ADDIS ABABA UNIVERSITY

አዲስ አበባ ዩኒቨርሲቲ
ጤና ሳይንስ ኮሌጅ

COLLEGE OF HEALTH SCIENCE -CDT-AFRICA

TREATMENT OUTCOMES OF PATIENTS WITH VISCERAL LEISHMANIASIS IN KONSO ZONE, SOUTHERN, ETHIOPIA

BY: GEYETO GARRA (MD, MSc FELLOW)

OCTOBER-2023

ADDIS ABABA, ETHIOPIA

አዲስ አበባ ዩኒቨርሲቲ
ጤና ሳይንስ ኮሌጅ

ADDIS ABABA UNIVERSITY COLLEGE OF HEALTH SCIENCECENTER FOR INNOVATIVE DRUG DEVELOPMENT AND THERAPEUTIC TRIALS FOR AFRICA

TREATMENT OUTCOMES OF PATIENTS WITH VISCERAL LEISHMANIASIS IN KONSO ZONE, SOUTHERN, ETHIOPIA

BY: GEYETO GARRA (MD, MSc FELLOW)

ACADEMIC ADVISOR: ASRAT HAILU (PROFESSOR)

A THESIS SUBMITTED TO ADDIS ABABA UNIVERSITY, COLLEGE OF HEALTH SCIENCE, CENTER FOR INNOVATIVE DRUG DEVELOPMENT AND THERAPEUTIC TRIALS FOR AFRICA, IN PARTIAL FULFILLMENT FOR THE REQUIREMENT OF MASTER OF SCIENCE DEGREE IN CLINICAL TRIAL.

OCTOBER -2023

ADDIS ABABA-ETHIOPA

DECLARATION

I hereby declare that this research is my original work and has not been presented for a degree by another person in this or any other university and all source material used for this compiled body work have been duly acknowledged.

Name: GEYETO GARRA (MD, MSc fellow)

Signature _____Date_____

The MSc in clinical trial a research thesis has been submitted for examination with my approval as a university academic advisor.

Name: ASRAT HAILU (PROFESSOR)

Signature _____Date_____

APPROVAL BY EXAMINED BOARD

Approval by the board of examiners

This thesis by Geyeto Garra is accepted in its present form by the board of examiners as satisfying thesis requirement for degree of masters in clinical trial

External examiner

_____	_____	_____
Full Name & Sig	Rank	Date

Internal examiner

_____	_____	_____
Full Name & Sig	Rank	Date

Academic advisor

_____	_____	_____
Full Name & Sig	Rank	Date

Contents

List of Figure

List of tables

ACKNOWLEDGMENT

Firstly, I would like to thank Almighty God for his mercy since my childhood. Following I would like to express my great thanks to Addis Ababa University, College of Health Sciences, Center for Innovative Drug Development, and Therapeutic Trials for Africa for allow me to commence my research.

I would like to express my sincere gratefulness to my academic advisor, Prof. Asrat Hailu for taking the time to review my document and me with feedback me with his precious comments, encouragement, and formative guidance that helped me to complete my thesis. Last but not least, I would like to thank Konso & Goma Zone health departments, Konso Zone health facilities, and Arbaminch General Hospital for providing me with important information for my study.

ABBREVIATIONS AND ACRONYMS

ALT- Alanine transaminase

AOR- Adjusted Odds Ratio

ART- Antiretroviral Therapy

AST- Aspartate aminotransferase

BUN- Blood Urea Nitrogen

COR- Crude Odds Ratio

Cr- Creatinine

DAT- Direct Agglutination Test

HBV- Hepatitis B virus

HC- Hematocrit

HCV-Hepatitis C virus

HG- Hemoglobin

HIV- Human Immunodeficiency Virus

NTDS- Neglected Tropical Diseases

PCR- Polymerase Chain Reaction

PM- Paromomycin

RBC- Red blood cells

RDT-Raped Diagnostic Test

Rk39- Recombinant kinesin antigen 39

SSG- Sodium stibogluconate

TB-Tuberculosis

VL-Visceral leishmaniasis

WB -Western blot

WBC- White blood cells

WHO- World Health Organization

Abstract

Background: Visceral leishmaniasis is one of the most neglected tropical diseases caused by protozoa of the genus Leishmania. Leishmaniasis is estimated to affect 0.7–1 million people, with 350 million people at risk, globally. It is characterized by a broad range of clinical and laboratory findings like fever, cachexia, hepatosplenomegaly, pancytopenia, hypo albuminuria, anemia, leucopenia, polyclonal hyper gamma globulinemia, or lymph node enlargement. So diagnosis and treatment of visceral leishmaniasis is difficult and without appropriate treatment, an estimated 95 % of VL patients will die.

Objective: This study aimed to analyze treatment outcomes of patients with visceral leishmaniasis in Konso Zone, Southwest, Ethiopia

Methods: Health facility -based, Cross-sectional, retrospective study was conducted among VL patients who were treated in Konso zone health facilities. Charts of all patients that have been treated from 2007 to 2022 in the zone that fulfills the inclusion criteria were reviewed. The data was entered and cleaned using SPSS 20 statistical packages and analysis was carried out using the SPSS 20 statistical packages. To identify factors associated with poor treatment outcomes, bivariate, and multivariable logistic regression were carried out.

Result: A total of 381 patient's charts were reviewed. The overall level of poor treatment outcomes was 6.6%. The presence of sepsis (AOR=3.323%, 95% CI :(1.191-9.273) P=0.022, ascites (AOR=5.919%, 95% CI: (2.269-15.444) P< 0.001, lymphadenopathy (AOR=4.879%, 95% CI:(1.875-12.694) P=0.001 and prolonged presentation to health facility of more than one month during illness (AOR= 0.366%,95% CI: (0.136-0.985) P=0.047 were found to be the independent predictors of treatment outcomes. Whereas treatment with the combination of SSG & PM as antileishmanial was inversely related with the poor treatment outcomes (AOR= 0.051%, 95% CI: (0.084-0.774) P=0.016.

Conclusion and recommendation: Sepsis, ascites, lymphadenopathy, and prolonged duration of illness at presentation were independent predictors of poor treatment outcomes, whereas treatment with the combination of SSG & PM as antileishmanial was inversely related with the poor treatment outcomes. Awareness creation in the community on signs and symptoms of VL and scaling up the health-seeking behavior to enhance early presentation to health facilities and training of health care providers on complications of VL patients are some of the strategies to be promoted in improving patient outcomes in VL control programs. Special attention and care should be given to VL patients with sepsis, ascites, and lymphadenopathy.

