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Statistical Analysis of the Risk Factors Associated with Visceral Leishmaniasis Patients at Marsabit County Referral Hospital

Elias Elema Guyo*, Tum Isaac Kipkosgei, Mathew Kosgei

Department of Mathematics, Physics and Computing, Moi University, Eldoret, Kenya

Email address:

eliasguyoelema@gmail.com (Elias Elema Guyo)

*Corresponding author

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Abstract: Visceral Leishmaniasis also known as Kala-azar, is a tropical infectious disease caused by female sandflies. It affects the internal organs, usually the spleen, liver and bone marrow. Globally, an estimated 700 000 to 1 million new cases of visceral leishmaniasis occur annually. In Kenya, 4000 cases occur while 5 million people are at risk of infection. The purpose of the study was to evaluate risk factors for visceral Leishmaniasis. The study adopted a retrospective cohort design. The study used secondary data from 2890 visceral leishmaniasis patients enrolled at Marsabit County referral hospital from September 2015 to September 2019. Cox proportional hazard model was used to establish the relationship between the survival time of visceral leishmaniasis patients and predictor variables. Data analysis was carried out using R statistical software. The risk factors which were significant predictors for survival time of visceral Leishmaniasis patients included; household design (cracked walls and thatched roof) [β =.435, p=.0001], living near anthills [β =.320, p=.0012], using bed nets [β= -.151, p=.0080], contact with infected dogs [β =.200, p=.0006], forest surroundings [β=.151, p=.0340] and sleeping outside at night [β =.169, p=.0260]. In conclusion, there was an increased case of visceral Leishmaniasis among patients who are not using bed nets, those living in cracked mud walls, those living near the forest, residing near ant hills, sleeping outside, and those in contact with infected dogs. The study recommended adopting appropriate practices such as avoiding contact with infected dogs, using bed nets at night, clearing forests surrounding homesteads, avoiding sleeping in the open at night, and reducing house proximity to ant hills and termite mounds to reduce the transmission from Visceral Leishmaniasis.

Keywords: Risk Factors, Survival Probabilities, Visceral Leishmaniasis

1. Introduction

Leishmaniasis is a parasitic infection caused by different species of Leishmania protozoa. It is transmitted through the bite of infected female sandflies from the Phlebotomus, Lutzomyia, and Psychodopygus species [4]. These insects bite from dusk to dawn and are often found in forests, stones, mud wall cracks, and animal burrows [7]. There are three main disease manifestations: self-healing but scarring Cutaneous Leishmaniasis, Mucocutaneous Leishmaniasis with the destruction of the mucosal tissues in the nose, mouth, and throat, and visceral Leishmaniasis in which parasites disseminate to the bone marrow, liver, and spleen, leading to high fever, hepatosplenomegaly, wasting, and death in the absence of treatment. Leishmaniasis is the most severe form of the Leishmaniasis family of diseases because death is inevitable if untreated [2]. An estimated 700,000 to 1 million new cases are expected, with 26,000 to 65,000 deaths worldwide yearly [12]. Visceral Leishmaniasis is endemic in 14 of Kenya's 47 counties; every year, 4,000 new cases are reported, and 5 million people are at risk of infection [3]. Northern Kenya had experienced multiple outbreaks of Visceral Leishmaniasis in the last ten years, with several counties being affected; in July 2006, a Visceral leishmaniasis outbreak was reported in Isiolo County, recording more than 60 cases. Wajir County experienced a

large outbreak in March 2018, where more than 180 cases were admitted, with a case fatality rate of 7.6%. A visceral leishmaniasis outbreak was reported in Marsabit County for the first time in 2014 [3]. The prevalence of visceral Leishmaniasis was reported in Turkana county, with the ratio of symptomatic to asymptomatic visceral Leishmaniasis was 1:6. Loroo sub-county had the highest prevalence of visceral leishmaniasis infection, followed by Karita and Amudat sub-counties at 31.9%, 14.6%, and 5.3%, respectively [10]. The number of Visceral Leishmaniasis cases reported in Marsabit County since the first prevalence is rising annually. Despite the disease's widespread prevalence, little is known about the ecology of the vector and the disease's transmission dynamics. In addition, the risk associated with visceral leishmaniasis transmission in Marsabit County remains largely undocumented.

2. Literature Review

This section offers a comprehensive summary of previous research on visceral Leishmaniasis.

