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STATISTICAL ANALYSIS OF RISK FACTORS OF MALARIA RELATED IN-HOSPITAL MORTALITY: A CASE STUDY AT BUSHULO MAJOR HEALTH CENTER, HAWASSA

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Abstract- ***Malaria is a major challenge to public health and socio-economic development worldwide and in sub –Saharan Africa in particular. It causes an estimated 300 to 500 million cases and 1.5 to 2.7 million deaths worldwide each year, of which 80% of the cases and 90% of the deaths occur in Sub-Saharan Africa. The main objective of this study was to identify the risk factors of malaria related in-hospital mortality; so that modeling and simulating the related risk factors. The data were taken from hospital records at Bushulo major health center from June 2009 to June 2012, Hawassa. From a total of 6594 laboratory confirmed malaria positive in the health center, a sample of 539 patients were selected using stratified random sampling technique. The data were analyzed using the classical logistic regression and Bayesian logistic regression approaches. In this effort the two approaches were compared using standard errors of model parameters. The results of the study showed that 78.5% of malaria patients were found to be discharged while the rest 21.5% died of malaria in the health center. From Bayesian simulation analysis age, residence, time from symptom onset to diagnoses, type of malaria species diagnosed, body temperature in the last diagnoses, malaria complicated, pregnancy cases, total length of stay in hospitalization, referral status and season when patient diagnosed, were found to be statistically significant at 5% level of significance. The classical logistic regression analysis could select the first eight of these as significant predictors. Model comparison also revealed that, the Bayesian modeling approach has given estimates of the parameters with smaller standard error values showing that, with appropriate choice of prior distributions, the Bayesian modeling approach might lead to a more accurate estimation than the classical approach. It can be concluded from this study that the most contributing risk factors of malaria related in-hospital mortality in the health center are under five age group, rural resident, P.falciprum type of malaria species, having malaria complicated cases, longer time (days) from symptoms onset to diagnoses, wet season, high body temperature in the last diagnoses, women of pregnancy cases, shorter time (days) of stay in hospitalization.***

Key words: Bayesian, Logistic regression, Malaria, Risk factors, In-hospital mortality Bushulo

1. INTRODUCTION

1.1. Background

Malaria is a vector-borne disease caused by Plasmodium parasites. The parasites are spread to people through the bites of infected Anopheles mosquitoes, called "malaria vectors". It remains to be a major challenge to public health and socio-economic development worldwide and in sub –Saharan Africa in particular. It causes an estimated 300 to500 million cases and 1.5 to 2.7 million deaths worldwide each year, of which 80% of the cases and 90% of the deaths occur in Sub-Saharan Africa (WHO, 2010).

In Ethiopia, it is also a leading public health problem, where 75 % of the country's land surface is malarious and 68% of the populations are at risk of malaria infection (FMOH & ENMIS, 2011). Thus, malaria is a public health concern and all age groups of the population are vulnerable. Children under five years of age and pregnant women are generally considered to be at a higher risk. In 2009, malaria was still the first leading cause of health problem accounting for 48% of out patient consultations, 25% admissions and 29.6% inpatient deaths (MOH, 2009). According to the MOH reports, approximately 70,000 people die of malaria each year in Ethiopia.

Nowadays, although malaria deaths do not occur as often as previously, it still remains a major public health problem and it is too early to reach any firm conclusion about the possibility of achieving MDGs, because of resistance of the parasite to antimalarial drugs, the complexity of disease, expensiveness of the control program, seasonal variability nature of the disease (WHO, 2010). In SNNPR, the high transmission season of malaria cases usually goes from August to December (Shargie et al., 2010). Even though, there is a little reduction of death cases, the results of the survey as well as the routine surveillance data demonstrated that malaria continues to be a significant public health challenge and a major public health problem in Hawassa (Shargie et al., 2010). However, measuring malaria burden in a population is a challenge in most developing countries, because most disease incidences and deaths occur outside of the formal health care, particularly at home (Lawrence et al., 2011). Instead, routine hospital data provide a proxy for measuring the incidence of severe malaria and for estimating

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mortalities or equivalent clinical indicators (Lawrence et al., 2011).

In spite of the fact that, various malaria related cases or issues are assessed in Hawassa, one of which has high malaria prevalence rates in Ethiopia, there has been no Bayesian modeling done so far about risk factors of malaria related in-hospital mortality. That is the motivation to undertake this study based on in-hospital mortality data collected at Bushulo major health center covering a period from June 2009 to June 2012 years among patients of laboratory confirmed malaria positives in the health center.

1.2. Statement of the Problem

Even though, the current malaria surveillance estimates indicate some encouraging signs in that the epidemic is stabilizing, it remains a major public health problem and infections with this parasite can be critical and which leads to death. This may be due to the fact that the parasite changes to complicated cases, seasonal variability nature of the vector disease and resistant to ant malarial drugs and its one of the leading causes of death in hospitals and health centers admissions (Lederberg and Oaks, 2012).

It is known that, measuring malaria burden in a population is a challenge in resource poor countries like Ethiopia. Because most disease incidences and deaths occur outside of the formal health care, particularly at home. Instead, routine hospital data provide a proxy for measuring the incidence of severe malaria and for crudely estimating morbidity rates or equivalent clinical indicators (Alexander and Patrick, 2012). Determining the major factors that may affect malaria related in-hospital mortality is important to design better strategy and ultimately improve the care provided or treatment condition at all levels of health care (Lawrence et al., 2011).

Furthermore, the Bayesian model approach which is a powerful statistical method in medical researches, in modeling and simulating malaria related hospital mortality using routine hospital data has been not yet addressed in this country. On account of this, the methodological framework is used to provide a useful tool for analyzing the data at hand and of similar structure. So, this study is intended to modeling and simulating the risk factors of malaria related in-hospital mortality. Accordingly, the central research question of this study is which factors have the major risk factors of malaria related mortality at Bushulo major health center?

1.3. Objectives of the Study

The general objective of this study is modeling the risk factors of malaria related in-hospital mortality at Bushulo major health center.