Keywords: Visceral leishmaniasis, treatment outcomes, Southwest Ethiopia.

CHAPTER ONE: INTRODUCTION

1.1 Background of the study

Visceral leishmaniasis is one of the most neglected tropical diseases caused by protozoa of the genus Leishmania (1, 3). Each time, NTDs have a substantial impact on overhead of 1 billion people worldwide, contributing to the damage of house hold incomes and impairment of particularly who are at advanced risks, including those with extreme poverty (4). Leishmaniasis is considered nearly to affect 0.7–1 million people, with 350 million people are largely prone worldwide (5, 6). Presently, 98 countries are more endemic for leishmaniasis (4, 7).

Leishmaniasis occurs after the infection of a mammalian host with the obligate, intracellular organisms. Leishmania species are classified into either Old World (OW) or New World (NW) species, depending on the different geographical locations in which they are endemic (8, 9). OW species are more found in Asia, the Middle East, the Mediterranean basin, and Africa, whereas NW ones are more endemic in the Americas (8). At least 20 Leishmania species are known to results human disease, of the Leishmania genus and Leishmania or Viannia subgenera (10).

VL is transmitted to humans through the bite of infected female phlebotomine sandflies (1). Some animal species, including domestic dogs, rodents, and some others, are the common host reservoir of VL in East Africa (1). Among the species of Leishmania, L. donovani and L. infantum are known to cause the visceral type of the disease. L. donovani is majorly endemic in East Africa and some geographical portions of Indian, while L. infantum occurs in Europe, North Africa, and Latin America (4).Visceral leishmaniasis is getting a growing public health trouble obtruding an estimated case burden of 50,000 – 90,000 people every year (11) There are some estimates that discloses as 90 % and above of VL cases are reported in only six countries, such as Bangladesh, Brazil, Ethiopia, India, Sudan, and South Sudan (11, 12).

Ancient, enervating , and stigmatizing, leishmaniases are among the NTDs causing a great impact nearly on two billion people (13) NTDs are aptly considered as "diseases of the poor" because they're all strongly related to poverty and poverty-stricken areas indeed in high-income countries (13). VL is characterized by a broad range of clinical and laboratory findings like fever, cachexia, hepatosplenomegaly, pancytopenia, hypo albuminuria, anemia, leucopenia, polyclonal hyper gamma globulinemia, or lymph node enlargement. (16, 17).

Some species of VL may cause dark discoloration of skin, particularly in India, which is due the production of adrenocorticotrophic hormone secondary to the release of cytokine (17). Therefore, VL was given the Hindu name kala-azar, which is to mean "black fever" (17). Two species are known to results in human VL, among the two L. donovani generally affects the OW and L. infantum affects the NW areas (3, 18)

Leishmaniasis has emerged or re-emerged in a variety of geographical areas worldwide, having a great impact on health and the economy (6). In the tropics, subtropics, and southern Europe,

leishmaniasis become endemic (6). In Ethiopia the first scientific reports of VL date back to 1942 (11, 19). In the East African area, Ethiopia has the third largest number of VL next to Sudan and South Sudan (21, 22). An official nationwide prevalence for either form isn't reported, however, a recent systematic review reported a national pooled prevalence of 19% (95% CI = 14–25%) (17). In Ethiopia, VL is prevalent in 6 of the country's twelve regions, in both lowlands in the south and southwest as well as the plains and highlands in the northeast (3). There are an estimated 2,000 new visceral leishmaniasis cases every time, with a population prone to acquire the disease are more than 3.2 million (18).

1.2 Statement of the Problem

The epidemiology of leishmaniasis is diverse and complex. Visceral leishmaniasis is being highly endemic in India, Brazil and East Africa. More than 90% of new cases are reported from six countries: Bangladesh, Brazil, Ethiopia, India, South Sudan and Sudan (11). The number of new cases worldwide each year is currently estimated to be 300 000. (11) Visceral leishmaniasis causes an estimated over 50,000 deaths annually, placing leishmaniasis ninth in a global analysis of infectious diseases (11).Patients and families affected by VL become poorer because of the high direct costs (costs for diagnosis and treatment of VL and indirect costs (loss of income) due to the disease itself (16).

VL is characterized by several complexities, and its clinical features are frequently confused with other acute febrile illnesses like malaria, typhoid fever, brucellosis, lymphoma, and leukemia making its clinical diagnosis difficult, especially in non-endemic areas (26). Misdiagnosis may be there with patients having fewer clinical manifestations causing delays in treatment and thus leading to death (26).

Recent literature points to the vulnerability pathways and burden of leishmaniasis on women (13). In some communities, women are at advanced threat for vector exposure if they spend further time in a home with livestock nearby or if they're assigned with responsibilities of animal care or fetching water, activities which carried out or occur in the morning or at dusk when the activity of sand-fly is heightened (13). The general insufficiency of healthcare in women is also considered an important factor contributing to their vulnerability to leishmaniasis (13). Compared to men,-women are less likely to seek healthcare instantly when they've sought authorization from their husbands, leading to more severe complications and, in the case of cutaneous leishmaniasis, there will be a greater risk of disfiguring (scarring) lesions (13). Late clinical presentations of women primarily stem from economic limitations and lack of knowledge about the disease (13). Moreover, a lack of women healthcare providers is a significant problem in places like Afghanistan, where women are frequently not allowed to visit male providers due to local cultural (13). To get treatment and avoid stigmatizing scars, women

may vend their means and suffer financially (13). Due to the burden of disease and stigma women are deprived their mobility their capacity to work, affecting future profitable openings (13). There is a general pattern of dwindling in incidence of VL with increasing age beyond 20 years, although the trend isn't significant for all studies (30).

Leishmaniasis in East Africa remains a major public health problem, with no signs of reduction in case trends. The situation is complicated by remoteness, and difficult to access, recurrent epidemics, a weak health system, lack of appropriate tools, malnutrition, concomitant infections including co infection with HIV and Leishmania, and insecurity in some of those areas and the difficulties of transporting diagnostic tests and medicines for case management. Konso zone is one of the zones with a high burden of visceral leishmaniasis in Southern Ethiopian region, Even though the zone has a similar burden of visceral leishmaniasis as another part of the country; to my knowledge retrospective study of treatment outcomes in patients with visceral leishmaniasis in the southern Ethiopian region in general, and particularly in Konso zone was not yet conducted. Thus, this study was conducted in all health facilities of Konso Zone and health facilities in other zones with possible access of referral, to analyze patient data retrospectively and coming up with up-to-date information on treatment outcomes in patients with visceral leishmaniasis.