Research on the relationship between visceral leishmaniasis infection and climatic changes based on rainfall patterns concluded that rainfall pattern is an important factor statistically correlated to Visceral Leishmaniasis spread in the region [11]. Cox proportional hazard model for visceral Leishmaniasis in their research, they discovered that a delay of more than 60 days between the onset of symptoms and therapeutic intervention was associated with a high mortality rate from visceral Leishmaniasis, similarly Children less than five years of age were at higher chances of premature death compared to other age structure they also identified that weakness and leishmaniasis HIV− co-infection, anemia and age between 50−60 years are the risk factor which needs to be recognized at the early stage of the disease in order to decrease mortality [8]. The Cox regression model, and they identified that dry leaves around the homestead, manure in the backyard, and sleeping predominantly outside at night increase the risk for visceral Leishmaniasis [1]. However, spraying insecticides in the house greatly reduced the risk of visceral Leishmaniasis. [5] carried out research on visceral Leishmaniasis using the hazard model, they found that gender and educational level were significant variables: women had a higher chance of knowing about the disease than men, and individuals with higher education were more likely to know about Leishmaniasis than those with no or only basic education. They also discovered that age was a protective factor, with people over 40 having a lower chance of living with many risk factors at home. A study on risk factors for visceral Leishmaniasis in north-western Ethiopia [14] discovered that sleeping outside under a bed net and smoking plant parts in the house at night were associated with a lower risk of infection with visceral Leishmaniasis [6] conducted malnutrition research as a risk factor for visceral Leishmaniasis, and they found that malnutrition is strongly linked to visceral leishmaniasis cases in northwest Ethiopia. [9] carried out research on the relationship between forest cover surrounding the homestead and the prevalence of visceral Leishmaniasis, they discovered a link between forest cover and disease transmission. Viana, G. M. *et al.* [13] carried out a cross-sectional study design in São Luis do Maranhão, Northeastern Brazil, on rainfall patterns and the prevalence of visceral Leishmaniasis; their research found that rainfall was directly proportional to visceral leishmaniasis cases reported in that region.

3. Methodology

3.1. Study Area

The study was conducted in Marsabit county, and secondary data was obtained from the Marsabit county referral hospital.

Cox-proportional Hazard Regression model for Visceral leishmaniasis risk factors.

The risk factors considered in the study were; Forest surrounding, contact with infected dogs, household designs, sleeping outside at night, use of bed nets, and proximity to ant hills and termite mounds. These risk factors increase mortality incidence from the disease. The probability of the endpoint death is called the hazard.

$$h(t) = h_0(t)\exp(b_1X_1 + b_2X_2 + \cdots + b_pX_p) \quad (1)$$

Where $h(t)$is the expected hazard at time t, $h_o(t)$ is the baseline hazard and represents the hazard when all of the predictors (or independent variables) $X_1, X_2 \ldots . X_p$ is equivalent to zero. $b_1, b_2 \ldots . b_p$ are regression coefficients.

This model can be illustrated using a ratio as

$$\frac{h(t)}{h_o(t)} = \exp(b_1X_1 + b_2X_2 + \cdots + b_pX_p) \quad (2)$$

Taking the natural logarithm (ln) of both sides, it is obtained as

$$ln\left\{\frac{h(t)}{h_0(t)}\right\} = (b_1X_1 + b_2X_2 + \cdots + b_pX_p) \quad (3)$$

3.2. Kaplan-Meier Estimator to Compare Survival Functions for Each Group

Kaplan-Meier was used to estimate the fraction of patients surviving beyond any age at time t; it involves computing the probabilities of the occurrence of an event at a certain point in time. These successive probabilities are multiplied by earlier computed probabilities to determine the final estimate. Assume we have a sample of n independent observations with their survival times denoted by $t_1, t_2, \ldots . t_n$ and indicator of censoring by $\delta_1, \delta_2, \ldots \delta_n$ where $\delta_i = 1$, death and where $\delta_i = 0$ for censored observations. The survival data are denoted by $(t, \delta_i), i = 1,2 \ldots . , n$.

Let;

$d_{(j)}$ = failure or death numbers at time $t_{(j)}$

$N_{(j)}$ = number of individuals at risk at $t_{(j)}$

The product limit estimator of survival function at time t:

$$\hat{S}_{KM}(t) = \left(1 - \frac{d_{(1)}}{N_{(1)}}\right)\left(1 - \frac{d_{(2)}}{N_{(2)}}\right) \ldots \ldots \left(1 - \frac{d_{(j-1)}}{N_{(j-1)}}\right) \quad (4)$$

$$= \prod_{t(j)<t}^{k} \left(1 - \frac{d_{(j)}}{N_{(j)}}\right) for\ t_{(k)} \leq t < t_{(k+1)}, K = 1,2, \ldots \ldots m$$

According to Kaplan-Meier (1958).

4. Results and Discussions

This section indicates the output after analysis, the study findings, and recommendations based on this study.

