FACTORS ASSOCIATED WITH TREATMENT OUTCOME AMONG PATIENTS WITH VISCERAL LEISHMANIASIS IN WAJIR WEST SUB-COUNTY, WAJIR COUNTY: 2017–2019

By

ALI NOOR MOHAMED

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DECLARATION

Declaration by Candidate

This thesis is my original work and has not been presented in any other university for the purposes of obtaining a degree. This thesis should not be reproduced without the prior permission of the author or Moi University.

Signature: _____ Date :_____

Ali Noor Mohamed

SPH/PGH/FE/07/17

Declaration by the Supervisors

This thesis has been submitted with our approval as the university supervisors

Signature: _____ Date :_____

Prof. Christina A. Otieno

Department of Environmental Health & Disaster Risk Management

School of Public Health,

Moi University,

ELDORET- KENYA

Signature: _____ Date :_____

Dr. Adam H. Haji

Deputy Director,

Preventive and Promotive Health,

Department of Health

Wajir County

DEDICATION

I dedicate this work to Kala-Azar patients in Wajir West Sub-county that have had their lives disrupted due to the infection and endured prolonged treatment periods.I hope that this work will count in ensuring that you get the best available treatment and care.

Special dedication to my dear mother, Hawa Haji, and my wife, Halima Abdi for their unwavering emotional and spiritual support that made this journey easier. To my daughters Mahadiya and Maymunah for their innocent curiosity and constant inquiries that lifted my spirit whenever I felt low. I love you and may God bless you all.

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ABSTRACT

Background: Leishmaniasis is a parasitic disease caused by intracellular protozoan parasite species of genus *Leishmania*. Visceral Leishmaniasis (VL) is the most severe of the three forms of leishmaniasis. Globally associated with 50,000-90,000 new cases annually with a mortality of up to 95% in untreated and 5-10% in treated cases. In Kenya, VL is endemic in arid and semi-arid counties and an estimated 2500 cases occur annually. In Wajir, 64% of all cases from 2014 to 2017 occurred in Wajir West sub-county. Data on treatment outcomes and associated factors in Wajir are scarce.

Objective: This study is aimed to characterize and identify factors associated with initial treatment outcomes among VL patients in Wajir west sub-county.

Methods: The study design was a cross-sectional mixed-method: a retrospective review of hospital records and qualitative data collection from June 22nd through July 25th, 2020 at Giriftu sub-county hospital, Arbajahan health centre, and Athibohol dispensary in Wajir West sub-county. Simple random sampling was used in selecting the patient records for review. A pretested standardized data abstraction tool was used to collect VL treatment data on socio-demographic, clinical, and laboratory information. A total of three Focus Group Discussions (FGDs) and four Key Informant Interviews (KIIs) were conducted for 42 Community Health Volunteers (CHVs) and 8 Healthcare Workers (HCWs) respectively. Interview guides were used in collecting socio-cultural, socio-economic, and healthcare related information and how it influenced treatment outcomes among patients with VL.

Quantitative data were analysed using Epi info version 7 software. Measures of central tendency and frequency listing were used for continuous and categorical variables respectively. Fisher's exact Chi-square tests were used to test for association among socio-demographic characteristics and VL treatment outcomes. Variables with $p < 0.20$ in bivariate were included in multivariate analysis. Variables with $p < 0.05$ in the final model were considered statistically significant. Qualitative data was transcribed and transcripts analysed thematically.

Result: A total of 195 VL patient records were included in the analysis.

The median age was 2.5 years (IQR: 3.3 years), 69.2% (135/195) were <5 years old, Males were 56.9 %(111/195) and 91.3 %(178/195) lived in Wajir-West Sub-county. Treatment outcomes at initial evaluation consisted of 93.8 % (183/195) cured (good-outcome) , 4.6% (9/195) mortality (poor outcome) and 1.5%(3/195) relapsed cases.

Independent factors associated with poor treatment outcome included Age ≥15 years (p value=0.006), Adverse drug event (p value=0.04) and Pneumonia (p value=0.04)

FGD-respondents reported distance to health-facility, self-treatment, husbandry-chores, and indirect costs as hindrances to Health-visits.

KII revealed lack of training, staff turnover, and stock-outs of drugs or test kits as the challenges.

Conclusion: VL is high in <5years, males, Factors associated with the poor outcome are; age ≥15yrs, pneumonia, and adverse drug events while the contributing factors include; distance to facility, home-treatment, indirect-costs, VL-kits, and drugs stock-outs, high staff turnover and lack of VL training.

Recommendation: Public education to mitigate VL burden, improved health interventions through staff training, timely supplies of VL kits/drugs, and close monitoring during treatment.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABBREVIATIONS AND ACRONYMS

ADE	Adverse Drug Events
AE	Adverse Effect
CDC	Centres for Disease Control
CL	Cutaneous Leishmaniasis
DALYs	Disability Adjusted Life Years
DAT	Direct Agglutination Test
DND*i*	Drug for Neglected Disease initiatives
EoT	End of Treatment
FELTP	Field Epidemiology and Laboratory Training Program
FGD	Focus Group Discussion
FIND	Foundation for Innovative New Diagnostics
HB	Haemoglobin
HIV	Human Immunodeficiency Virus
HSB	Health Seeking Behaviour
IREC	Institutional Research and Ethics Committee
ISC	Indian Sub-continent
KA	Kala-Azar
KEMRI	Kenya Medical Research Institute
KII	Key Informant Interview
MCL	Muco-cutaneous Leishmaniasis
MoH	Ministry of Health
NTD	Neglected Tropical Disease
PM	Paromomycin
PKDL	Post Kala-Azar Dermal Leishmaniasis

RDT	Rapid Diagnostic Test
RK39	Repeat Kinesin 39
SSG	Sodium Stibogluconate
TB	Tuberculosis
ToC	Test of Cure
VL	Visceral Leishmaniasis
WHO	World Health Organization

DEFINITION OF TERMS

At initial assessment (between 2 and 4 weeks after initiating treatment) these are the outcomes to be recorded (MoH, 2017).

Confirmed non-response: Signs and symptoms persist or recur during treatment with parasitological confirmation (smear showing parasite density equal to or greater than before treatment)

Death: Any death, whether related to VL or not

Defaulter: The patient does not complete treatment for VL

Good treatment outcome: Is considered when the patient is clinically cured of VL as measured by laboratory or through use of clinical criteria (resolution of fever, regression of size of the spleen, increase in hemoglobin, and weight gain)

Initial cure: A full course of drugs has been completed and the patient has clinically improved. Clinical criteria for initial cure include; resolution of fever, regression of splenomegally, return of appetite, and or gain in body weight**.**

Loss to initial follow-up: The patient does not present for assessment after completion of treatment.

Poor treatment outcome: Means 1. Non-adherence (A patient who was lost to follow up or took less than recommended doses due to the patient leaving the hospital) 2. Treatment failure/non-response (Patient who experiences a recurrence of VL symptoms after initial cure) or 3. Death due to VL.

Probable non response: Signs and symptoms persist or recur during treatment without parasitological confirmation.

Relapse: A patient who experiences a recurrence of VL symptoms with parasitological confirmation at any time point after initial cure. VL relapses are usually observed within 6 months of completing therapy.

CHAPTER ONE

INTRODUCTION

1.1 Background

Leishmaniasis is among the 20 Neglected Tropical Diseases (NTD) currently listed by WHO (WHO, 2020). VL is caused by an obligate intracellular protozoan parasite of genus *Leishmania* (Siqueira-Neto *et al.,* 2012). The disease has four main clinical syndromes: Cutaneous Leishmaniasis (CL), Muco-cutaneous Leishmaniasis (MCL), Post Kala-Azar Dermal Leishmaniasis (PKDL), and Visceral Leishmaniasis (VL) also known as Kala-Azar which is the most severe form of leishmaniasis (Chappuis *et al.,* 2007;Roque *et al.,* 2014). VL is mainly caused by *Leishmania donovani* and is transmitted by female the *Phlebotomine* sand fly (Yared *et al.,* 2014). It usually presents with fever, splenomegally, and or wasting (Y. K. Mueller et al., 2014a).

VL is endemic in 65 countries distributed in five regions; Europe, Asia, the Middle East, Africa, and America (WHO, 2010). Globally an estimated 50,000 to 90,000 VL cases occur every year causing fatality of up to 95% in untreated cases (WHO, 2018). In East Africa, endemic foci of VL are found in remote parts of Kenya, Eritrea, Somalia, Sudan, Ethiopia, and Uganda (Ritmeijer *et al.,* 2014). VL is reported to be fatal if left untreated with an estimated global annual fatality of up to 59,000 cases and associated 2,356,000 Disability Life Adjusted Years (DALYs) (Den Boer *et al.,* 2011).

In Kenya, VL is endemic in arid and semi-arid counties namely; Wajir, Marsabit, Mandera, Baringo, Turkana, Kitui, and Machakos (Njau, 2010).

It is estimated that about 2500 cases occur annually and 6.81 million people are at risk of infection (MoH, 2017).

The first reported major VL outbreaks in Wajir occurred in 2001 and this was followed by other outbreaks in 2006 through 2008 (Malaria Consortium, 2010; Njau, 2010). More recent waves were reported in 2014 and 2017 (FELTP/MoH surveillance data analysis report; 2019).

VL treatment outcome is an important indicator used in monitoring treatment activities (MoH, 2017) . Even in the presence of treatments mortality is up to 5% when using antimonials and may reach up to 11% in impoverished populations (Kimutai *et al.,* 2017).

Data on treatment outcome will enable policy makers, frontline healthcare providers and funding organizations to identify priority areas for addressing VL management in Wajir County. Although VL treatment strategy was initiated back in 2001, no treatment outcome study was done creating information gaps. Hence, this study aims to identify factors associated with VL treatment outcome among VL patients that were initiated on treatment at Giriftu sub-county hospital, Arbajahan health centre and Athibohol dispensary in Wajir West sub-county.

1.2 Problem Statement

VL is endemic in Wajir County and the burden remain high with frequent outbreaks from 2001 through 2018 (Njau, 2010). Following recent VL outbreaks (2014 to 2017), The highest proportion of VL cases (70.8%) were reported in Wajir West sub-county (FELTP/MoH surveillance data analysis report; 2019). The relatively high number of VL cases in Wajir West sub-county may be driven by environmental and climatic factors such as termite hills, *Balanite* trees, acacia trees, black cotton soil plus high temperature and humidity that provide suitable habitat for sandfly vector (Njau, 2010)**.**

VL infection is associated with death in up to 95% in untreated cases and 5-10% in treated cases (WHO, 2018; Kimutai *et al.,* 2017). In endemic areas, seeking diagnosis and treatment for VL is often associated with huge financial strain in an already meagre financial situation (Okwor *et al.,* 2016).

To control VL, the MoH guideline recommends the use of active surveillance, a process that requires health workers and community health volunteers to carryout house to house search for cases, test and initiate treatment at the nearest health facility. However, in Wajir surveillance remain passive where health worker wait for patient to visit the health facility (FELTP/MoH surveillance data analysis report; 2019). The passive process allows other factors such as distance to health facility, illiteracy, cost of transport, existence of alternative treatments, home chores, and severity of the condition to play a role thereby delaying diagnosis and treatment. These and similar factors have been shown to influence health seeking behavior thereby affecting VL diagnosis and treatment often leading to poor outcome (Garapati *et al.,* 2018;Lotukoi *et al.,* 2017).

The other control method is by use of antimonial treatment drugs. These drugs are recommended for use in Kenya but associated with prohibitive cost, toxicity, painful injections, long treatment periods, defaults, relapse, and mortality of up to 5-10% of the treated cases (Kimutai *et al.,* 2017;MSF, 2011). These drug related factors have been shown to affect health seeking behavior hence delayed treatment and development of drug resistance as was shown in India and Bangladesh where delay in diagnosis resulted in poor clinical indicators and death (Pascual *et al.,* 2012; Den Boer *et al.,* 2011).

1.3 Justification

In Kenya, the MoH guideline on VL recommends in addition to active surveillance, the integration of pharmacovigilance and treatment outcome monitoring as part of routine surveillance (MoH, 2017). This entails, regular monitoring of treatment activities, follow-up after treatment, and training of personnel on best practices in managing adverse drug effects.

Similarly, studies that were done in East Africa and southeast Asia on VL treatments, underscore the need for close monitoring of treatment outcomes to determine the safety, efficacy, drug exposure, and therapeutic responses (Kimutai et al., 2017; Ostyn *et al.*, 2014). Never the less, gaps exist in Wajir where VL surveillance remains passive and no pharmacovigilance or treatment monitoring study has been done. This poses great risk for VL patients who are mainly pastoralists, making it difficult to diagnose cases earlier and or initiate treatment for better outcome.

In the Indian sub-continent (ISC) where similar antimonials like Sodium stibogluconate (SSG) were used for VL treatment, effectiveness waned over years. This was mainly due to sub-optimal doses, incomplete duration of treatment, and use of sub-standard drugs leading to treatment failures (Sundar *et al.,* 2001). If such changes (treatment failures) occur without notice, they will have serious social and health consequences for the community. It will increase the indirect cost of treatment, duration of hospital stay, worsen prognosis and hence impede overall control and of the disease. This will also hamper the implementation of VL control policies and guidelines leading to a more costly intervention.

Understanding the factors associated with VL treatment outcomes in Wajir west is important in designing evidence-based interventions. The information generated by

this study will be vital for decision making by healthcare providers, policymakers, and funding organizations to plan VL control interventions**.**

1.4 Research question

What are the VL treatment-associated factors that may influence treatment outcomes among VL patients in Wajir west sub-county?

1.5 Broad objectives

To determine factors associated with initial treatment outcome among patients treated for visceral leishmaniasis in Wajir West sub-county from January 2017 to October 2019.

1.5.1 Specific objectives

1. To describe socio-demographic, Clinical and Laboratory related factors associated with initial treatment outcome among VL patients in Wajir West
2. To determine proportion of initial outcomes following VL treatment interventions
3. To identify quantitative and Qualitative factors associated with initial VL treatment outcomes

CHAPTER TWO

LITERATURE REVIEW

2.1. Overview

Leishmaniasis is a vector-borne disease caused by protozoa of genus *Leishmania and* it is transmitted by sand-fly of genus *Phlebotomus* and *Lutzomyia* in the old and new world respectively (Georgiadou *et al.,* 2015). Leishmaniasis is among the 20 neglected diseases that largely affects people of low socioeconomic levels, mainly in developing countries (WHO, 2010).

Visceral leishmaniasis (Kala-Azar) is the most severe form of leishmaniasis and is mainly caused by *L.donovani* and *L. infantum* and is responsible for causing global severe health problem**s** in 400,000 people and death in up to 40,000 people annually (Ready *et al.,* 2014). VL is estimated to cause 1.98 million Disability Adjusted Life Years (DALYs) and is of great public health concern in low-income countries (Soosaraei *et al.,* 2018). It is reported that 90% of VL infected individuals do not develop the classical form, while a small group among the infected progress to a severe form that is unresponsive to treatment (P. L. Santos et al., 2016).

2.2 Epidemiology of Visceral leishmaniasis in Kenya

2.2.1 Parasite and vector

In Kenya, VL is caused by *L. donovani* and the main sand-fly vector is *P.martini* which breeds in termite mounds, animal burrows and in cracks of vertisols (Elnaiem, 2011). Other possible vectors identified in Northeastern Kenya include *P.celiae* and *P. vansomerenae*, both of which are associated with termite hills (Marlet *et al.,* 2003).