Specific Objectives:

Specific objectives of the study are:

- To identify the risk factors of malaria related mortality at Bushulo major health center.
- To develop Bayesian logistic regression model and Simulate the chance of discharged/death status of laboratory confirmed malaria positive patient.
- To compare the Classical and Bayesian logistic regression approach in parameter estimation of the model.
- To provide information for policy makers and researchers.

1.4. Significance of the Study

The outcome of the research will help health care workers to inform patients about the related risk factors of death they might encounter. Moreover, clinicians can decrease mortality among malaria positives by early diagnosis and appropriate intervention.

The result of the study might ultimately improve the care provided at all levels of health care to assist in monitoring and planning resource needs in a health system and designing appropriate interventions, tailored towards communities at high risk and enable clinicians and policy makers to enhance the awareness of the society about factors which increase the probability of death in- hospital of malaria patients. Furthermore, the result of this study can also be used as a source of information to other researchers for further study to identify important risk factors of malaria related in-hospital mortality.

2. METHODOLOGY

2.1. Data

The study is retrospective, which was retrieved from the patient cards of malaria positives. So in this study, the data were obtained from record reviews of all inpatient malaria cases of laboratory confirmed malaria positive admitted to the pediatric ward from June 2009 to June 2012. Data were collected in October 2012 using a structured format and carried out by enumerators to get available information for this study Thus, in this research we use secondary data which was collected from patient admission card of laboratory confirmed malaria positives and a total of 6594 patients are recorded as confirmed malaria positive from 2009 to June 2012 in Bushulo major health center.

2.2. Sampling Design and Sampling Procedures

The target population for this study was recorded patients of laboratory confirmed malaria positive at Bushulo Major Health Center from June 2009 to June 2012. The 6594 patients who were laboratory confirmed malaria positive were taken as the population of the study. In this study, stratified random sampling method was adopted as an appropriate sampling design for selecting a representative sample of laboratory confirmed malaria patients. These were stratified into two strata based on their place of residence (urban and rural). So that the required sample size for the study was determined from each stratum. Hence the divisions /stratifications of a population are:

Stratum 1: Patients who are laboratory confirmed malaria positives in the health center from urban residence with population size N_1 and sample size n_1.

Stratum 2: Patients who are laboratory confirmed malaria positives in the health center from rural residence with population size N_2 and sample size n_2.

Let $N= N_1+ N_2$ be total number of laboratory confirmed malaria patients admitted to the major health center and

$n=n_1+n_2$ be total sample size of patients that was used in the study.

2.3. Sample Size Determination

In spite of the fact that, there are several formulas developed for sample size calculation that conform to different research situations, the sample size determination techniques for this study is based on stratified random sampling techniques. In stratified random sampling, a sample is drawn from each stratum of the population of which is assumed to be divided into subpopulations /strata according to a specific characteristic. The sample size determination formula that is adopted in this study is described as follows (Cochran, 2007):

$$n = \frac{\sum_{i=1}^{L} \frac{N_i^2 p(1-p)}{W_i}}{\frac{N^2 d^2}{Z_\alpha^2} + Np(1-p)}$$

where, n = the sample size needed, N = the total population size, Z_α = Standard normal distribution that correspond to the α level of confidence, p= the probability of dying of malaria in hospital in the stratum (i) , d = the level of precision, L= the total number of strata(urban and rural residence), N_i = the size of stratum (i), which is the size of the population in each residence and the stratum weight, W_i = the estimated proportion of N_i to N. According to Mesganaw et al. (2011) 24.1% in-hospital death was due to malaria at Butajira Hospital, SNNP Region. Therefore, p=0.241 was taken as the probability of death due to malaria in each stratum. The sampling error is called level of precision in sampling context denoted by d gives the researcher some idea relating to the accuracy of the statistical estimate. The level of precision taken for this study was 3.5% (i.e., d= 0.035). The level of confidence that is used in this study was 95%.

In this study the total population N=6594, the level of precision, d=0.035, the probability of dying due to malaria in-hospital, p=0.241, level of significance, α=0.05 were used as inputs to compute sample size. The total required sample size was 539. The health center gives service for both urban and rural residence, which was considered to be strata for this study. The size of the sample in each stratum was determined based on appropriate sample size allocation to each stratum. In this study proportional allocation method were used to yield 284 and 255 from urban and rural stratas respectively. Finally, using patient's admission cards of their unique identification number from each residence a simple random sample of laboratory confirmed malaria patients was selected from each stratum.

2.4. Variables in the Study

The variables included in the study were selected based on some previous studies and those that are expected to be risk factors/determinants of malaria related in- hospital mortality.

The Dependent Variable

The response or dependent variable in this study is the binary response variable which is named as "Discharged/Death status" of patients leveled as whether persons died of malaria in hospital or not. This status of patient is coded as 1, if the patient died in hospital and 0, if the patient discharged of malaria positive under laboratory confirmed.

The Independent Variables

The explanatory variables that are included in the study and assumed to be risk factors of malaria related mortality in the major health center are presented in Table 2.1.

2.5 Method of Statistical Analysis

In this study, since the response variable is a dichotomous variable, that is discharged/death status of patients (discharged =0 or death =1) so the effect of explanatory variables on the dependent variable can be investigated using logistic regression model that can be formulated under the classical or the Bayesian set up. Both approaches are considered in this study.

2.5.1 Classical Logistic Regression Model

Logistic regression analysis extends the techniques of multiple regression analysis in which the outcome variable is categorical. It is used when the dependent variable is dichotomous (binary), such as (discharged or died, presence or absence, success or failure, and etc) logistic regression is used (Stephenson, 2010). There are two main uses of logistic regression: Firstly, it is useful to predict the group membership. Since logistic regression calculates the probability of success over the probability of failure, the results of the analysis are in the form of an odds ratio. Secondly, it explains the relationships and strengths among the variables.

