MODELLING RISK FACTORS, TRANSMISSION AND MORTALITY RATE OF *Visceral leishmaniasis* AT MARSABIT COUNTY REFERRAL HOSPITAL

BY

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(B.ED EDUCATION)

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DECLARATION

Declaration by the student

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DEDICATION

I dedicate this thesis to my beautiful, loving and caring wife, Sabdio for her unfathomable moral support, prayer and motivation while writing this work and to my family and friends.

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ABSTRACT

Visceral leishmaniasis (V.L.), also known as visceral leishmaniasis, is a tropical infectious disease caused by female sand flies. This type of Leishmaniasis affects the internal organs, usually the spleen, liver, and bone marrow. Globally, an estimated 700 000 to 1 million new cases of V.L. occur annually. In Kenya, 4000 cases arise, while 5 million people are at risk of infection annually. The purpose of the study was to evaluate the risk factors; estimate the transmission and mortality rate of visceral leishmaniasis at Marsabit County referral hospital and give an insight understanding of V.L. dynamics to create awareness. The study's specific objectives were to: Evaluate the risk factors associated with mortality among V.L. patients, estimate the mortality and transmission rate of V.L. and establish the level of endemicity of V.L. 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 V.L. patients and predictor variables. The Susceptible, Infected, and Recovered (S.I.R.) model was fitted to estimate the transmission and mortality rates and establish the disease's endemic nature. Data analysis was carried out using R statistical software. The risk factors that were found to be 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]. The mortality and transmission rates were estimated at 13.19% and 13.63%, respectively. The control reproductive number (level of endemicity) was 0.0141, implying that the disease was not endemic. In conclusion, there was significantly higher mortality among patients who are not using bed nets, those living in cracked mud walls, those living near the forests, residing near ant hills, sleeping outside, and those in contact with infected dogs. The study recommends the adoption of appropriate practices such as avoiding contact with infected dogs, use of bed nets at night, clearing forests surrounding homesteads, avoiding sleeping in the open at night, repair wall cracks,reduce house proximity to ant hills and termite mounds to reduce the transmission and subsequent mortality from Visceral leishmaniasis.

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ABBREVIATIONS AND ACRONYMS

C.L – Cutaneous Leishmaniasis.

D.F.E-Disease Free Equilibrium.

E.E-Endemic Equilibrium.

G.I.S –Geographical Information System.

H.I.V – Human immunodeficiency virus.

I.R.S – Indoor Residual Spraying.

K.M-Kaplan Meier.

L.D- Leishmaniasis Donovani.

L.I-Leishmania Infantum

N.T.D-Neglected Tropical Disease

O.D.E -Ordinary Differential Equation.

P.D.E -Partial Differential Equation.

P.K.D.L-Post Visceral leishmaniasis dermal leishmaniasis.

P.L.E-Product Limit Estimator.

S.I.R – Susceptible Infectious and Recovered.

S.L.I.R-Susceptible Latent Infectious and Recovered

S.S.G- Sodium stibogluconate.

V.L. -Visceral leishmaniasis.

WHO -World Health Organization.

DEFINITION OF TERMS

Visceral leishmaniasis - A chronic and potentially fatal parasitic disease of the viscera (especially the liver, spleen, bone marrow, and lymph nodes) caused by Leishmania donovani infection. Visceral leishmaniasis is another name for it.

Basic reproductive number – Refers to the number of people among the susceptible population that can be infected by an infected sand fly on average throughout the infectious period.

Control Reproductive Number- Refers to the number of people among the susceptible population that can be infected by an infected sand fly on average throughout the infectious period with control to treatment.

Survival time is the time from a defined point to the occurrence of a given event, e.g., death.

Risk Factors – Refer to something that increases the chances of developing a disease, e.g., interaction with infected dogs is a risk factor for V.L.

Transmission rate - The rate at which a communicable disease pathogen spreads from an infected host individual or group to another individual or group, regardless of whether the other individual was previously infected.

Mortality rate – The number of deaths in a specific population per unit of time.

Symptomatic Individuals- Refers to individuals who exhibit the signs and symptoms of a particular disease.

Asymptomatic Individuals – Refers to individuals who do not show signs and symptoms of disease yet are infected.

Infection rate – The likelihood or risk of infection in a population.

CHAPTER ONE: INTRODUCTION

1.0 Overview.

This chapter begins by giving the background of the study, a statement of the problem, research objectives, significance of the study and assumptions of the study.

1.1 Background to the study.

Leishmaniasis is a parasitic infection caused by various Leishmania protozoa species. The bite of infected female sand flies of the Phlebotomus, Lutzomyia, and Psychodopygus species spreads it. From dusk to dawn, these insects bite and are commonly found in the forests, stone, mud wall cracks and animal burrows. Although Leishmaniasis is clinically divided into three major categories - cutaneous, mucocutaneous and visceral - it receives little attention. There are three types of Leishmaniasis: 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 spread to the bone marrow, liver and spleen, resulting in high fever, hepatosplenomegaly, wasting and death in the absence of treatment Visceral leishmaniasis is the most severe form of Leishmaniasis because death is unavoidable if not treated (salih, 2020). Leishmaniasis has been endemic in parts of Kenya since the early twentieth century (kanyina, 2020). In 1940s, visceral leishmaniasis was reported in troops of the King's African Rifles stationed north of Lake Turkana in southwest Ethiopia. A severe outbreak of visceral leishmaniasis was reported in the Kitui district in 1952, with 303 cases, and peaked in 1953, with 2,142 cases. In the same year, 157 cases were reported in the neighbouring Meru district. In 1966, 1,500

cases of visceral leishmaniasis were reported in the Meru district. The Visceral leishmaniasis vector was identified as the Phlebotomus martini Parrot during that epidemic. Further outbreaks of Visceral leishmaniasis were reported in the Machakos and Kitui districts in the 1970s and 1980s, respectively (Tinui, 2006).

In 1955, Baringo and neighboring districts such as West Pokot were identified as Leishmaniasis foci. Visceral leishmaniasis caused by Leishmania donovani is endemic in Kenya's Baringo District. The disease in Baringo had a concentrated distribution in the dry, hot areas below 1500 meters and the infections can be classified as follows: a disease that is asymptomatic, subclinical, and self-limiting (not medically identifiable), as well as clinically manifest disease (that is medically identifiable).

Half of the reported visceral leishmaniasis patients are between ages 5 and 14 and 66% are males. In 1999, the Baringo district reported 305 cases of visceral leishmaniasis (Martha, 2016)

Three Maasai children were diagnosed with visceral leishmaniasis in the early 1990s in Kenya's Rift Valley district of Kajiado. L. donovani was isolated, but a survey of other school children in the district revealed no additional cases (Tinui, 2008). Northern Kenya had experienced multiple outbreaks of V.L. in the previous decade, affecting several counties. A Visceral leishmaniasis outbreak was reported in Isiolo County in July 2006, with more than 60 cases. In March 2018, Wajir County experienced a large outbreak, with over 180 cases admitted and a 7.6% case fatality rate. For the first time in history, a V.L. outbreak was reported in Marsabit County in 2014 (Kanyina, 2020b).

In 2014 the following information was retrieved from research conducted by Kanyina “a total of 136 cases were confirmed where 77.2 % (105) were male, and 22.8 % (31) were female with 9.6% (13) cases mortality rate and all these cases were admitted at Marsabit County referral hospital, Kenya” (Kanyina, 2020a).“ The overall prevalence of visceral leishmaniasis infection in Pokot County was 17.2%, but the community's prevalence of symptomatic infection was 2.5%. The symptomatic to asymptomatic visceral leishmaniasis ratio was 1:6. Loroo sub-county had the highest prevalence of Visceral leishmaniasis infection (31.9%), followed by Karita and Amudat sub-counties (14.6%) and 5.3%, respectively" (Odoch, 2013). The total number of cases of visceral leishmaniasis reported in Marsabit County since the first prevalence tally to (2890) cases. Despite the disease's widespread prevalence, little is known about the vector and the disease's transmission dynamics. In addition, the risk associated with visceral leishmaniasis (V.L.) transmission in Marsabit County remains largely undocumented.

Visceral leishmaniasis is associated with a fatality rate of 85% in untreated patients and less than 50% in treated patients (Stauch, 2011). The first instances of visceral leishmaniasis were reported in 2014 at Marsabit County referral hospital, which caused health panic as the available medical personnel could not handle the cases, resulting in high mortality rates. Marsabit is partly arid and semi-arid; it has limited access to essential health services due to household poverty, complicating diagnosing and treating Leishmaniasis. After malaria, the second most deadly tropical disease is visceral leishmaniasis (Spickler, et al., 2017). An estimated 700,000 to 1 million new cases are expected, with 26,000 to 65,000 deaths worldwide yearly (Myrsini et al.,2020). V.L. is found in 14 of Kenya's 47 counties the counties are (Marsabit 9%,Wajir 11%,Garisa

15%, Mandera 17%, Turkana 5%, Pokot 12%,Baringo 8%, Isiolo 8%, Meru 6%, Kajiado 14%, Kitui 12%, Samburu 8%, Tana River 11% and Bomet 3%) (Jahn, 2018). Every year, 4,000 new cases are reported, and 5 million people are at risk of infection. (Kanyina, 2020a). "The study identified V.L. endemic foci in Marsabit County, where the disease significantly burdens the current devolved health care system. The county's preparedness for an outbreak was inadequate and hence high mortality incidence"(Kanyina, 2020a). Therefore, the need to avert the situation with appropriate control and preventative measures. "Because Visceral leishmaniasis is mostly unknown outside of endemic areas, outbreaks are frequently detected late due to inadequate surveillance or because they are initially misdiagnosed as malaria or other acute febrile illnesses. If not addressed promptly, these outbreaks can have a high mortality rate" (Alvar et al., 2021). A model was used to evaluate the mortality and transmission rate of V.L. Instead of the basic reproduction number, the control reproductive number (R_C) was estimated and used to assess the level of endemicity in the presence of treatment. When $R_C > 1$, the model ensures disease persistence. When $R_C < 1$ corresponds to disease eradication. A treatment model was considered. This was a critical assumption because untreated patients die relatively quickly (sundar, 2004).

1.2 Statement of the problem.

Most research in Marsabit County on Visceral leishmaniasis was based on qualitative approaches; there is a need for more focus on awareness at the community level, so the need to evaluate the risk factors, estimate mortality rate and transmission rate, level of endemicity to reduce suffering, death and improve the general well-being of the communities and advice the stakeholders appropriately.

1.3 Objectives of the study

This subsection highlights the general objectives and specific objectives.

1.3.1 General objective

The general objective of this study was to evaluate risk factors, transmission and mortality rates due to visceral leishmaniasis at Marsabit County referral hospital.

1.3.2 Specific objectives

The specific objectives of the study were to:

1) Evaluate risk factors associated with mortality among visceral leishmaniasis patients admitted at Marsabit County referral hospital.
2) Estimate mortality and transmission rate of visceral leishmaniasis at Marsabit County referral hospital.
3) Determine the level of endemicity of visceral leishmaniasis at Marsabit County referral hospital.

1.4 Significance of the study

The information obtained from the model for this disease's transmission rate and mortality rate is significant to the authorities and other relevant parties for policies and decision-making. The findings provided sufficient statistical information particularly significant predictors of survival time in visceral leishmaniasis patients. This will help raise general awareness of the risk factors for visceral leishmaniasis. As a result, this would serve as a foundation for health study education for infected patients and the general public to reduce disease occurrence.

1.5 Assumptions of the study

There is an interacting population of hosts and vectors which is assumed to mix homogeneously.

The population consists of three types of individuals; Susceptible, Infectious, and Recovered.

There is a homogeneous mixing of the infected and susceptible populations.

Both populations have the same probability of contracting the disease.

The host-vector ratio changes over time.

CHAPTER TWO: LITERATURE REVIEW

2.0 Introduction

This chapter discusses model development for visceral leishmaniasis; the model is used to estimate risk factors, mortality rate and calculate the control reproductive number to estimate the level of endemicity.

2.1 World prevalence of visceral leishmaniasis;

The epidemiology of Leishmaniasis is diverse with the Indian Sub-Continent, Brazil and East Africa having the highest prevalence, visceral leishmaniasis is a global infection affecting 88 Countries with 500,000 reported annually with 556 million people are at risk. Globally 90% of visceral leishmaniasis cases have been reported in Sudan, Brazil, India, Bangladesh, and Nepal (Hailu et al., 2010). Leishmania donovani (LD) and Leishmania infantum (LI) are the main causes of Infections. LDs are restricted to the (sub-) tropics of Asia and Africa while LI is restricted in the drier parts of Latin America as well as in the Mediterranean climate regions. Cutaneous Leishmaniasis (CL) causing organisms having been accounted for 73% of the CL infection globally with Afghanistan, Iran, and Syria (Ready et al., 2014).

In Africa, visceral leishmaniasis is endemic in West Africa, North, Central, East and the Horn of Africa. The presence of visceral leishmaniasis infection was first reported in Niger in 1911. Based on this information, visceral leishmaniasis is proposed to be endemic in a belt running from Mauritania, Gambia, and Senegal in the west to Nigeria and Cameroon in the east (Menkir et al., 2015). East Africa is the second-largest visceral leishmaniasis focus in the world estimated at 30,000 and related deaths at 4000 especially

in Sudan, Ethiopia, and Kenya, visceral leishmaniasis is associated with high mortality and morbidity, exacerbated by poor nutritional status and the remote location of visceral leishmaniasis endemic areas (Hailu et al., 2010) affecting several communities in the following endemic Countries; Sudan, South Sudan, Kenya, Uganda, Somalia and Ethiopia (Al salim et al., 2016). The disease affects socially marginalized and poor communities in semi-arid and arid areas in Kenya and its 85% fatal if not treated (Kalan et al., 2013). Visceral leishmaniasis is fatal if not well managed. Even with treatment, the mortality rate was high (10%) (Berman el.at, 1997). In 2005, a national visceral leishmaniasis elimination programme was launched jointly by the health ministries from Bangladesh, India and Nepalto eliminate visceral leishmaniasis by 2015 (WHO, 2004). In Bangladesh, the goal of the elimination programme was to reduce visceral leishmaniasis cases below 1 per 10 000 people in the visceral leishmaniasis endemic sub districts (known as Upazila). The strategies for visceral leishmanisis elimination included active detection of post visceral leishmaniasis dermal leishmaniasis (PKDL) cases, adequate treatment of visceral leishmaniasis and PKDL cases, interruption of disease transmission through integrated vector management, and social mobilization (WHO, 2005). Since 2006, several operational research activities have been conducted by government and non- government organizations to support the national elimination programme in Bangladesh. These programmes revealed that the passive case detection (existing surveillance system) highly under estimated visceral leishmaniasis cases in Bangladesh (Mondal el.at, 2009). In 2008, a study conducted in the Rajshahi district showed that the incidence of visceral leishmaniasis was 27 times higher than the elimination target. It also found that the knowledge of the community about visceral leishmaniasis and its

vector was poor and their health seeking behavior was also unsatisfactory (Mondal el.at, 2010). Similar to visceral leishmaniasis case reported, the mortality rate of visceral leishmaniasis was also highly under estimated in Bangladesh. Until now, there is no well-designed study to measure visceral leishmaniasis mortality in highly visceral leishmaniasis endemic areas of Bangladesh. According to the directorate general of health Services, the reported annual number of visceral leishmaniasis deaths varied from 6 to 36 during 1999–2009, this appears to be highly underestimated because a community-based study in a small endemic area reported a high visceral leishmaniasis mortality rate (about 10.0%) in 2003 (Mohfw el.at, 2011). The possible reason for the high under estimation of visceral leishmaniasis deaths might be a shortfall in the passive reporting system which does not include tertiary hospitals under visceral leishmaniasis case surveillance. Visceral leishmaniasis patients who are poor and living in remote communities far from healthcare facilities often die at home without seeking treatment or preferred traditional healers for their healthcare and do not report to the public health facilities. Under estimation of deaths contributes to visceral leishmaniasis remaining a major neglected tropical disease. Thus, there is a need to investigate the magnitude of visceral leishmaniasis deaths and its risk factors through a well- designed study and by using adequate tools for investigation of death.