Table 1. *Variables and parameter estimate.*

Covariate of interest	Symbol	Parameter (β)	p-values	Hazard
Drugs given	X_1	− 0.3846	0.0001	0.6807
Cracked walls	X_2	0.4350	0.0001	1.5449
Residence near ant hills	X_3	0.3203	0.0012	1.3776
Use of bed nets	X_4	− 0.1513	0.0080	0.7633
Contact with infected dogs	X_5	0.2004	0.00059	1.2219
Forest surrounding	X_6	0.1507	0.0340	1.1626
Sleeping outside at night	X_7	0.1696	0.0260	1.1848

$$ln\{\lambda_t\} = -0.3846X_1 + 0.4350X_2 + 0.3203X_3 - \ 0.1513X_4 + 0.2004X_5 + \ 0.1507X_6 + 0.1696X_7 \quad (5)$$

In the above equation, household design (cracked mud wall) (X_2), residence near ant hills (X_3), contact with infected dogs (X_5), the forest surrounding (X_6), and sleeping outside at night (X_7) had positive parameter coefficients which indicated that these predictor variables are associated with worse prognosis or decreased survival among visceral leishmaniasis patients at Marsabit referral hospital while drug administered (X_1) and use of bed nets (X_4) had negative parameter coefficient indicating that it had a protective effect or associated with improved survival or decreased risk of the death among visceral leishmaniasis patients.

Kaplan Meier Curves for Survival Probabilities.

4.1. Survival Probability for Household Design (Cracked Walls and Thatched Roof)

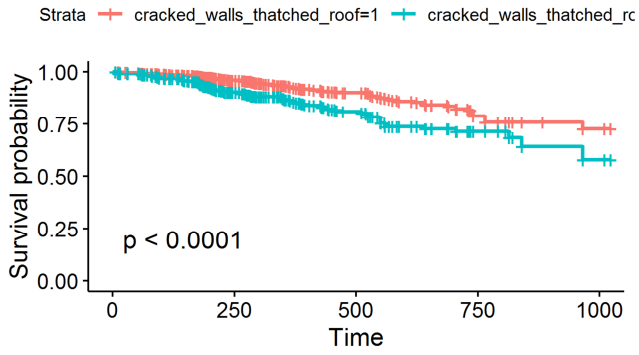

Figure 1. *Kaplan Meier curve to show survival probabilities of patients in households with cracked walls and thatched roof.*

Those living in cracked mud walls were coded 1, while those not living in cracked mud walls were coded 2. The log-rank p-value is significant (0.0001), and the survival probabilities for the two groups differ significantly. Those living in cracked walls and thatched roof houses have a higher risk of contracting the disease.

4.2. Survival Probability for a Residence Near Ant Hills

Those residing near ant hill were coded 1, while those not residing near ant hill were coded 2. The log-rank p-value is significant (0.0012), and the survival probabilities for the two groups differ significantly. Those living near ant hills have a higher risk of contracting the disease.

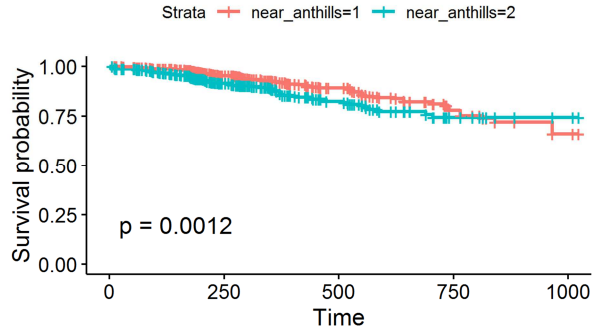

Figure 2. *Kaplan Meier curve to show survival probabilities of patients' residence near ant hills.*

4.3. Survival Probability for Bed Net Use

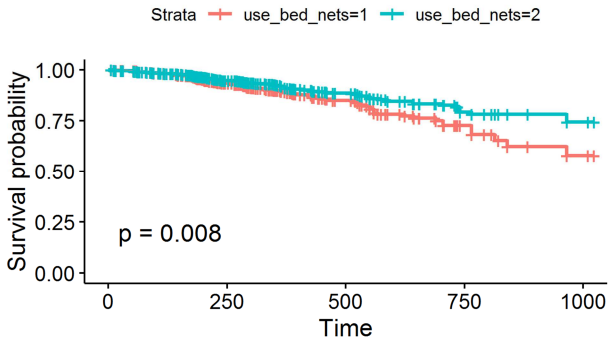

Figure 3. *Kaplan Meier curve to show survival probabilities of patients using bed nets.*

Those using bed nets were coded 1, while those not were coded 2. The log-rank p-value (0.008) is statistically significant. Those without bed nets had a higher risk of contracting the disease.