Table 2.1: List of Variables with their Codes and Descriptions

Explanatory Variables	Categories
Sex of patient	(0) Male (1) Female
Age of patient	(0) < 5 years (1) 5-14 years (2) 15-44 years (3) ≥ 45 years
Residence of patient	(0) Urban (1) Rural
Season when patient diagnosed: dry season (Oct.-March) wet season (April-September)	(0) Dry (1) Wet
Type of malaria species diagnosed	(0) Plasmodium Falciprum (1) Plasmodium Vivax (2) Mixtured
Referral status	(0) No (1) Yes
Time from symptom onset to diagnoses (days)	(0) < 3 days (1) 3 – 5 days (2) > 5 days
Body temperature in the first diagnosis (°C)	(0) 35 – 37 (°C) (1) 38 – 40 (°C) (2) ≥ 41 (°C)
Body temperature in the last diagnosis (°C)	(0) 35 – 37 (°C) (1) 38 – 40 (°C) (2) ≥ 41 (°C)
Malaria complication	(0) No (1) Yes
Malaria in pregnancy cases	(0) No (1) Yes
Total length of stay in hospitalization	(0) < 3 days (1) 3 - 5 days (2) > 5 days
Treatment given (drugs)	(0) Quinine (1) Chloroquine (2) Other

2.5.2 Model Description

Since the response variable in this study is dichotomous and we will denote it as Y, and denote the event Y=1, when the subject has the characteristic of interest and Y=0, when the subject does not have that characteristic of interest. In logistic regression, a single outcome variable Y_i (i=1,…,n)

follows a Bernoulli probability function that takes the value 1 with probability of success p_i or the value 0 with probability of failure 1-p_i. The binary logistic regression model is described as follows. Let Y_{nx1} be a dichotomous outcome random variable with categories 1 (died in hospital) and 0 (discharged). Let $X_{nx\ (k+1)}$ denote the collection of k-predicator variables of Y, where

$$\boldsymbol{X} = \begin{bmatrix} 1 & X_{11} & X_{12} & X_{13} & . & . & . & X_{1k} \\ 1 & X_{21} & X_{22} & X_{23} & . & . & . & X_{2k} \\ . & . & . & . & . & . & . & . \\ 1 & X_{n1} & X_{n2} & . & . & . & . & X_{nk} \end{bmatrix}$$

X is called regression matrix and without the loading column of 1's is termed as predictor data matrix. Then, the conditional probability that a malaria patient died in hospital given the X_i set of predictor variables is denoted by $P(Y_i =1/X_i) =p_i$. Then p_i can be expressed in the form:

$$P_i = \frac{e^{\beta_0+\beta_1 x_{i1}+....+\beta_k x_{ik}}}{1+e^{\beta_o+\beta_1 x_{i1}+....+\beta_k x_{ik}}} = \frac{e^{X_i'\beta}}{1+e^{X_i'\beta}} = \frac{1}{1+e^{-X_i'\beta}} \quad .....(1)$$

Where: β = (k+1) x1 vector of unknown parameters and $x_i' = (1, x_{i1}, \ldots, x_{ik})$, i=1, 2, …, n.

However, the relationship between the predictor and response variables is not a linear function in logistic regression; instead, the logarithmic transformation of equation yields the linear relationship between the predictor and response variables.

So an alternative form of the logistic regression equation is the logit transformation of P_i given as follows:

$$\text{logit}(P_i) = \log\left(\frac{P_i}{1-P_i}\right) = \beta_0+\beta_1 X_{i1}+\beta_2 X_{i2}+.....+\beta_k X_{ik} \quad .....(2)$$

The coefficients can be interpreted as the change in the log-odds associated with a one unit change in the corresponding independent variable keeping the other variables constant or the odd increases multiplicatively by e^{β} for every one unit change increase in x.

2.5.3 Parameter Estimation for the Binomial Logistic Regression

The maximum likelihood estimation is the most computing estimation methods used in fitting logistic regression model (Hosmer – Lemeshow, 2011). Hence, in this study the maximum likelihood estimation technique will be applied to estimate parameters of the model. Consider the logistic model

$P_i = \frac{e^{X_i'\beta}}{1+e^{X_i'\beta}}$, since observed values of Y say, Y_i's (i=1, 2,…,n) are independently distributed as binomial and, the maximum likelihood function of Y is given by:

$$L(Y;\beta) = \prod_{i=1}^{n} P(y_i \mid X_{i1}, X_{i2}, \ldots, X_{ik}) = \prod_{i=1}^{n} \left[\frac{e^{X_i'\beta}}{1+e^{X_i'\beta}}\right]^{y_i} \left[\frac{1}{1+e^{X_i'\beta}}\right]^{(1-y_i)} \quad ..... \quad ....(3)$$

The fact that the parameters $\hat{\beta}_o, \hat{\beta}_1, \ldots, \hat{\beta}_k$ and estimates of P_i for each subject could be facilitated by the widely available Statistical software such as SAS, SPSS, STATA, GLIM and WinBUGS. But in this study SPSS and WinBUGS softwares were used.

2.5.4 Bayesian Logistic Regression Model

Bayesian modeling is concerned with generating the posterior distribution of the unknown parameters given both the data and some prior density for the unknown parameters. Bayesian modeling approach provides a much more complete picture of the uncertainty in the estimation of the unknown parameters, especially after the confounding effects of nuisance parameters are removed (Draper, 2008; Lee, 2010; Tanner, 2011). Suppose we observe a random variable Y and assume the parameter β is random variable having prior distribution f (β). The conditional probability distribution of the posterior probability distribution function is defined as:

$$f(\beta \mid y) = \frac{f(y \mid \beta) f(\beta)}{f(y)} \quad ..... \quad ....(4)$$

where $f(y) = \int .....\int f(y|\beta)\ f\ (\beta)\, d\beta$ is a normalizing constant.

2.5.5 Bayesian Inference for Logistic Regression Parameters

A computationally tractable Bayesian inference for logistic regression models with parametric link is derived utilizing a Markov Chain Monte Carlo algorithm to simulate from the joint posterior distribution of the regression and the link parameter. Classical statistical inference is based on maximum likelihood estimation. Maximum likelihood estimation chooses the parameters that maximize the likelihood of the data, and is intuitively appealing. In maximum likelihood estimation, parameters are assumed to be unknown but fixed, and are estimated with some confidence. Instead of considering just a single value for a model parameter, as done by maximum likelihood estimation, it is known that Bayesian approach provides a very different approach to the problem of unknown model parameters in that the uncertainty about the unknown parameters is quantified using probability distributions so that the unknown parameters are regarded as random variables.