1.3 Significance of the Study

Visceral leishmania is still one of the world's most neglected diseases, affecting largely the poorest of the poor, mainly in developing countries that are transmitted between humans and other mammalian hosts by phlebotomine sand flies. Studs conducted so far deal among visceral leishmania case that had HIV confection and their associated factors on treatment outcome (11). Besides the limited studies undertaken on treatment outcome and associated factors in Ethiopia, there is no research based evidence in my study area of interest on treatment outcomes and it's influencing factors in VL patients so far. Therefore, this study aims at assessing the treatment outcome of VL among patients in Konso Zone health facilities. The study may significantly help in planning and implementing the future strategies for control of the disease. Moreover, this study may provide pathways and information for other researchers who want to conduct further study on the issue; consequently findings will help as a baseline data for future studies.

CHAPTER TWO

2. REVIEW OF LITERATURE

2.1 Treatment outcomes and it's influencing factors in a patients with VL

Visceral leishmaniasis is a treatable and curable disease if properly treated but it is fatal if left untreated in over 95% of cases. So early diagnosis and effective treatment prevent disability and death. The treatment of leishmaniasis depends mainly on its form and the parasite species involved (11, 19, 20). Since there is a limited armory of drugs and protective vaccines against leishmaniasis to date, chemotherapy is the only remaining option. Anti-leishmanial drugs such as liposomal -amphotericin B, pentavalent antimonial drugs, including sodium stibogluconate (SSG) and meglumine antimoniate, paromomycin sulfate (PM), and miltefosine showed therapeutic efficacy against VL (16). In Ethiopia, a combination of SSG and PM given for 17 days has been considered the first-line treatment for VL. However, in cases of treatment failure, relapse, and severe toxicity cases liposomal -amphotericin B is recommended as second-line treatment. Despite the introduction of these drugs, mortality is still high in Ethiopia. This is directly or indirectly related to poor treatment outcomes, which occur for several reasons. The risk factors for poor treatment outcomes and responses to the different anti-leishmanial drugs are highly variable in different populations. For example, the rate of resistance to SSG is very high in the Indian population, unlike the East African countries with low resistance. Risk factors for poor treatment outcomes are also variable and include age, duration of illness, malnutrition, presence of anemia, co-infections, ethnicity, and high baseline parasite load (1). Thus, the determination of local data about treatment outcomes and the risk factors of poor treatment outcomes is very crucial for national control, prevention, and elimination of VL. A better understanding of treatment outcomes helps policymakers, clinicians, and funding organizations to develop strategies for improving outcomes. Studies that determine VL treatment outcome at some intervals are vital to prevent the occurrence of drug resistance in our region even though resistance is not a common problem in East Africa at present (1). In Eastern African countries where the causative agent for VL (L. donovani) is highly virulent, drug unresponsiveness had been reported (1).

CHAPTER THREE

3. OBJECTIVES OF THE STUDY

3.1 General objective

This study aimed to assess the treatment outcome of patients outcomes with visceral leishmaniasis in the health facilities of Konso Zone, Southern Ethiopia.

3.2 Specific objectives

- To assess the treatment outcome of patients with VL.
- To identify factors influencing treatment outcomes of patients with VL.

CHAPTER FOUR

4. METHODS AND MATERIALS

4.1 Study Setting.

This study was conducted in Konso Zone Southern Ethiopia. Konso zone is one of the zones in SNNPRS which is located at 595km from Addis Ababa. The population of the zone is estimated to be 311,657 in the year 2022 of whom 51% was considered to be females and the remaining 49% was male population. There are 2 primary hospitals and 14 health centers in the zone. One of the hospitals (Karat Hospital) in the zone serves clients from the Teltele district of Oromia, Alli, and Burji special districts of SNNPRS in addition to the population of the Zone.

4.2 Study Design

A health facility-based cross-sectional study was conducted by retrospective Chart review.

4.3 Study period

This study was conducted for the patients with VL and enrolled to standard treatment 2007 to 2022 in all health facilities of Konso Zone and in facilities outside Konso where referrals were in place.

4.4 Source population All patients who presented to a health facility and diagnosed to have VL in the health facilities of Konso Zone from 2007-2022.

4.5 study population

Patients with fever who were diagnosed to have VL and started on standard treatment during the study period.

4.6 Eligibility Criteria

4.6.1 Inclusion Criteria

The inclusion criteria for diagnosis of VL were laboratory methods that were performed according to Ethiopian Ministry of Health guidelines using a positive recombinant kinesin antigen rapid diagnostic test, DAT, and microscopic examination of aspirates from spleen, bone marrow, and/or lymph node in a patient presented with sign and symptoms suggestive of VL.

4.6.2 Exclusion criteria

Charts with incomplete medical records of treatment outcome or chart with any missing data were excluded from the study.

4.7 Sample size determination

All clients with a well-established diagnosis of VL and who attended treatment at any health facility in Konso Zone or referred to a health facility out of Konso Zone, whose chart had full information; from 2007 to 2022 were included in this study.

4.8 Sampling Technique

All charts of patients with VL diagnosis were sampled.

4.9 Data Collection Procedure &Measurement

Data extraction was carried out by ten clinical staffs. It was done by drawing from stored medical records and electronic sources; patient charts were drawn by the clinical staffs from all health institutions of Konso Zone and Arbaminch General Hospital. The record review was carried out by the clinicians under the supervision of principal investigator. Standard formats with few variations to address the objective of the study was used to collect the data

4.10 Data quality management

Data collectors were trained to maintain the quality of data for a day on standard tool which was prepared in English. The training was given to the data collectors about proposal objectives, sampling procedures, data collection mechanisms, and tools to collect data by the principal investigator. Information on clinical evaluations, treatment outcomes, and laboratory result forms were cross-checked with collected data to check for absoluteness, accuracy, clarity, and consistency by the principal investigator on a daily basis. Any errors such as incompleteness were corrected consequently. The data was intensively cleaned up before its analysis.