VL transmission in Kenya is anthroponotic and man remains the only confirmed reservoir with no animal reservoir yet identified (Mutinga *et al.,* 1989; Ready *et al.,* 2014).

2.2.2 Occurrence and Geographical distribution

In Kenya, VL is endemic in West Pokot, Baringo, Turkana, Meru, Tharaka, Isiolo, Kitui, Machakos, Wajir, Mandera, and Garissa Counties (formerly districts) (Lawyer *et al.,* 1989;Marlet *et al.,* 2003; Njau, 2010; Malaria Consortium, 2010).In Baringo 66% of the reported human cases were male and 50% were between 5–14 years of age(Tonui, 2006).

In Wajir, VL was first detected in 1935 among soldiers manning the northern border during the second world war (Ashford *et al.,* 1987). In 1998 there was an outbreak of VL reported in the Dadaab refugee camp and Wajir involving mainly nomadic people (MSF, 2011). In 2001, another outbreak occurred where a total of 904 cases were reported in Wajir, Mandera, and Dadaab refugee camps involving mainly children (Marlet *et al.,* 2003).This was attributed to severe drought in 1996 that resulted in food shortages, migration, and severe malnutrition (among children) increasing the risk of VL infection (Boussery *et al.,* 2001). More frequent outbreaks reported from September 2006 to April 2007 with 40–60 cases, then another wave between April and July 2008 that resulted in 92 cases and 7 deaths (Njau, 2010). The most recent outbreaks occurred from 2014 through 2019 with a total of 607 VL cases (MoH/FELTP VL investigation report, 2019).

2.3 Transmission

The VL infection starts with the bite of an infected female sandfly that injects parasites into a susceptible host (Ready *et al.,* 2014). Several species of animal

including Dogs, cats, rodents, mongoose, foxes, jackals, bats, primates, sheep, and other domestic animals are known to be the reservoir hosts that maintain transmission in different localities (Dereure *et al.,* 2003; Roque *et al.,* 2014; Rohousova *et al.,* 2015).

Leishmania donovani infections are restricted to sub-tropics of Asia and Africa where transmission is mainly anthroponotic (human to human transmission) while *Leishmania infantum* occurs in Latin America and Mediterranean regions where domestic dog served as the main reservoir host (Ready *et al.,* 2014).

The incubation period for VL ranges from 2 to 6 months but can be as short as 2 weeks in immunocompromised hosts (MoH, 2017).

2.4 Clinical signs

It presents with fever, anemia, hepato-splenomegally, general malaise, and wasting (Mueller et al., 2014).

2.5 Differential diagnosis for Visceral leishmaniasis

The symptoms of VL which include prolonged fever, lack of appetite, enlargement of the abdomen due to splenomegaly or hepatomegaly mimics symptoms in Malaria, Tuberculosis, brucellosis, Typhoid fever and hydatid disease (Leishmaniasis, 2014; Sunyoto et al., 2018).

2.6 Diagnosis of Visceral leishmaniasis

In Kenya, VL diagnostic procedure is outlined in MoH guideline(MoH, 2017) as follow;

2.6.1 Clinical diagnosis

This is achieved based on standard clinical cases definition: A VL suspect is any person from a VL endemic area who presents with fever for more than 2 weeks and splenomegally or weight loss AND in whom malaria has been ruled out or has not shown clinical response to effective antimalarial treatment (MoH, 2017).

2.6.2 Laboratory diagnosis

2.6.2.1 Parasitological diagnosis

A clinically suspected case can be confirmed using spleen or bone marrow aspirate. Splenic aspirates are more sensitive (95%) than aspirates of bone marrow(60–85%) (Sundar, 2002). Splenic and bone marrow aspirates are limited to hospital settings or health facilities where there is adequate equipment and trained staff to manage complications appropriately (MoH, 2017). Parasites can be identified as either amastigote in smears from tissue aspirates stained by one of the Romanowsky stains (Giemsa, Wright, or Leishman stains) and examined under oil immersion or promastigotes in culture (Sundar, 2002).

2.6.2.2 Serological diagnosis

These are immunological tests that detect antibodies against Leishmania. Serological tests include a direct agglutination test (DAT) and an Rk-39 based rapid diagnostic test (RDTs). The tests measure the serological response to surface-borne antigens of the whole *Leishmania donovani* (Hirve *et al.,* 2017).

1. rK39 Rapid Diagnostic Test (rK39-RDT)

rK39 is a cloned antigen of 39 amino acid repeats of the kinesin-like gene found in *Leishmania chagasi.* The antigen is specific for all members of *Leishmania*

donovani complex (*L.chagasi*, *L.donovani*, and *L.infantum*) and seroreactivity correlates with active disease (Amulundu, 2013).

According to MoH guideline on VL diagnosis, RDT is a rapid diagnostic test which is a serological method that relies on lateral flow immune-chromatographic test techniques.

An RK-39 based RDT is a simple, point of care test that can be used in all levels of the health care services including peripheral services to permit prompt diagnosis to initiate treatment. It is a qualitative membrane-based immunoassay for the detection of antibodies to Leishmania causing VL. It is the first test in all primary VL cases and does not require a laboratory and highly skilled technical staff. The currently available rK39 RDTs can be performed easily by health personnel with results available within 10–20 minutes. In case RDT turns negative, DAT is performed.

2. Direct Agglutination Test (DAT)

According to MoH guideline on VL diagnosis, DAT is a sensitive and specific test. It is relatively simple and can be performed under field circumstances. However, it requires training, a cold chain, and standardization. It can be performed using a dried blood spot (on filter paper) or serum.

The test is semi-quantitative and the antibody titers used at field level range from 1:100 up to 1:51200. The cut-off point for positive DAT is 1:3200 in endemic areas. It requires a well-trained laboratory technical staff to undertake the procedure over 2–3 days. It is a highly sensitive (> 95%) and specific (> 85%) test when performed according to standardized procedures. If the DAT result is borderline, the test is repeated not earlier than one week later, or a parasitological test must be performed. If the DAT result is negative another disease has to be considered.

2.7 Treatment of Visceral leishmaniasis

Globally, the main drugs available for VL treatment include systemic agents like Antimony, Amphotericin, Paromomycin, and oral Miltefosine (Moore *et al.*, 2010).

In 2010 WHO approved the use of combined therapy using intravenous Sodium Stibogluconate (SSG) and intramuscular Paromomycin (PM) as first-line treatment for all primary VL cases in Eastern Africa (Kimutai *et al.*, 2017; MoH, 2017).

In Kenya, the choice of VL treatment drug depends on efficacy and safety, patient's age, concomitant infection, availability, and cost (MoH, 2017)**.**

2.7.1 First line treatment drug

Combination therapy is the first-line treatment that is recommended by MoH against all primary VL cases in Kenya. The combined therapy involves: Sodium Stibogluconate (SSG) at 20 mg/kg per day intramuscularly or intravenously plus Paromomycin(PM), 15 mg [11 mg base] per kg body weight per day intramuscularly, for 17 days (Kimutai *et al.*, 2017).

Health facilities in endemic areas are allowed to use Sodium Stibogluconate (SSG) alone as a monotherapy in situations where Paromomycin (PM) is not available or is contraindicated due to ototoxicity, injection site pain, and raised liver enzymes (Moore *et al.*, 2010). The treatment as monotherapy is SSG 20 mg/kg per day intramuscularly or intravenously for 30 days.

Use of SSG can be withdrawn during treatments (when used either as combination or as monotherapy) due to severe and sometimes life-threatening adverse side effects such as acute pancreatitis, aberration of creatinine, jaundice, high liver function test (LFT) values of >5x normal values, cardiac toxicity (arrhythmia, prolonged

electrocardiographic rate), low white blood cell counts and uninterrupted vomiting (MoH, 2017; Chappuis *et al.,* 2007).

According to a pharmacovigilance study conducted in East Africa (Uganda, Kenya, Ethiopia, and Sudan), involving 3126 VL patients, the combined SSG and PM resulted in an overall SADEs rate of 1.9% (60/3126) and the most common SADEs were infections, a blood disorder, gastrointestinal disorder and ear and labyrinth disorder (Kimutai *et al.,* 2017). Similarly, in a retrospective cohort study on the use of SSG and PM as routine treatment in eastern Sudan, 4% (33/809) of the patients discontinued their treatment mainly due to side effects such as hearing problems, jaundice, and severe anaemia (Atia *et al.*, 2015).

2.7.2 Second line treatment drug

Liposomal amphotericin B (Ambisome) is used in treating pregnant women, severely ill patients, children <2 years, adults older than 45 years, VL-HIV co-infected patients, lack of response or contraindication to SSG or PM treatment (MoH, 2017). The recommended dose in Kenya is 3–5mg/kg body weight per daily dose by infusion given over 6–10 days up to a total dose of 30 mg/kg. Side effects are rare but it may result in fever, chills, low backache, hypokalemia transient nephrotoxicity, and anaphylactic reactions (Lockwood *et al.,* 2010). Liposomal Amphotericin B (Ambisome) was reported to be less effective in treating VL relapse cases than primary VL cases. This was shown in a retrospective study conducted in Ethiopia where its use in 79 HIV positive relapse VL cases resulted in a 38% initial cure rate as compared to its use in 116 HIV positive primary VL cases where it resulted in a 74% cure rate (Ritmeijer *et al.,* 2011).

2.8 Treatment outcome for Visceral leishmaniasis

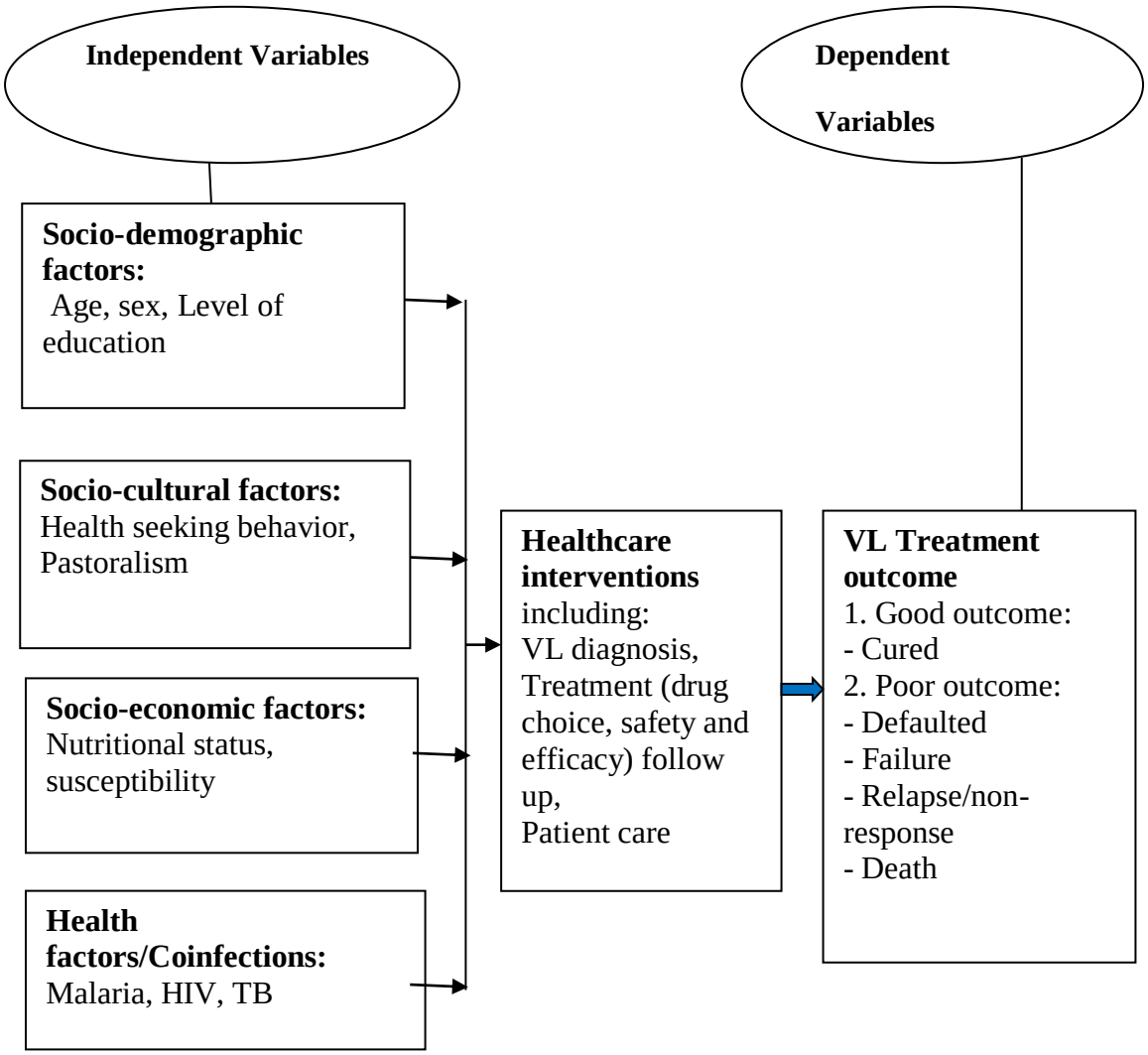
VL treatment can be achieved with various outcomes, mainly; cure, relapse, death during treatment, and or discontinuation or default during treatment (Collin *et al.*, 2004). However, treatment outcomes are dependent on prevailing factors such as socio-demographic, socio-economic, and socio-cultural, and health-related factors such as the severity of the disease and the presence of co-infections. This was shown in various studies.

In Muzaffarpur district, India, a hospital-based case-control study on risk factors associated with defaulting VL treatment (using SSG and Miltefosine), reported a 16.3%(89/544) treatment defaults (Kansal *et al.,* 2017). This, according to the study was attributed to a patient seeking a second opinion and preferring to be treated in specialized VL treatment centres. In Georgia, a retrospective study on risk factors for VL relapse among 300 patients treated using SSG reported a delayed diagnosis of >90days, Hb level of <60g/l, and age of <1 year as significant factors associated with the VL relapse (Kajaia *et al.,* 2011).

In South Sudan, a retrospective hospital-based study on VL risk factors and trends involving 8800 primary VL and 621 relapse cases, reported an increased risk of relapse following VL treatment. The study found that 17 day SSG/PM combination therapy was associated with two-fold higher odds of relapse than 30 day SSG alone (Gorski *et al.,* 2010).In northwestern Ethiopia, a retrospective review of 241 VL patients' records reported 92(38%) cases of HIV-VL coinfection. This resulted in an increased odds of death and treatment failure by about five and nine times respectively (Hurissa *et al.,* 2010).

2.9 Conceptual Framework

VL treatment outcome is influenced by the interaction between independent variables such as socio-demographic, socio-cultural, socio-economic, and co-infections and healthcare interventions such as diagnosis, choice of drugs, and follow-up after treatment.



2.10 Factors Associated with Visceral leishmaniasis treatment outcome

2.10.1 Socio-demographic factors

2.10.1.1 Age

In a pharmacovigilance (PV) prospective cohort study on safety and efficacy of SSG and PM conducted in East Africa (Kenya, Ethiopia, and Sudan) involving 3126 VL patients, age was found to affect the outcome. Age of <35 years was significantly associated with higher initial cure and lower death rate compared to ≥35 age group (Kimutai et al., 2017). In Sudan, a retrospective health facility-based study that involved 3076 VL patients (treated using SSG), reported a four times greater risk for death among age group ≥45 years old (Seaman, 1996).