2.5.6 Likelihood Function

The likelihood function of the Bayesian formulation for n independent Bernoulli trial is given by, let $y_1, y_2, \ldots, y_n$ be independent with success probabilities $P_1, P_2, P_3, \ldots, P_n$, that is $Y_i = 1$ with probability P_i or $Y_i=0$ with probability 1-P_i, for i= 1,2,…,n. The likelihood contribution from the i^{th} subject is given by:

$$L(\beta \mid y) = \prod_{i=1}^{n} \left[P_i^{y_i} (1 - P_i)^{(1-y_i)} \right] \quad ..... \quad ..... \quad ..... \quad ..... \quad ..... \quad (5)$$

we know that, in equation (1) the probability of success written as:

$$P_i = \frac{e^{\beta_0 + \beta_1 x_{i1} + \ldots + \beta_k x_{ik}}}{1 + e^{\beta_0 + \beta_1 x_{i1} + \ldots + \beta_k x_{ik}}}$$

Where: P_i = the probability of i^{th} patient has died of malaria in-hospital and the likelihoods function over a data set of subjects is:

$$L(\beta \mid y) = \prod_{i=1}^{n} \left(\frac{e^{\beta_o + \beta_1 x_{i1} + \ldots + \beta_k x_{ik}}}{1 + e^{\beta_o + \beta_1 x_{i1} + \ldots + \beta_k x_{ik}}} \right)^{y_i} \left(1 - \frac{e^{\beta_o + \beta_1 x_{i1} + \ldots + \beta_k x_{ik}}}{1 + e^{\beta_o + \beta_1 x_{i1} + \ldots + \beta_k x_{ik}}} \right)^{(1-y_i)} \quad \ldots\ldots\ldots (6)$$

2.5.7 Prior Distribution

Existing evidence about the parameters of interest may be available from earlier studies or from experts' opinions and can be formalized into what is called prior distribution of the parameter of interest. A prior distribution can be non informative, informative, or very informative. Non informative prior distributions are used in cases in which no extra-sample information is available on the value of the parameters of interest (Clark et al., 2002 and Mila et al., 2003). Informative prior distributions are used when some prior knowledge about the parameters of interest is available, such as when existing belief or evidence indicates that a parameter should take a value within a range. Formally, this knowledge is represented with a distribution that has a known mean and large variance. Very informative prior distributions are used when very strong prior knowledge about the parameters of interest should be a specific value. In statistical terms, this knowledge can be represented with a distribution that has a known mean and small variance. So a critical feature of any Bayesian analysis is the choice of a prior. The choice can include also informative prior distributions if something is known about the likely values of the unknown parameters $\beta_0, \beta_1, \ldots, \beta_k$ or non-informative priors if either little is known about the coefficient values or if one wishes to see what the data themselves provide as inferences.

One may prefer to provide prior information on the odds-ratio=exp (β) scale, and transform back to the logistic scale. For this purpose, we will use the most common priors for logistic regression parameters, which are of the form: $\beta_j \sim N(\mu_j, \sigma_j^2)$. This implies the normal distribution with mean μ_j and with variance σ^2_j. It can be expressed as follows:

$$f(\beta_j) = \frac{1}{\sqrt{2\pi\sigma_j^2}} \exp\left\{ \frac{-1}{2} \left(\frac{\beta_j - \mu_j}{\sigma_j^2} \right)^2 \right\} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (7)$$

2.5.8 Posterior Distribution

Given the likelihood of logistic regression and the prior distribution given above, the posterior distribution of the Bayesian logistic regression model is derived by multiplying the prior distribution over all parameters by the full likelihood function. We can write posterior distribution as:

$$f(\beta \mid y) = \prod_{i=1}^{n} \left[\left(\frac{e^{\beta_o + \beta_1 x_{i1} + \ldots + \beta_k x_{ik}}}{1 + e^{\beta_o + \beta_1 x_{i1} + \ldots + \beta_k x_{ik}}} \right)^{y_i} \left(1 - \frac{e^{\beta_o + \beta_1 x_{i1} + \ldots + \beta_k x_{ik}}}{1 + e^{\beta_o + \beta_1 x_{i1} + \ldots + \beta_k x_{ik}}} \right)^{(1-y_i)} \right] \prod_{j=0}^{k} \frac{1}{\sqrt{2\pi\sigma_j^2}} \exp\left\{ \frac{-1}{2} \left(\frac{\beta_j - \mu_j}{\sigma_j} \right)^2 \right\} \ldots\ldots (8)$$

In this study, the likelihood function is based on the data set that was obtained from a review of patient cards of laboratory confirmed malaria patients in Bushulo major health center. In regard to prior distributions for model parameters, non informative prior distributions of the type given above were used. Computing the estimate of β of the posterior distribution may be difficult; on account of this, we need to use non analytic method such as simulation techniques. The most popular method of simulation technique is the Marcov Chain Monte Carlo (MCMC) methods and that was applied in this study.

2.5.9 Markov Chain Monte Carlo (MCMC) Methods

A major difficulty towards more widespread implementation of Bayesian approaches is that obtaining the posterior distribution often requires the integration of high–dimensional functions. MCMC methods are attempted to simulate direct draws from some complex distribution of interest such as posterior distribution. A popular way of simulating from a general posterior distribution is by using MCMC methods. Markov Chain Monte Carlo techniques enable quantitative researchers to use highly complicated models and estimate the corresponding posterior distributions with accuracy. In this way, MCMC methods have greatly contributed to the development and propagation of Bayesian theory. Simulation can also be used to estimate and visualize the posterior distribution of f (β|y) itself. The main problem in the above mentioned procedure is how to generate from the posterior density f (ß|y) random sample. The operation of a Marcov Chain until it reaches its stationary distribution is exactly the process employed in MCMC. Generally the most commonly used MCMC techniques are Metropolis-Hasting and Gibbs sampler algorithm. In this study we give the details of Gibbs sampler algorithm as follows.