2.2 Prevalence of Visceral leishmaniasis in Kenya.

Traditionally, visceral leishmaniasis was considered more prevalent in arid counties of eastern and northern regions, while cutaneous leishmaniasis was more prevalent in the semi-arid counties of western and central areas of Kenya; however, the current outbreak had

extended to the western and southern counties as well. The ever-expanding and migrating human population for survival or trade, mainly the pastoral community and refugees, the interaction of humans with the animal population, environmental changes, and social unrest may be some of the factors playing a role in the shift of the disease foci to the earlier non-endemic areas. There are several challenges in the control of visceral leishmaniasis in Kenya which have led to a persistent increase in the number of cases as well as the geographical shift of the disease. The interventional strategies of diagnosis, management and control of the disease have not proven effective; however, they have remained unchanged even in the face of the changing epidemiology of visceral leishmaniasis (Dagne el.at, 2021).

There are several other gaps in understanding the disease, such as the pastoral epidemiology, the effect of natural calamities, animal reservoirs and zoonotic transmission, and refugee movement, which need to be filled to implement adequate control and prevention measures for visceral leishmaniasis in Kenya. In addition to the already existing challenges, the COVID-19 pandemic had highly impacted countries like Kenya concerning healthcare resources and had left the neglected diseases more neglected.

During the pandemic, there had been severe disruption in activities such as mass drug administration, case detection, treatment, and vector control (Dagne el.at, 2021)

The access of patients to the health care systems had been severely compromised amidst the COVID-19 pandemic regarding timely attention and availability of beds to those who needed them, leading to the community spread of the disease. Despite the many measures taken by the WHO and the government in the prevention of visceral leishmaniasis by

formulating evidence- based policies, facilitating public and private collaborations to aid the management of the disease, provision of medical supplies from the WHO's global emergency stockpile, and other measures, visceral leishmaniasis remains a problem of public health in Kenya (Alvar et.al, 2022).

2.3 Development of the model.

There have been few investigations of elements of V.L. utilizing numerical models. In 1988, Christopher Dye and Daniel M. Wolpert acquainted with the first anthroponotic V.L. deterministic model for capturing temporal dynamics (Dye, 1996). Their model was utilized to clarify the V.L. between the scourge periods from 1875 to 1950 in Assam, India. They surveyed the effect of control measures in endemic regions utilizing properly modified models. They presumed that the noticed sensational rise in V.L. cases might be ascribed to "characteristic" (host and vector elements birth and demise rates) factors. In 1996 Dye Presented a four-condition Susceptible-latent-infectious-resistant (S.L.I.R) model to portray the visceral leishmaniasis pandemic. S.L.I.R, separately, addresses the susceptible, latent, infectious, and resistant populations of visceral leishmaniasis. Also, the model thought about the changes among these populaces. Nonetheless, Dye didn't know about the practices of canine and vector in the model. (Courtenay et al., 2002) further developed Dye's model using the canine populace integrated into the S.L.I.R model. (Ribas et al., 2013) constructed an O.D.E model for visceral leishmaniasis transmissions among people, canines and vectors. Their model used (11) O.D.E conditions, which included susceptible (canine, sand, fly and human), Latent (canine, vector and human populace), infected (canine, vector and human populace) and resistant (canine and human) populace. Even though the model they used was introduced with no

information reenactment, it was the principal model to depict practices for all species engaged with visceral leishmaniasis. Since WHO assignment of Visceral leishmaniasis as a Neglected Tropical Disease (N.T.D) in 2015, a plenitude of studies has zeroed in on creating numerical models of Visceral leishmaniasis (Zhao et al., 2016) fostered a (12) condition O.D.E showing an instinctive Leishmaniasis scourge. They improved the model by incorporating a hospitalized populace into the O.D.E framework; this populace had a greater chance of endurance because of efficient medication.

Their research showed that the equilibrium of visceral leishmaniasis is strongly related to a critical model parameter(R_c), as the pandemic threshold value for (R_0). (R_0) Is the expected number of cases generated by a single case in a populace where all individuals are vulnerable to infection while (R_C) is the number of secondary cases per infectious case in a populace made up of both susceptible and non-susceptible hosts with control to treatment.

Similarly, (Subramanian et al., 2015) came up with a compartment-based O.D.E of Visceral leishmaniasis to clarify transmission of disease in symptomatic visceral leishmaniasis, asymptomatic visceral leishmaniasis and Post Visceral leishmaniasis dermal leishmaniasis disease classes. (Bi et al., 2018) worked on 12-condition O.D.E from (Zhao et al., 2016) to an 8-condition O.D.E by partitioning canine and vector into susceptible and infected populace. Using a worked O.D.E model, scientists decreased the framework sensitivity analysis and decreased the parameters assumed. This model likewise effectively recreated the 2011 visceral leishmaniasis pandemic in Southern Sudan. (Abubakar et al., 2014), Moved the O.D.E in (Ribas et al., 2013) by considering a canine populace as a primary reservoir for Visceral leishmaniasis. Subsequently, their

numerical model included eight variables comparing the susceptible, latent, infectious and recovery populace of canines and humans. (Le Rutte et al., 2018) analyzed three O.D.E and compared results and taught about indoor spraying. The contrast between the models was the means by which connections between P.K.D.L and the recuperation populace were displayed. Their examination anticipated that, utilizing 60%–80% indoor residual spraying (I.R.S) inclusion, visceral leishmaniasis could be eradicated in three years in Bihar, India. Likewise, different scientists have made gradual commitments utilizing different O.D.E Visceral leishmaniasis pandemic models. (Bi et al., 2018), presented a two-dimensional P.D.E dependent on an O.D.E model. Their work considered human age and time as two measurements since authentic information have emphatically proposed that instinctive Leishmaniasis infection rates was exceptionally connected to human age since kids and teens (matured from 0 to 20) are bound to become infected contrasted with other ages. Their work utilized simulation and numerical investigation to clarify their work in accordance with recorded Visceral leishmaniasis endemic information distributed by W.H.O models based on real-world data (Chappuis et al., 2007). Visceral leishmaniasis data was used generally in three ways; utilization of detailed information to construct measurable models, utilization of authentic information to anticipate future pervasiveness and utilization of existing information to adjust model boundaries in numerical endemic models.

(Da Rocha et al., 2018) used census data to investigate the prevalence of visceral leishmaniasis in various regions of Brazil. They tracked down a positive relationship between visceral leishmaniasis rates and homes surrounding the forest cover. (Bi et al., 2018) expanded past work by investigating and contrasting outcomes from 21 factual

models as per human and canine visceral leishmaniasis information in Brazil, they discovered relationships between home in regions with green vegetation and infected canines and between the human disease rate and urbanization. (Thompson et al., 2002) researched on the relationship between visceral leishmaniasis infection and climatic changes based on rainfall patterns. Their research concluded that rainfall patterns are essential factors statistically correlated to visceral leishmaniasis spread in the region. The area of residence of an individual was considered as a risk factor for the spread of visceral leishmaniasis, the areas researched included; residence near ant hills, termite mounds, urban cities, rural areas and plains. The ant hills and termite mounds residence populace statistically showed an increased risk from visceral leishmaniasis infection compared to other populace considered in the study. De araujo's considered a measurable model with information and tracked down that spatial information is more precise for visceral leishmaniasis pandemic review and analysis hence, they applied a statistical model to evaluate risks from visceral leishmaniasis using obtained data from Belo Horizonte and Brazil (de Araújo et al., 2013). Their research identified that risk factor for Visceral leishmaniasis was correlated to the income of the individual, the education level of the individual and the proportions of infected canine to a resident of the area; however, as opposed to their past study discoveries, home in regions with green vegetation did not indicate critical relationships to hazard from Visceral leishmaniasis. Several other methods were used to anticipate the trend of visceral leishmaniasis pandemics with different variables. (Elnaiem, 2011) summed up information from eastern Sudan in Ggeographical Information System and utilized that information to construct present models of Visceral leishmaniasis diseases dependent on rainfall intensity.

(Mubayi et al., 2010) used 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 5 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 an early stage of the disease in order to decrease mortality.

(Coura-Vital et al., 2013) used the Cox regression model, and they identified that the presence of dry leaves around the homestead, manure in the backyard, sleeping predominantly outside at night increased the risk of visceral leishmaniasis. However, spraying insecticides in the house significantly reduced the risk from visceral leishmaniasis. (Margonari et al., 2020) 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 northwestern Ethiopia (Yared et al., 2014a) 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 from Visceral leishmaniasis. (Mengesha et al., 2014) conducted malnutrition research as a risk factor for visceral leishmaniasis; they found that malnutrition is strongly linked to visceral

leishmaniasis cases in northwest Ethiopia. (Ngere et al., 2020) 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 et al., 2011) 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 V.L. cases reported in that region.

According to a research conducted in Kacheliba Sub county Kenya visceral leishmaniasis is endemic and remains to be the second most prevalent parasitic disease after malaria, their findings agree with previous reports that ranked Visceral leishmaniasis as second most lethal parasitic disease (Y.Song et,al., 2020). They discovered that there is a multiplex relationship between Visceral leishmaniasis cases and climate change, an increase in global temperatures and a decrease in rainfall amount tend to significantly influence Visceral leishmaniasis cases and these relationships agree with reports in earlier studies (Gebresilassie et al., 2015).

The observed surges in Visceral leishmaniasis cases towards the end of dry season as well as just after the rains, while remaining relatively low during cold weather season depict the level of interaction between climate change-induced seasonal weather variability and their impact on visceral leishmaniasis incidents among other vector-borne diseases (Bhunia et al, 2010). Seasonal weather variability influence on vector habits was further demonstrated by the increase in Visceral leishmaniasis cases during low precipitation period, this may be attributed to elevated vector population as well as vector expansion to uncommon areas towards the end of dry seasons. Summer season is usually

characterized by varying humidity as well as wide range of temperature variations; these observations support previous reports by (H.Elomari et al., 2020) which indicated a positive correlation between vector abundance and increased temperature variability. Overall, climate change induced prolonged drought results in depletion of available surface water and rangeland pasture coverage, hence, triggers mass movement of humans and animals into high vector density areas (Koirala,et.al.,2004). The significantly associated environmental factors like existence of seasonal rain water channels, presence of acacia tree, and anthills in and around human houses with high visceral leishmaniasis infection rates may indicate the complexity of interaction between ecological and lifestyle factors predisposing the communities to disease. Big woody plants on the lowland areas particularly along seasonal riverbanks and swamps remain green and provide shades from scotching sun to both herders and their livestock during hot weather dry season. Likewise, these plants as well as riverbank form humid vector preferred hiding and breeding zones, hence providing potentially risky areas of infection (Czheng,et.al 2019). During flooding periods, these seasonal rain water pathways tend to move the sand fly larvae from the endemic zones to new different places, hence, increasing risk of transmission as well as vector expansion to new areas (Rajesh, et al.,,2019). The moderately humid atmosphere and plenty of hiding areas inside the anthill holes are believed to form perfect resting and breeding environment for the sand fly; thus, its presences around the human houses increase the risk of infections (Alebie, et.al, 2019). The flowers and secretions of the acacia tree provide both feed and water to the sand fly, while its bark provides perfect resting and breeding place hence, presence of acacia in and around the compound poses risk of

attracting the vector and exposing those living nearby to visceral leishmaniasis (Argaw et al., 2013).

Presence of animal sheds and chicken shelter as well as movement of houses from time to time to new temporary compounds and locations was associated with risk of visceral leishmaniasis infection, and this poses complication in disease control as these practices are both economic and cultural in nature. Many times, constructed animals and chicken shelters tend to be wet during rainy seasons which create humid environment that are believed to attract the vector while the structure provides resting place (Younis et al.,2020). Traditional nomadic culture of frequently moving houses and people to new geographical area which is commonly practiced by the pastoral community living in the vector endemic arid and semi-arid areas was associated with increased risk of infection. The risk was believed to be arising from the high vegetation density in the newly settled temporary compound which may be already infested with the vector or attract it as a result of human activities such as newly cultivated agricultural fields (Macharia et al.,2018). The impact of environmental factors and climate change induced seasonal weather pattern variability emerges as an important factors that influence vector distribution and habitats as well as number of Visceral leishmaniasis cases in kacheliba sub county (bulle et al., 2022). Considering the fast setting-in of climate change effect which triggers frequent alterations on seasonal weather pattern, both the global prevalence and emergence of vector-borne diseases in uncommon areas are expected to rise (Tidman et al., 2021), regardless of phlebotomine species involved and reservoir behaviors, weather fluctuations and environmental modifications are considered strong factors that may influence the occurrence of Visceral leishmaniasis (Short.et.al, 2017).

Similarly, global warming and climate change-induced alteration in temperature and precipitations variability remain to be significant factors affecting vector epidemiology in terms of abundances and activeness (Yal.et al.,, 2019). In African where more than seventy percent of the population lives in rural areas, it is expected that the continent will experience more of the effect of climate change and global warming as a result of the emerging new settlements and wide spread alteration of environment through deforestation which may promote creation of more vector breeding sites (Githeko et.al, 2000). Increase in temperature is believed to favor sand fly multiplication while also increasing its period of activity (Omari et al., 2020). Environmental factors surrounding homesteads including presences of certain plant species, seasonal rain water pathways-created land fissure and crevices and presence of animal sheds are thought to influence the presence as well as activity of the vector (Kristein et al., 2014).