A retrospective study on determinants of adverse outcome of Kala-Azar among 3365 VL patients in South Sudan reported age of ≥45 years and <2 years as a risk factor for death among adults and children respectively (Collin *et al.,* 2004). Similarly, a retrospective VL treatment data analysis study involving 3483 VL patients in Eastern Uganda reported the main risk factor for in-hospital deaths as being aged <6 and >15 years with a strikingly higher case fatality of up to 29% in >45 years of age (Mueller et al., 2014b).

In Peru where a case-control study on risk factors for pentavalent antimonial (SSG) treatment failure indicated that young age of <16 years as a strong predictor for treatment failure (Llanos-Cuentas *et al.,* 2008). In Bihar India, an observational retrospective cohort study on risk factors for relapse involving 8749 VL patients treated using Liposomal Amphotericin B(Ambisome) found the age of <5 and ≥45 years as a statistically significant factor in VL relapse (Burza *et al.,* 2014).

2.10.1.2 Gender

In a retrospective study on the determinant of adverse outcomes among 3365 VL patients in South Sudan, gender significantly affected the outcome of treatment. The study identified Vomiting as an independent factor with an increased odds of death, conversely, among patients aged 16 – 24 years and 25 – 34 years, Female subjects were almost three times more likely to experience vomiting than male patients (Collin *et al.,* 2004).

In Bihar India, an observational retrospective cohort study on risk for VL relapse found a statistically significant association between male gender and relapse (Burza *et al.,* 2014). Also, another hospital-based case-control study in the same area on risk

factors associated with defaulting from VL treatments, more than half (50.6%) of 87 defaulter cases were women (Kansal *et al.,* 2017).

2.10.1 3 Level of education

A cross-sectional study on the prevalence of malnutrition and associated risk factors among 403 VL patients in Northwest Ethiopia, indicated that 73% of the adult VL patients were illiterate (Mengesha *et al.*, 2014).

Similarly, in Bihar India, a case-control study on risk factors for VL treatment default reported 49.3% (43/87) of VL treatment defaulters as illiterate (Kansal *et al.*, 2017). In Gadaref state, Sudan, an unmatched case-control study involving 198 cases and 801 controls, reported illiteracy as one of the determinants of VL occurrence (Nackers *et al.*, 2015).

2.10.2 Socio-cultural factors

2.10.2.1 Nomadic-pastoralism and cross-border migration

Nomadic pastoralism involves movement with livestock from place to place in search of mainly pasture and water. VL epidemics are often associated with occupational exposures and movement of none immune people into pre-existing transmission cycles (WHO, 2018; Argaw et al., 2013).

Cross-border migration due to civil unrest is reported to result in VL epidemics. This was shown in South Sudan where VL epidemics that occurred in 1983, 2005, and 2014 was strongly linked to naïve migrants who entered VL endemic areas following civil unrests (Al-Salem *et al.*, 2016).

In Sudan, the VL situation and gap analysis report cited various VL outbreaks concerning the migration of nomadic pastoralists (Malaria Consortium, 2010). For

example; a major VL outbreak was reported to have occurred in the unity state of Southern Sudan between 1984 and 1994 which may have been triggered by pastoralists from the Blue Nile. In 1990 and 1991, 200 patients were diagnosed with VL following importation from Bentiu area of unity state into Kordofan state. In 1994, another outbreak was reported following the return of people from food distribution in Barbar El-Fugara village which is a VL endemic zone of the Al-Qadarif region of eastern Sudan (Sunyoto *et al.,* 2018).

In Kenya, VL spatial clustering and an epidemiological study conducted among agro-pastoral communities in Parkarin and Loboi villages of Baringo attributed the introduction of VL to the area by nomadic Turkanas from the North (Ryan et al., 2006b).

2.10.2.2 Health Seeking Behavior (HSB)

Preference for alternative treatment influences health seeking behavior, especially among pastoralists where health facilities are inadequate. This was shown in a cross-sectional risk factor study involving 341 respondents that were carried out in Turkana Kenya where 58% of the Kala-Azar cases resorted to traditional healers, applied cow dung, or made an incision to the affected area (Lotukoi *et al.*, 2017).

In Bihar India, a cross-sectional survey conducted among 120 PKDL patients on health seeking behavior revealed a delay to the first medical consultation (patient delay) from 15 days to 5475 days (15 years). Poor PKDL knowledge, type of lesion, and distance to the Primary healthcare were significantly associated with the patient delay (Garapati *et al.,* 2018).

In another cross-sectional study on health seeking behavior of 200 PKDL patients in India, the patient delay ranged from 10 days to 4745 days (13 years). This was significantly associated with the patient's age, education, occupation, and residential status (Basher *et al.,* 2013).

2.10.3 Socio-economic factors

2.10.3.1 Poverty

The occurrence of VL is more prevalent among the poor with low socio-economic status. In East Africa, low socio-economic status was found to increase the risk of VL occurrence (Kolaczinski *et al.,* 2009). A similar study in India showed 84% of the VL cases had a very low standard of living (SIDDIQUE *et al.,* 2018). This leads to malnutrition, poor housing conditions, lack of preventive measures, and illiteracy.

Poverty can be reflected in housing quality and this was shown in a systematic review of 103 studies on housing and Leishmaniasis in Lima Peru. The study reported that mud-walled houses with cracks and holes, provide favorable conditions for sandfly breeding and resting (Calderon-Anyosa, *et al.,* 2018). Similarly, in a case-control study in north-western Ethiopia on risk factors for VL, people living in a cracked wall houses were six times more likely to be infected with VL (Yared *et al.,* 2014).

Poverty is also associated with poor nutrition and this was found to increase the risk of VL progression to clinically manifested disease (Alvar *et al.,* 2006).

A review article on the social and economic burden of VL, diagnosis, and treatment of VL in endemic areas put a huge financial strain on families with consequences of delay in seeking treatment thus influencing outcome (Okwor *et al.*,2016). A retrospective study on access to VL treatment in Bihar, India, showed that lower caste

with VL had significantly delayed access to treatment and with poorer indicators at admission (Pascual *et al.,* 2012).

2.10.3.2 Malnutrition

Malnutrition is the cellular imbalance between the supply of nutrients and energy and the body's demand for them to ensure growth, maintenance, and specific functions (Atassi, 2019).

A study on protein-energy malnutrition (PEM) as a risk factor for VL infection indicates that malnutrition impairs elements of adaptive innate immunity increasing susceptibility and progression of VL (Malafaia, 2009).

According to the WHO VL fact sheet, poor protein-energy, lack of iron, vitamin A and zinc increase the risk of progression to clinically manifest VL infection (WHO, 2010).In north-western Ethiopia, a facility-based case-control study on factors associated with VL infection showed that 44% (48/109) of VL cases were malnourished and that malnutrition was significantly associated with VL infection (Bantie *et al.,* 2014).

In Brazil, a hospital-based retrospective study that involved 250 VL patients showed malnutrition as an indicator for VL poor prognosis (Braga *et al.,* 2013). Similarly, in north west Ethiopia, an institutional-based cross-sectional study on the nutritional status of 379 adult VL patients reported 74% (280/379) of them being undernourished (Weldeabezgi *et al.,* 2017) In a similar study in Ethiopia, the magnitude of malnutrition among VL patients was found to be 74% (Weldeabezgi *et al.,* 2017).

Among VL patients in Southern Sudan, there was an increased risk of death among adults with body mass index (BMI) <13 and in children with medium height for

weight less than 60% (Collin et al., 2004). Malnutrition was also cited as one of the markers of poor prognosis in VL cases (Elinor *et al.,* 2013).

2.10.4 Healthcare interventions

2.10.4.1 Delay in VL Diagnosis

Delay in VL diagnosis can allow rapid progression of the disease worsening the prognosis. Delay can be a patient delay (the time between symptoms and first medical consultation) or system delay (the time between first medical consultations to start of treatment) (Garapati *et al.,* 2018).

In pastoral and rural communities where health facilities and or knowledge on the need for early diagnosis are limited, the patient delay was shown to affect treatment outcomes. This has been shown in northwestern Ethiopia where VL patients who were admitted to a treatment centre with a delay of ≥29 days were found to be four times more likely to develop poor treatment outcomes(Welay *et al.,* 2016). In Georgia, delay in diagnosis of VL was attributed to a relapse rate of up to 7% following VL treatment(Kajaia *et al.,* 2011).

In a cross-sectional study on the health-seeking behavior of 200 PKDL patients in India, the system delay ranged from 0 days to 1971 days (5.4 years). This was significantly associated with the patient educational status, occupation, number of treatment providers, and first healthcare provider (Basher *et al.,* 2013).

In another study in Bihar, India, it was found that defaulting was significantly associated with place of treatment. This was attributed to differences in functioning and care provided at individual Health facilities (Kansal *et al.,* 2017).

The effect of delay in diagnosis and treatment outcome has also been reported in South Sudan (Collin *et al.,* 2004) and Peru (Llanos-Cuentas *et al.,* 2008). The cause of delay in seeking conventional treatment was also been explored in Bihar, India where 81% of VL patients were found to seek treatment from unqualified private practitioners (Hasker *et al., 2010)*.

2.10.4.2 Choice of VL treatment drugs

Chemotherapy remains the best means to cure VL and Pentavalent antimonials are the drugs of choice for treatment of VL since 1920 (Ponte-Sucre *et al.*, 2017). In Kenya, according to MoH and WHO VL guideline, Sodium stibogluconate (SSG) and Paromomycin (PM) are first-line drugs of choice while Liposomal amphotericin B (Ambisome) is considered as second-line in case of children < 2 years of age and pregnant mothers(MoH, 2017).

According to a pharmacovigilance study in East Africa, SSG and PM have an initial cure rate of 95.1% but associated with at least one adverse effect (AE) in 34% of patients (Kimutai *et al.*, 2017). In Sudan following the use of SSG and PM, 4% of the patients discontinued treatment due to drug side effects (Atia *et al.,* 2015).

In eastern Uganda, the in-hospital case fatality rate of 3.7% was reported following the use of pentavalent antimonials (SSG) and the main risk factors for in-hospital death include drug-related adverse events (Mueller *et al.,* 2009).

2.10.4.3 VL drug resistance

Besides the treatment drug-related factors, drug resistance remains the fundamental determinant of treatment failures. For example, in the Bihar district of India, the treatment failure rate of up to 65% was reported in the use of pentavalent antimonial compounds like SSG (Sundar, 2010). This was attributed to sub-therapeutic doses,

incomplete duration of treatment, and use of sub-standard drugs. Based on the findings, the use of antimonials is largely suspended in the Indian sub-continent (ISC). On the other hand, a clinical trial in East Africa in the Use of paromomycin at 15mg/kg was reported to have shown an efficacy rate of <50% making it unsuitable as monotherapy (Croft *et al.*,2011). Similarly, in Northwestern Ethiopia, use of antimonial drugs was attributed to treatment failures that resulted in a 6% poor treatment outcome (Welay *et al.,* 2016).

2.10.5 Co-infections

VL is a chronic infection that results in immunological dysfunction which may predispose a patient to co-infections. The common VL-coinfections include HIV, malaria, and TB (MoH, 2017).

2.10.5.1 Co-infection with HIV

In the Mediterranean region, Kala-Azar co-infection with HIV may manifest without typical splenomegally but commonly with atypical organ involvement such as of lungs and gastro-intestinal system (Norman *et al.,* 2014). The HIV co-infection with Kala-Azar is thought to cause immunological imbalances that may lead to deterioration of patient condition worsening the progression and thereby increasing the risk of treatment failure.

This has been shown in northwestern Ethiopia where 38% of HIV co-infection with Kala-Azar and was associated with 31.5% of treatment failure (Hurissa et al., 2010). The same study showed that VL relapsed in 36.8% of HIV positive cases. In another study, mortality and relapse rate for patients known to be HIV positive were 18.1% and 16.1% respectively (*Burza et al.*, 2014).

The cure rate among HIV-VL co-infected patients is low compared to non-HIV-positive patients. This was shown in northern Ethiopia where the cure rate among HIV-positive patients was 16% in primary VL and 58% in relapsed cases (Ritmeijer *et al.,* 2011).

2.10.5.2 Co-infection with Malaria

Malaria is regarded as one of the main differentials diagnoses for Kala-Azar, especially in tropics and sub-tropics where malaria is also endemic.

In northwestern Ethiopia a prevalence of 4.2% co-infection of VL with malaria was reported (Ferede *et al.,* 2017). In Uganda a prevalence of VL co-infection with Malaria was 21% and this was found to be a contributing factor to mortality during treatment (Mueller *et al.,* 2009).

2.10.5.3 Co-infection with TB

A case study in southern Sudan suggested the increasing nature of co-infections between TB and parasitic diseases especially in developing countries. It indicated that co-infection can occur and TB as immunosuppressive can allow quick progression of VL and on gthe other hand VL can reactivate latent TB (Shweta *et al.,* 2014). Concomitant TB-VL infection was seen in 27% of HIV positive and 6% HIV negative VL patients and were four times likely to have treatment failures (Hurissa *et al.,* 2010).

CHAPTER THREE

METHODOLOGY

3.1 Study Area

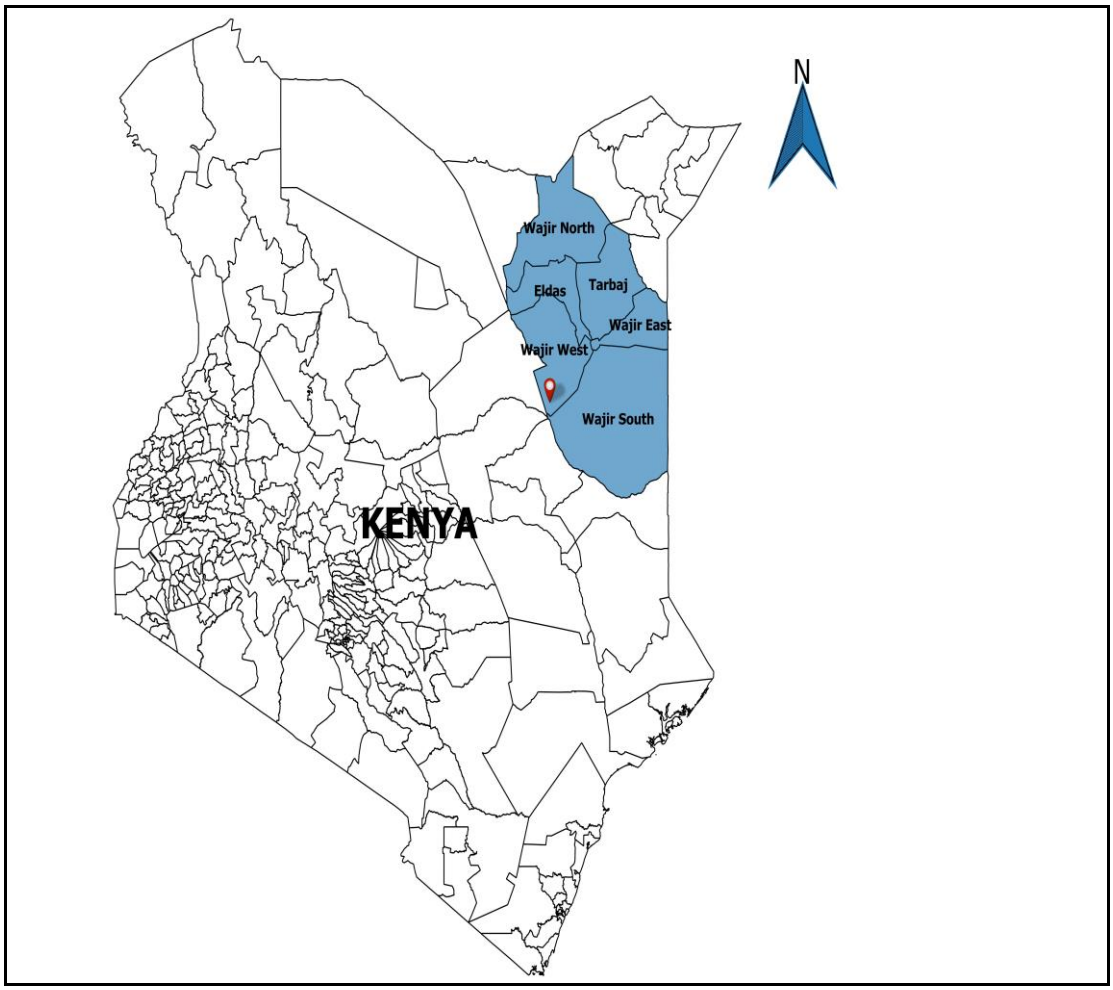


Figure 1: Map Showing study area, Wajir County
Source: QGIS version 2.18.14)

Wajir County is located in the northeastern region of Kenya and is in the arid and semi-arid ecological zone (IV—V). It covers an area of 56,685 Km2 and as per the 2019 population census, its general population is 781,263 (KNBS, 2019). The County has six sub-counties namely Wajir East, Tarbaj, Wajir West, Eldas, Wajir North, and Wajir South. The study was conducted in Wajir West. The sub-county has a population of 121,828 as of 2019 and covers an area of 9,044 square kilometers

(KNBS, 2019). Over ninety percent of the population keep livestock and practice pastoral nomadism.