4.11 Data processing and analysis

The data were entered and cleaned using SPSS 20 statistical packages and analysis was carried out using the SPSS 20 statistical packages. Descriptive statistics like percentages, frequency, mean values, and standard deviations were used to describe our findings. To identify factors associated with poor treatment outcomes, bivariate, and multivariable logistic regression were carried out. Crude odds ratio were computed to selected candidate variables for the final model and those variables with p-value <0.25 were fitted for adjusted odds ratio using binary logistic regression.To identify independent predictos of treatment outcome.

4.12 Operational definitions

Good treatment outcome: cure at the end of treatment, reduction is of signs and symptoms after completion of standard treatment (resolution of fever, increase in hemoglobin, weight gain, and regression of spleen size), and absence of parasites on the smears. (1)

Poor treatment outcome: Is defined as the experience of death, treatment failure, or relapse (1)

4.13 Ethical Considerations

Ethical approval was obtained from the Research and Ethical Review Committee of Addis Ababa University, College of Health Sciences, Center for Innovative Drug Development and Therapeutic Trials for Africa after waiver of informed consent was applied (Ref.No-CDT/5611/22). Furthermore, the ethical approval was essentially a request for a waiver of consent, so a letter of support was secured from Konso & Gamo Zone health departments (Ref No ጉ-29/8375/14, Gzm01-710-79) respectively and from all district health offices of Konso zone. Oral permission was obtained from respective hospitals and health centers as well. This study

planned to analyze geographic distribution, socio-demographic characteristics, clinical features, laboratory results, and patient outcomes in VL cases that were treated with various regimens of anti-leishmania by retrospective review of medical records of individuals who were diagnosed to have VL and attended treatment at health facilities of the Zone for the last 15 years. Names and card numbers of the patient were not included. The results of the research did not affect the clinical care of the individuals since the study was retrospective.

4.14 Dissemination of the Results

The results of this study are to be presented as a thesis at Addis Ababa University, College of Health Sciences, and Centre for Innovative Drug Development and Therapeutics Trials for Africa. It is also planned to publish the results in a peer-reviewed journal.

CHAPTER FIVE

5. RESULTS

5.1 Socio-demographic characteristics of Patients with VL.

There were a total of 1659 patients treated at different health facilities in Konso Zone from January 2007 to December 2022, but only 381 fulfilled the inclusion criteria. So majority, (77%), had incomplete records and/or missing data. Of these, medical records with missing data ((96.4%) were from the karat health center where they were totally unavailable and the rest were from karat primary hospital which lacks baseline laboratory investigations like CBC, liver enzymes, renal function tests, and with incomplete patient history.

The mean age of the study participants was 19.09 ± 11.65 years. Three hundred and three (79.5%) were males with a male-to-female ratio of 4:1. More than half of the patients were those aged 16 years and above (53.3%). The majority of the study participants were protestant followers in religion (75.1%). Nearly half of the study subjects were students by occupation (48.55%), followed by farmers (45.13%) and very few were employees (0.52%). Three hundred and fifty-six (93.4%) were Konso by ethnicity and hundred percent of the study participants were from rural residents (Table 1).

Table 1 Socio-demographic characteristics of VL patients treated in Konso zone health facilities, Southwest, Ethiopia from January-2007-December-2022(N=381)

Variables	Category	Frequency	Percent
Sex	Male	303	79.5
	Female	78	20.5
Age	0-5 Years	21	5.5
	6-15 Years	157	41.2
	>=16 Years	203	53.3
Religion	Protestant	286	75.1
	Orthodox	91	23.9
	Others	4	1
Level of education	Illiterate	125	32.8
	Can read & write	27	7.1
	Primary (1-8)	148	38.8
	Secondary (9-12) & above	37	9.7
	No information	44	11.5
Occupation	Farmer	172	45.13
	Student	185	48.55
	Employer	2	0.52
	No information	22	5.8
Marital status	Single	275	72.2
	Married	93	24.4
	Divorced	3	0.8
	Widowed	1	0.3
	Others	9	2.4
Ethnicity	Konso	356	93.4
	Ali	15	3.9
	Hamer	3	0.8
	Others	7	1.8
Residence	Rural	381	100
	Urban	0	0

5.2 Distribution of VL cases by Woreda

The majority of the study participants were from Karat Zuria Woreda (44.5%) followed by Kolme cluster (25.5%) and Kena Woreda (20.5%) (Fig1).

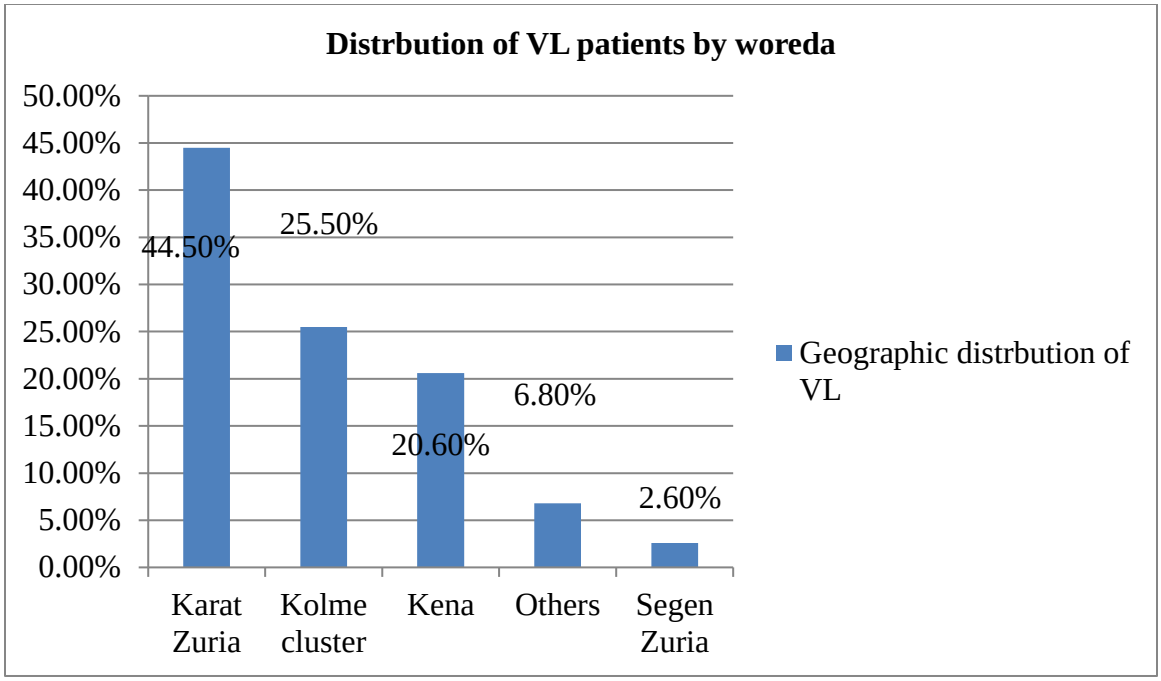

Figure 1 Geographic distribution of VL patients who were treated in Konso zone health facilities, Southwest, Ethiopia, from January 2007-December 2022 (N=381)