With the devastating effect of global warming and climate change coupled with prevalent low individual immune system and social weakness in the visceral leishmaniasis endemic zones, cases of visceral leishmaniasis are expected to get aggravated, thus, the need to undertake epidemiological studies particularly in endemic areas (Carvalho et al.,2020).

Environmental factors such as mining, dam building, and large irrigation schemes with road construction in developing countries may all lead to an increase in the number of sand fly and hence visceral leishmaniasis. It worth mentioning that in 1996 in Kabul, the capital of Afghanistan, the resurgence of visceral leishmaniasis had occurred because of deficiencies in the control of the vector (sand-fly) and lack of access to medical treatment due to the cost and increasing drug resistance to first-line treatment. HIV/AID increases susceptibility to infections with visceral leishmaniasis approximately by 100–1000, one

challenge for African countries was how to deal with an increased in the number of individuals who suffer from visceral leishmaniasis and HIV infection (Coleman el.at, 2016).

Inequalities between the indigenous population and the mushrooming of the small centers or towns have led to the growth of bigger towns and or settlements leading to a close social interaction between Man, environment and the biological vectors in Marsabit County this, in turn, leads to poor social-economic factors to the inhabiting population predisposing them to poverty, poor housing conditions, poor sewerage and sanitary condition leading to ideal breeding and resting sites for visceral leishmaniasis and associated vectors with ease in access of the susceptible population due to the associated overcrowding conditions in such settings (Desjeux et al., 2001), (Hasket et al., 2012). High Illiteracy has been associated with poor knowledge, attitude and, practices on the risk factors, control, and prevention strategies (Debroy, 2017). According to a prospective study done on the visceral leishmaniasis risk factors in India and Nepal, the results showed risk of visceral leishmaniasis were strongly associated with the low economicand social-economic status noting that for those living in households with low socio economic status the risk was higher.

According to another study done in Bangladesh on the association of overcrowding, close stay, and association with previously infected visceral leishmaniasis patients it was found out that overcrowding (<50 meters household overcrowding) had a higher risk intensity and pre-infection. There was a 26 times likelihood of developing an infection in the household with a previous case of visceral leishmaniasis (Bern C et al., 2010). Leishmaniasis is climate-sensitive to rainfall, temperature and humidity change

(Rodriguz et al, 2006) the changes in temperature, rainfall and humidity can have strong effects on vectors and reservoir hosts by altering their distribution and influencing their survival and population sizes; Slight fluctuations in temperature can have a significant effect on the Developmental cycle of Leishmania promastigotes in sand flies in areas with low transmission for the disease; Drought, famine and flood resulting from the global warming and land degradation causes population displacement and migration of the affected population to areas with high transmission of visceral leishmaniasis, and poor nutrition couldin turn compromise immunity (Asfaram et al, 2017).

According to the study on the geographical continuous area in Bihari, India in identifying the risk factors associated with incidence on the various climatic and geographical variations various were different locations was a protective factor (Hasker et al, 2012). In a research study on "Modeling the ecological niche " aim at assessing the environmental factors interdependence with visceral leishmaniasis spread in Bangladesh, the study found out that high visceral leishmaniasis manifestations in warmer and low to moderate precipitations were agreeing with the disease distribution probability (Abdullah et al., 2017).

Globally Malnutrition and the presence of the underlying opportunistic disease have been associated with disease severity (Desjeux et al, 2014). According to the visceral leishmaniasis risk factors studies to assess on Hypernatremia and other risk factors for death in human visceral leishmaniasis: new insights from a cross-sectional study in Brazil showedthat most of the Non-survivor's had significant lower levels of albumin associated with protein-energy malnutrition among other protein malnutrition

conditions, , energy malnutrition , lower levels of iron does iron deficiencies , vitamin A, hypernatremia among other electrolyte imbalances reported (Daher et al., 2017). Parasite proliferation was abundant in the spleen and the liver leading to hepatosplenomegaly in 75-90% of deaths, bone marrow infections pancytopenia and generalized reduction in blood cell count resulted to super infection and immunosuppression (Ready et al., 2014). According to a prospective study done in Northeast Brazil it was found out that a possible malnutrition was a possible risk factor to severe visceral leishmaniasis with coupled close association with debilitating disease (Cerf et al., 1987).

Seasonal migration and grazing patterns have been associated with an imbalance in an individual immunity (Sharma et al., 2008) leading to the introduction of the non-immune persons into an area where there's enzootic or endemic transmission leading to a possible outbreak in such an area. Seasonal grazing and migratory movements may also spread the disease, with the return of migrants to non-endemic areas, as appears to have occurred in the highlands of Ethiopia in the 2000s. Herding activities that are being associated with migration and grazing predisposes the populations mostly the young youthful Men into sleeping outside under acacia trees and living in houses constructed of grassy material, appears to increase has been found to increase the risk for the disease (Gebremichael et al., 2018).

European article review on the assessment of the emergency and the re-emergence of visceral leishmaniasis in Europe it was found out that human and domesticated animal's movement from endemic Continents is responsible for the upsurge of visceral

leishmaniasis casesin Europe (Ready et al., 2010).

This study aimed to contribute to the body of knowledge on visceral leishmaniasis in achieving the World Health Organization's neglected tropical diseases road map target 2021 to 2030 and sustainable development goal number 3.3 which target to end neglected topical disease epidemics by 2030, as well as Kenya's ministry of health 2021-2025 strategic plan for control of visceral leishmaniasis and vision 2030. The present study endeavors to ascertain climate change and environmental influence on visceral leishmaniasis in Marsabit County in order to provide essential information to help in up scaling strategies to reduce visceral leishmaniasis burden.

2.4 Mortality from Visceral leishmaniasis

Visceral leishmaniasis is a fatal vector-borne disease if not treated. The World Health Organization classifies it as a neglected tropical disease. Since 2016, the global incidence of visceral leishmaniasis has decreased by more than 30%. The W.H.O.'s (2021-30) N.T.D road map has set an ambitious target for global disease eradication. Milestones included less than 1% mortality due to primary Visceral leishmaniasis in 56 countries by 2025 and 64 countries by 2030 (representing 85% of all endemic countries) (Sunyoto, 2017). East Africa is the world's most affected region, accounting for 45 percent of all visceral leishmaniasis cases reported to W.H.O. in 2018. Visceral leishmaniasis is still a poorly understood and under reported disease that has devastating consequences for some of the most vulnerable populations (jervis, 2017).

Only seven countries account for roughly 90% of the global burden of V.L. four of which are in Eastern Africa (Sudan, South Sudan, Ethiopia, and Kenya), two in Southeast Asia

(India and Bangladesh), and Brazil, which accounts for nearly all cases in South America. Research conducted in Baringo and Pokot areas showed that there was high endemicity of V.L. since 1980 which affects the impoverished tribal nomadic population. In other areas, V.L. outbreaks were associated with periods of drought (Burns, 1980).

According to a study conducted in Marsabit County, although visceral leishmaniasis is curable, it has significant mortality in humans due to a lack of earlier identification by healthcare providers, late medication and poor case management. V.L. has a high death rate in Marsabit County if left untreated (Kanyina, 2020c).

The hazard of death among relapse visceral leishmaniasis patients was 3 times higher than that of primary visceral leishmaniasis patients; this implies that a significant proportion of patients with relapse visceral leishmaniasis are dying compared to patients with primary visceral leishmaniasis (Assumpcao el.at, 2011).

Visceral leishmaniasis patients who had toxicity during treatment were at increased risk of mortality than those patients who had no toxicity, this finding was in line with a study in Uganda–and national guideline since most anti-leishmanial drugs are toxic, the development of drug toxicity such as arrhythmia, pancreatitis, and others are common, leading to poor compliance and further deterioration of the patient to cause death (Mueller el.at, 2009).

The hazard of death among visceral leishmaniasis patients with comorbidity was higher than those without comorbidity, this finding was based on studies in Eastern Uganda, Brazil, India, and Ethiopia Probably ascribed to the double burden associated with the comorbidity. Moreover, patients with concomitant disease/comorbidity had to take more

drugs so they might have more risk of toxicity and drug–drug interaction, which causes a severe form of the disease and end up with the death of the patient (Das el.at, 2016).

The hazard of death among visceral leishmaniasis patients who had nasal bleeding was higher than those patients who did not had nasal bleeding, this finding based on results of studies conducted in Northern Ethiopia (Tigray), America and Sudan. Nasal bleeding among visceral leishmaniasis patients occurs probably due to a combination of deficient clotting factors (Lyon el.at, 2003). According to a study conducted by Gedaref state of Sudan, America and Brazil the patients who had jaundice at admission were at increased risk of death than their counterparts, this could be possibly due to the presence of liver dysfunction among visceral leishmaniasis patients with jaundice (jaundice is usually the sign of liver dysfunction); therefore, visceral leishmaniasis patients with jaundice might have decreased plasma protein synthesis, inability to detoxify drugs and impairment of other liver functions compared to visceral leishmaniasis patients without jaundice (Karthick el.at, 2016).

Those bed ridden visceral leishmaniasis patients had an increased risk of death compared to ambulatory visceral leishmaniasis patients, this findings was based on a study in Kahsay Abera Hospital-This might be linked to the majority of bedridden patients (64%), in the study, had concomitant diseases such as HIV/AIDS, tuberculosis and pneumonia, which ultimately increased the risk of death compared to ambulatory patients. A similar studies conducted in Brazil, stated that most severely ill patients had an increased risk of concomitant diseases that increased their risk of death. Furthermore, severely ill patients usually do not respond to their medication easily and do not take adequate food as well. (werneck el.at, 2003).

Secondary bacterial infections are known to be an important cause of death among visceral leishmaniasis infected individuals (Queiroz el.at, 2010). Many studies showed that the presence of co-infections was a strong predictor of adverse evolution of visceral leishmaniasis.

2.5 Endemicity of visceral leishmaniasis.

Visceral leishmaniasis is endemic in 78 countries, but it primarily affects the poor in East Africa, Southeast Asia and Brazil. Southeast Asia has historically had the highest burden of Visceral leishmaniasis, with an estimated 270,900 cases in 2007 and 350,279 in 2019 (Alvar et al., 2021).

Leishmaniasis has been known to be endemic in parts of Kenya from as far back as early in the 20th century. These areas include Turkana, Baringo, Kitui, Machakos, Meru, West Pokot and Elgeyo Marakwet districts which have been reported to be endemic for V.L. Recent outbreaks of V.L. have been reported in the previously non-endemic districts of Wajir and Mandera in North Eastern Kenya between May 2000 and August 2001 (Tinui, 2008).

V.L. is endemic in the arid and semi-arid regions of Kenya including the Rift Valley and provinces in the east and north east of Kenya caused by *L. donovani*. Confirmed visceral leishmaniasis endemic regions are focused in the arid lowlands and include Baringo, Turkana, Marakwet, Samburu, Pokot, Laikipia and Kajiado, Machakos, Mwingi, Meru, Wajir, and Keiyo. There is inadequate information on the prevalence, burden and spatial distribution of the disease. In the Eastern Region, foci have been documented in Isiolo,

Kitui, Machakos, Makueni, Marsabit, and Tharaka Nithi counties. In Rift Valley, the disease is more common and has been documented in Baringo, Pokot, Turkana, Samburu, Kajiado and Laikipia Counties (Jones & Welburn, 2021).

The disease foci may change to areas previously not known to be endemic as a result of climate change and population movements. There have been several outbreaks of the disease in Kenya; the most recent was confirmed in Isiolo, Marsabit and Wajir counties (Kanyina, 2020a).

The study overall goal was to estimate the transmission and mortality rate associated with Visceral leishmaniasis in Marsabit county referral hospital. This thesis focuses on addressing a gap that other researchers had not addressed by providing an analysis of transmission and mortality rate due to Visceral leishmaniasis at Marsabit county referral hospital with specific consideration to the risk factors using the Cox proportional hazard model and S.I.R model; other research conducted in Marsabit county did not consider a quantitative approach to this disease.

CHAPTER THREE: METHODOLOGY

3.0 Introduction.

This section describes the study's design, Source of data, ssurvival analysis models used, S.I.R model used, Calculation of control reproductive number and ethical clearance.

3.1 Study Design, Area, and Population

A retrospective research design was adopted. The study used secondary data from 2890 visceral leishmaniasis patients enrolled at Marsabit County referral hospital from September 2015 to September 2019.

3.2 Source of data

The data was extracted from existing database at Marsabit referral hospital department of disease surveillance.

3.3 Data Analysis Techniques

Data cleaning was done before being analyzed to remove outliers and thus remain with the data’s essential aspect. R-software version 4.0.2 was used for data analysis. A descriptive baseline summary of patients' clinical characteristics was created using iteration R codes, with frequency distributions and summary statistics used where appropriate. A unique identification number was assigned to patients to avoid double counting, which may arise from relapses.

3.4 Inclusion criterion

The data included all residents of Marsabit County who are present during the study period.

3.4.1 Exclusion criterion

The analyzed data does not include nonresidents of Marsabit County and travellers into the five compartment model.

3.5 Ethical Clearance, Data Safety, and Confidentiality

NACOSTI provided the ethical clearances. The study relied on secondary data obtained from Marsabit county referral hospital department of disease surveillance. The result of the study will be provided to relevant authorities and interested parties for the decision-making process.

3.6 Cox-proportional Hazard Regression model for V.L. Risk Factors.

Cox proportional hazards analysis is one of the most widely used regression techniques for predicting survival outcomes. There are several critical assumptions for using the Cox proportional hazards regression model correctly, including

i) Survival times in the sample are independent.

ii) The predictors and the hazard have a multiplicative relationship.

iii) Over time, the hazard ratio remains constant.

Cox regression can be used to investigate the impact of various risk factors for visceral leishmaniasis on survival. These factors are; the forest surrounding, contact with infected dogs, household designs, sleeping outside at night, use of bed nets, and proximity to ant hills and termite mounds (Moncaz, 2012). The probability of the endpoint death is called the hazard.

The hazard is modeled using the approach used by (Ariyanti et al., 2021)

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

(3.0)

Where $h(t)$ denotes the anticipated hazard at time t, the baseline hazard represented by $h_o(t)$ which is the hazard when all of the predictors (independent variables) $X_1, X_2 \ldots . X_p$ are equal to zero, $b_1, b_2 \ldots . b_p$ are regression coefficients. The predicted hazard $h(t)$ is the product of the baseline hazard $h_0(t)$ and the exponential function of the linear combination of the predictors. As a result, the predictors multiply the predicted hazard.

A ratio can be used to illustrate this model.