The Sub-county borders Isiolo County to the West and Garissa County to the South-east. It lies in the western arid lowlands of Wajir County and receives an annual rainfall of 150–300mm. It is characterized by black cotton soil, grasslands, acacia trees, shrubs, and termite mounds that provide habitat for sandflies which has led to the high burden of visceral leishmaniasis (Njau, 2010). It has a harsh climate that is hot and dry most of the year with mean annual temperatures of 31◦C. The sub-county is divided into four wards and it has a total of eighteen public and four private health facilities.

3.2 Study Design

This was a cross-sectional hospital-based mixed-method study that had two phases where both quantitative and qualitative data were collected.

3.3 Target Population

The target population was VL suspected patients in Wajir West sub-county, Wajir County.

3.4 Study Population

The study population was patients who were initiated on VL treatment at Giriftu sub-county hospital, Arbajahan health centre, and Athibohol dispensary anytime from January 2017 to October 2019.

The key informants were healthcare workers specifically; clinicians, nurses, laboratory technologists, and surveillance officers who were directly involved in the diagnosis or treatment of VL patients.

The FGD respondents were community health volunteers who are part of the community unit of the target facility. They are involved in routine linking of the local community with the Health facility and engaged in activities like defaulter tracing for vaccination programs.

3.5 Sampling Technique and Sample Size

3.5.1 Sample size calculation

From literature reviews, no documented study was found that had been done in Kenya to assess factors associated with VL treatment outcome. A retrospective hospital-based study on VL treatment outcome in northwest Ethiopia was identified as the basis for sample size calculation.

To estimate the sample size, Cochran's formula (1977) was used

Sample size, $\mathbf{n= Z^2p\ (1\text{-}p)/d^2}$

n= desired sample size

p= estimated prevalence of cure rate among VL patients: 84.6% (Hurissa *et al.,* 2010)

z= statistic for a level of confidence (The standard normal deviation at the required 95% confidence level = 1.96）

d= desired level of precision (5%)

The minimum sample was $[1.96*1.96*(1\text{-}0.85)*0.85]/0.05^2$

Based on the calculations, the minimum sample size was 195 VL case records.

3.5.2 Sampling procedure for quantitative data

The study was conducted at three health facilities in Wajir West sub-county. A visit was made to all three facilities to identify VL treatment records, incomplete records were excluded, data was abstracted and captured on notebooks. A total of 228 complete VL treatment records were identified: Giriftu sub-county hospital (160

records), Arbajahan health centre (62 records), and Athibohol dispensary (6records). Proportionate to the number of complete records, the 195 desired sample records were distributed among the three facilities. At the facility, the list of complete records (sampling frame) were subjected to simple random sampling to identify records for review.

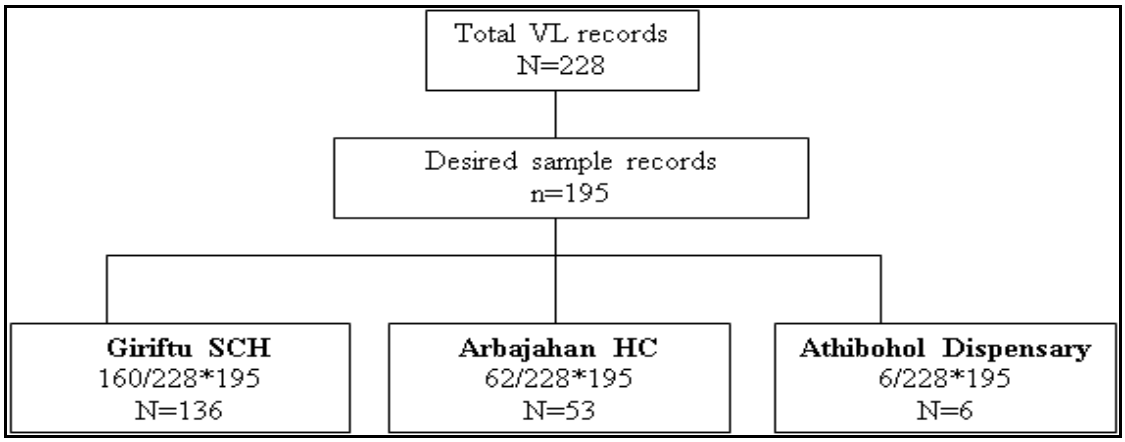


Figure 2: Sampling flow for VL records

3.5.3 Sampling procedure for Qualitative data

Healthcare workers were purposively sampled based on their role in VL surveillance, diagnosis, and management. Using duty roster as a sampling frame, a total of eight (8) healthcare workers (HCW) were identified and they included two clinicians, three nurses, two lab technologist, and a surveillance officer.

Community Health Volunteers (CHVs) were sampled from a register(sampling frame) at community unit of the target health facilities. Each community unit comprised 17 CHVs of mixed gender. The CHV list from each unit was stratified into two groups based on gender. Each stratum was then subjected to simple random sampling using excel random number generator and at the end, a total of 7 male and 7 female members were selected from each of the three facilities (42 respondents).

3.6 Inclusion and exclusion criteria

3.6.1 Inclusion and exclusion criteria for Quantitative data

This study included patients who were initiated on VL treatment at Giriftu sub-county hospital, Arbajahan health centre, and Athibohol dispensary between January 2017 and October 2019.

Excluded from this study were; VL patients who were transferred from target Health facilities to other facilities for advanced treatment, those patients with incomplete records (treatment outcome).

3.6.2 Inclusion and exclusion criteria for Qualitative data

Included were respondents such as HCWs who were involved in VL patient care through routine laboratory and clinical management of VL patients and CHVs who were registered with the target facility as part of the community unit.

Excluded were those HCWs who were not directly involved in VL patient care and unregistered CHVs.

3.7 Study Period

This study was undertaken over a period of one month starting from June 22nd to July 25th 2020. This coincided with containment period for Covid-19 and dry season of the year.

3.8 Study Procedure

Data were collected by the principal investigator and two research assistants. The research assistants were recruited based on their training. One was public health officer and the other was a community health extension worker.

The principal investigator trained the research assistants on the study objectives, inclusion-exclusion criteria, respondent recruitment process, how to obtain consent from study participants, ethical issues, and the entire process of data collection.

At the start of the study, the officer in-charge of the health facility was briefed on research objectives and permission sought to proceed with data collection.

3.9 Baseline survey

A pilot study was conducted one week before actual data collection at Garsenqoftu dispensary. This was to pretest the electronic-based data abstraction tool, paper-based FGD, and KII interview question guides. The participants were recruited and consent was obtained for participation. For quantitative data, random selection was done for twenty treatment forms out of twenty-eight available forms. For KII, the nurse on-duty was identified and for the FGD, two female and four male members of CHVs were identified.

1. Limitations of study tools and challenges during Baseline survey

During data abstraction, the electronic-based data abstraction tool was not able to pick the age in months and decimals in Hb level.

A section like the village of VL exposure where the patient got infected was also missing.

During the FGD, female respondents were less interactive and requested the need to have a separate meeting from that of males for purpose of having more interactive discussions and in compliance with their Islamic beliefs.

2. Changes adopted from Baseline survey

Before actual data collection, corrections and additions (village of VL exposure) were made to the electronic-based data abstraction tool.

A suitable FGD seating plan was drawn (Sketched) and a separate male-female session approach was adopted.

3.10 Data Collection

3.10.1 Data collection tool for quantitative data

An Epi-info software-based standardized data abstraction tool (Appendix A) was used to collect VL data from treatment forms. A trained research assistant reviewed the VL treatment forms and extracted the VL patient data. Each entry was given a unique identifying number and the data was later uploaded onto an excel database for analysis. In addition to treatment data, the tool was also used in collecting Global Positioning System (GPS) coordinates of the visited facilities.

3.10.2 Data collection tool for Qualitative data

1. **Key informant interview (KII) guide**

KII question guide was used to collect health information from HCWs. The questions covered three main aspects of routine health service practice towards VL management and they include; VL diagnosis, treatment, and patient care (Appendix B). A face to face interviews were conducted with each respondent at his or her office and the responses were captured verbatim using a notebook. Each interview took 45 minutes and at the end, a total of two clinicians, three nurses, two laboratory technologists, and one surveillance officer were interviewed.

2. Focus Group Discussion (FGD)

FGD question guide was used to collect information from CHVs. The questions covered socio-cultural (thematic areas; nomadic pastoralism and health seeking behavior) and socio-economic (thematic areas; poverty and malnutrition) issues that are known to influence VL susceptibility and treatment outcome (Appendix C). At each facility, a separate session was conducted for seven male and seven female members taking into consideration the Islamic culture of the respondents (mixing of the gender is a taboo) and minimizing dominance by the male gender. All the sessions were conducted at the patient waiting area of the target facilities and each session lasted 90 minutes. During the sessions, the participants were seated in a hollow square seating arrangement (Appendix E) maintaining adequate social distance. This style was adopted for all the sessions to allow unimpeded interaction between the moderator and the group and also between the group members. Each session was moderated by an experienced public health officer and data was captured verbatim using a notebook and mobile phone-based voice recorder. In the end, a total of 42 CHVs were interviewed with a male to female ratio of 1:1

3.10.3 Variables

The variables collected using standardized data abstraction tool included;

Independent variables: patient identity number, age, sex, occupation, level of education, residence, duration of sickness, weight, height, pregnancy status (for women), type of patient (relapse or primary), mode of VL diagnosis (clinical or serological), comorbidities, concomitant infections, Hb level, date of symptom onset, Village of exposure, date of diagnosis, the start date of treatment, duration of treatment, treatment drugs, and adverse events.

Dependent variables: cured (good outcome) and death (poor outcome) were recorded to evaluate the initial End of treatment (EoT) outcome.

GPS coordinates captured included**:** Latitude and Longitude of the visited facilities.

The variables captured using the Key informant question guide under thematic areas include respondents' knowledge towards; VL diagnostic procedures, recommended VL treatment drugs, treatment precautions, and nutritional care.

The variables captured using the FGD question guide under the thematic areas include factors associated with; nomadic pastoralism, health seeking behavior, poverty, and malnutrition.

3.11 Data Management and Analysis

3.11.1 Data entry

All the data from VL treatment forms were abstracted into an electronic (Tablet) based standardized data abstraction tool. Each record was given unique identity, and saved without the patient's name. After every twenty entries, the principal investigator (PI) verified the abstracted data for completeness and errors before marking VL treatment forms to avoid double entry. After all the entries were made, the data was synched with the original template on the principal investigator's personal computer for storage and analysis.

KII verbatim notes taken during the face-to-face interview were transcribed and organized into themes using Microsoft word 2010. The information was then stored under a password on PI's personal computer for analysis.

FGD verbatim and audio recordings were transcribed and organized into themes using Microsoft word 2010 and stored under a password on PI's personal computer for analysis.

3.11.2 Data Analysis

Quantitative data was cleaned using Ms. Excel (Microsoft, One Microsoft Way, Redmond, Washington, U.S. 2010) and data analysis was carried out using Epi info version 7(Centers for Disease Control and Prevention, Atlanta, GA, USA) software. Descriptive analyses were performed for continuous variables while counts and frequencies for categorical variables. Association between clinical or demographic factors and VL treatment outcome was analyzed using bivariate analysis. Odds ratio (OR) with 95% confidence intervals (CI) were reported.

Pearson's chi`-square test was used as a statistical test of significance and a P-value of <0.05 was considered statistically significant**.** Exposures of interest included age, duration before diagnosis, concomitant infections, adverse drug events, anemia, and malnutrition.

Multivariate analysis was carried out to identify independent factors associated with VL treatment outcome using a stepwise forward selection **a**pproach in which variables with a p-value of ≤0.20 at bivariate were included.

The final model included all the variables and only those with a P-value of ≤0.05 were considered significant.

GPS coordinates in the CSV file were uploaded into Quantum Geographic Information System (QGIS) software version 2.18.14 and a map of the visited sites was generated superimposed on the Kenyan County's map (Figure 3).

Qualitative data were analyzed using NVIVO software. Data obtained through KII were coded and every response was grouped and summarized under three thematic areas of VL diagnosis, treatment, and patient care.

Information obtained through FGD were coded and every response was grouped and summarized under four thematic areas; nomadic pastoralism, health seeking behavior, malnutrition, and poverty.

3.11.3 Data presentation

The findings from this study were prepared and summarized in prose, frequency tables' bar graphs, and geocode maps.

3.12 Ethical Consideration

3.12.1 Ethical approval

At Moi University School of Public Health, the concept to carry out this study was reviewed and approved.

The draft proposal was then subjected to ethical reviews and approved by Moi University's Institutional Review and Ethics Committee (IREC) (Appendix F).

The IREC approved document was then submitted to National Commission for Science, Technology, and Innovation (NACOSTI) which issued a research license (Appendix G). Before commencement of the field study, permission was obtained in writing from the County director for health in Wajir County.

At the start of the study, the Principal Investigator (PI) met with officers' in-charge of each health facility, introduced the research objectives, and was granted access.

Each study participant was informed of the study purpose and provided with informed consent (Appendix D). The consent was in English and translation into local Somali was done for community health volunteers. There was no cost or inducements and the participants were given the liberty to take part or withdraw without fear of penalty. To protect the participants' identity, no names were included in the data collection, unique identifiers were used instead. Participants were assured that their information

will be kept confidential and the result will be disseminated or published without revealing their identity.