5.3 Baseline clinical features of VL at presentation.

The clinical manifestations commonly observed in patients with VL in the locality were: fever, weight loss, splenomegaly, and loss of appetite. Skin lesions, abnormal respiratory sounds, and jaundice were infrequent clinical manifestations. Weight loss, splenomegaly, fever, and loss of appetite respectively were reported in 379 (99.5%), 379 (99.5%), 378 (99.2%), and 346(90.3%) in VL patients (Table2).

Table 2 Baseline clinical features of VL-patients terated in Konso zone health facilities Southwest, Ethiopia, from January-2007-December 2022 (N=381)

Clinical feature	Number (%) positive
Fever	378(99.2)
Weight loss	379(99.5)
Ascites	81(21.3)
Loss of appetite	346(90.8)
Diarrhea/Vomiting	102(26.8)
Cough	192(50.4)
Bleeding /Epistaxis	98(25.7)
Skin lesion /petechiae	7(1.8)
Lymph node enlargement	86(22.6)
Edema	81(21.3)
Abnormal respiratory sound	26(6.8)
Fatigue	224(58.8)
Jaundice	79(20.7)
Splenomegaly/Abdominal swelling	379(95.5)
Hepatomegaly	80(21)
Headache	179(41)
Joint pain	98(25.7)

5.4 Concomitant infections in patient with VL

The frequent concomitant illnesses were sepsis (24.4%) followed by pneumonia (15.2%), malaria (10.8%) and Intestinal parasitosis (10.8%), whereas TB (2.6%), HIV infection (0.8%) and HCV infection (0.5%) were the least frequent concomitant illness (Table3).

Table 3 Common concomitant infections reported by VL patients treated in Konso zone health facilities, Southwest, Ethiopia from January 2007-December 2022(N=381)

Concomitant illness	**Number (%) positive**
Malaria	41(10.8)
Intestinal parasitosis	41(10.8)
Pneumonia	58(15.2)
Pulmonary tuberculosis	8(2.1)
Sepsis	93(24.4)
UTI	26(6.8)
Acute Kidney Injury	2(0.5)
HBV infection	10(2.6)
HCV infection	2(0.5)
Acute gastro enteritis	5(1.3)
Otitis Media	4(1)
Hyper-reactive malarial splenomegaly	2(0.5)
HIV	3(0.8)

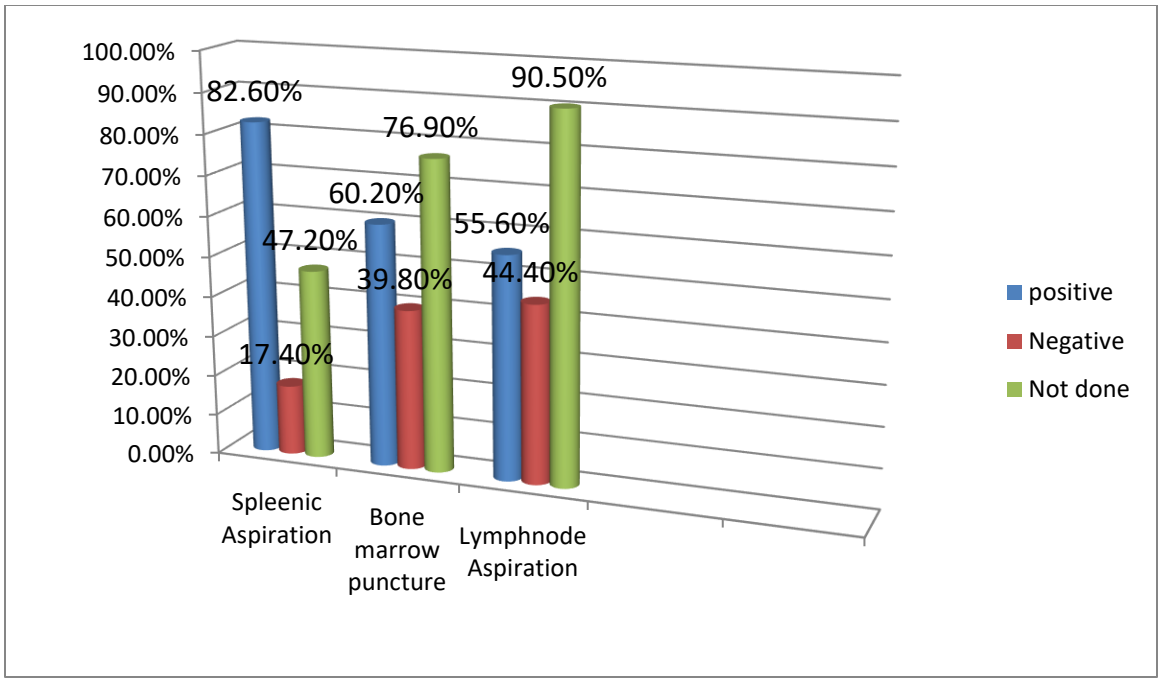

Figure 2 Site of tissue aspiration for parasitic investigation among VL patients treated in Konso zone health facilities, Southwest, Ethiopia from January 2007-December 2023 (N=381)

5.5 Baseline hematologic findings

Among the serologic tests, rK39 was the most commonly performed test (n=287, 75.3%) with less DAT (n=100, 26.2%). Concerning the tissue aspiration procedure splenic aspiration was done for 201 participants of whom 166(82.6%) were positive whereas bone marrow puncture was performed for 88 individuals and 53(60.2%) were found to be positive and among 36 study subjects for whom Lymph node aspiration done 20(55.6%) were positive. The positivity rate was 82.6% in the spleen, 60.2% in bone marrow puncture, and 55.5% in lymph node aspirations. The following table shows hematologic parameters concerning treatment response before and after the treatment. The majority of patients had decreased hematological parameters at admission. All hematological parameters improved after treatment which was more dramatic in platelet counts. At admission 92.7% (n=353) of the patients were leukopenic, 95.8% (n=365) were anemic, and 80.8% (n=308) were thrombocytopenic. But the number of patients with leucopenia, anemia, and thrombocytopenia decreased to 287(75.3%), 313 (82.2%), and 156(40.9%) respectively at discharge (Table 4).