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

(3.1)

Obtaining natural logarithm (ln) on both side

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

(3.2)

The relationship between the risk factors $(X_1, X_2, \ldots X_p)$ and the outcome are of particular interest. The coefficients of regression $(b_1, b_2 \ldots . b_p)$ quantify the associations. In the Cox proportional hazards regression model, the estimated coefficients, such as b_1, represent the change in the expected log of the hazard ratio relative to a one-unit change in X_1, while holding all other risk factors constant. The antilog of an estimated regression coefficient $\exp(b_1)$ gives the hazard ratio. If a risk factor's hazard ratio is close to one, that risk factor does not affect survival. If the hazard ratio is below one, the risk factors are protective (associated with decreased mortality). If it is more than one, the risk factors are associated with an increased risk of mortality (decreased survival) (khidakhsh, 2019).

3.6.1. Kaplan-Meier Estimator to compare survival functions for each group

Kaplan-Meier (K.M) estimates are non-parametric survival functions commonly used to describe and compare the survival of a study population. One of the best statistical methods for calculating the likelihood of a patient surviving for a given period after treatment is to use K.M. estimators. The Kaplan-Meier employs curves to calculate events, censoring, and survival probability. Kaplan Meier estimate is another name for Product Limit estimate (P.L.E). The product-limit formula calculates the percentage of patients who survive beyond any age at time t; it entails calculating the chances of an event occurring at a given time. These successive probabilities are multiplied by any previously computed probabilities to arrive at the final estimate. Assume that n independent observations with survival times denoted by $t_1, t_2, \ldots . t_n$ and censoring indicator by $\delta_1, \delta_2, \ldots \delta_n$where $\delta_i = 1$, death and where $\delta_i = 0$ for censored observations. Let $(t, \delta_i)\,, i = 1,2 \ldots ., n$ denotes survival data. The Kaplan-Meier estimator can be obtained by ordering the survival times as $t_1 < t_2 \ldots ., t_n$ respectively. Subsequently, assume that among the n observations, there are $m \leq n$ failures that occurred at distinct m time. Thus, the parameters used to estimate the product limit are given as follows;

$d_{(j)}$ = number of mortality at time $t_{(j)}$

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

The Kaplan Meier estimator for survival at time t can be obtained as;

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

(3.3)

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

Kaplan-Meier claims that;

If $t = 0, S(0) = 1$. This means that at time 0 all the subjects were alive. The greenwood formula is used to estimate the variance of the survival function using the Kaplan-Meier estimator:

$\widehat{Var} S_{(t)} = \left[\widehat{S_{(t)}}\right]^2 \sum_{t_{(i)} \leq t} \frac{d_i}{ni(ni-di)}$ (S.sawyer, 2003)

(3.4)

Where d_i represent number of event (death) that happens at time t_i and n_i represent the individuals known to have survived (have not yet had an event or been censored) up to time t_i. The $(1-\alpha)^*100\ \%$ confidence interval for the survival function (skm (t)) at time t is:

$\widehat{S_{km}}(t) \pm Z_{\frac{\alpha}{2}} S.e\left(\widehat{S_{km}}(t)\right)$

(3.5) where S_{km} refer to Kaplan- Meier estimator.

In order to develop a procedure here, considered the total number of observations, number of persons at risk, and serial number, which play the important role in the calculation of probabilities. The n denotes the number of subjects in the sample and n_i denotes the number of persons at risk at time t_i . k is the serial number in reverse order of those times at which censoring occurred; e.g., if the first observation is censored then it has the highest serial number and if the second observation is censored it has the second highest number and so on. Then the weight is defined by

$$w_i=\left(1-\frac{k*I_{ci}}{n*r_i}\right)$$

(3.6)

Where

I_{ci}-is an indicator function

I_{ci}=1 if the observation is censored

I_{ci}=0 otherwise

3.7 Model Framework for Visceral leishmaniasis Transmission using S.I.R model

The V.L. transmission cycle occur through a female phlebotomine sand fly bite. A numerical model was utilized where the host and sand fly are expected to blend homogeneously (Biswas, 2017b). The density of humans denoted is by $N_h(t)$ and N_v(t) the density of sandflies. The elements inside the human populace are modeled using compartments which included, the susceptible individuals$S_h(t)$, asymptomatic $A_h(t)$, infected $I_h(t)$, hospitalized$T_h(t)$, and recovered $R_h(t)$; thus come up with a model used by (Biswas, 2017b).

$$N_h = S_h + A_h + I_h + T_h + R_h$$

(3.6)

The sand fly population is divided into susceptible $S_v(t)$ and infectious $I_v(t)$, with

$N_v = S_v + I_v$.

(3.7)

Diagrammatic representation of the human and vector population interaction

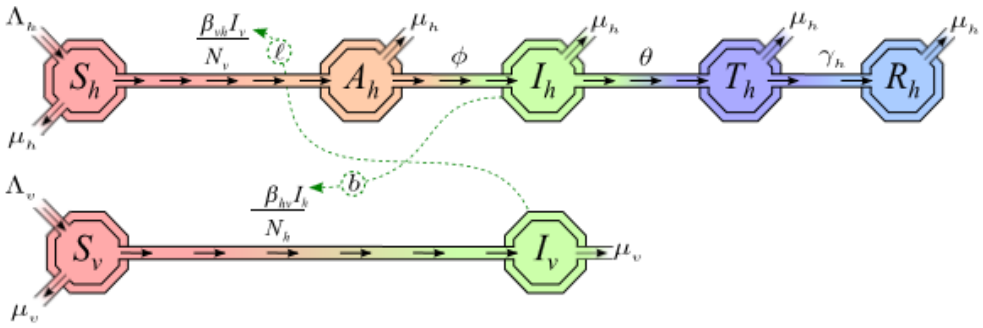

Figure 3.1 Vector and human interaction

Below are the definitions and their respective parameters

Exposure to sand fly b, landing rate of the sand fly ℓ, the rate at which sand fly leaves compartment μ_v , time t for treatment-seeking by patient θ_h, rate at which clinical signs develop ϕ_h, probability of transmission from sand fly to human β_{vh}, probability of transmission from human to sand fly β_{hv}, the rate at which human leave compartment μ_h.

A diagrammatic illustration of interactions between compartments (Biswas, 2017a).

All new case for human follow symptomless stage (A_h). After some weeks, humans develop symptoms at the rate (ϕ_h) ; once an individual develops signs and symptoms he/she is transferred to the third compartment (I_h) which consists of infected individuals. After developing signs and symptoms, some individuals seek treatment at the rate (θ_h), on receiving treatment, an individual recovers at the rate (γ_h). A sand fly enters the compartment at the rate (λ_v) and leaves the compartment through mortality at (μ_v). λ_h Is the rate at which an individual enters into the compartment, μ_h rate at which individual leaves compartment; N_h extend to $\frac{\lambda_h}{\mu_h}$ when t extend to ∞, thus it is assumed that $N_h = \frac{\lambda_h}{\mu_h}$.

The rate of infection of visceral leishmaniasis in humans (force of infection on a human) is obtained using λ_{vh} where

$$\lambda_{vh} = b\beta_{vh}\frac{N_v I_v}{N_h N_v} = b\beta_{vh}\frac{I_v}{N_v} \quad (3.8)$$

This is a product of sand fly bite (b), β_{vh} the transmission probability from vector to human and the ratio of an infected sand fly in sand fly population $\frac{I_v}{N_v}$.

A Susceptible vector is infected by feeding on the blood of an infected human at the rate λ_{hv} (force of infection on the vector). The rate λ_{hv} obtained by

$$\lambda_{hv} = b\beta_{hv}\frac{I_h}{N_h}$$

(3.9)

which is a product of the biting rate of the vector (b); the likelihood of transmission from human to sand fly (β_{hv}); the ratio of infected individuals to the human population ($\frac{I_h}{N_h}$). New individuals enter the compartment while other individuals leave the asymptomatic compartment. The changes to this populace are obtained by;

$$\frac{dA_h}{dt} = \lambda_{vh}S_h - (\phi_h + \mu_h)A_h$$

(3.10)

The asymptomatic individual enters the infectious compartment at the rate (ϕ_h) the change in populace is given by;

$$\frac{dI_h}{dt} = \phi_h A_h - (\mu_h + \theta_h)I_h$$

(3.11)

Considering (θ_h) treatment rate while μ_h rate at which an individual exit compartment and individual enter the treatment compartment (T_h) at the rate (θ_h). After receiving treatment, an individual recovers at the rate (γ_h), this changes, in the population was obtained by:

$$\frac{dT_h}{dt} = \theta_h I_h - (\gamma h + \mu h)T_h \tag{3.12}$$

After receiving the treatment, individuals recover while the population decreased by mortality is obtained by:

$$\frac{dR_h}{dt} = \gamma h T_h - \mu_h R_h \tag{3.13}$$

There are changes in the population of sand flies due to new vectors entering compartments at a rate (λ_v) and others exiting compartments (μ_v). The change in the population for vector is obtained by

$$\frac{dS_v}{dt} = \lambda_v - \lambda_{hv} S_v - \mu_v S_v \tag{3.14}$$

The populace of the infected vector was obtained at the rate (λ_{hv}) and reduction as a result of the death of the vector at the rate(μ_v). This change was obtained by

$$\frac{dI_v}{dt} = \lambda_{hv} S_v -$$

$$\mu_v \quad (3.15)$$

The parameters put together to give the transmission rate as follows;

$$b\beta_{hv}(\frac{S_h}{N_h} + \frac{I_h}{N_h})S_v$$

(3.16)

Where $b\beta_{vh}S_v \frac{I_h}{N_h}$is the proportion of sand fly bites that result into the transmission of Visceral leishmaniasis while $b\beta_{vh}S_v \frac{S_h}{N_h}$ is the proportion that does not result into the transmission and therefore, $\beta_{vh} bS_v$ is defined as the feeding rate per unit of time.

3.8 Modeling the Mortality from Visceral leishmaniasis

To model how V.L. transmitted by sand flies eventually leads to mortality in humans, investigate the consequences of infection-related mortality by incorporating a mortality probability into the S.I.R equations (Song et al., 2020), let m be a disease-related mortality rate for infected people. Let the probability of an individual in the infectious group dying from V.L. be ρ .

From the *S.I.R* equation

$$m = \frac{\rho}{I-\rho}(\gamma_h + \mu_h).\frac{I_h}{N_H} \quad (3.17)$$

Where ρ represents the probability of an individual being in infectious compartments. γ_h represent the recovery rates, and μ_h represent the rate at which an individual exists the compartments due to mortality. I_h the infected human population and N_H represent the entire human population of Marsabit County.

This can be combined to give infection dynamics to be

$$\frac{dI}{dt} = \beta SI - \frac{(\gamma_h + \mu_h)}{1-P}\text{I} \qquad (3.18)$$

Where S represents susceptible vector population, I represent the number of infected individuals in the entire human population of Marsabit County and p probality of an individaul been in infectious compartment.

Marsabit County, the assumptions of the S.I.R model holds when calculating the mortality rate and transmission rate for visceral leishmaniasis. The outcome of this model is necessary to the authorities and other relevant parties in order to understand the transmission dynamics and subsequent mortality so as to reduce disease morbidity in Marsabit County.

3.9 Calculation of Control Reproduction Number ($\mathcal{R}_C$) for V.L.

The control reproduction number (R_C) refers to, in a completely susceptible population, the average number of people infected by an infected sand fly throughout the infectious period when introduced into a susceptible population of size N ≈ S_0 in a compartment where treatment (θ_h) is continuously available. R_C was computed using the next generation operator method, which necessitates the computation of the matrix of new infection F and the matrix of transition between compartments V. Consider the infected sub-population $I_h(t), A_h(t)\ and\ I_v(t)$. Let F denote, the rate of new infections into the infected compartment, and V the rate of human entry into the infected compartment.

$$\frac{d}{dt}\begin{bmatrix} A_h \\ I_h \\ I_v \end{bmatrix} = f - v = \begin{bmatrix} \frac{bm_{v:h}\,\beta_{vh} I_v S_h}{N_v} \\ \frac{b\beta_{hv} I_h S_v}{N_h} \\ \end{bmatrix} - \begin{bmatrix} (\phi_h + \mu_h)A_h \\ -\phi_h A_h + (\theta_h + \mu_h)I_h \\ \mu_v I_v \end{bmatrix}$$

(3.19)

Using the next generation operator method, where F is the vector of rates of new infection inflow in each compartment and V = $V^+ + V^-$ is the vector of individuals transfer rates into and out of the infective compartment by all processes. Taking the Jacobean matrix of each vector with respect to each of the infectious classes and evaluating at E_0= (λ_h/μ_h,0,0,0,0,λ_v/μ_v) gives

$$= \begin{bmatrix} 0 & 0 & bm_{v:h}\beta_{vh} \\ 0 & 0 & 0 \\ 0 & \frac{b\beta_{hv}\lambda_v\mu_h}{\lambda_h\mu_v} & 0 \end{bmatrix} \text{ and}$$

$$\text{V} = \begin{bmatrix} G_1 & 0 & 0 \\ -\phi_h & G_2 & 0 \\ 0 & 0 & \mu_v \end{bmatrix} \qquad (3.20)$$

Computing FV^{-1} obtain

$$FV^{-1} = \begin{bmatrix} 0 & 0 & \frac{bm_{v:h}\beta_{vh}}{\mu_v} \\ 0 & 0 & 0 \\ \frac{b\beta_{hv}\lambda_v\mu_h\phi_h}{\mu_v\lambda_h G_1 G_2} & \frac{b\beta_{hv}\lambda_v\mu_h}{\mu_v\lambda_h G_2} & 0 \end{bmatrix}$$

(3.21)

Using the next generation matrix operator's spectral radius $\rho(FV^{-1})$ gives

$$R_C = \rho(FV^{-1}) = \sqrt{\left(\frac{b\beta_{hv}}{\mu_v}.\frac{b\beta_{hv}\phi_h}{(\phi_h+\mu_h)(\theta_h+\mu_h)}.m_{v:h}\right)} \tag{3.22}$$

Thus the control reproductive number in terms of treatment θ_h was obtained as

$$R_C(\phi_h) = \sqrt{\left(\frac{\phi_h}{(\mu_h+\theta_h)} \times \frac{\beta_{vh}\ell}{(\mu_h+\theta_h}\right) \times \left(\frac{b\beta_{hv}}{\mu_v}\right)} \tag{3.23}$$

where ℓ is sand fly landing rate, b sand fly biting rate, and β_{vh} is the transmission probability from vector to human. The expression in Equation 3.23 is referred to as the control reproduction number because it depends on treatment control of the population of size $N_h \approx S_h$ and $N_v \approx S_v$. The model includes two equilibria: Disease-Free Equilibrium (D.F.E) and Endemic Equilibrium (E.E).