All the abstracted data collected using the standardized abstraction tool and the transcribed information from question guides of KII and FGD were stored in a zip folder on PI's personal computer. The data is also backed up on a hard drive with password protection. The analyzed data and reports generated thereof were also stored in the same folders and backed up on the same hard drive. The data and backups were accessible only to the principal investigator.

3.13 Dissemination of Study Findings

Report from this study will upon approval by the supervisors be shared with the County Department of Health, Wajir County. The dissemination will also be done through the presentation in thesis defense and publication journals

CHAPTER FOUR

RESULT

4.1 Characterization of Visceral leishmaniasis (VL) cases

4.1.1 Socio- demographic characteristics

A total of three public health facilities were visited namely; Athibohol Dispensary hospital (catchment population, 10,000).Arbajahan health centre (catchment population, 11,000**),** and Giriftu sub-county hospital (catchment population, 16000). The three facilities provide diagnosis and treatment services for VL patients (Figure 3).

A total of 195 VL patient records were included in the analysis. The median age was 2.5 years with an interquartile range of 3.8 years, more than half of them (135, 69.2%) were <5 years of age, and male were 111(56.9%). The majority 178(91.3%) were residents of the Wajir West sub-county and only 17(8.7%) were cases from neighbouring sub-counties (Table 1). Among the 21 adolescent VL cases (>10 years of age), herders formed the highest proportion with 15(71.4%) cases.

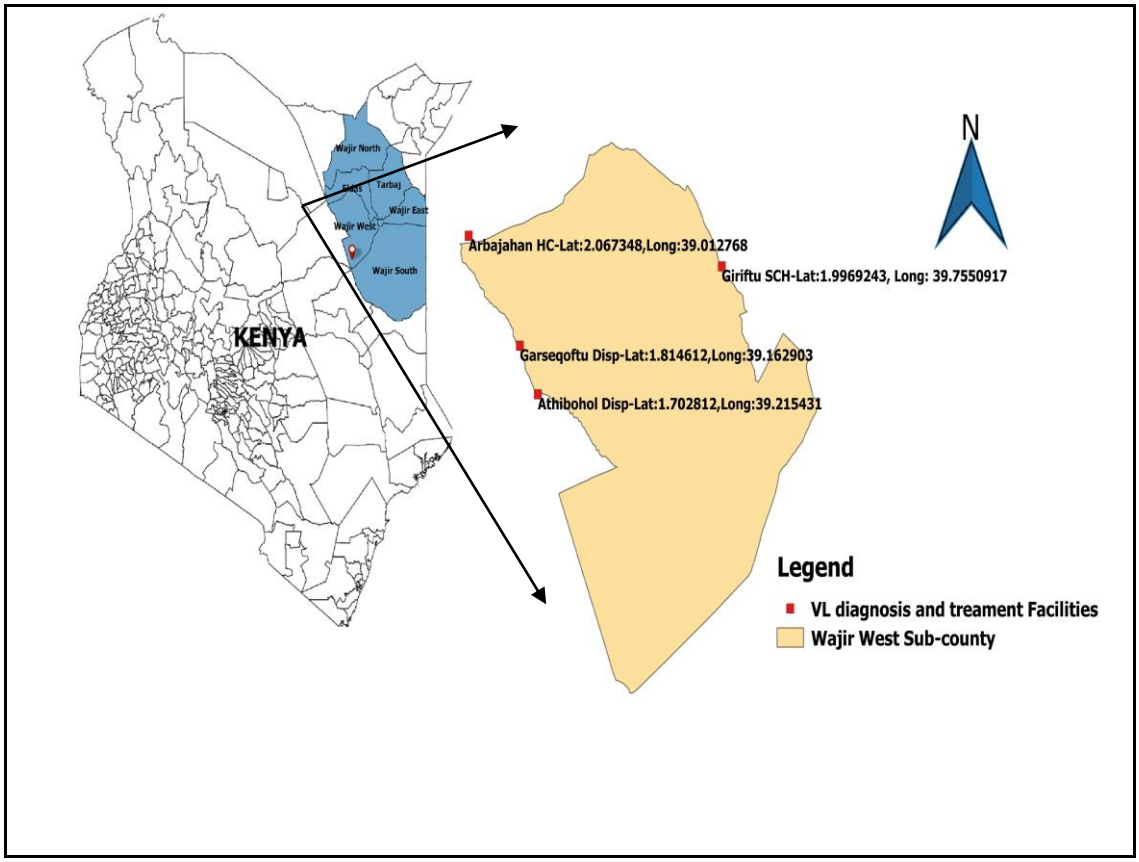


Figure 3: Map of health facilities and their relative location

Table 1: Socio-demographic characteristics of VL patients (n=195)

Characteristics	Frequency	%
Age		
<5	135	69.2
5 – 14	50	25.7
≥15	10	5.1
Gender		
Male	111	56.9
Female	84	43.1
Level of Education		
None	190	97.4
Primary incomplete	4	2.1
Primary complete	1	0.5
Occupation		
Child	174	89.2
Animal herder	15	7.7
House-wife	1	0.5
Student	5	2.6
Sub-county of residence		
Wajir west	178	91.3
Eldas	17	8.7

4.1.2 Laboratory characteristics

All VL suspected patients were first diagnosed based on clinical case definition then subjected to RDT and or DAT tests depending on the availability of the test kits. Among the 195 suspected VL patients, 167(85.6%) tested positive on RDT, 8(4.1%) tested positive on DAT, and 20(10.3%) diagnosed based on clinical case definition (Figure 4).

Based on diagnosis, patients were categorized as either primary VL or relapse (Table 2). Diagnosis for suspected relapse cases involves the use of parasitological analysis of splenic aspirates. However, none of the health facilities did the splenic aspiration and therefore solely relied on clinical symptoms and history of previous treatment. In addition to VL diagnosis, Laboratory samples were also analyzed for Hb level, and presence of comorbidities or co-infections with HIV, Malaria, and tuberculosis (TB). Among all the suspected VL cases, 178(91.3%) had their Hb level checked and the mean Hb was 7.5g/dl with a standard deviation (SD) of ± 2.3g/dl. None of the tested patients turned positive for HIV, Malaria, and TB

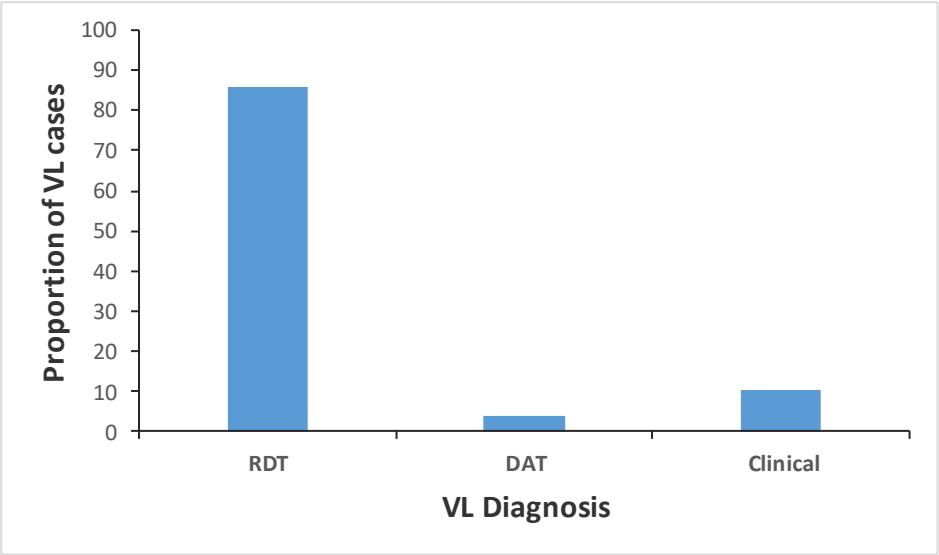


Figure 4: Proportion of VL cases by Lab. result, Wajir West sub-county.

Table 2: Laboratory characteristics of VL patients by Hb level and VL category

Laboratory Characteristics	Frequency	Percent
Patient category		
Primary VL	192	98.5
Relapse	3	1.5
Hemoglobin Level		
Severe <5g/dl	35	19.7
Mild/Moderate 5-9g/dl	88	49.4
Normal >9g/dl	55	30.9

4.1.3 Clinical characteristics

The time between VL symptoms onset to hospital diagnosis (Patient delay) ranged from 3 to 97 days, with a median of 22 days. The time between diagnoses to the start of VL treatment (System delay) ranged from 0 to 31 days with a median of 1 day**.** The main clinical signs and symptoms included fever (98%), abdominal pain (77%), and splenomegally (52%) (Table 3). The mean hospital stay period during treatment was 18.4±5.9 days. Co-morbidities were severe anemia (Hb<5g/dl) and severe malnutrition

4.2 Visceral leishmaniasis treatment and initial outcomes

Overall, a good outcome (cured) was achieved in 183(93.8%) patients **(**Table 4**).** There were nine deaths by end of treatment giving case fatality rate of 4.6%. Three patients (1.5%) were categorized as relapse cases (excluded from the initial outcome). The highest proportion of cases (77.9%) was treated using SSG and PM. The overall treatment compliance was 100% with no defaulters to the standard course of VL drugs. The common ADEs were jaundice, renal complications, and bleeding. Of the 12 ADEs, 9(75%) occurred following SSG/PM, while the rest in Pentosam (SSG).

Table 3: Clinical profiles of VL patients (n=195)

Characteristics	Frequency	Percent
Patient status		
Inpatient	143	73.3
Outpatient	52	26.7
VL onset to diagnosis(patient delay)		
<14 days	25	12.8
14 to 28 days	90	46.2
≥29 days	80	41.0
Diagnosis to treatment(system delay)		
0 to 1 day	163	83.6
1 to 7 days	21	10.8
>7 days	11	5.6
Clinical signs and symptoms		
Fever	191	97.9
Abdominal pain	151	77.4
Splenomegally	101	51.8
Hepatomegally	16	8.2
Fever + Abdominal pain	150	76.9
Fever + splenomegally	100	51.2
Fever + hepatomegally	16	8.2
Concomitant infection		
Pneumonia	64	32.8
Septicemia	20	10.3
Otitis media	5	2.6
Comorbidities		
Severe anaemia	35	17.9
Severe malnutrition	9	4.6

Table 4: Treatment drugs and initial treatment outcome (n=195)

Variables	Frequency	Percent
VL drug Received		
Combined SSG and PM	152	77.9
Pentostam (SSG)	27	13.8
Liposomal Amphotericin B	16	8.2
Complications		
Adverse drug events(ADEs)	12	6.2
Initial treatment outcome		
Initial cure	183	93.8
Death	9	4.6

4.3 Factors associated with Visceral leishmaniasis treatment outcome

4.3.1 Quantitative factors

In Bivariate analysis, treatment factors such as Adverse drug events, Age ≥15 years, pneumonia, severe anaemia (Hb<5g/dl), delayed diagnosis (≥29 days), and severe malnutrition were found to be associated with treatment outcome. However, in the multivariate logistic regression analysis, only adverse drug events, Age (≥15 years), and pneumonia remained significantly ($p< 0.05$) associated with poor VL treatment outcomes (Table 5).

VL patients who were aged ≥15 years were 18.1 times at greater risk of death(poor outcome) from treatment complications than those less than 15 years of age (aOR, 18.1; 95%CI, 2.30–143.14; p=0.01).

VL patients with adverse drug events during treatment for VL were almost 9 times at greater risk of death (poor outcome) than those without adverse event (aOR, 8.6; 95%CI, 1.10–67.87; p=0.04).

VL patients who had pneumonia as a concomitant infection during VL treatment were about 7 times at greater risk of death (poor outcome) than those without pneumonia (aOR, 6.7; 95%CI, 1.06–41.91; p=0.04).

Note: Relapse cases were considered as follow-up outcomes and thus excluded from bivariate and multivariate analyses of the factors associated with the initial outcome.

Table 5: Bivariate and multivariate logistic regression analysis

	Treatment Outcome					
Variables	**Cured**	**Death**	**cOR (95% CI)**	***P***	**aOR (95% CI)**	***P***
Adverse event						
Yes	8	4	9.67(1.31,53.86)	0.013	8.6(1.10,67.87)	0.04*
No	175	5	1.00		1.00	
Age						
>=15 years	7	3	12.6(1.64,73.83)	0.007	18.1(2.30,143.14)	0.006*
<15 years	176	6	1.00		1.00	
Pneumonia						
Yes	54	7	8.4(1.51,84.10)	0.005	6.7(1.06,41.91)	0.04*
No	129	2	1.00		1.00	
Hb level(g/dl)						
Hb <=5g/dl	29	5	6.6(1.32,35.04)	0.009	5.1(0.88,29.57)	0.07
Hb >5g/dl	154	4	1.00		1.00	
Days to diagnosis						
>=29 days	72	7	5.4(0.98,54.19)	0.027	1.8(0.28,11.94)	0.52
<29 days	111	2	1.00		1.00	
Malnutrition						
Yes	6	2	8.4(0.69,58.75)	0.048	4.4(0.31,62.49)	0.3
No	177	7	1.00		1.00	

cOR, crude odds ratio; aOR, adjusted odds ratio; CI, confidence interval; *p-value ≤0.05

4.3.2 Qualitative factors

4.3.2.1 Key informant interview (KII)

Theme 1: understanding VL diagnosis

All the interviewed HCWs were familiar with the procedures involved in diagnosing VL in their facilities.

Clinicians and lab technologists were aware of the diagnostic algorithm as per the WHO/MoH guide, however, to mitigate challenges posed by chronic shortages of test kits and drugs, the current practice (especially at Giriftu sub-county hospital, the only facility with in-patient care service) was as follow;

Admission before serological testing: Key informants reported that all the **s**uspected patients with persistent fever, abdominal pain, splenomegally, hepatomegaly, from the endemic village and not responding to treatment especially antipyretic were first subjected to rK39 tests.

If no splenomegally but with persistent fever and other signs, he/she will be admitted for monitoring (2-3 days). One of the key informants at Giriftu sub-county hospital reported that *"We admit patients after clinical suspicion and this allows us to treat any other concomitant infections, monitor progress and in the meantime stabilize the patient by providing nutritional supplements and blood transfusion for severely anemic before testing for VL" This* practice according to the key informant was adopted in late 2018 and was aimed to minimize misdiagnosis and sparingly manage the VL diagnosis and treatment kits. The other two facilities adopted the same diagnostic procedure but refer severe cases for admission and blood transfusion to Giriftu sub-county hospital.

Use of testing algorithm as per WHO/MoH guideline*:* Laboratory technologists reported that they use the standard procedure. They reported that if a patient turns positive on rK39, they are started on treatment but if rK39 is negative, the samples are subjected to DAT. The titre levels for DAT used in making the decision were; 1:200 – 1600 is regarded as negative and the patient is treated for other condition. Titre of >1600 to 3200 are regarded as borderline and the decision is made by the clinician and the patient is either put on treatment or the test is repeated after 1 week. A titre of 6400–204800 is regarded as VL positive, and the patient is put on treatment.