2.5.10 The Gibbs Sampling Algorithm

The Gibbs sampler (Geman and Geman 2009) is most widely use MCMC technique. One advantage of the Gibbs sampler is that, in each step, random values must be generated from univariate distributions for which a wide variety of computational tools exists (Gilks et al., 2011). In spite of the fact that there are different widely available Software for Bayesian statistical inference such as Win BUGS/BUGS, BayesX, R, BACC, but in this study Win BUGS/BUGS and R software was implemented. The Gibbs sampler algorithm was implemented by sampling the set of full conditional distributions or up on in turn from the k-conditional posterior distributions as follows:

$$\{\Pi(\beta_1 \mid \beta_2, \beta_3, \ldots, \beta_k), \Pi(\beta_2 \mid \beta_1, \beta_3, \ldots, \beta_k) \ldots \Pi(\beta_k \mid \beta_1, \beta_2, \ldots, \beta_{k-1})\} \ldots\ldots\ldots\ldots\ldots (9)$$

It is essential that there be a definable conditional statement for each coefficient in the β vector and completely articulated so that it is possible to draw samples from the described distribution. This requirement facilitates the iterative nature of the Gibbs sampling algorithm described and stated as follows:

1. Start with an initial value $\beta^{0} = (\beta_1^{\circ}, \beta_2^{\circ}, ..., \beta_k^{0})$
2. Sample for each i = 0, 1, 2,...., n-1

Generate $\beta_1^{(i+1)}$ from $f\left(\beta_1 \mid \beta_2^{(i)}, \beta_3^{(i)}, ..., \beta_k^{(i)}\right)$

Generate $\beta_2^{(i+1)}$ from $f\left(\beta_2 \mid \beta_1^{(i+1)}, \beta_3^{(i)}, ..., \beta^{(i)}{}_k\right)$

⋮

Generate $\beta_k^{(i+1)}$ from $f\left(\beta_k \mid \beta_1^{(i+1)}, \beta_2^{(i+1)}, ..., \beta_{k-1}^{(i+1)}\right)$

3. Return $\beta^{(1)}, ..., \beta^{(n)}$.

2.5.10.1 Convergence of the Algorithm

The empirical results from a given MCMC analysis are not deemed reliable until the chain has reached its stationary distribution. On account of this, the term convergence of an MCMC algorithm refers to whether the algorithm has reached its equilibrium (target) distribution. If this is true, then the generated sample comes from the correct target distribution. Hence, monitoring the convergence of the algorithm is essential for producing results from the posterior distribution of interest. Convergence diagnosis was adopted sampler has reached its stationary distribution (Albert, 2010)

2.5.10.2 Tests for Convergence Diagnostics

Generally it is unclear how much we must run an algorithm to obtain samples from the correct target distributions. Several diagnostic tests have been developed to monitor the convergence of the algorithm. Among several ways, the most popular and straight forward convergence assessment methods are Autocorrelation, Time series plots, Gelman-Rubin statistic, and Density plot.

3 RESULTS AND DISCUSSION

3.1 Results

3.1.1 Descriptive and Test of Association Results

The data were obtained from records of 539 patients who were laboratory confirmed malaria positive in-patients during June 2009 to June 2012. The results displayed in Table 1 shows percentages and counts of discharged/death status of patient with respect to the explanatory variables. Out of the 539 patients considered, 423 (78.5%) patients were discharged while 116 (21.5%) were died. The association between the outcome variable and each predictor of the variables with chi-square and likelihood ratio tests, frequency distributions of each category of predictor variables was included in detail in Table 1.

Table 1: Test of Association between Discharged/Death Status and Explanatory Variables

Variable	Category	Discharged/death status				Total		Chi-square (Sig.)	LR (Sig.)
		Discharge		Death					
		Count	%	Count	%	Count	%		
Sex of patient	Male	207	82.1	45	17.9	252	46.8	3.762 (0.152)	3.795 (0.151)
	Female	216	75.3	71	24.7	287	53.2		
Age of patient	<5	121	62.5	48	37.5	169	31.4	44.961 (0.000)	48.422 (0.000)
	5 -14	177	82.1	14	17.9	191	35.4		
	15 -44	70	71.6	42	28.4	112	20.8		
	≥45	55	92.7	12	7.3	67	12.4		
Residence of patient	Urban	252	88.7	32	11.3	284	52.7	37.36 (0.000)	38.207 (0.000)
	Rural	171	67.1	84	32.9	255	47.3		
Season when p diagnosed (wet or dry)	Dry	188	83.9	39	16.1	227	42.1	4.375 (0.016)	4.454 (0.015)
	Wet	235	70.3	77	29.7	312	57.9		
Type of malaria s diagnosed	P. Falciprum	213	63.4	77	36.6	290	53.8	14.413 (0.000)	15.497 (0.000
	P. Vivax	171	84.2	25	15.8	196	36.4		
	Mixtured	38	76.1	14	23.9	52	9.6		
Referral status	No	343	86.4	54	13.6	397	73.7	55.596 (0.002)	51.086 (0.001)
	Yes	80	56.3	62	43.7	142	26.3		
Time from symptom on diagnoses (days)	< 3 days	255	93.4	18	6.6	273	50.6	105.044 (0.000)	101.945 (0.000)
	3- 5 days	116	75.3	38	24.7	154	28.6		
	> 5 days	52	56.4	60	43.6	112	20.8		
Body temperature in th diagnoses (°C)	38-40 (°C)	254	80.2	59	19.8	313	58.1	3.154 (1.476)	3.127 (1.477)
	≥ 41 (°C)	169	74.8	57	25.2	226	41.9		
Body temperature in th diagnoses (°C)	35-37 (°C)	410	96.7	14	3.3	424	78.7	391.983 (0.000)	361.375 (0.000)
	38-40 (°C)	13	13.1	86	86.9	99	18.4		
	≥ 41 (°C)	0	0.0	16	100.0	16	3.0		
Malaria complication	No	295	87.2	25	12.8	320	59.4	87.634 (0.000)	88.620 (0.000)
	Yes	128	58.4	91	41.6	219	40.6		
Pregnancy cases	No	183	81.5	17	18.5	200	37.1	106.771 (0.000)	93.103 (0.000)
	Yes	33	47.9	54	52.1	87	16.1		
Total length of sta hospitalized(days)	< 3 days	127	61.7	79	38.3	206	38.2	65.711 (0.000)	70.921 (0.000)
	3-5 days	198	84.3	12	15.7	210	39.0		
	> 5 days	98	89.7	25	10.3	123	22.8		
Treatment given (drugs)	Quinine	252	73.5	91	26.5	343	63.6	11.014 (0.045)	11.901 (0.042)
	Chloroquine	171	87.2	25	12.8	196	36.4		