D. F. E of the Model exists if $R_C < 1$ and the E.E exist when $R_c > 1$

For the above equation to fit in estimating the control reproductive number the following assumptions hold; There is an interacting population of hosts and vectors which is assumed to mix homogeneously, the population consists of three types of individuals; Susceptible, Infectious, and Recovered, there is a homogeneous mixing of the infected and susceptible populations, both populations have the same probability of contracting the disease, the host-vector ratio changes over time. The outcome of the control reproductive number is essentials to estimate the prevalence of the disease in Marsabit County. When $R_c > 1$ indicate continuous morbidity and mortality of visceral leishmaniasis in Marsabit County, while when $R_c < 1$ the disease is manageable given appropriate measures to the risk factors responsible for the disease.

CHAPTER FOUR: RESULTS AND DISCUSSIONS

4.0 Introduction

This chapter presents the study's findings and discussions for each objective.

4.1 A descriptive summary of patients' demographic characteristics.

Age of the patients admitted at Marsabit county referral hospital.

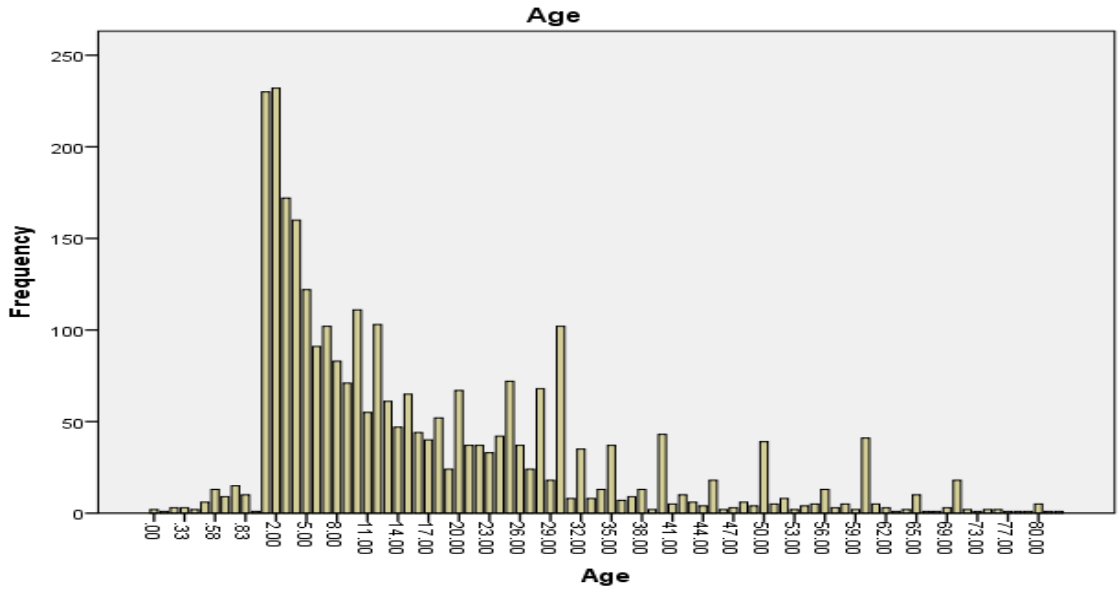

Figure 4.1 Age distributions for visceral leishmaniasis patients

The eldest patient was 80 years, while the youngest had 6 months. The mean for age is 16.80 years and the median age was 29.50 years with a standard deviation of 16.07.

Patients' admission in terms of gender

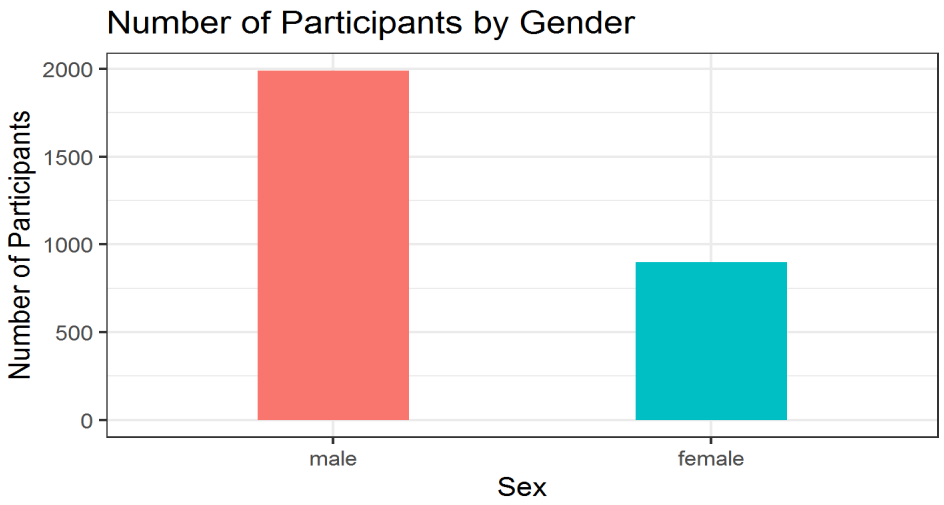

Figure 4.2 Number of participants by gender.

From the study, more males were infected as compared to females.

A number of patients survived /died.

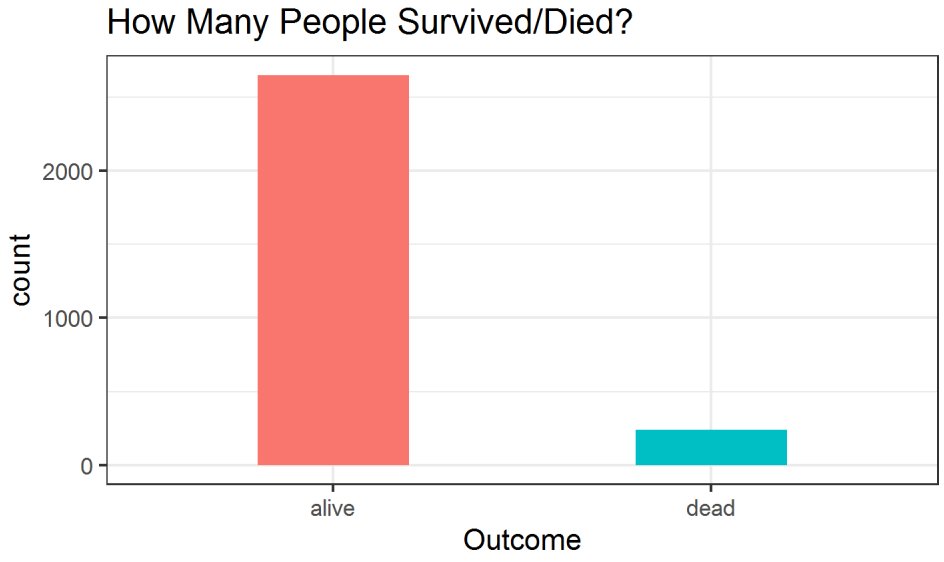

Figure 4.3 Outcomes by survival and death.

2,530 people survived, while 239 people died.

Types of drugs administered to the patients at Marsabit referral hospital.

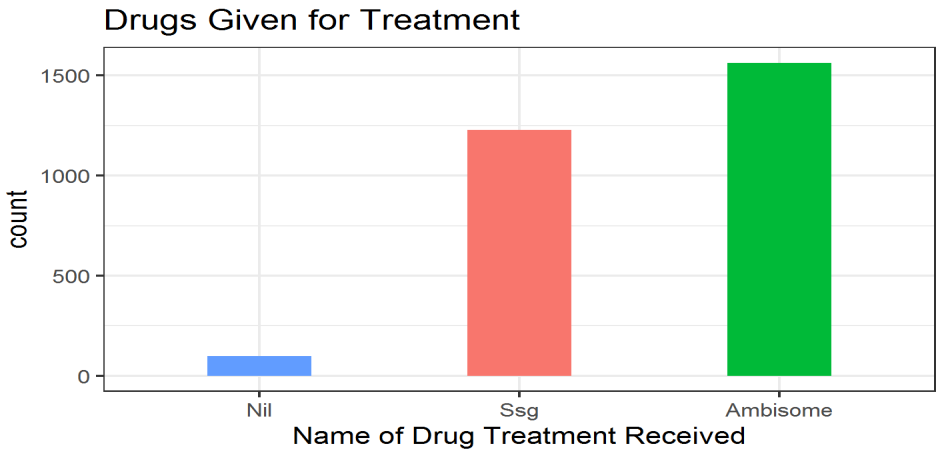

Figure 4.4 Treatments administered to patients

Most patients were subjected to treatment Ambisome (1,542), while Sodium stibogluconate was 1,227.

4.2 Evaluate the risk factors associated with mortality among visceral leishmaniasis patients admitted at Marsabit referral hospital.

This section demonstrates how to investigate the final multivariate Cox proportional hazard model that met model development and evaluation criteria. In the study, the Cox model had household design (cracked mud walls), drugs given for treatment, residence near ant hills, use of bed nets, contact with infected dogs, the forest surrounding, and sleeping outside at night as its explanatory or predictor variables and time to the death as the dependent variable also known as survival time. The hazard values were multiplied

for each category within the variable, and the natural logarithm of the product was used to calculate the parameter.

Table 4.1 Variables and parameter estimate.

Covariate of interest	**Symbol**	**Parameter ($\boldsymbol{\beta}$)**	**p-values**	**Hazard**
Drugs given	X_1	-0.3846	0.0001	0.6807
Household design(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

From the table, the following equations were derived

$$ln\{\lambda_t\} = -0.3846X_1 + 0.4350X_2 + 0.3203X_3 - 0.1513X_4 + 0.2004X_5 + 0.1507X_6 + 0.1696X_7 \quad (4.1)$$

In the 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 indicating that these predictor variables are associated with a poor prognosis or a lower survival rate among Visceral leishmaniasis patients at Marsabit referral hospital while drug administered (X_1) and use of bed nets (X_4) had a negative parameter coefficient indicates that it had a protective effect or was associated with improved survival or lower risk of death in patients with Visceral leishmaniasis.

4.2.1 Survival probability for household design (cracked walls and thatched roof)

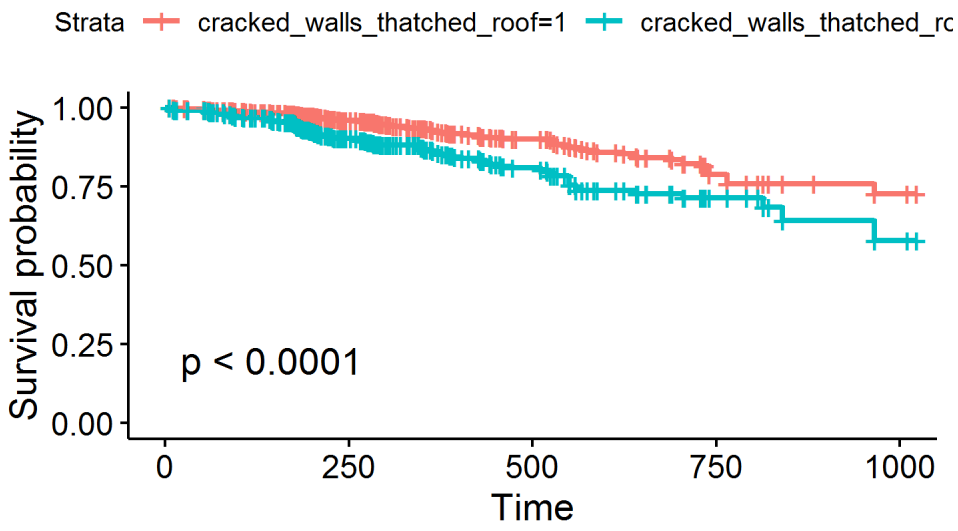

Figure 4.5 Kaplan Meier curve to show survival probabilities of patients in households with cracked walls and thatched roof

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 two groups'

survival probabilities differ significantly. Those living in cracked walls and thatched roof houses have lower survival probabilities.

4.2.2 Survival probability for a residence near ant hills

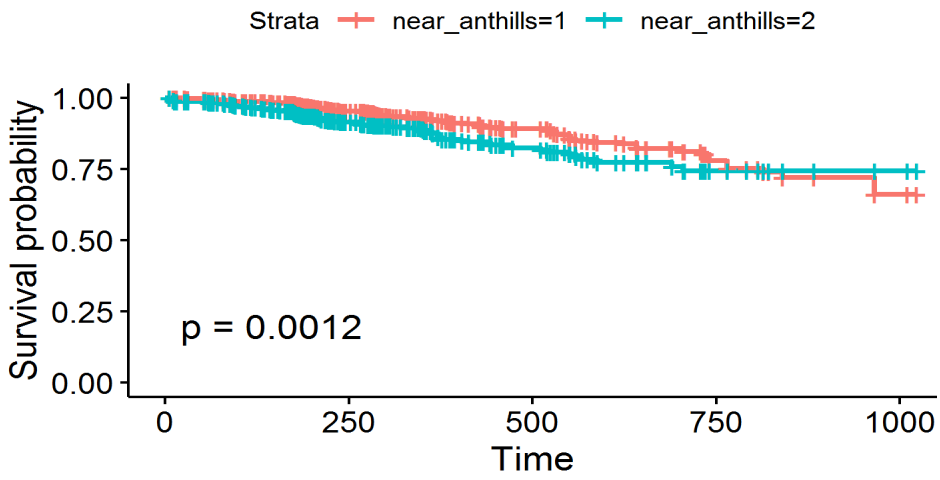

Figure 4.6 Kaplan Meier curve to show survival probabilities of patients' residence near ant hills.

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 two groups' survival probabilities differ significantly. Those living near ant hills have lower survival probabilities.

4.2.3 Survival probability for bed net use

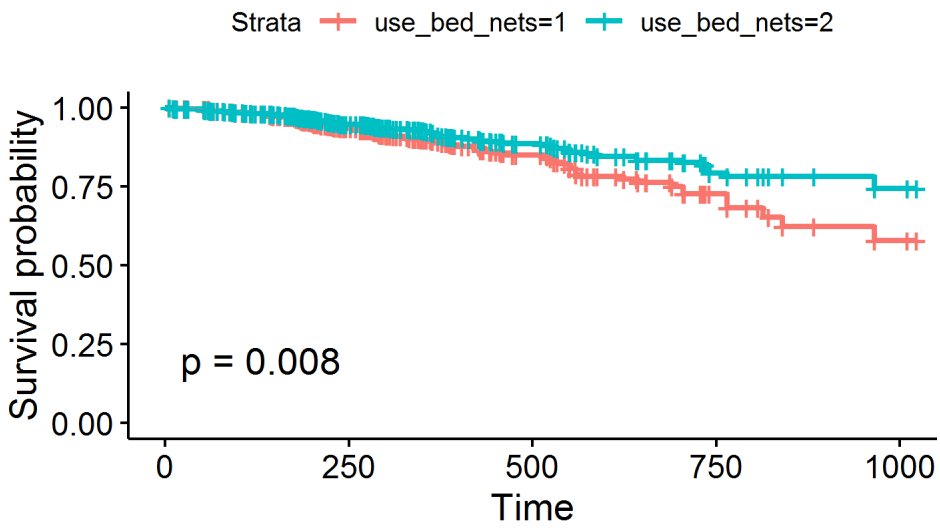

Figure 4.7 Kaplan Meier curve to show survival probabilities of patients using bed nets

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 have lower survival probabilities.