Differentiating primary and relapse VL cases: According to Lab technologists, the use of serological diagnostic kits (rK39 and DAT) could not tell the primary from

relapsed VL cases. Serological tests are reported to show positive for 2-3 years after treatment even if the person is feeling well. They reported that relapse can only be confirmed through the demonstration of parasites in the splenic aspirate. However, according to them, none of the facilities collect splenic aspirate and currently rely on the conventional methods used for confirmation of primary VL (clinical, history, Epidemiological, and RDT/DAT). This, was due to lack of training on splenic aspiration techniques and the absence of necessary tools. The main challenge in regards to diagnosing relapse cases was provision of false history by the patient and or guardian. According to the key informants' locals are familiar with RDT giving positive for already treated cases, therefore they try to present the patient as a new case or switch facility. One lab technologist explained it as "*locals are aware that if someone was treated previously, he or she could be denied test or treatment so they always give scant information on past visits"*

Knowing the differential diagnosis for VL, concomitant infections, and co-morbidities: All the respondents knew the existence of other diseases that resembled VL in terms of clinical presentations. They reported malaria, TB, and HIV as the main differentials tested for in all VL suspects as per the MoH guideline. However, the respondent reported to also suspect and sometimes test for brucellosis and meningitis.

They reported common concomitant infections as lower respiratory tract infections and otitis media. Anaemia and malnutrition were reported to be the common co-morbidities.

Challenges in diagnosis and treatment of VL: The respondents reported frequent stock outs of diagnostic kits and treatment drugs as the main challenge. In addition, they mentioned staff turnover, lack of training, and limited facility as one of the

challenges in managing patients, especially during outbreaks. One of the key informants explained the challenge as **"***here in Giriftu sub-county hospital, during outbreaks patients are referred from other peripheral facilities and villages. These patients share the same ward with other non-VL patients and since VL patients take at least 7 days and others up to 60 days, they occupy the bed making it unavailable for other patients. This strains our capacity and at times create emergencies"*

In Giriftu sub-county hospital, it was reported that only 19 % (4/21) (a nurse, clinician, lab tech, and a medical officer) were trained out of the total 21 HCWs (10 nurses, 5 clinicians, 4 lab techs, and 2 medical officers). This, according to a clinician is sub-optimal given the endemicity of VL in the area.

One of the key informants explained the resultant challenge as; **"***during VL outbreaks and when a VL management trained officer is on leave, the few that are left in the facility become overwhelmed and this necessitates the involvement of non-trained officers. This had in various instances led to an increased number of complicated cases that ended up being transferred to County referral hospitals"*

Theme 2: VL Treatment

Recommended VL treatment regimen: All the respondents were aware and familiar with the treatment regimen as outlined in the MoH guideline. The clinicians and nurses reported using the following VL drug regimens; SSG (20mg/kg i.v) for all primary cases, >2years and none severe cases and PM (15mg/kg i.m) for 17 days while those <2years, pregnant and severely sick and >45 years were put on Ambisome (Liposomal amphotericin B) 3-5mg/kg for 6-10 days (some days are escaped to limit toxicity).in the absence of Ambisome, SSG(Pentosam) 20mg/kg for 30days is used.

***Precautions for VL drug use*:** Clinicians and nurses understood the necessary precautions as per the MoH guideline and are always keen on severely sick patients. However, the informants reported that the choice of drug for a particular patient is sometimes hindered by frequent stock outs. This was explained by a clinician as "*Treatment regimen is ideally as per protocol but sometimes the decision is made as per availability of the drug"*

In case of a severe acute event following VL treatment, respondents reported managing it by first discontinuing drug use and monitoring the progress, then switching to a safer regimen e.g. Ambisome.

If alternative drug was unavailable, the situation was monitored for 2-3 days and restarted on the same drug and in the meantime monitoring vital parameters.

***Effectiveness of VL drugs*:** the informants observations were that the current regimen was highly effective with no known cases of unresponsiveness or ADE. In the explanation a clinician said; *most patients respond by 3rd day of treatment regardless of the regimen and usually, the fever goes down, appetite improves and weight improves indicating the effectiveness of the drug*.

According to the respondents, there were two levels of patient evaluation; during and before discharge from the facility. During treatment, progress is monitored and any adverse event, default, or death are noted. On completion of the treatment course the patients were evaluated and status categorized as an initial cure, probable non-response, and or confirmed non-response. None of the facilities carried out a test of cure or followed up for six months after treatment as per MoH guidelines. One of the key informants explained why facilities didn't follow up patients for six months as "*Majority of the VL patients are from remote villages, are nomadic pastoralist and*

most of them have no telephone contacts making it difficult to trace, therefore, currently no mechanism is in place"

Theme 3: VL Patient care

Requirement for support of VL patients: All the respondents reported provision of diagnosis, treatment, and nutritional supplementation as the main VL patient care services. All the facilities provide free diagnosis, treatment, and nutritional supplements to VL patients. In addition, inpatient ward and blood transfusions were provided for at Giriftu sub-county hospital. One of the respondents explained the patient care service as follow;*"The VL patient treatment compliance is excellent and there are zero defaulters, this is because the local communities have known that VL is a fatal disease and our free service is providing immense relief"*.

The respondent reported provision of fortified porridge, plumpy'supTM, and plump'NutTM as the main nutritional foods available for all malnourished patients including VL. These nutritional supplements are reported to be consistently provided by UNICEF and World Food Program (WFP). On the other hand, VL diagnostic kits and treatment drugs were provided free through support by international NGOs mainly; Foundation for Innovative New Diagnostics (FIND) and the Drugs for Neglected Disease *initiative* (DND*i*). WHO, Kenya Medical Research Institute (KEMRI), and the Neglected Tropical Disease unit (NTD).

4.3.2.2 Focus Group Discussion (FGD)

Theme 1: Nomadic pastoralism and risk of VL infection

All the respondents were aware of VL occurrence and presence of its vector in Wajir county and in particular their area of residence; within the towns and villages of Wajir West sub-county. One of the male respondents described the VL situation as *"I have*

known VL since I was young, I was once a victim and one of my children also got it and I came to realize that it always leads to death if the person doesn't get treated at the hospital"

Concerning nomadic pastoralism, the respondents concurred that the practice does increase the risk of VL infection.

The main factors that were mentioned by the respondents were:

Transhumance and vector presence- the respondent explained that the sandfly that transmits VL are known to inhabit trees like *Acacia Seyal* (Qura'c) and *Balanites aegyptica* (Quud) that are commonly found in the grazing area. This according to them poses an obvious risk to herders and those using stock routes.

Temporary Housing**:** The pastoralists in Wajir tend to live in *tulads;* small temporary villages with 5-10 households where housing is predominantly made of sticks and mud or dung plastered walls. The *tulads* are usually located in the middle of the bushes with no access roads**.**

This type of housing was not able to provide protection against sand fly thereby increasing the risk of bite and or VL infection.

Environmental risk factors- Within Wajir West there are natural environmental features that make it more prone to VL. The features were an abundance of specific vegetation like *Acacia* and *Balanite* trees and also the black cotton soil (*Boji*). One man reported as; *all the endemic villages are along the stretch of about 20km in Wajir West sub-county with black cotton soil (Boji) – during the dry season the soil cracks allowing sand flies to inhabit and attack people from there. The fly usually emerge during the evening and especially when it rains and water gets in. The fly also*

inhabits the hair around the Camel hump and <u>*Acacia*</u> <u>*Senegalensis*</u> (cadaad geri/xabag) *trees which is common in this area.*

Pastoral behaviours – Herders tend to sit on ant hills as a vantage point to monitor grazing animals and sleep on the ground whenever they want to rest. This behaviour is thought to increase the risk of the sandfly bite. A female respondent explained the practice that is thought to increase the risk of sandfly bite as *"almost all pastoralists dress scantly, especially when herding animal to avoid entangling with thorny trees and they also prefer outdoor sleeping to avoid high indoor temperature"*

Also, the camel herders are reported to dress scantly and detest the use of bed-nets for fear of scaring camel especially when it's blown by the wind.

Theme 2: Influence of pastoralism on treatment seeking by VL patients

Nomadic pastoralism was reported to influence the need to seek or delay VL diagnosis and treatment. This was due to the following factors;

Remote villages**:** most of the pastoral villages are reported to be in bushes far away from permanent settlements, with no paved roads and inaccessible except by foot. This limits the access to health facility that is usually located in permanent settlements and hence delays in seeking treatment. One female respondent described the situation as *"Health facilities are always out of reach because most VL affected pastoralists stay in remote villages with no access or transport"*

Home treatment: it is reported that most people self-treat conditions that present with fever or pain with pain relief tablets from local shops. Respondents agreed that almost all VL cases are at first treated using pain relief drugs for both adults and children delaying health facility visits and in the process allowing the progression of VL. One male respondent explained; "*here in our town people always rely on Panadol (pain*

relief tabs) which is easily available, to treat all sorts of pain, if this fails then it becomes necessary to seek hospital treatment"

***Husbandry chores*:** it was observed that the majority of the locals keep livestock and that there is little time to rest. House heads are always busy either herding, fencing, trekking in search of pasture, or caring for a sick animal. This coupled with the already mentioned factors allows procrastination thus delaying trips to the health facility and in the process allowing the progression of VL.

This was explained by one of the female respondents as *"in a pastoral household, there are few numbers of people or none in the household during the day and most are away with animal making it a challenge to take care of the sick"*

Illiteracy – there is a low level of literacy among the residents leading to barrier in understanding the dynamics of disease transmission and progression. They agreed that illiteracy affects health-related aspects that include personal hygiene, nutrition, seeking treatment, and disease prevention measures.

Theme 3: Health seeking behaviour among the locals

The majority of the respondents believe that the public perception towards Healthcare service is shifting since the start of devolution in 2013. This has made conventional Healthcare a preferred treatment avenue for ailments especially VL compared to home or traditional care during previous years. The respondents mentioned two main factors that may influence health-seeking behavior as follow;

Lack of VL knowledge on symptoms among the locals – This influenced if the patient visited health facility for diagnosis and treatment or not. It was reported that, despite the frequent recurrence of VL little was done especially on differentiating the symptoms from other diseases. One Female respondent explained; "*Despite the*

frequent recurrence of VL in Wajir west and the availability of free diagnosis and treatment, the locals could not recognize the symptoms as they do for other diseases like measles"

It was reported that patient preferred to self-treat and if it failed self-refer for treatment thus allowing the progression of the disease.

Seeking alternative treatment – The Somali community usually sought homecare treatment for almost all the diseases before seeking conventional treatment. Firstly they resort to Quran reading, where divine intervention is sought followed by a period of monitoring and at the same time using over-the-counter antipyretics like Panadol™

This practice is said to be encouraged by lack of health facilities in remote villages, lack of transport to health facilities, husbandry chores that limit the available time, and lack of knowledge on the dynamics of VL.

Theme 4: **Poverty influence on susceptibility and progression of VL**

Poverty related factors were:

High indirect cost of VL treatment – Despite the provision of free diagnosis and treatment at government facilities, access is limited due to distance and indirect costs that are incurred on transport, boarding and lodging during the long treatment period. The nearest VL endemic village to anyone facility was estimated to be 40km with the farthest being 80 km this according to them can cost 20k to 40k respectively on private transport alone. This cost is reported to be quite prohibitive and concerning this, one male respondent explained the challenge as; "*among pastoralists, money is a rare commodity and any activity that require funding had to wait for the animal to be identified and taken to market for sale before the money is available for use. This process will in itself contribute to delay and thus allow progression of the disease*"

Lack of basic needs - Lack of good nutrition, good housing, and good hygiene were reported to contribute and make one more susceptible to VL infections

Theme 5: Malnutrition influence on recovery from VL

Malnutrition among the residents was reported to be prevalent and it is was considered as one of the factors that influences the progression and recovery from VL in the following ways;

Weakening body condition and immunity against diseases - Those with weak body conditions especially children were reported to quickly progress to severely sick levels.

Malnourished patients were reported to be at higher risk of death after infection with VL. This was reported to be based on the fact that VL causes loss of appetite and if someone is already malnourished may get worsened.

Prolonged convalescence and relapse **-** Some respondents reported that VL patients take several months from the discharge period to completely get back to normal body condition.

This was common among those who were severely malnourished. one respondent explained that "*I witnessed two cases that were taken back to Health facility after having completed treatment some six to eight-month ago and both were tested like they were new cases and put on treatment"*

Co-infection **-** Malnutrition weakens the body and immunity allowing onsets of other diseases, especially pneumonia. It is a common occurrence to find pneumonia among VL patients and this was attributed to malnutrition and the resultant weak immunity.

Special diets for VL patient **-** Most respondents reported that Camel milk tend to delay the onset of symptoms and at diagnosis those patient turn negative on RK39. This they said is also known to healthcare workers. Conversely, the use of mutton and cow milk is reported to enhance onset of symptoms and allow quick diagnosis. Therefore, during the convalescent period, the locals were reported to refrain from a diet with cow milk and or mutton, for fear of VL re-occurrence.

CHAPTER FIVE

DISCUSSION

5.1 Quantitative data

5.1.1 Socio-demographic characteristics

In this study, the highest proportion (69%) of VL cases occurred in <5 years, and among males and in Wajir West sub-county. This finding is contrary to the findings where a study on risk factors for VL infection reported a higher proportion of 60% and 62.2% among >15 years age group in Turkana and north-western Ethiopia respectively (Lotukoi *et al.,* 2017; Yared *et al.,* 2014). The difference in the finding could be due to the differences in the approach.

Despite that, other age groups are also affected, the higher proportion among <5 years of age in this study could be due to low immunity as compared to older ages.

This was reported in a situational gap analysis report on Leishmania control in Eastern Africa, where a higher risk of VL infection among children in endemic areas was attributed to lowered immunity as compared to adults who acted as reservoirs (Malaria Consortium, 2010). Similar age-based VL dynamics were reported in Ethiopia where a VL incidence study indicated susceptibility among all age groups in places where VL was recently introduced unlike the endemic areas (Ali & Ashford, 1994).

In this study, more than half (57%) of VL patients were male. This was comparable to findings in Turkana where males were 52.8 % (28/53**)** of the VL cases (Lotukoi *et al.,* 2017). Similarly in Bihar India, males were 69% (93/134) of the cases (Siddique *et al.,* 2018), and in north-western Ethiopia, where males constituted 85.6% (77/90) of the VL cases (Yared *et al.,* 2014). This gender difference was attributed to gender

roles or activities, behaviours, and practices in Turkana, Bihar, and north-western Ethiopia. However, the observed gender difference could also be potentially due to physiological differences (hormones interacting with immune effectors) rather than behaviour or role-related exposures. The physiological relation was confirmed in an eco-epidemiological study conducted in Ethiopia where VL incidence was significantly higher in males in the first year of life (Kirstein *et al.,* 2018).

5.1.2 Treatment outcome

In this study, the proportion of cured following initial evaluation after VL treatment was 93.8%. This was comparable to a prospective cohort study conducted in East Africa on safety and efficacy of SSG and PM combination for VL treatment involving 3126 VL patients enrolled from sentinel sites in Sudan(1962), Kenya(652) Ethiopia(322), and Uganda(190) that reported cure rate of 95.1% (Kimutai *et al.,* 2017). Similar findings were reported from Eastern Sudan where a hospital-based retrospective cohort study involving 1252 VL patients treated using SSG and PM resulted in a cure rate of 93% (Atia *et al.,* 2015). In contrast, according to an observational retrospective cohort study in Bihar India, a VL treatment involving 8588 VL patients using intravenous Liposomal Amphotericin B (Ambisome) for 4–10 days, resulted in an initial cure rate of 99.4% (Burza *et al.,* 2014).