It was shown above Table 1 that out of thirteen categorical predictor variables, only two predictor variables, namely sex of patient and body temperature in the first diagnosis have no significant association in the response. Eleven predictor variables have significant association with the response variable. But using multiple logistic regressions by the Forward Stepwise (Likelihood Ratio) method in SPSS, only eight predictor variables were selected by the model. These are age of patient, residence of patient, type of malaria species diagnosed, time from symptom onset to diagnoses (days), body temperature in the last diagnoses (°C), malaria complicated, pregnancy cases and total length of stay in hospitalization (days) contributed significantly to the Discharged/Death status of patients with p-value, 0.034, 0.001, 0.000, 0.009, 0.000, 0.02, 0.038, and 0.019 which is less than level of significance, α= 0.05, respectively (See Table 2).

We note that the exp($\hat{\beta}$) which is also called odds multiplier or odds ratio, in Table 2 column presents the extent to which raising the corresponding measure by one unit influences the odds ratio.

Table 2: Variables in the Final Logistic Regression Model (Bushulo Major Health Center, Oct. 2012)

Predictor Variable	$\hat{\beta}$	S.E.($\hat{\beta}$)	Wald	Df	Sig.	Exp(B)	95.0% C.I. for Exp(B)	
							Lower	Upper
Age(Ref)			7.594	3	0.034			
Age(1)	-1.840	0.826	4.959	1	0.026	0.159	0.031	0.802
Age(2)	-1.533	0.778	3.880	1	0.039	0.216	0.047	0.992
Age(3)	-2.079	0.787	6.983	1	0.008	0.125	0.027	0.585
Resid(1)	1.607	0.521	9.526	1	0.001	4.989	1.798	11.843
Typemalaspecdiag(Ref)			14.518	2	0.000			
Typemalaspecdiag(1)	-3.329	0.945	12.402	1	0.000	0.036	0.016	0.229
Typemalaspecdiag(2)	-2.984	0.984	9.195	1	0.043	0.051	0.019	0.348
Timesymptodiag(Ref)			9.528	2	0.009			
Timesymptodiag(1)	0.897	0.693	1.674	1	0.044	2.452	0.630	9.536
Timesymptodiag(2)	1.204	0.731	2.712	1	0.025	3.334	0.795	11.977
Bodytemplastdiag(Ref)			24.56	2	0.000			
Bodytemplastdiag(1)	1.178	0.275	18.34	1	0.000	3.249	1.895	5.571
Bodytemplastdiag(2)	1.922	0.501	14.69	1	0.000	6.835	2.558	18.26
Malcomp(1)	1.213	0.516	5.522	1	0.020	3.364	1.223	9.254
Pregncase(1)	0.733	0.534	1.887	1	0.038	2.082	0.731	5.930
TLS(Ref)			5.979	2	0.019			
TLS(1)	-1.364	0.658	4.292	1	0.045	0.256	0.070	0.929
TLS(2)	-0.415	0.323	1.648	1	0.038	0.661	0.351	1.244

* Ref; in the brackets indicates the reference category for each predictors.

We can interpret Exp ($\hat{\beta}$) as changes in odds. If the value exceeds 1 then the odds of success occurring increase (death due to malaria); if the value is less than 1, any increase in the predictor variables leads to a drop in the odds of dying. The results in Table 2 show that the values of the odds ratio interpretation of age categorized as < 5, 5-14, 15-44 and ≥ 45 years. The patient of 5-14 age group was 0.159 times less likely to die of malaria than the reference category (< 5 years) patient. Also for individuals in the age group 15-44 years and ≥ 45 years the odds of dying of malaria is 0.216 and 0.125 times less likely than for under five children age (the reference category) respectively. This implies that, death to malaria is high for those in the age group of less than five years. When we come to see the odds ratio of resident of patient, it is categorized as urban and rural. Apparently, the results shown that the odds of death due to malaria for rural resident are 4.989 times more likely than for patients from urban areas and other results are interpreted accordingly.

3.1.3 Bayesian Logistic Regression Analysis

The Bayesian logistic regression modeling were used to make inference and the Gibbs sampler algorithm was implemented with 30000 iterations in three different chains, 15000 burn-in terms discarded, so that the 15000 iterations are sampled from the full posterior distribution. The model identified those all eight significant variables (in classical logistic regression method) and additional two predictor variables as having significant impact on malaria inpatient discharged/death status (see Table 3). The algorithm uses different convergence tests and the convergence of the chain can be initially checked visually using trace plots and MC error in comparison to its posterior standard errors (Ioannis, 2009 and Gelman, 2005).

Time series plot: The time series plot in Bayesian simulation indicates a good convergence where three independently generated chains will mix together or overlapped and the Win BUGS package gives the plot with iteration number on the X-

axis and parameter value on the Y-axis for each predictor variables. (See Figure 1).