4.2.4 Survival probability for interaction with dogs.

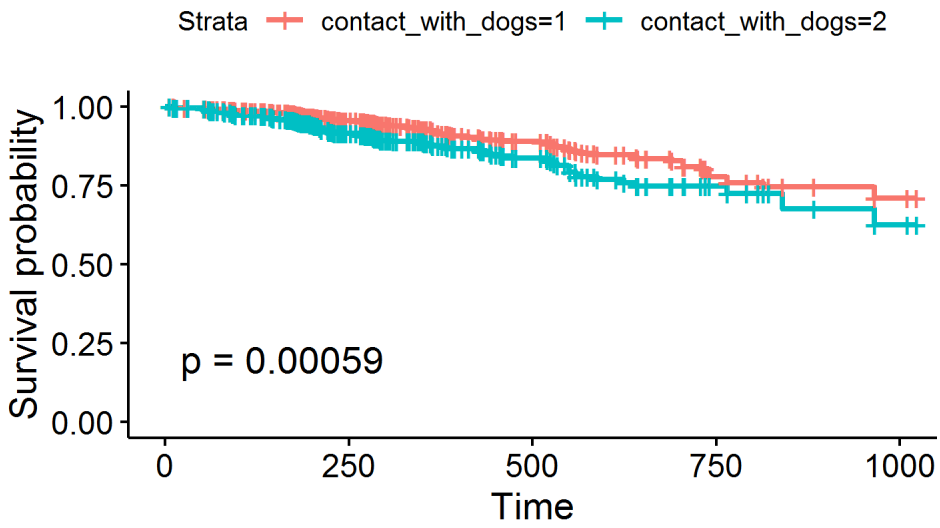

Figure 4.8 Kaplan Meier curve to show survival probabilities of patients' contact with dogs

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 interacting with infected dogs have lower survival probabilities.

4.2.5 Survival probability for forest cover surrounding the homestead.

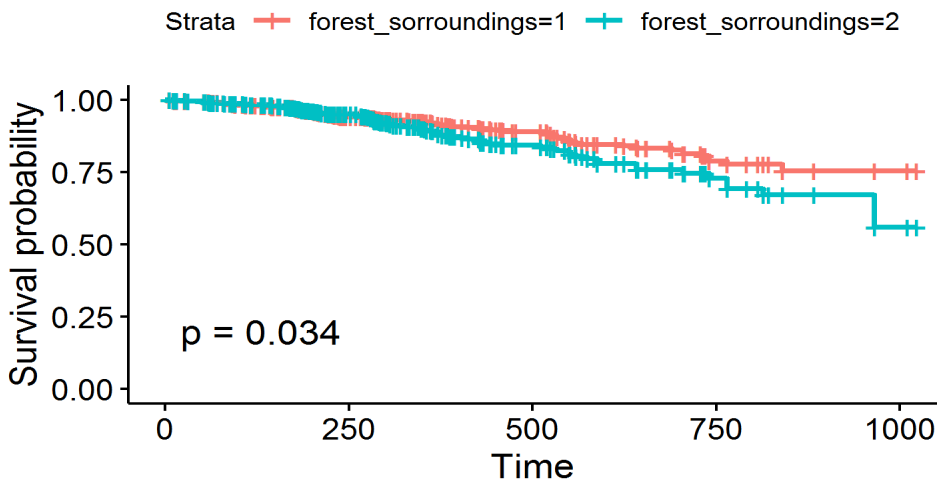

Figure 4.9 Kaplan Meier curve to show survival probabilities of patients around the forest.

Those living near forest were coded 1 while those not were coded 2. The log-rank p-value is significant at (0.0340). Those who live near the forests have lower survival probabilities.

4.2.6 Survival probability for sleeping outside at night.

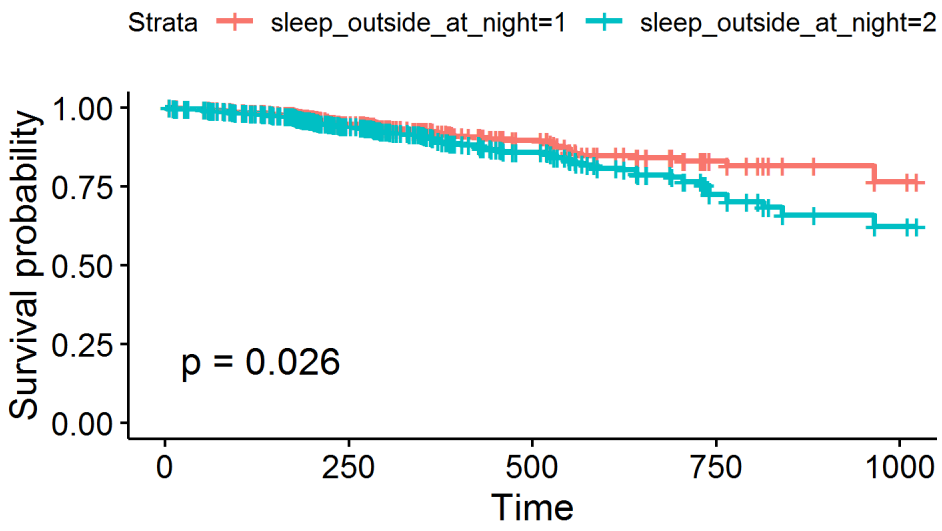

Figure 4.10 Kaplan Meier curve shows survival probabilities of patients sleeping outside at night.

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 at night lower survival probabilities.

Table 4.2 Household design risk analysis

HOUSEHOLD DESIGN (cracked mud walls, thatched grass house)

Outcome	Exposed	Non-Exposed	Total
Negative	1998	653	2651
Positive	139	100	239
Total	2137	753	2890
	Risk Exposed	Risk Non Exposed	Rt
	Estimate	Lower95% CI	Upper
Risk	2.04	1.60	95%CI
Risk difference (Re − Rne)	0	0.44	2.60
			−0.56
Risk ratio	1.28		
Midp. exact	$2.96255e^{-08}$		
Fisher. exact	$3.25763e^{-08}$		
Chi-square	$6.436038e^{-09}$		

The level of exposure to surrounding nature and the residence's construction (using local and affordable building materials and, most importantly, how those materials are refined and finished), number of floors, number of rooms, dirt floor, damp earthen floors, and houses with cracked mud or thatched plastered house walls are closely related to human health. Housing condition provides an environment for the transmission of Visceral leishmaniasis, and hence cracked mud wall was correlated with the spread of Visceral

leishmaniasis. However, 2137(73.94 %) were exposed to this risk, while 753 (26.06 %) were non-exposed. Those exposed to the risk and survived were 1998 (93.50%) while 139 (6.50%) died. The risk in the exposed and non-exposed groups is (2.04) and (1.6), respectively. The log-rank p-value was significant at (0.0001) and the survival probabilities for those not living in cracked mud walls increased over time. The risk of contracting the disease was higher for those living in cracked walls/thatched houses. This is consistent with similar research carried out in Loima and Turkana west it discovered a link between housing and Leishmaniasis infection (Abarca, 2021).

Table 4.3 Residence near ant hills risk analysis

Residence area near ant hills

Outcome	Exposed	Non-Exposed	Total
Negative	1995	656	2651
Positive	157	82	239
Total	2152	738	2890
	Risk Exposed	Risk Non-exposed	Rt
	Estimate	Lower95%CI	Upper95%CI
Risk	1.52	1.18	1.35
Risk. Difference.(Re − Rne)	0	0.34	0.17
Risk ratio	1.36		
Midp. exact	0.001605		
Fisher. exact	0.001875		
Chi-square	0.001164		

Residents near ant-hills were also associated with the transmission of visceral leishmaniasis. Ant hills and termites mounds provide a conducive breeding site for the vector of the sand fly. People who engage in outdoor activities near sand fly breeding

areas during the day increase the risk of being bitten by an infective sand fly. As a result, knowing where sand flies rest is useful for taking precautions against vector bites and planning vector control activities. Residence near ant hill provides an environment for the transmission of Visceral leishmaniasis and hence correlated with the spread of Visceral leishmaniasis; however, 2152 (74.46 %) were exposed to this risk, while 738(25.54 %) were non-exposed. Those exposed to the risk and survived were 1995 (92.70 %), while 157 (7.30%) died. Those non-exposed who survived were 656 (88.88 %), while 82 (11.11%) died. The risk for the non-exposed group (those not living near anthills) was low (1.18) as compared to those living near anthills (1.52). The log-rank p-value is significant (0.0012). Those living near anthills are at higher risk of contracting the disease; this was consistent with similar studies in Fangak County, South Sudan (Elsa, 2008) and America (Belo et al., 2013).

Table 4.4 use of bed nets risk analysis

Use of bed nets

Outcome	Exposed	Non-exposed	Total
Negative	1823	828	2651
Positive	144	95	239
Total	1967	923	2890
	Risk Exposed	Risk non-exposed	Rt
	Estimate	Lower 95 CI	Upper 95 CI
Risk	1.40	1.09	1.80
Risk Ratio	1.28		
Risk difference (Re − Rne)	0	0.31	− 0.4
Midp. exact	0.007841		
Fisher. exact	0.008973		
Chi-square	0.006844		

Insecticide-treated bed nets are known to kill sand flies and have proven repellent properties that reduce the number of sand flies entering the house. An individual who did not sleep under treated bed nets had a higher probability of being infected with visceral leishmaniasis given a bite from an infected female sand fly. Therefore, not using

insecticide-treated bed nets was highly correlated to the spread of the disease. The human populace was categorized into exposed and non-exposed. 1967(68.06 %) were exposed to this risk while 923(31.94) were none exposed. Those exposed to the risk and survived were 1823 (92.68 %), while 144 (7.32%) died. Those non-exposed who survived were 823(89.17 %), while 95 (10.87%) died. The risk in non-exposed group is 1.09, while the risk in the exposed group is 1.4. The log-rank p-value (0.008) is statistically significant. The use of bed nets showed an increased survival probability. Therefore, not using bed nets increased the transmission of the disease. This was consistent with a similar study conducted in Bangladesh (Chowdhury et al., 2019) and (Mondal et al., 2013) and in west Pokot, Kenya (Kolaczinski et al., 2008).

Table 4.5 Interaction with dogs risk analysis

Interaction with dogs

Outcome	Exposed	Non-exposed	Total
Negative	1954	697	2651
Positive	150	89	239
Total	2104	786	2890
	Risk exposed	Risk Non-exposed	Rt
	Estimate	Lower 95% CI	Upper 95%CI
Risk	1.59	1.23	2.04
Risk ratio	1.29		
Risk difference	0	0.36	−0.45
Midp. Exact	0.000405		
Fisher.Exact	0.000454		
Chi.Square	0.000270		

Most of the Marsabit county residents are pastoralists who keep dogs for security. Visceral leishmaniasis can be transmitted from dogs to humans. Humans most frequently contract this disease when bitten by a sand fly that had previously bitten an infected dog. Dogs act as a reservoir for the parasite causing the disease. Thus, close contact with them increases the probability of contracting the disease. The population was categorized into exposed and non-exposed. 2104 (72.80 %) were exposed to this risk while 786 (27.20%) were non-exposed. Those exposed to the risk and survived were 1954 (92.87 %), while 150 (7.13%) died. Those non-exposed who survived were 697(88.68 %), while 89 (11.32%) died. The risk for exposed was (1.59) and non-exposed group was (1.23). The log-rank p-value was significant (0.00059) and the risk of contracting the disease was higher for those in contact with infected dogs. This study was consistent with a similar study in Turkana county (Abarca, 2021) and Northwestern Ethiopia (Yared et al., 2014a).

Table 4.6 Forest cover surrounding the house risk analysis

Forest covers surrounding the house.

Outcome	Exposed	Non-exposed	Total
Negative	1883	768	2651
Positive	152	87	239
Total	2035	855	2890

	Estimate	Lower 95 CI	Upper 95 CI
Risk	1.36	1.06	1.75
Risk difference (Re − Rne)	0	0.3	−0.39
Risk ratio	1.28		

Mid. point exact	0.017803
Fisher. exact	0.017851
Chi-square exact	0.015917

Forest covers surrounding as a risk for visceral leishmaniasis at Marsabit county referral hospital. The population was categorized into exposed and non-exposed. 2035 (70.41 %) were exposed to this risk, while 855 (29.58 %) were non-exposed. Those exposed to the risk and survived were 1883 (92.53 %), while 152(7.47 %) died. Those non-exposed who survived were 768 (89.25 %), while 87 (10.18 %) died. The risk in the exposed group was 1.36, while the risk for the non-exposed group was 1.06. The risk difference was (0.3) among the two groups. The log-rank p-value was significant (0.0340). Therefore forest surrounding the house was highly correlated to the transmission of visceral leishmaniasis. Those living near forest surrounding are at higher risk of the disease compared to the non-exposed group. This study was consistent with a similar studies conducted in Brazil (Margonari et al., 2020) and Gilgil Kenya (Ngere et al., 2020).

Table 4.7 Sleeping outside at night risk analysis

Sleeping outside at night

Outcome	Exposed	Non-exposed	Total
Negative	1480	1171	2651
Positive	151	88	239
Total	1631	1259	2890

	Estimate	Lower 95 CI	Upper 95 CI
Risk	1.32	1.03	1.70
Risk difference (Re − Rne)	0	0.29	−0.38
Risk ratio	1.3		
Midp. exact	0.027649		
Fisher. exact	0.0293070		
Chi-square	0.0281348		

Sleeping near an animal shelter, under acacia trees and near farm areas at night exposes an individual to the risk of been in contact with sand flies; this increases the likelihood of disease transmission to humans. The human populace was categorized into exposed and non-exposed. 1631(56.44 %) were exposed to this risk while 1259(43.56%) were non-exposed. Those exposed to the risk and survived were 1480 (90.74 %), while 151 (9.3 %) died. Those non-exposed who survived were 1171(93.01%), while 88 (6.99 %) died. The risk for non-exposed group is 1.03, while that for the exposed group is 1.32. The risk

difference was (0.29). The risk ratio was 1.3; this value is more than 1 implying an increased risk in the exposed group. The log-rank p-value was significant (0.026). The survival probability improves with time for those not sleeping outside at night; the risk was high for those sleeping outside at night. Therefore, this study agreed with previous research conducted in Western Ethiopia (Yared et al., 2014b) and Turkana County, Kenya (Abarca, 2021).