On the other hand, the proportion of death during treatment in this study was 4.6% and this was lower than in similar studies in Ethiopia (23.7%), India(22.6%), Brazil (5.3%) and southern Sudan (10.9%)(Welay *et al.,* 2016; Burza *et al.,* 2014; M. A. Santos *et al.,* 2002; Seaman, 1996) . However, it is higher than that found in Uganda(3.7%) (Mueller *et al.,* 2009). This could be due to differences in the study design, setting, and subjects involved in the study.

5.1.3 Factors associated with VL treatment outcome

In In this study, poor outcome (death) during VL treatment was associated with age ≥15 years, adverse drug events, and pneumonia. In Eastern Africa, a study on the safety and efficacy of VL treatment using SSG and PM involving 3126 VL patients (in Sudan, Ethiopia, and Kenya) reported; advanced age (>15 years), sepsis, anemia, and renal related adverse events as the main factors associated with death during VL treatment (Kimutai *et al.,* 2017), Similarly, in northwest Ethiopia, death among 595 VL patients following treatment using SSG at 20mg/kg/day for 30 days was associated with late diagnosis (>29 days), severe illness at admission (inability to walk) and co-infection with HIV (Welay *et al.,* 2016) In eastern Uganda, in-hospital death following VL treatment using SSG and Amphotericin B was associated with the age of <6 years and >15 years, co-infection with TB, and drug-related adverse events (Mueller *et al.,* 2009). In addition to various factors, pneumonia was reported to be independently associated with death during VL treatment. This was shown in studies conducted in Brazil where pneumonia was reported to be significantly associated with mortality among hospitalized VL cases (Ahmed *et al.,* 2016;Braga *et al.,* 2013).

In previous studies, similar varied factors were also shown to be associated with death. For instance, in Southern Sudan, death among 3076 VL patients treated using SSG was associated with markers of disease severity such as age of ≥45 years, duration of illness of ≥5 months, severe anemia (Hb <60g/L), and low body mass index of <12.2kg/m2 (Seaman *et al.*, 1996). From the subsequent study in southern Sudan, death among 3365 VL patients treated using SSG was associated with the age of <2 and ≥45 years, malnutrition, anemia (Hb <6mg/dl), duration of illness of ≥5 months, and episodes of diarrhea (Collin *et al.*, 2004).

5.2 Qualitative factors

5.2.1 Health intervention factors

5.2.1.1 Diagnosis of Visceral leishmaniasis

According to KII, VL diagnosis follows the MoH outlined algorithm; clinical case definition, RDT, and DAT. None of the facilities carry out spleen or bone marrow aspirations as a VL diagnostic method. This finding is comparable to a study on epidemiology, diagnosis, and treatment of VL where the use of serological (rK39) method was reported to provide the best diagnostic option while splenic aspiration is associated with increased risk of hemorrhage and fatal complications (Georgiadou et al., 2015). Similarly, a study on clinical epidemiology, diagnosis, and treatment of VL involving 4,831 VL patients in Pokot Kenya reported the use of rK39 based diagnostic tests as a sufficiently accurate method to replace direct agglutination and splenic aspiration as a first-line diagnostic procedure (Mueller *et al.*, 2014).

5.2.1.2 Treatment of Visceral leishmaniasis

The KII respondent reported to follow WHO and MoH recommended protocols in diagnosis and management of VL suspected cases.

The protocol contains various treatment regimens and necessary precautions required to limit adverse effects. In the protocol, Liposomal Amphotericin B was recommended as a first-line treatment regimen for severe, pregnant, and those aged <2 and >45 years of age. This recommendation is based on its high efficacy (>96%) and low toxicity (MoH, 2017). However, the findings from the quantitative analysis are contrary to protocol guidelines. This is because, out of the total 69 cases that were <2 years, only 14(20.3%) of these cases were treated using Liposomal Amphotericin B (Ambisome).

This finding is nevertheless consistent with KII respondents that reported using the regimen based on availability. The frequent unavailability of Ambisome could be attributed to its high cost as compared to SSG and PM which are relatively cheap (Sundar & Singh, 2016**;** DNDi, 2018).

Despite the MoH recommendation, that witching from Liposomal Amphotericin B to SSG alone or in combination with PM will not be less effective and or pose an increased risk of toxicity. This was shown in one of the studies carried out in southern Sudan where MSF used SSG among a war-torn malnourished population in VL epidemics since 1990 3076 VL patients were treated using 30 days 20mg/kg SSG where it resulted in an 83.3% cure rate with minimal associated side effects and death (Seaman, 1996).

Subsequent studies by MSF in Southern Sudan where SSG was used in treating 3365 VL patients between 1998-2002 resulted in a cure rate of 91.9% with minimal toxicities (Collin *et al.,* 2004).

More recent studies have shown comparable efficacy in the use of the combination (SSG and PM) and SSG alone therapy. In South Sudan, a large retrospective field evaluation study by MSF-Holland resulted in a cure rate of 97% and 92.4% among VL patients treated using combined SSG/PM (for 17 days) and SSG alone (for 30 days) respectively (Melaku *et al.,* 2007). This finding was further strengthened by a more recent multicenter trial study in East Africa where the use of combined SSG/PM and SSG alone resulted in a cure rate of 91.4% and 93.9% respectively (Musa *et al.,* 2012).This makes both regimens suitable for VL treatment in East Africa.

5.2.1.3 VL patient care

According to the KII respondents, VL patient care services provided at Wajir west facilities include free VL diagnosis, treatment, and nutritional supplementation. These, was achieved through continued support by national government institutions such as the Neglected Tropical Disease unit (NTD), Kenya Medical Research Institute (KEMRI), and non-governmental organizations such as Medecins Sans Frontieres (MSF) and Drugs for Neglected Disease Initiatives (DNDi). KEMRI is reported to spearhead research in regards to VL vectors and treatment drugs, While DNDi is involved in the provision of free treatment drugs. As documented in a situational analysis report (Tonui, 2006).

The continued support to VL diagnosis, treatment, and care in Kenya by DNDi and MSF was also reported in Pokot VL treatment centers of Amudat (in Uganda) and Kacheliba (in Kenya) (Mueller et al., 2014). Nutritional supports are provided for all malnourished regardless of VL status and it's by UNICEF and the World Food Program (WFP).

Additionally, inpatient services, blood transfusion, and regular monitoring are only done at Giriftu sub-county hospital. None of the facilities reported to carryout active surveillance, vector surveillance, case finding during outbreaks, and parasitological analysis as per WHO and MoH guidelines (MoH, 2017).

5.2.2 Socio-cultural factors

5.2.2.1 Nomadic pastoralism and increased risk of VL infection

FGD respondents reported nomadic pastoralism-related factors such, as the movement in search of pasture, temporary housing, and pastoral behaviors such as scant dressing and sitting on ant hills as the main risks for VL infections. This corroborates the

findings from quantitative analysis where 91.3% of the patients were reported to have been exposed in rural villages of Wajir West sub-county. This finding is comparable to a systematic review on rural housing characteristics which indicated risk factors for VL where mud walls with crack and holes, damp and dark houses were found to be risks for VL transmission (Calderon-Anyosa *et al.,* 2018). Similar findings on poor housing as a risk for sandfly bite were reported in Baringo where significantly higher VL seroprevalence occurred in a village with more mud and stick houses (Ryan *et al.,* 2006a).

The movement in search of pasture for livestock was reported to increase exposure to sandfly habitats. The existence of environmental habitats such as *Balanites* tree, *Acacia*, and ant hills in Wajir West and its association with sandfly bites has been reported (Njau, 2010).

Another prominent environmental driver reported by FGD was the existence of vertisols or black cotton soil (Boji). This is the predominant soil type in almost all parts of Wajir west and especially in all the known VL endemic villages. This finding is consistent with the Wajir land-form and soil profile report (L.Touber, 1991). The soil type was reported to provide lash mineral-rich pastures that encourage frequent migration by nomadic pastoralists. This soil type is characterized by a high content of smectitic clay minerals which swell when hydrated and shrink upon desiccation causing deep cracks during dry season allowing sandflies to inhabit. This was shown in an eco-epidemiological study conducted in a VL endemic village of Ethiopia where persons living close to to vertisols were more likely to be bitten by sandflies than those away from it (Kirstein *et al.,* 2018).

5.2.2.2 Influence of nomadic pastoralism on VL treatment

Factors associated with pastoralism such as remoteness of the village which increases the distance to the health facility, home treatment, husbandry chores, illiteracy, and indirect costs influence the need to seek VL treatments. This finding is comparable to findings in Gadaref, Sudan where a study on community perspective on access barriers to VL diagnosis and care reported seeking alternative treatment, indirect costs, distance to the health facility, and illiteracy as main factors that impeded seeking for conventional treatment and care (Sunyoto *et al.,* 2018). Similarly, a study on pastoralism and delay in diagnosis of TB in Ethiopia found nomadic pastoralism, illiteracy, and distance to health facility as the main factors associated with patient delay in seeking healthcare services (Gele *et al.,* 2009). Similar findings were reported in the Pokot VL endemic area where the relocation of MSF treatment center from Amudat to Kacheliba which is closer to endemic zones resulted in earlier VL patient presentation (Mueller *et al.,* 2014a).

Self-treatments were also noted as a factor in causing a delay in seeking treatment. This is comparable to findings among Somali nomadic pastoralists where self-treatment became a barrier to prompt bio-medical diagnosis of TB thereby limiting its control (Gele *et al.,* 2010). This finding provides basis for the need to educate locals on the availability of better treatments.

Nomadic pastoralism and its related activities such as husbandry chores (herding, nursing sick animal, and trekking in search of pasture) were pointed out and thought to delay health facility visits for VL diagnosis and treatment. Similar findings were shown in a study on pastoralism and delay in TB diagnosis where nomadic pastoralism, lack of knowledge on TB, and distance to health facility were shown to be the main factors on diagnosis and treatment (Gele et al., 2009)**.**

5.2.2.3 Health seeking behavior

During the FGD, most of the respondents concurred on the lack of VL knowledge among the locals (especially on symptoms) as the main driver in seeking for most convenient rather than effective treatment. This could be the possible factor contributing to the level of delays where, 90% of the patients had a delay of ≥14 days post-onset of symptoms. A similar finding was shown in a study on barriers in access to diagnosis and treatment completion of TB in western Nepal, where the distance to the health facility, lack of TB knowledge, and seeking alternative treatment was found to influence health-seeking behavior (Marahatta *et al.,* 2020)**.**

5.2.3 Socio-economic factors

5.2.3.1 Poverty influence on VL susceptibility and progression

Indirect costs were reported to be one of the major impediment to seeking health care services. The indirect cost involves the need to spend out of pocket on transport, lodging, and boarding. This finding is comparable to that reported in Gadaref, Sudan where delay to VL diagnosis and treatment was predominantly linked to indirect costs (Sunyoto *et al.,* 2018).

5.2.3.2 Malnutrition influence on recovery from VL

Malnutrition results in weakened body condition, reduced immunity, a prolonged period of convalescence, increase susceptibility to coinfection, and relapse. This is consistent with quantitative findings where malnutrition was found to be significantly associated with poor outcomes. These findings are consistent with those in study on Protein Energy Malnutrition (PEM) as a risk factor for VL, which showed that mild to severe malnutrition in children caused up to a nine-fold increase in the risk of VL progression than a child with mild or normal nutrition (Malafaia, 2009)**.**

5.3 Limitations

This study has some notable limitations that should be considered when interpreting its results. These include;

1. The quantitative data were retrospectively abstracted from patient records and some important variable like Hb level was not recorded for 45(23.1%) patients and this may have led to under or overestimation of the outcome.
2. The adverse events that were reported present for 12 patients was specified (named e.g. bleeding) only in 3 patients limiting further characterization of those with adverse events.
3. The relapse cases that were reported were based on the clinical exam rather than the standard method that involves confirmation of parasites in the splenic aspirate
4. No predictors of relapse could be determined from this data

CHAPTER SIX

CONCLUSIONS AND RECOMMENDATION

6.1 Conclusion

Our findings indicate that there were more VL cases among males, <5 years old, and in those from Wajir West sub-county. The main risk factor for death among VL patients was mainly the age of ≥15 years, pneumonia, and Adverse Drug Events. At the community level, distance to the health facility, husbandry chores, and home treatment were the main hindrances to health facility visits. At the health facility level, lack of VL related training, staff turnover, inadequate inpatient services, and frequent stock out of diagnostic and treatment supplies posed great challenges to VL service delivery.

6.2 Recommendations

a. Short-term intervention

Based on our study findings, County Government should carry out public education on exposure to sandflies, VL diagnosis, and treatment dynamics to mitigate the VL burden and improve treatment outcomes among Wajir West residents. At health facilities, the frontline staff involved in VL treatment should give special attention to those VL patients with concomitant infections, comorbidities, and at risk of adverse drug events to help minimize poor outcomes. At the National level, the MoH NTD unit should undertake training for frontline staff especially clinicians, nurses, and lab-technologists on splenic aspiration and precautions in the use of VL drugs and develop policies aimed at ensuring sustainable and adequate supply for VL drugs and diagnostic kits

b. Long-term interventions

MoH/FELTP should research VL predisposing factors among male gender and <5 years age group in Wajir County.

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APPENDICES

Appendix A: Data abstraction tool

PART I: Health facility Information

County_____ Sub-county _____Ward _____

Health facility name _____

OP/No: _____

Data abstraction Date (dd/mm/yyyy): _____ / _____ /_____

Abstractor name _____ Contact/Tel _____

PART II: Demographic Information

2.0 **Enrolment Date**: ____/___/_____

2.1. **Patient ID** _____

2.2. **Year of birth:** _____ Age _____ (Years)

2.3 **Gender:** 1 ☐ Male 2☐ Female

2.4 If Female, was she pregnant? 1☐ Yes 2 ☐No;

Pregnancy test1 ☐ not done2 ☐ positive3 ☐Negative

2.5. **Residence:** 1Ward _____2 Village _____3_Nearest Health facility ___

2.6. **Occupation: 1** ☐ None 2 ☐student 3 ☐ Animal herder 4 ☐self-employed

5 ☐home maker 6 ☐others (Specify) _____

2.7 **Education level: 1** ☐ None 2 ☐ Primary 3 ☐Secondary 4 ☐post-secondary

2.8 **Name of Contact person:** _____ Phone number of contact person ____

Part III: Clinical information at enrolment

1. Weight _____ (kg) height _____ (CM) Temperature _____**(◦C)**

2. **History of disease**

   a) 1Days since onset of symptoms _____(Days)

   b) 2Date of onset of symptoms ___/___/____(dd/mm/yy)

   c) 3Visited traditional healer: 1 ☐Yes 2 ☐No

   d) 4 Has patient been admitted for VL before?1 ☐Yes 2 ☐ No

   If yes, when 1 ☐3months ago, 2 ☐6month ago 3 ☐1year ago, 4 ☐ >1year

3. Has patient had fever for 2 weeks before enrolment 1 ☐Yes 2 ☐No

4. Has patient had abdominal pain?1 ☐Yes 2 ☐No

5. Were the organs enlarged? **Liver:1** ☐Yes 2 ☐No **Spleen:1** ☐Yes 2☐No

6. Presence of concomitant infection at presentation**:1** ☐Yes 2 ☐No

   If yes, name them **_____, _____, _____**

Part IV: Laboratory information

1. Rapid diagnostic test (rK39) result 1 ☐Not done 2 ☐Positive 3 ☐Negative 4 ☐Inconclusive

   If negative (rK39) have you done DAT? 1 ☐Yes 2 ☐No if not why? _____

2. DAT result 1 ☐Positive(titre:___) 2 ☐Negative 3 ☐Borderline (titre:_____)

3. HIV status 1 ☐Positive 2. ☐Negative 3 ☐Inconclusive

4. Hemoglobin level (g/dl):_____

5. Tissue aspiration 1 ☐Not done 2☐Bone marrow 3 ☐Lymph node,4 ☐ Spleen

6. Splenic/bone marrow aspirate result: 1 ☐Not done2 ☐positive 3 ☐ Negative

7. Microscopy result:1 ☐Positive 2 ☐Negative 3 ☐Not known

8. Final diagnosis/Patient category: 1☐Primary 2 ☐Relapse 3 ☐PKDL 4 ☐ others (specify)__

Part V: Treatment/Hospitalization

IP No. _____ Hospital Ward _____ Data of Admission __/__/___

Date VL treatment started ___/__/__

1. Treatment regimen given to the patient:

a) 1☐combination (SSG and paromomycin) Dosage _____

b) 2☐Pentostam (SSG) Dosage _____

c) 3☐ Glucantime Dosage _____

d) 4☐Liposomal amphotericin B Dosage _____

e) 5☐Other (Specify):_____ Dosage _____

2. Number of treatment days: _____

3. Was the treatment completed? 1 ☐Yes 2 ☐No if No, Why? _____

4. What are the initial treatment outcome?

1 ☐ Initial cure

2 ☐ Probable non-response

3 ☐ Confirmed non-response

4 ☐ Default

5 ☐ Death

5. Was there any severe adverse event following treatment? 1 ☐ Yes 2 ☐ No

If yes, name the drug: _____, _____, _____

If yes, name the Severe Adverse Event (s) _____, _____, _____

6. Was there any other condition that was treated during VL treatment?

1 ☐ Yes 2 ☐ No If yes, name the disease/condition _____,

Part VI: Follow up examination

1. Was there any follow up after treatment?**1** ☐ Yes 2 ☐ No

If yes, what were the final treatment outcome?

