations are suggested for the prevention of malaria relapse in patients after treatment, which include refining the causes of malaria relapse on the basis of available evidence, creating effective treatment protocols and providing effective malaria treatment against parasites resistance. Prevalence rates of infection among babies and under-aged children were not covered in this study, which needs further research.

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