Table 4 Hematologic parameters concerning before and after treatment in VL clients treated in Konso zone health facilities Southwest, Ethiopia from, January 2007-December 2022 (N=381)

Variables	Before treatment Number(percent)	After treatment Number (percent)
Anemic	365 (95.8%)	313 (82.2%),
Leukopenic	353 (92.7%)	287 (75.3%),
Thrombocytopenic	308 (80.8%)	156 (40.9%)

Table: 5 Comparison of hematological Findings before and after treatment in VL clients treated in Konso Zone health facilities Southwest, Ethiopia from January 2007-December 2022(N=381)

Table:5 Comparison of hematologic findings before and after treatment in VL patients treated in Konso zone health facilities Southwest, Ethiopia from January 2007-December 2022(N=381)

Parameters	before treatment	after treatment	P-value
Total WBCs (10^3/µl)	2.28±1.348	3.77±3.45	< 0.001
Hb (g/dl)	7.21±2.14	10.25±2.81	< 0.001
Hct (%)	23.56±5.09	31.61±14.60	< 0.001
Plt (10^3/µl)	103.30±49.89	190.63±130.78	< 0.001

WBC white blood cell, Hb hemoglobin, Hct hematocrit, Plt-platelet, P-value, 0.05 considered statistically significant

In this study the hematologic parameters after treatment mean WBC count (3.77±3.45×103) Hb (10.81±2.14 g/dl) and Hct values (31.51±14.60), platelet count (103.30±49.89x103) showed a dramatic rising compared to before treatment, WBC count (2.28±1.348×103/µl), Hb (7.21±2.14 /g/dl, Hct (23.56±5.09), and Platelet count (190.63±130.78 x103) respectively. This finding is similar with the study conducted at University of Gondar Hospital; Leishmania Research and Treatment Center Northwest, Ethiopia where the result demonstrated that RBCs parameters majorly after treatment mean RBC count (3.77±0.84×106/µl), Hb (10.5±2.1 g/dl) and Hct values (32.2±6.81) displayed a substantial increment compared to pre-treatment one; when RBC count (3.34±0.82×106/µl), Hb (8.9±2.2 g/dl) and Hct (27.3±6.5), respectively (39).

5.6 Renal function test and liver enzymes of patients with VL

There is more or less no change in BUN findings in response to treatment but there is a slight change in Cr level in response to treatment i.e from 39% to 29.7%, 32.2% to 42.3% and 4.6% to 1.3% in low, normal and high values respectively. Among the liver enzymes; AST values in patients with normal values at baseline, were decreased from 52% to 37% during discharge whereas those with high AST values were increased from 22.3% to 35.7% during discharge. But there is unremarkable change in ALT values in response to treatment (Table 6)

Table 6 Renal function tests and liver enzymes of clients with VL before and after treatment who were treated in Konso zone health facilities southwest, Ethiopia, from January 2007-December 2022(N=381)

Renal function test	Category	Frequency	percent
BUN at Admission	Low	0	0
	Normal	83	21.8
	High	203	53.3
	Not done	95	24.9
BUN at discharge	Low	1	0.3
	Normal	78	20.5
	High	201	52.8
	Not done	101	26.5
Creatinine. at Admission	Low	149	39
	Normal	123	32.2
	High	16	4.6
	Not done	93	24.2
Creatinine at discharge	Low	113	29.7
	Normal	161	42.3
	High	5	1.3
	Not done	102	26.8
Liver Enzym			
AST at Admission	Low	1	0.3
	Normal	198	52
	High	85	22.3
	Not done	97	25.5
AST at discharge	Low	0	0
	Normal	141	37
	High	136	35.7
	Not done	104	27.3
ALT at Admission	Low	2	0.5
	Normal	243	63.8
	High	39	10.2
	Not done	97	25.5
ALT at discharge	Low	1	0.3
	Normal	214	56.2
	High	62	16.3
	Not done	104	27.3

Table 7 Comparison of renal function tests and liver enzymes before and after treatment in VL clients treated in Konso zone health facilities, Southwest, Ethiopia, from January 2007-December 2022(N=381)

Parameters	before treatment	after treatment	P-value
Cr	0.91±2.85	0.79±0.63	<0.001
BUN	25.00±8.07	24.77±13.95	<0.001
AST	47.17±37.43	56.25±40.03	<0.001
ALT	36.09±32.29	46.77±32.48	<0.001

ALT- Alanine transaminase, AST- Aspartate aminotransferase, BUN- Blood urea nitrogen, Cr- Creatinine ,P-value, 0.05 considered statistically significant

In this study it was revealed that there was slight decrement in creatinine value after treatment than before but there was more or less no change in blood urea nitrogen values whereas there was dramatic increment in both liver enzymes test values after treatment than before the treatment (table7)

5.7 Type of treatment given to VL patients

Concerning treatment type, 51.2% of the VL cases has been treated by a combination of SSG & PM followed by AmBisome and SSG, 19.4%, 19.2% respectively (Fig3).