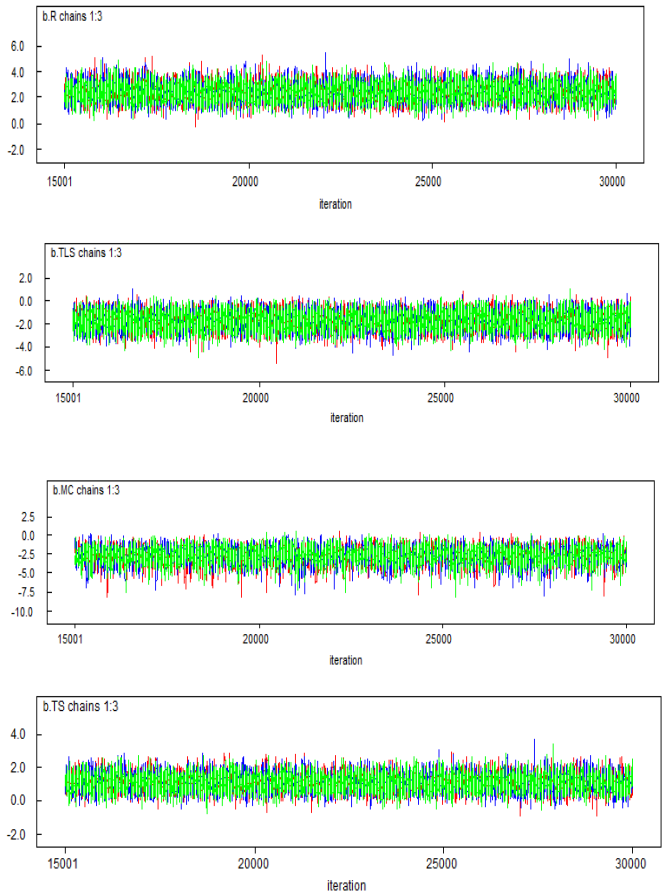

Figure 1: Convergence of Time Series Plots for the Bayesian Simulations of Posterior Distribution of the Model Parameters for Selected Predictors.

Autocorrelation Plot: The plots show that the three independent chains were mixed or overlapped with each other and pass out for higher lags and hence this is an evidence of convergence. (See in Figure2).

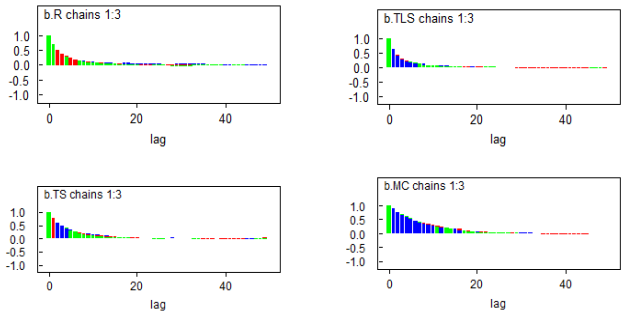

Figure 2: Convergence of Autocorrelation Plots for the Bayesian Simulations of Posterior Distribution of the Model Parameters for Selected Predictors.

Gelman –Rubin Statistic: Gelman-Rubin convergence statistic with width of the pooled runs green, the average width of within the individual runs blue and their ratio red ratio close to 1 so that it is an indication of convergence (see in Figure 3).

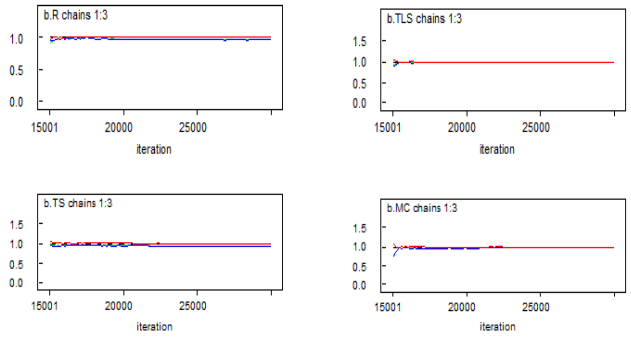

Figure 3: Convergence using Gelman-Rubin Statistic Plots for the Bayesian Simulations of Posterior Distribution of the Model Parameters for Selected Predictors.

Density plot: The plots for most predicator variables indicate the coefficient has normal distributions (bimodal density) and hence the simulated parameter value indicates convergence (see Figure 4).

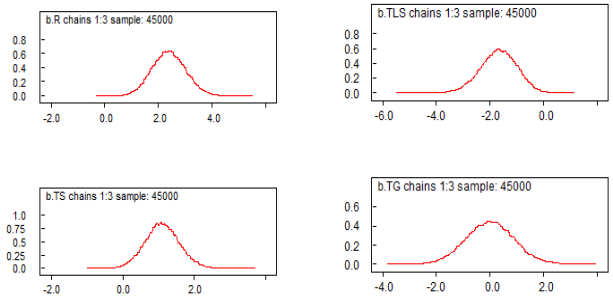

Figure 4: Convergence of Density Plots for the Bayesian Simulations of Posterior Distribution of the Model Parameters for Selected Predictors.

3.1.4 Assessing Accuracy of Bayesian Simulation

If the Monte Carlo error value in MCMC algorithm of Bayesian simulation is low in comparison to its posterior standard error, then the posterior density is estimated with accuracy. Especially, to have accurate posterior estimates the simulation should be run until the Monte Carlo error for each parameter of interest is less than about 5% of its posterior standard error, since small values of MC error will indicate that we have calculated the quantity of interest with precision and hence evidence for accuracy of posterior estimate is accomplished. In Table 3, MC error for each significant predictor is less than 5% of its posterior standard error. This implies convergence and accuracy of posterior estimates are attained and the model is appropriate to estimate posterior statistics also the 95% confidence intervals of parameters do not contain zero.

Table 3: Summary Statistics of the Posterior Distribution of the Model Parameters

Node	Mean($\hat{\beta}$)	S.E($\hat{\beta}$)	MC error	95% CI	
				Lower	Upper
b.Age	1.1920	0.3072	0.002301	0.4226	2.0420
b.Body temp.in last the diag.	2.9280	0.9010	0.007040	1.9770	5.3500
b.Malaria complicated	-2.7960	0.7590	0.008005	-5.1240	-0.9592
b.Pregnancy cases	0.8962	0.5912	0.009220	0.1417	1.4940
b.Residence	2.4020	0.5333	0.002564	1.1880	3.6810
b.Referral status	-1.9120	0.7987	0.007820	-3.8930	-0.3261
b.Season when patient diag.	1.5510	0.6170	0.008450	0.1709	3.0100
b.Total length of stay in hospitalize.	-1.6760	0.6057	0.002073	-3.0750	-0.3870
b.Type of malaria species diag.	0.8326	0.3258	0.002067	0.1589	1.5610
b.Time from symptom	1.1100	0.4241	0.004918	0.2000	2.0590

1.1.1. Model Comparison

For model comparison purposes, the results of the techniques that used to compare Bayesian and classical logistic regression analyses were displayed in Table 4; SE_B and SE_C stands for standard error of Bayesian and classical methods, respectively. So we can say that the Bayesian logistic regression model to generate the posterior distribution of the unknown parameters using MCMC simulation technique can be more preferable than the classical logistic regression method.