4.3 To evaluate mortality and transmission rate due to visceral leishmaniasis at Marsabit county referral hospital.

Using a S.I.R approach, the mortality was evaluated by considering different compartments of transmission of Visceral leishmaniasis from vector to human; The probability of an individual being in the infectious compartment from a sample of 2890 cases reported, 2769 (95.81%) tested positive for Visceral leishmaniasis which gives a probability of an individual getting infected while in the compartment (ρ) to be (0.9581). At infectious stages, patients develop signs and symptoms, which include; fever that lasts for weeks and months, chills, anemia, weight loss, splenomegaly, weakness, cough and enlargement of the liver. Patients seek medical treatments from nearby health centers, but most cases are referred to Marsabit referral hospital to get specialized treatment. The recovery rate was considered a critical parameter (γ_h) in evaluating the mortality rate. This rate was estimated at 0.8754, the rate at which an individual exits the compartment due to mortality (μ_h) was estimated at a probability (0.0863) this was obtained by considering 239 patients who died divided by 2,769 who tested positive.

Using S.I.R model

$$M = \frac{\rho}{1-\rho}.(\gamma_h + \mu_h).\frac{I_h}{N_H}$$

(4.2)

Where M = mortality from Visceral leishmaniasis

$\rho -$ Probability of patient been in infectious compartment

$\gamma_h -$ Recovery rate of patients on receiving treatments

$\mu_h -$ Rate at which patients exit the infectious compartment

$I_h =$ Infected human population

N_H = Population size of Marsabit county (459,785) (KNBS, 2019).

Estimate for the probability of patients been in the infectious compartment ($\boldsymbol{\rho}$)

$$\rho = \frac{total\ patients\ who\ tested\ positive}{Total\ sample\ size}$$

$$\rho = \frac{2{,}769}{2890}$$

$$\rho = 0.9581$$

Estimate for recovery rate (γ_h)

2,530 patients recovered from the disease after receiving treatments. The rate can be obtained by

$$\gamma_h = \frac{2530}{2890}$$

$$\gamma_h = 0.8754$$

Estimate for the rate at which humans exit infectious compartment (μ_h)

239 patients died while in this compartment; this rate can be estimated as

$$\mu_h = \frac{239}{2{,}769}$$

$$\mu_h = 0.0863$$

To evaluate mortality, substitute the parameter values to obtain visceral leishmaniasis mortality at Marsabit County referral hospital.

$$M = \frac{0.9581}{1-0.9581}\ (0.8754 + 0.0863) \times \frac{2769}{459785}$$

$$M = \frac{0.9581}{0.0419}\ (0.9617) \times 0.0060$$

$$M = (22.8663)(0.9617)(0.0060)$$

M= 0.1319

M=13.19%

The value of 0.9581 represent the proportions of infected individuals in the human population which was obtained by dividing those who turned positive for visceral leishmaniasis with total human population of Marsabit County, the value 0.8754 was obtained from the portions of those who seek medication after been infected with visceral leishmaniasis, the value 0.0863 represented the rate at which an individual leaves compartment due to mortality, the value 2769 represented the infected individual in the human population and the value 459,785 represented the total human population of Marsabit County as at 2019 census data.

The mortality rate from visceral leishmaniasis at Marsabit County referral hospital was 13.19%, indicating that the mortality incidence was 131 deaths per year in 1000 people. This indicate that the mortality incidence can been reduced by controlling the risk factors which are responsible for the spread of visceral leishmaniasis.

4.3.1 Transmission rate for visceral leishmaniasis at Marsabit referral Hospital.

To calculate the transmission rate, consider the biting rate of 0.0061; this was obtained by considering α which is rate at which a particular human is bitten by a particular sand fly 0.5 (Rohani, 2007), Multiplied by total susceptible vectors and divided by the total human population of Marsabit county. The transmission probability from vector to human was estimated at 0.6595 obtained by considering the average number of patients who turns positive daily. (Matoke-Muhia et al., 2016) carried out research on sand fly

distribution in the endemic regions in Kenya. A total of 14,000 sand flies were collected: Baringo (52.3%), Nakuru (8.6%), and Marsabit (37.2%). 40% were *P. martini*. In the Marigat sub-county of Baringo, *P. martini* was the only vector trapped, while in the East Pokot sub-county, *P. dubosciq* (40%) and *P. martini* (30%) were prevalent. In Gilgil (Nakuru), *P. guggiesbergi* (60%) was prevalent; however, this number keeps varying as the vector population is not constant. The total population of the vector as of 2019 was estimated from (Matoke-Muhia et al., 2016) by considering the vector growth rate. The proportions of the infected individual in the human population were obtained by considering 2769 that tested positive of the sample population of 2890 patients.

To evaluate the transmission rate from the above parameter.

Transmission rate = $b\beta_{hv}(\frac{S_h}{N_h}+\frac{I_h}{N_H})S_v$ and to obtain the transmission which can result into the transmission of Visceral leishmaniasis to human can be obtained by;

Transmission rate of V.L. = $b\beta_{vh}S_v\frac{I_h}{N_H}$ (4.3)

Estimate for biting rate for sand fly (b)

$$b = \alpha \times \frac{Total\ vectors\ in\ marsabit}{Total\ population\ of\ marsbit\ county}$$

$\alpha = 0.5$ (Prob.that a specific human is bitten by a specific sand fly) (Rohani, 2007)

The total vector of Marsabit as of 2016, 37.2% = $\frac{372}{1000} \times 14{,}000 = 5{,}208$ vectors. (Matoke-Muhia et al., 2016)

To estimate the total vector population as of 2019, consider the vector growth rate. It takes 2-3 days for a pupa to develop into an adult sand fly; that means, on average, it takes 2.5 days for 1 sand fly to develop then; how many sand flies can be developed in a year ($365\ ^1/_4$ days)

$$\frac{365.25\ days\ \times 1\ sand\ fly}{2.5\ days}$$

This estimates to 146.1 sand flies in a year; multiply this by 3 years since 2016 to estimate for the next three years to obtain the vector population as of 2019. This will evaluate to 438 vectors in the next three years and add this to the vector population as of 2016, which were 5,208 vectors. This estimate to 5,646 vectors as of 2019. The total population of Marsabit County was 459,785 as of 2019. The value of b can thus be estimated as

$b = 0.5 \times \frac{5,646}{459,785}$

b = 0.0061.

Estimate for transmission probability from vector to human.($\boldsymbol{\beta_{vh}}$)

2,890 cases were reported over the period between 2015-2019.

2,769 were reported to have tested positive for V.L.

The average number of people who turn positive annually was $\frac{2,769}{5} = 553.8$ people

How many people turn positive in a day $\frac{553.8}{365.25} = 1.5162$ per day.

The rate at which an individual turn positive in a day can thus be obtained as $\frac{1}{1.5162} = 0.6595$

Thus the transmission probability from vector to human can be estimated as

$$\beta_{vh} = 0.6595$$

I_h= 2,769 (Those who turned positive)

$$N_h = 459{,}785$$

Solving the above

$$\text{Transmission rate} = 0.0061 \times 0.6595 \times 5646 \times \frac{2769}{459{,}785}$$

$$\text{Transmission rate} = 0.0061 \times 0.6595 \times 5646 \times 0.0060$$

$$\text{Transmission rate} = 0.1363$$

$$= 13.63\%$$

This represents the number of new infections from visceral leishmaniasis per unit of time generated by an infected sand fly.

4.4 To estimate the level of Endemicity of Visceral leishmaniasis.

The Jacobean method used for the S.I.R model yields a reasonableR_0. Still, for more complex compartmental models, especially those with more infected compartments, the method is hard to apply as it relies on the algebraic Routh-Hurwitz conditions for stability of the Jacobean matrix, an alternative method proposed by Diekmann, Heesterbeek, and Metz (1990) and elaborated by Van den Driessche and Watmough (2002) (Diekmann et al., 1990) gives a way of determining R_0 for an O.D.E compartmental model by using the next generation matrix.

Evaluation for control reproductive number

$$R_C(\phi_h) = \sqrt{\left(\frac{\phi_h}{(\mu_h+\theta_h)} \times \frac{\beta_{vh}\ell}{(\mu_h+\theta_h)}\right) \times \left(\frac{b\beta_{hv}}{\mu_v}\right)}$$

(4.4)

Where

Estimate for the rate at which clinical signs develop (ϕ_h)

For V.L., a person takes about three months to develop signs and symptoms of the disease after infections. If an individual takes three months to develop signs, then what is the rate that an individual can develop signs in a day.

$$\phi_h = \frac{1}{30 \times 3} = \frac{1}{90}$$

Thus the rate of an individual developing signs and symptoms in a day can be estimated at

$$\phi_h = 0.0111$$

Estimate for the rate at which sand fly exist compartment (μ_v).

The average life expectancy of a sand fly is two weeks (14 days)

$$\text{Number of } sand\ fly\ daily\ death = \frac{An\ individual\ sand\ fly}{No.of\ days}$$

$$\text{Number of sand fly daily death } = \frac{1}{14}$$

Daily mortality rate of sand fly = 0.0714.

Estimates for transmission probability from Human to Vector (β_{hv}).

Consider the probability of transmission from vector to a human estimated above at 0.6595; then transmission probability from human to vector can be obtained by ;

$$\beta_{hv} = 1 - 0.6595$$

$$\beta_{hv} = 0.3405$$

The rate at which humans are administered with drugs at the hospital (θ_h).

From the study, most patients were subjected to treatment Ambisome (1,542) while Sodium stibogluconate was 1,227. The total number of patients treated were

1542 + 1227 =2,769

The sample size was 2,890 patients; therefore, the rate at which humans were administered with treatment can be obtained by

$\theta_h = \frac{2769}{2890} = 0.9581$ per person.

To evaluate control reproductive number;

$$\mathcal{R}_C(\phi_h) = \sqrt{\left(\frac{\phi_h}{(\mu_h + \theta_h)} \times \frac{\beta_{vh}\ell}{(+\theta_h}\right) \times \left(\frac{b\beta_{hv}}{\mu_v}\right)}$$

Where

ϕ_h = 0.0111 rate at which clinical signs develop.

$\mu_h =$ 0.0863 rate at which humans exit compartments due to mortality.

θ_h= 0.9581 rate at which humans are administered with treatment.

β_{vh} = 0.6595 transmission probability from sand fly to human.

ℓ = 0.8 (Gebresilassie et al., 2015) sand fly landing rate on humans.

b = 0.0061 average number of bites per sand fly.

β_{hv}= 0.3405 transmission probability from human to sand fly.

μ_v = 0.0714 rate at which sand flies exit the compartment due to mortality.

$$\mathcal{R}_c = \sqrt{\frac{0.0111}{(0.0863+0.9581)} \times \frac{0.6595 \times 0.8}{(0.0863+0.9581)} \times \frac{0.0061 \times 0.3405}{0.0714}}$$

$$\mathcal{R}_C = \sqrt{\frac{0.0111}{1.0444} \times \frac{0.5276}{1.0444} \times \frac{0.0021}{0.0714}}$$

$$\mathcal{R}_c = \sqrt{0.0106 \times 0.5052 \times 0.0294}$$

$$\mathcal{R}_c = \sqrt{0.0002}$$

$$\mathcal{R}_c = 0.0141$$

This means a single case caused by a sand fly bite generates 0.0141 other cases of visceral leishmaniasis; hence a disease-free equilibrium exists since $\mathcal{R}_c < 1$ at Marsabit County referral hospital. Control reproductive rate (R_c) is the key measure in estimating the ability of a new pathogen to spread. When R_c is greater than 1, the epidemic is growing. The R_c values have important implications for disease control. It indicates level of mitigation efforts needed to bring an epidemic under control. Mitigation measures

include rapid case identification, quarantine measures, and physical distancing to prevent secondary transmissions. An R_c of below 1 suggests the outbreak is coming to an end, as it can produce less than its existing number with time.

From the result R_c was less than one this indicated that the disease can be managed putting into consideration the risk factors which needs to be control so as to obtain a smaller value of R_c in Marsabit County.

CHAPTER FIVE: CONCLUSIONS AND RECOMMENDATIONS

5.0 Introduction

This chapter presents the study's conclusions and recommendations; section 5.2 provides conclusions derived from the results and section 5.3 offers study recommendations.

5.1 Conclusions

The following risk factors were found to be a significant predictor of survival of visceral leishmaniasis patients; Household design, which included cracked mud walls and grass-thatched houses, was significant in transmitting visceral leishmaniasis. Residence near ant hill was associated with an increased risk of disease transmission. Not using treated bed nets were a significant risk factor in the study; individuals who do not use treated bed nets are at high risk of infection with visceral leishmaniasis compared to those using treated 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 and mortality rates from visceral leishmaniasis at Marsabit County referral hospital. The mortality and transmission rates were estimated at 13.19% and 13.63%, respectively. The control reproductive number (level of endemicity) was 0.0141, implying that the disease was not endemic. There is a need for community awareness on the risk factors for the visceral leishmaniasis so as to reduce the transmission rate of visceral leishmaniasis and subsequent mortality from the disease. Controlling the risk factors have the effect of lowering the R_c which in return

reduces the prevelence of the disease hence increase the survival probabilities of the visceral leishmaniasis patients at Marsabit County referral hospital.

5.2 Recommendations

All people living in leishmaniasis endemic areas to; sleep under iinsecticide treated bed nets to prevent human to vector contact, avoid sand fly breeding and resting sites especially for the boys when grazing animals, repair cracks in walls of houses to minimize entry and resting sites of sand flies, clear vegetation around the homestead to reduce resting sites for sand flies and destroy inactive termite hills and animal burrows around home steads to reduce breeding sites for sand flies. They should also recognize early symptoms and signs of leishmaniasis and seek immediate medical attention as soon as possible (early diagnosis and treatment). Mobilization and education of the community with effective behavioral change interventions must always be locally adapted. Partnership and collaboration with various stakeholders and other vector-borne disease control programmes is very critical. There should also be minimal interaction with an animal reservoir for visceral leishmaniasis which means that dogs, cattle and rodents should stay in well-screened or air-conditioned areas to avoid contact with the vector in order to reduce mortality rate as a result of visceral leishmanias infections.

Further research to be done by considering non resident of Marsabit County into the S.I.R compartment and also putting into consideration other risk factors e.g. malnutrition, H.I.V co-infection , environmental and climatic changes.