4.4. Survival Probability for Interaction with Dogs

Those who interacted with dogs were coded 1, while those

who did not interact with dogs were coded 2. The log-rank p-value is significant (0.00059), and the survival probabilities differ significantly among the two groups. Those who interacted with infected dogs had a higher risk of contracting the disease.

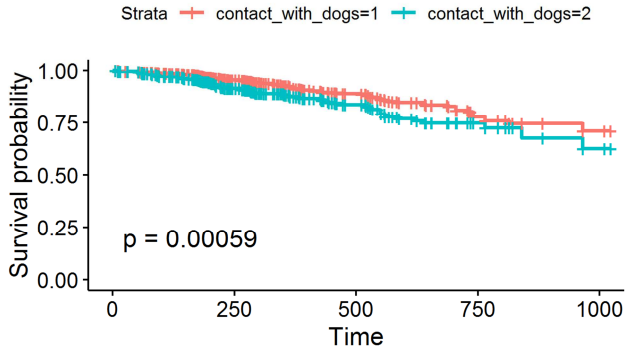

Figure 4. *Kaplan Meier curve to show survival probabilities of patients' contact with dogs.*

4.5. Survival Probability for Forest Cover Surrounding the Homestead

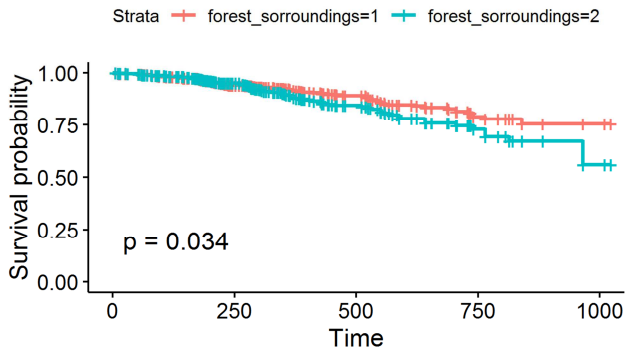

Figure 5. *Kaplan Meier curve to show survival probabilities of patients around the forest.*

Those living near the forest were coded 1, while those not living near the forest were coded 2. The log-rank p-value is significant at (0.0340). Those living near forest surroundings are at a higher risk of contracting the disease.

4.6. Survival Probability for Sleeping Outside at Night

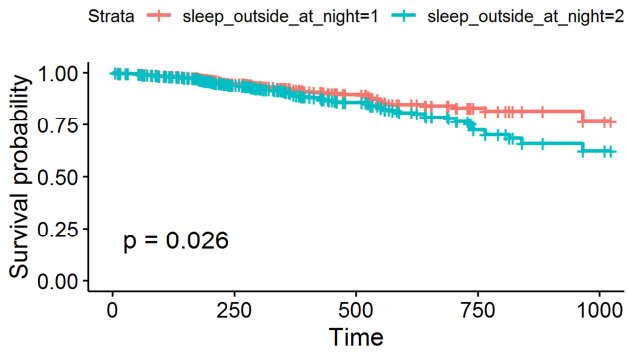

Figure 6. *Kaplan Meier curve shows survival probabilities of patients sleeping outside at night.*

Those sleeping outside at night were coded 1, while those not sleeping outside were coded 2. The log-rank p-value is significant at (0.0260). Those sleeping outside are at higher risk of contracting the disease.

5. Conclusions

The survival probability curves indicated that household design, which included cracked mud walls and the grass-thatched house were significant to the transmission of visceral Leishmaniasis. Residence near ant hill was associated with an increased risk of disease transmission. Bed nets were a significant risk factor in the study; individuals who do not use bed nets are at high risk of infection with Visceral Leishmaniasis compared to those using bed nets. Interaction with dogs was a significant risk factor in this study because those who interacted with dogs had a higher probability of contracting visceral Leishmaniasis. Forest cover surrounding the homestead was associated with increased transmission of visceral Leishmaniasis in Marsabit County. Sleeping outside at night was another factor associated with increased transmission of visceral Leishmaniasis. The above risk factors heightened the transmission rate from visceral Leishmaniasis at Marsabit County referral hospital.

6. Recommendations

To minimize the transmission from visceral leishmaniasis the following measures are to be adopted by the residence of Marsabit County;

1) Sleep under insecticide-treated bed nets to prevent human-to-vector contact.
2) Minimize residence in thatched grasses houses as it is associated with increased transmission of the disease.
3) Repair cracks in walls of houses to minimize entry and resting sites of sandflies.
4) Clear vegetation around the homestead to reduce resting sites for sandflies and destroy inactive termite hills and animal burrows around homesteads to reduce breeding sites for sandflies.

Conflicts of Interest

The authors have not declared any conflict of interest.

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