Table 4: The Model Comparison Based on Standard Error (Bushulo Major Health Center, Oct. 2012)

Variables	Classical logistic results		Bayesian logistic results		SE Comparison
	Mean($\hat{\beta}$)	$SE_C(\hat{\beta})$	($\hat{\beta}$)	$SE_B(\hat{\beta})$	
Age of patient	1.088	0.390	1.192	0.3072	$SE_B < SE_C$
Residence of patient	2.147	0.598	2.402	0.5333	$SE_B < SE_C$
Referral status	-1.825	0.879	-1.912	0.7987	$SE_B < SE_C$
Season when patient diagnosis	1.389	0.688	1.551	0.6170	$SE_B < SE_C$
Malaria complicated	-2.319	0.952	-2.796	0.7590	$SE_B < SE_C$
Time from symptom to diagnosis	0.994	0.452	1.110	0.4241	$SE_B < SE_C$
Type of malaria species diagnosis	0.741	0.350	0.8326	0.3258	$SE_B < SE_C$
Body temp. in the last diagnosis	3.350	1.033	2.9280	0.9010	$SE_B < SE_C$
Pregnancy cases	0.8962	0.5912	1.484	0.570	$SE_B < SE_C$
Total length of stay in hospitalization	-1.364	0.658	-1.676	0.6057	$SE_B < SE_C$

3.2 Discussion

This study attempted to modeling and simulating the risk factors of malaria related in-hospital mortality at Bushulo Major Health Center, Hawassa. The results of the study showed that, out of a sample of 539 patients hospitalized for malaria from June 2009 to June 2012, 78.5% were patient discharged while 21.5 % were patient died of malaria. In the Bayesian approach of logistic regression model the Gibbs sampler algorithm with Win BUGS software was implemented with 30000 iterations in three independent different chains, 15001 burn-in terms were discarded, so as to obtain 15000 samples from the full posterior distribution.

The Bayesian simulation of logistic regression identified ten predictor variables, including all eight significant variables in classical approach and two others. The fact that the variables referral status and season when patient has been diagnosed come out to be significant in the Bayesian approach, but not in the classical approach is in line with the studies conducted by Lawrence et al. (2011) in Zomba district hospital in Malawi and Bachou et al. (2011) in Mulago hospital in Uganda and Guyatt et al. (2010) in Kenya, were found to be the major risk factors of malaria patient discharge/death status. The Bayesian logistic regression approach took more predictor variables than the classical approach. To have accurate posterior estimates, the simulation was run until the Monte Carlo error for each parameter of interest is less than 5% of its posterior standard error, and hence evidence for accuracy of posterior estimates in Bayesian simulation of logistic regression is accomplished. In this study MC error for each significant predictor was found to be less than 5% of its posterior standard error. This implies convergence and accuracy of posterior estimates of the Bayesian simulation were attained. As we can see in the Table 4 in Bayesian approach the standard error values for ten predictor variables were less than that of classical approach. So we can say that Bayesian approach might leads to a better accurate estimation than the classical one.

Finally, in this study using Bayesian modeling and simulation of MCMC algorithm, similar results for age of patient, resident of patient, malaria complicated, type of malaria species diagnosed and total length of stay in hospitalization have significant impact and relationship with malaria patient discharge/death status as study in Zomba district hospital in Malawi by Lawrence et al. (2011). The results for time from symptom onset to diagnoses, were also similar with the study reported in Ethiopia by Mesganaw et al. (2011) and in Uganda by Bachou et al. (2011) and also for pregnancy cases the result confirms with the study by Newman et al. (2008) in Ethiopia. Similar results were also reported in earlier studies in South Africa in St. Augustines Hospital, were found that body temperature of patient in the last diagnoses were significant to the risk of malaria patient death (Zungu et al., 2011).

4 CONCLUSIONS AND RECOMMENDATIONS

4.1 Conclusions

- Among the samples considered for the study, the death rate due to malaria was estimated to be 21.5%. The health status of malaria patients at the center was found to be significantly associated with age of patient, residence of patient, season when patient diagnosed, type of malaria species diagnosed, referral status, time from symptom onset to diagnosis (days), body temperature in the last diagnosis (°C), malaria complication, pregnancy cases, total length of stay in hospitalization (days) and treatment given. Factors levels with higher risk to death due to malaria in the health center were found to be: under five age group, rural resident, P.falciprum type of malaria species diagnosed, longer time (days) from symptoms onset to diagnosis, having malaria complicated cases, high body temperature in the last diagnosis, women of pregnancy cases, and shorter time (days) of stay at the center.
- Moreover, the estimates of the parameter value of standard errors in Bayesian approach were found to be smaller than that of the classical method and also, more predictor variables were selected by the model in Bayesian approach than in the classical method.
- Finally, we conclude that the application of Bayesian logistic regression model to generate the posterior distribution of the unknown parameters given both data and prior densities of the unknown parameters using MCMC simulation technique particularly, Gibbs sampler might lead to a more accurate estimation than the classical logistic regression method.

4.2 Recommendations

- To minimize the risk of dying in hospital due to malaria, health workers should be cautious when a patient has a complicated malaria cases, high body temperature in the last diagnosis and laboratory confirmed plasmodium falciprum type of malaria species. When this is the case appropriate clinical and special attention should be given. For the population at risk of malaria death particularly the most vulnerable groups, children under 5 years of age and pregnant women special attention should be given like early detection and prompt diagnosis.
- Moreover, patient from rural residents are particularly at high risk of death than patients from urban residents hospitalized in the health center. In order to address this problem, governmental and non-governmental organizations those working in the areas should focus on continuous awareness creation of early diagnoses and treatment to the health facility.
- Finally, the concerned body has to expand and maintain health promotions on designing appropriate interventions, tailored towards communities at high risk and effective treatment at home or with community.
- Methodologically, this model can easily be adapted to analyze other health indicator of similar structure and in like settings. Moreover, further modeling researches might be necessary, in order to model risk of malaria related hospital mortality with data from a number of hospitals. May be Geostatistical modeling or Spatial modeling could considered, since malaria data are geographically referenced.

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