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APPENDIX I: R-codes

```
## -----------------------------------------------------

#Load required packages


library(tidyverse)

library(readxl)

library(knitr)

library(janitor)

library(psych)


#Load the data set


dataset <- read_excel("data.xlsx", sheet = "Sheet1") %>%

  clean_names()


#Encode categorical variables accordingly


dataset$sex <- factor(dataset$sex, levels = c(1,2),

                                   labels = c("male","female"))


dataset$rdt_rk39 <- factor(dataset$rdt_rk39, levels = c(1,2),

                                             labels = c("positive","neg

ative"))
```

```
dataset$drugs_given_for_treatment <- factor(dataset$drugs_given_for_tre
atment,
                                        levels = c(1,2,3),
                                        labels = c("Ssg","Ambisome","Nil")
)

dataset$outcome <- factor(dataset$outcome, levels = c(1,2),
                                              labels = c("alive","dead"))



levels <- c(1,2)
labels <- c("yes","no")

dataset$cracked_walls_thatched_roof <-
  factor(dataset$cracked_walls_thatched_roof,
         levels = levels,
         labels = labels)

dataset$near_anthills <- factor(dataset$near_anthills, levels = levels,
                                                        labels = labels)

dataset$use_bed_nets <- factor(dataset$use_bed_nets, levels = levels,
                                                      labels = labels)

dataset$contact_with_dogs <- factor(dataset$contact_with_dogs,
```

```
                                    levels = levels,
                                    labels = labels)

dataset$forest_sorroundings <- factor(dataset$forest_sorroundings,
                                      levels = levels,
                                      labels = labels)

dataset$sleep_outside_at_night <- factor(dataset$sleep_outside_at_night
,
                                         levels = levels,
                                         labels = labels)

dataset$sub_county <- factor(dataset$sub_county)




## ------------------------------------------------------
#Descriptive statistics


dataset %>%
  group_by(sex) %>%
  summarise(mean = mean(age),
            min  = min(age),
            max  = max(age),
            sd   = sd(age),
```

```
            skew = skew(age)) %>%
  knitr::kable()



## -------------------------------------------------------
dataset %>%
  group_by(sex) %>%
  summarise(n = n()) %>%
  knitr::kable()


ggplot(dataset, aes(x = sex, fill = sex)) +
  stat_count(width = 0.4) +
  theme_bw() +
  labs(title = "Number of Participants by Gender",
       x = "Sex",
       y = "Number of Participants") +
  theme(legend.position = "none")



## -------------------------------------------------------


dataset %>%
  group_by(cracked_walls_thatched_roof) %>%
  summarise(n = n()) %>%
  knitr::kable()
```

```
ggplot(dataset, aes(x = outcome, fill = outcome)) +
  stat_count(width = 0.4) +
  theme_bw() +
  labs(title = "How Many People Survived/Died?",
       x = "Outcome") +
  theme(legend.position = "none")


## -------------------------------------------------------


dataset %>%
  group_by(sub_county) %>%
  summarise(n = n()) %>%
  arrange(desc(n)) %>%
  knitr::kable()


ggplot(dataset[!is.na(dataset$sub_county),],
       aes(x = reorder(sub_county,sub_county, FUN = length),
                     fill = sub_county)) +
  stat_count() +
  theme_bw() +
  coord_flip() +
  labs(title = "Number of Participants Per Sub-County",
       x = "Sub County Name") +
  theme(legend.position = "none")
```

```
## -----------------------------------------------------


dataset %>%
  group_by(rdt_rk39) %>%
  summarise(n = n()) %>%
  arrange(desc(n)) %>%
  knitr::kable()


ggplot(dataset[!is.na(dataset$rdt_rk39),],
       aes(x = reorder(rdt_rk39,rdt_rk39, FUN = length),
                     fill = rdt_rk39)) +
  stat_count(width = 0.4) +
  theme_bw() +
  labs(title = "Result of Specific type of Test Done",
       x = "Lab Test Results") +
  theme(legend.position = "none")



## -----------------------------------------------------


dataset %>%
  group_by(drugs_given_for_treatment) %>%
  summarise(n = n()) %>%
  arrange(desc(n)) %>%
```

```
  knitr::kable()


ggplot(dataset[!is.na(dataset$drugs_given_for_treatment),],
       aes(x = reorder(drugs_given_for_treatment,drugs_given_for_treatm
ent,
                       FUN = length),
                   fill = drugs_given_for_treatment)) +
  stat_count(width = 0.4) +
  theme_bw() +
  labs(title = "Drugs Given for Treatment",
       x = "Name of Drug Treatment Received") +
  theme(legend.position = "none")




## -------------------------------------------------------


dataset %>%
  group_by(cracked_walls_thatched_roof) %>%
  summarise(n = n()) %>%
  arrange(desc(n)) %>%
  knitr::kable()


ggplot(dataset,
       aes(x = reorder(cracked_walls_thatched_roof,
```

```
                        cracked_walls_thatched_roof,
                        FUN = length),
                    fill = cracked_walls_thatched_roof)) +
  stat_count(width = 0.4) +
  theme_bw() +
  labs(title = "Cracked walls thatched roof",
       x = "") +
  theme(legend.position = "none")




## -----------------------------------------------------


dataset %>%
  group_by(near_anthills) %>%
  summarise(n = n()) %>%
  arrange(desc(n)) %>%
  knitr::kable()


ggplot(dataset,
       aes(x = reorder(near_anthills,near_anthills,
                        FUN  = length),
                        fill = near_anthills)) +
  stat_count(width = 0.4) +
  theme_bw() +
```

```
  labs(title = "Near anthills",
       x = "") +
  theme(legend.position = "none")




## ------------------------------------------------------


dataset %>%
  group_by(use_bed_nets) %>%
  summarise(n = n()) %>%
  arrange(desc(n)) %>%
  knitr::kable()


ggplot(dataset,
       aes(x = reorder(use_bed_nets,use_bed_nets,
                       FUN  = length),
                       fill = use_bed_nets)) +
  stat_count(width = 0.4) +
  theme_bw() +
  labs(title = "Use Bed Nets?",
       x = "") +
  theme(legend.position = "none")


## ------------------------------------------------------
```

```
dataset %>%
  group_by(contact_with_dogs) %>%
  summarise(n = n()) %>%
  arrange(desc(n)) %>%
  knitr::kable()


ggplot(dataset,
       aes(x = reorder(contact_with_dogs,contact_with_dogs,
                       FUN  = length),
                       fill = contact_with_dogs)) +
  stat_count(width = 0.4) +
  theme_bw() +
  labs(title = "Contact with Dogs?",
       x = "") +
  theme(legend.position = "none")


## -------------------------------------------------------


dataset %>%
  group_by(forest_sorroundings) %>%
  summarise(n = n()) %>%
  arrange(desc(n)) %>%
  knitr::kable()
```

```
ggplot(dataset,
       aes(x = reorder(forest_sorroundings,forest_sorroundings,
                       FUN  = length),
                       fill = forest_sorroundings)) +
  stat_count(width = 0.4) +
  theme_bw() +
  labs(title = "Forest Surroundings?",
       x = "") +
  theme(legend.position = "none")



## -----------------------------------------------------


dataset %>%
  group_by(sleep_outside_at_night) %>%
  summarise(n = n()) %>%
  arrange(desc(n)) %>%
  knitr::kable()


ggplot(dataset,
       aes(x = reorder(sleep_outside_at_night,sleep_outside_at_night,
                       FUN  = length),
                       fill = sleep_outside_at_night)) +
  stat_count(width = 0.4) +
  theme_bw() +
```

```
  labs(title = "Sleep outside at night?",
       x = "") +
  theme(legend.position = "none")



## ------------------------------------------------------
#require(devtools)
#install_version("epicalc", version = "2.15.1.0",
                #repos = "http://cran.us.r-project.org")


library(epitools)


data2 = dataset


data2$cracked_walls_thatched_roof =
  relevel(data2$cracked_walls_thatched_roof, "yes")



res1 = riskratio.wald(table(data2$cracked_walls_thatched_roof,
                      data2$outcome))



res1$data %>%
  knitr::kable()
```

```
res1$measure %>%
  knitr::kable()



## -------------------------------------------------------

data2$near_anthills =
  relevel(data2$near_anthills, "yes")

res2 = riskratio.wald(table(data2$near_anthills, data2$outcome))

res2$data %>%
  knitr::kable()

res2$measure %>%
  knitr::kable()



## -------------------------------------------------------
data2$use_bed_nets =
  relevel(data2$use_bed_nets, "no")

res3 = riskratio.wald(table(data2$use_bed_nets, data2$outcome))

res3$data %>%
```

```
  knitr::kable()


res3$measure %>%
  knitr::kable()



## ------------------------------------------------------
data2$contact_with_dogs =
  relevel(data2$contact_with_dogs, "yes")


res4 = riskratio.wald(table(data2$contact_with_dogs, data2$outcome))


res4$data %>%
  knitr::kable()


res4$measure %>%
  knitr::kable()



## ------------------------------------------------------
data2$forest_sorroundings =
  relevel(data2$forest_sorroundings, "yes")


res5 = riskratio.wald(table(data2$forest_sorroundings, data2$outcome))
```

```
res5$data %>%
  knitr::kable()


res5$measure %>%
  knitr::kable()




## ------------------------------------------------------
data2$sleep_outside_at_night =
  relevel(data2$sleep_outside_at_night, "no")


res6 = riskratio.wald(table(data2$sleep_outside_at_night,
                            data2$outcome))


res6$data %>%
  knitr::kable()


res6$measure %>%
  knitr::kable()




## ---- fig.width=8.5, fig.height=4-----------------------
#install.packages(c("survival", "survminer"))
```

```
library("survival")

library("survminer")


set.seed(2021)



model_data <- read.csv("data3.csv")


#Cox proportional hazard model


res.cox <- coxph(Surv(time, outcome) ~ age + sex +

                   drugs_given_for_treatment +

                   cracked_walls_thatched_roof +

                   near_anthills + use_bed_nets +

                   contact_with_dogs +

                   forest_sorroundings + sleep_outside_at_night,

                   data = model_data)


#summary(res.cox)



## -------------------------------------------------------

bh = read.csv("beta_hazard.csv")


bh %>%
```

```
  knitr::kable()



## ---- fig.width=6.5-------------------------------------

ggforest(res.cox, data = model_data)




## ------------------------------------------------------
#S.I.R Modeling

library(deSolve)
library(reshape2)

# Model inputs

initial_state_values=c(S=999999,I=1,R=0)
parameters=c(gamma=0.2*365,beta=0.4*365,mu=1/70,b=1/70)

# Time points

time = seq(from=1,to=400,by=1/365)

time2 = seq(min(model_data$time), max(model_data$time), 1/365)
```

```
# SIR model function


sir_model2 <- function(time2,state,parameters){
  with(as.list(c(state,parameters)),{
    N=S+I+R
    lambda=beta*(I/N)
    dS=-lambda*S-mu*S+b*N
    dI=lambda*S-gamma*I-mu*I
    dR=gamma*I-mu*R


    return(list(c(dS,dI,dR)))
  }
  )
}




# Solving the differential equations:
output <- as.data.frame(ode(y=initial_state_values,
                            func = sir_model2,
                            parms= parameters,
                            times = time2))


out_long = melt(output,id="time")
```

```
#Plotting the prevelance over time
ggplot(data = out_long,
       aes(x = time, y = value/1000000,
           colour = variable, group = variable)) +
  geom_line() +
  xlab("Time (years)") +
  ylab("Prevalence")   +
  scale_color_discrete(name="State")



## ------------------------------------------------------
# Fit survival data using the Kaplan-Meier method

surv_object <- Surv(time = model_data$time, event = model_data$outcome)

fit1 <- survfit(surv_object ~ drugs_given_for_treatment,
                   data = model_data)
#summary(fit1)



## ------------------------------------------------------
ggsurvplot(fit1, data = model_data, pval = TRUE)
```

```
## ------------------------------------------------------

#Examine the predictive values of bed net use


fit2 <- survfit(surv_object ~ use_bed_nets,

                   data = model_data)

#summary(fit2)


ggsurvplot(fit2, data = model_data, pval = TRUE)




## ------------------------------------------------------

#Examine the predictive values of house condition


fit3 <- survfit(surv_object ~ cracked_walls_thatched_roof,

                   data = model_data)

#summary(fit2)


ggsurvplot(fit3, data = model_data, pval = TRUE)




## ------------------------------------------------------
```

```
#Examine the predictive values for near anthils


fit3 <- survfit(surv_object ~ near_anthills,
                   data = model_data)
#summary(fit2)


ggsurvplot(fit3, data = model_data, pval = TRUE)




## ---------------------------------------------------------
#Examine the predictive values for near anthils


fit3 <- survfit(surv_object ~ contact_with_dogs,
                   data = model_data)
#summary(fit2)


ggsurvplot(fit3, data = model_data, pval = TRUE)



## ---------------------------------------------------------
#Examine the predictive values for near forest surroundings


fit3 <- survfit(surv_object ~ forest_sorroundings,
                   data = model_data)
```

```
#summary(fit2)


ggsurvplot(fit3, data = model_data, pval = TRUE)




## -------------------------------------------------------
#Examine the predictive values for those who sleep outside at night

fit3 <- survfit(surv_object ~ sleep_outside_at_night,
                   data = model_data)
#summary(fit2)

ggsurvplot(fit3, data = model_data, pval = TRUE)



## -------------------------------------------------------
#Examine the predictive values in terms of gender

fit3 <- survfit(surv_object ~ sex,
                   data = model_data)
#summary(fit2)

ggsurvplot(fit3, data = model_data, pval = TRUE)
```

```
## ------------------------------------------------------

library(mudens)

fit <- mudens(model_data$time, model_data$outcome)

#summary(fit)

plot(fit)
```

APPENDIX II: MAP

MARSABIT COUNTY MAP

Marsabit is a county in Kenya covering a surface area of 66.923,1 square kilometres; Marsabit is the largest county in Kenya. Its capital is Marsabit town, and its largest town is Moyale. According to the 2019 census, the County had a population of 459,785

APPENDIX III: RESEARCH PERMIT

REPUBLIC OF KENYA

NATIONAL COMMISSION FOR SCIENCE,TECHNOLOGY & INNOVATION

Ref No: 641663

Date of Issue: 20/February/2021

RESEARCH LICENSE

This is to Certify that Mr.. ELIAS ELEMA GUYO of Moi University, has been licensed to conduct research in MARSABIT on the topic: MODELLING MORTALITY AND TRANSMISSION RATE OF VISCERAL LEISHMANIASIS A CASE STUDY OF MARSABIT COUNTY for the period ending : 20/February/2022.

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APPENDIX IV ANTI-PLAGIARISM CERTIFICATE

SR163

THESIS WRITING COURSE

PLAGIARISM AWARENESS CERTIFICATE

This certificate is awarded to

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16th /02/2023