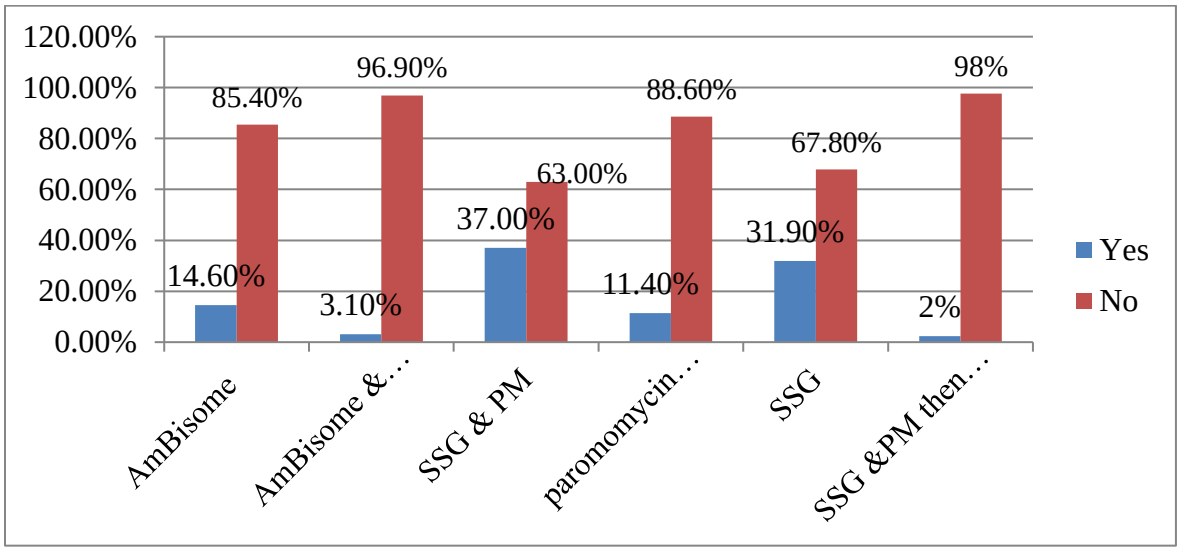

Figure 3 Types of treatment prescribed among VL patients who were treated in Konso zone health facilities, Southwest, Ethiopia from January 2007- December 2022 (N=381)

5.8 Antibiotics and other medications are prescribed for concomitant illnesses among patients with VL.

The frequently prescribed medication for concomitant infections was Ceftriaxone 127(33.3%) followed by Azithromycin 22(5.8%) and artemisinin-lumefantrine (AL) 41(10.8%), whereas fluconazole 1(0.3%), Ceftazidime 2(0.5%) and ART medications 3(0.8%) were the least frequently prescribed concomitant medications (Table 8).

Table 8 Antibiotics / other medications prescribed for concomitant illness among patients with VL treated in Konso zone health facilities, Southwest, Ethiopia from January 2007-December 2022(N=381)

Type of anti-biotic/medication s	Category	Frequency	Percent
Ceftriaxone	Yes	127	33.3
	No	254	66.7
Tinidazole	Yes	17	4.5
	No	364	95.5
Azithromycin	Yes	22	5.8
	No	358	94.2
Anti-tuberculosis drugs	Yes	8	2.1
	No	373	97.8
Vancomycin	Yes	7	1.8
	No	374	98.2
Ceftazidime	Yes	2	0.5
	No	379	99.5
Cotrimoxazole	Yes	14	3.7
	No	367	96.3
Fluconazole	Yes	1	0.3
	No	380	99.7
Ciprofloxacin	Yes	11	2.9
	No	370	97.1
Augmentin	Yes	10	2.6
	No	371	97.4
Artemether lumefantrine (Coartem)	Yes	41	10.8
	No	340	89.2
ART	Yes	3	0.8
	No	378	99.2

5.9 The duration between Diagnosis and initiation of treatment

For the majority of the study participants (95.81%) treatment was initiated within the first 4 days of diagnosis and for very few participants (0.79%) treatment was initiated after 29 days of diagnosis (Table 9).

Table 9 Duration between diagnosis and treatment initiation for VL patients who were treated in Konso zone health facilities Southwest, Ethiopia from January 2007- December 2022 (N=381)

The duration between diagnosis and initiation of treatment in days	Number of patients treated (%)
0-4 days	365(95.8)
5-8 days	7(1.83)
9-12 days	3(0.79)
13-16 days	2(0.52)
17-20 days	1(0.26)
21-24days	0(0)
25-28 days	0(0)
>=29 days	3(0.79)

5.10 Treatment outcomes

The overall good treatment outcome was 93.4% with only a poor outcome of 6.6%. Among the 25 patients with poor outcomes, 10 (40%) were deaths, 9 (36%) were relapse, and 6 (24%) patients had experienced treatment failure and needed second-line treatments. The immediate cause among the 10 deaths was overwhelming sepsis in 2 patients and hepatic failure secondary to drug-induced hepatotoxicity in 2 patients whereas the cause of death in 6 patients was not documented (Fig4).

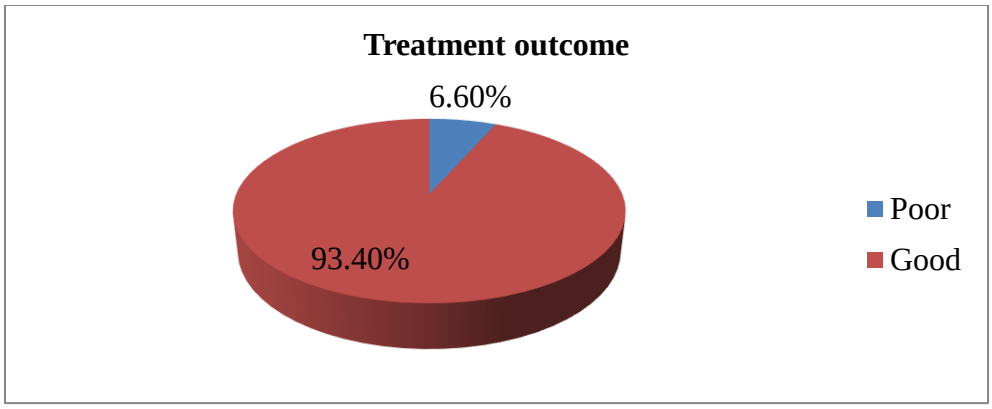

Figure 4 Treatment outcomes reported by Vl patients in Konso zone health facilities Southwest< Ethiopia from January 2007-December 2022(N=381)

5.11 Factors associated with poor treatment outcome in patients with VL.

Binary logistic regression analysis

Of the seven variables that fulfilled the inclusion criteria to be a potential candidate in bivariate logistic analysis, five variables were found to be significantly associated with poor treatment outcomes of a patient with VL and were included in the final model after adjustment was made for confounders. Results of the multivariable analysis showed that sepsis, ascites, lymphadenopathy, duration of illness of more than one month during presentation were significantly associated with poor treatment outcomes whereas treatment with SSG &PM combination as antileishmanial treatment has inverse relation with poor treatment outcome (Table 10.)