1 ☐ Final (definitive) cure

2 ☐ Relapse

3 ☐ Death

4 ☐ Loss to follow up

Was there any signs of PKDL? 1 ☐ Yes 2 ☐ No

If No follow up, what were the reason? _____, _____, _____

Appendix B: Key Informant Interview Guide

KII No. _____

Name of Health Facility: _____

Cadre of the respondent: _____

Respondent ID (code): _____

Date_____

Starting time_____

Ending time_____

Dear Colleague

Thank you for taking the time to join us today to share your thought and experiences. My name is Ali Noor Mohamed and I will be moderator for today's session. I am joined by my colleague _____, who will be assisting in note taking. The session will take approximately 45 minutes. We will be having a discussion on factors associated with treatment outcome among patients with visceral leishmaniasis between 2017 and 2019 in Wajir West sub-county, Wajir County. It should be noted that:

1. You would be contributing to a research study

2. Such information would be instrumental in improving VL treatment interventions carried out in Wajir west sub-county

While responding, please observe the following:

3. Accuracy and completeness of submitted information

4. Consulting other colleagues who could help in providing relevant information

5. Supporting your responses with documents, whenever possible

Healthcare interventions for Kala-Azar patients

1. **Diagnosis of Kala-Azar**

- I would like to know your involvement in diagnosing Kala-Azar in this facility
- From your experience, what are the common practice in this facility in diagnosing Kala-Azar?

  Probe: what are the standard procedures for diagnosing Kala-Azar? How can you tell if it's new or relapse case? What are the common diseases that resemble Kala-Azar in this area? What method does this facility use in diagnosis Kala-Azar? What could contributes to misdiagnosis?
- From your experience, what special challenges does this facility has in terms of diagnosing Kala-Azar and how best do think it should be addressed?

2. **Treatment of VL (Kala-Azar)**

- What are the recommended regimen for use in treating Kala-Azar in this facility?

  Probe: what precautions exist for use of these drugs? In case of severe drug effects how do you manage cases? How can you establish that the available drug is working on the disease?

3. **Patient care**

- I would like to know what local community feel about Kala-Azar treatment offered at Health facilities. What expectations do VL patients have when they come to Health facility for VL treatment?

  Probe: Do people prefer certain kind of treatment? What determines the choice of drug?

- What are standard nutritional requirements for Kala-Azar patients during treatment?

  Probe: What do you think could contribute to patient non response to the drug? What could contribute to drug failures in this facility? Why do patients default/ interrupt treatment?

I have no more questions. Thank you for taking the time to answer our questions today.

Appendix C: Focus group discussion interview guide

FGD Number_____

Location_____

Date_____

Starting time_____

Ending time_____

1. **Introduction**

Good morning, thank you for taking the time to join us today to share your thoughts and experiences. My name is Ali Noor MoHamed and I will be the moderator for today's session. I am joined by my colleague_____, who will be assisting in note taking. The session will take approximately 60 – 90 minutes. We will be having a discussion on factors associated with treatment outcome among patients with visceral leishmaniasis between 2017 and 2019 in Wajir west sub-county, Wajir County. The information collected today will provide us with knowledge about various factors that may influence VL treatment and thereby help us understand ways to improve outcome and thus mitigate the impact of Kala-Azar.

We will be using a tape recorder to record what is discussed today. We will not use your personal names to ensure confidentiality.

Ground Rules

1. 60-90 minutes (tape recorded -- observer and note taker)
2. Speak clearly/one at a time
3. Conversation/all participate

4. No right or wrong answers

5. Assurance of anonymity and confidentiality

1. Socio- cultural factors

Nomadic pastoralism

- In your experience, how does pastoral nomadism increase the risk of Kala-Azar infection in this area?
- In your opinion how does pastoral nomadism influence the need to seek treatment for Kala-Azar?

Probe: what influences the need to seek conventional Healthcare? What other treatment options besides conventional Healthcare is available to the community? What do you think contributes to delay in seeking Healthcare services?

Health seeking behavior

- What are the common perceptions on seeking treatment for diseases at Health facilities?

Probe: how does neighbors opinion or religious beliefs influence the need to seek conventional treatment? How does distance to Health facility influence need to seek Healthcare service? What do you think contributes to poor Health seeking behavior among VL patients?

2. Socio-economic factors

Poverty

- In your experience, what costs are involved in seeking Kala-Azar treatment?

Probe: what are the costs of diagnosis and treatment at public facilities? What are the alternative cheaper sources of drugs in the locality?

- In your experience, how does standard of living influence the need to seek Healthcare services in this locality?

Probe: How do you think poverty influences susceptibility and progression of VL?

Malnutrition

- Why do you think malnutrition influence recovery from Kala-Azar? What are the special diets required by Kala-Azar patients?

I have no more questions. Thank you for taking the time to answer our questions today.

Appendix D: Informed Consent form

Title of Study: Factors Associated With Treatment Outcome Among Patients With Visceral Leishmaniasis In Wajir West sub-county, Wajir County From January 2017 to May 2019

Principal Investigator: Dr. Ali Noor Mohamed

Who has allowed this study to take place?

Moi University ethical committee have carefully looked at this work and agreed that the study is important, relevant to Wajir and follows nationally and internationally agreed on study guidelines. This includes ensuring that all participants' rights are respected. Permission has been granted by the County Director of the department of Health Wajir County

Sponsors: Ministry of Public Health Kenya, in collaboration with Centre for Diseases control through Kenya Field Epidemiology Laboratory Training Program

Invitation: I Dr. Ali request you to take part in this study. The study aims to determine treatment outcome for VL among patients treated in Wajir West sub-county. The study will describe the factors that are associated with treatment outcome helping the department in planning measures that will improve treatment outcomes. The interview sessions are expected to last about 1 hour (for KII) to Ninety minutes (For FGD). During this time, you will be asked some questions about VL treatment.

Risks and benefits: The study will not pose any risks to you and seeks to help improve treatment outcome. There will be no costs to you for taking part in this study.

Confidentiality: All Information obtained about you will be kept confidential and will be used only for the purposes of the study. Your name will not be required. The results of the study may be published or disseminated without revealing your identity.

Consent: You are free to take part or to withdraw from the study now and whenever you want, there will be no penalty.

Questions: If you have any questions, concerns or complaints about the study, please call Dr. Ali Noor Mohamed -0722386917

Signatures: Your signature below indicates that you agree to participate in this study. You will receive a copy of this signed document.

I---------- (participant's code) have had the study explained to me. I have understood what has been explained and had all my questions answered well.

- ✓ I agree to take part in this study.
- ✓ I understand that I can change my mind at any stage and it will not affect me in any way.

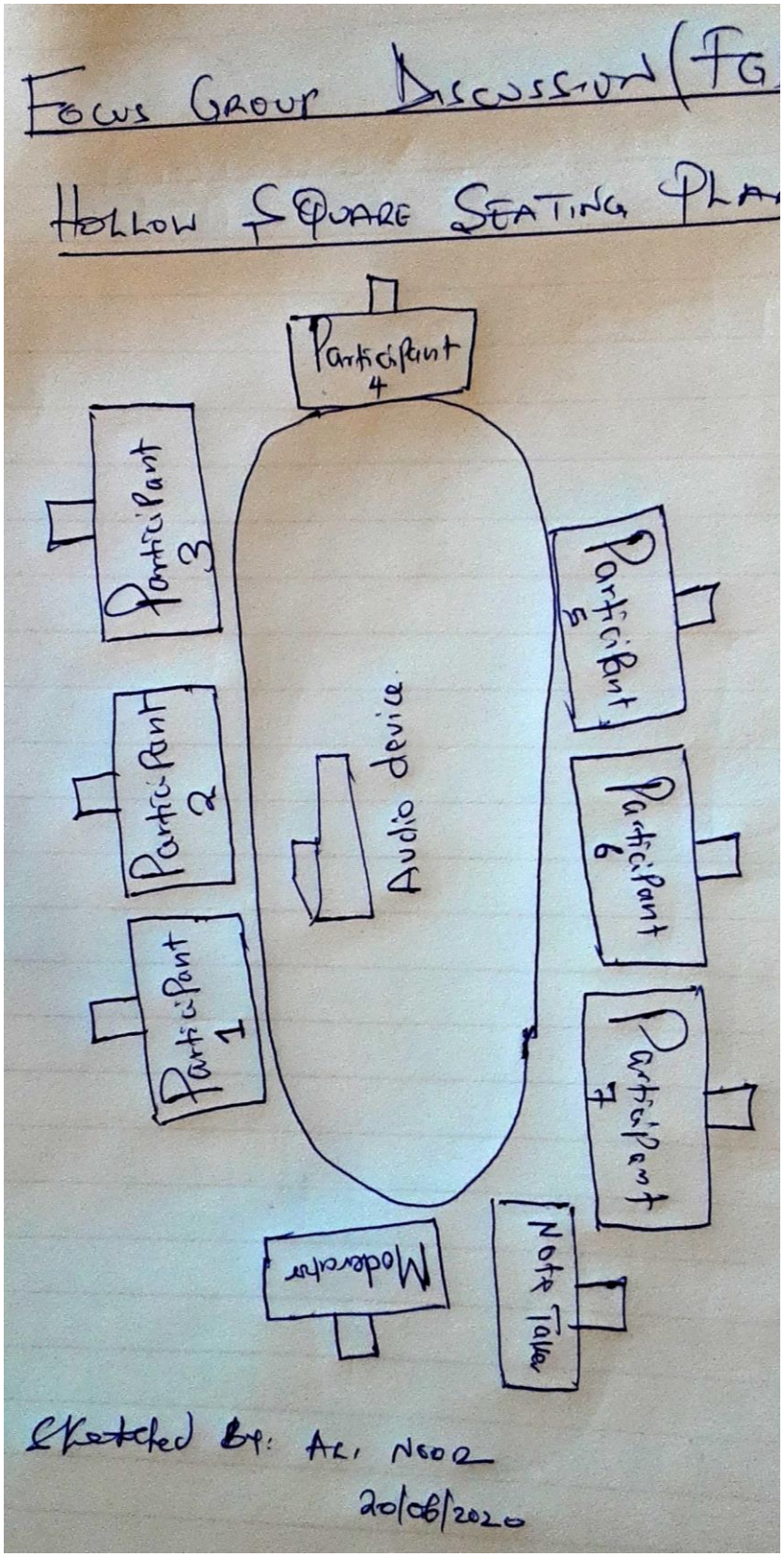
_____ _____

Signature of participant Date

_____ _____

Signature of interviewer/PI Date

Appendix E: FGD seating plan



Appendix F: IREC approval

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471/2/3

MOI UNIVERSITY
COLLEGE OF HEALTH SCIENCES
P.O. BOX 4606
ELDORET
Tel: 33471/2/3

Reference: IREC/2019/209
Approval Number: 0003453

5th December, 2019

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
05 DEC 2019
APPROVED
P.O. Box 4606-30100 ELDORET

Dr. Ali Noor Mohamed,
Moi University,
School of Public Health,
P.O. Box 4606-30100,
ELDORET-KENYA.

Dear Dr. Mohamed,

FACTORS ASSOCIATED WITH TREATMENT OUTCOME AMONG PATIENTS WITH VISCERAL LEISHMANIASIS BETWEEN 2017 AND 2019 IN WAJIR WEST SUB-COUNTY, WAJIR COUNTY, KENYA

This is to inform you that ***MU/MTRH-IREC*** has reviewed and approved your above research proposal. Your application approval number is ***FAN:0003453***. The approval period is **5th December, *2019 – 4th December, 2020.***

This approval is subject to compliance with the following requirements:

i. Only approved documents including (informed consents, study instruments, MTA) will be used.
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by ***MU/MTRH-IREC***.
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to ***MU/MTRH-IREC*** within 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to ***MU/MTRH-IREC*** within 72 hours.
v. Clearance for export of biological specimens must be obtained from relevant institutions.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
vii. Submission of an executive summary report within 90 days upon completion of the study to ***MU/MTRH-IREC.***

Prior to commencing your study you will be expected to obtain a research license from National Commission for Science, Technology and Innovation (NACOSTI) https://oris.nacosti.go.ke and also obtain other clearances needed.

Sincerely,

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc	CEO	-	MTRH	Dean	-	SOP	Dean	- SON
	Principal	-	CHS	Dean	-	SON	Dean	- SOD

Appendix G: NACOSTI research License

REPUBLIC OF KENYA

NATIONAL COMMISSION FOR SCIENCE,TECHNOLOGY & INNOVATION

Ref No: **890615**

Date of Issue: **19/February/2020**

RESEARCH LICENSE

This is to Certify that Dr.. Ali Noor Mohamed of Moi University, has been licensed to conduct research in Wajir on the topic: FACTORS ASSOCIATED WITH TREATMENT OUTCOME AMONG PATIENTS WITH VISCERAL LEISHMANIASIS BETWEEN 2017 AND 2019 IN WAJIR WEST SUB-COUNTY, WAJIR COUNTY, KENYA. for the period ending : 19/February/2021.

License No: **NACOSTI/P/20/3503**

890615

Applicant Identification Number

Director General
NATIONAL COMMISSION FOR SCIENCE,TECHNOLOGY & INNOVATION

Verification QR Code

NOTE: This is a computer generated License. To verify the authenticity of this document, Scan the QR Code using QR scanner application.

Appendix H: Research Ethics certificate