Table 10treated in Konso zone health facilities, Southwest Ethiopia, from January 2007-December 2022(N=381) Multivariable logistic regression analysis of the factors associated with poor treament outcomes among VL patients

Variables	Category	Outcome		COR	AOR	P value
		Poor	Good			
Sepsis	Yes	12(12.9%)	81(87.1%)	3.134(1.376-7.136)	3.323(1.191-9.273)	0.022
	No	(4.5%)	275(95.5%)	1	1	
Ascites	Yes	15(18.5%)	66(81.5%)	6.591(2.835-15.322)	5.919 (2.69-15.444)	0.000
	No	10(3.3%)	290(96.7%)	1	1	
	No	15(5%)	285(95%)	1	1	
Lymphadenopathy	Yes	15(17.4%)	71(82.6%)	6.021(2.596-13.966)	4.879(1.875-12.694)	0.001
	No	10(3.4%)	285(96.6%)	1	1	
Duration of illness during presentation	< 1 month	15(5.3%)	268(94.7%)	1	1	
	≥1 month	10(10.2%)	88(89.8%)	2.8(2.647-9.136)	3.66 (1.982-8.953)	0.047
SSG +PM	Yes	6(3.1%)	189 (96.9%)	1	1	
	No	19(10.2%)	167(89.8%)	3.584(1.398-9.185)	5.321 (1.833-15.442)	0.002

CHAPTER SIX

6. DISCUSSION

This study revealed that the overall poor treatment outcomes was 6.6%. This finding is harmonious with a study conducted at Arba Minch general hospital among VL patients enrolled at the leishmaniasis treatment center from January 2011-December 2015 where 8.6 % of patients had poor treatment outcomes (11). But, this finding is lower than a study conducted at ACSH, Tigray region, Northern Ethiopia & Kahsay Abera Hospital in northwestern Ethiopia, where poor treatment outcomes were found to be 12.1% and 23.7% respectively (1,42). The possible reason for this difference could be; in the case of ACSH, there was majority proportion of patient with VL cases were co-infected with TB &HIV, and in the case of Kahsay Abera Hospital advanced proportion of VL patients were co-infected with TB. In this study, it was identified that sepsis, ascites, lymphadenopathy and prolonged duration of illness of further than one month during presentation were significantly associated with poor treatment outcomes. The odds of VL patients co-infected with sepsis were about three times higher to have poor treatment outcomes as compared to those who didn't witness sepsis. This finding is consistent with a study conducted at Arbaminch General Hospital Leishmania Research & Treatment Center where VL patients with sepsis had four times higher poor treatment outcomes as compared to their counterparts (11). cases with VL and sepsis had a higher risk to die than VL cases not having sepsis (11). In our study patients, those who presented to health institution of more than one month of illness were about 3.7 times more likely to have poor treatment outcomes compared to those who presented earlier one month of illness. This is analogous to the finding at Kahsay Abera Hospital in northwestern Ethiopia; VL patients who were admitted to the treatment center with a delay of more than a month (≥ 29 days) from the onset of symptoms were four times more likely to have poor treatment outcomes than patients who presented and were admitted earlier (42). In the current study subjects who were treated with other anti-leishmanial medications were 5.3 times more likely to have poor treatment outcomes compared to those who were treated with combination of SSG & PM. This has parallels with the study done in Eastern Africa where it was revealed that the overall effectiveness at the end of treatment or initial cure rate of SSG-PM was 95.1%(43). This finding is also harmonious with the finding of the study conducted at the Leishmaniasis Research and Treatment Center of the University of Gondar, where VL cases were found to have a high end-of-treatment cure rate of SSG and paromomycin combination therapy (99.0%) among HIV-negative VL patients (44). In this particular study, subjects who developed ascites were almost 6 times more likely to have poor treatment outcomes than those who didn't (AOR=5.919%, 95% CI: (2.269-15.444) P< 0.001. Those participants who had lymphadenopathy were 5 times more likely to have poor treatment outcomes than those who didn't have lymphadenopathy (AOR=4.879%,95% CI:(1.875-12.694) P<0.001. Ascites and

lymphadenopathy could be associated with prolonged duration of illness at presentation or other severe concomitant illnesses.

Among the serologic tests, rK39 was the most commonly performed test (n=287, 75.3%) with less DAT (n=100, 26.2%). Of the tissue aspirate procedures; splenic aspiration was the commonest procedure employed in 201(52.8%) (figure 2) followed by bone marrow puncture 88(23.1%). (Figure 2) Among the tissue aspirate procedures performed (spleen, bone marrow puncture, and lymph node) aspiration was positive in 166(43.6%), 53(13.9%), and 20(5.2%) cases respectively. The positivity rate was 82.6% in the spleen, 60.2% in bone marrow puncture, and 55.5% in lymph node aspirations.

In this study it was demonstrated that the pre-treatment leukopenia was 92.7% which was advanced than the study conducted at the University of Gondar Hospital; Leishmania Research and Treatment Center 83.4% (39), and report from India, which ranged from 37.4% to 60.5% (45) The difference in the prevalence of pre-treatment leukopenia of between studies could be due to variations in the sample size, threshold values used for judgments of leukopenia, and study design but it is comparable with another study from Gonder 95.4% (44). Leukopenia may be associated with symptoms that last for a long time and are caused by splenomegaly (39).

The overall prevalence of pre-treatment anemia in the current study was 95.8% which was analogous to studies reported from Gondar, where the prevalence ranged from 94.4% to 97.4% (46) and New Delhi, India (94.4 -100%) (38). In our study, the overall frequency of post-treatment anemia was 82.2%, which was lower than the report from Gondar, which had a prevalence of 93% (46). but greater than the study from the University of Gondar Hospital; Leishmania Research and Treatment Center 58.3% (39). The difference in the frequency of anemia between studies could be due to variations in the sample size, threshold values used for judgments of anemia, and study design. Anaemia can be caused by a variety of factors, including RBC sequestration and destruction in an enlarged spleen, immunological mechanisms, and changes in RBC membrane permeability in VL patients (39). The rate of pre-treatment thrombocytopenia was 80.8% which was slightly advanced than a study done at the University of Gondar Hospital; Leishmania Research and Treatment Center 75.8%, (39) but it is harmonious with a study done in India which ranges from 83.7% to 85% (46). But, this result was greater than a report from New Delhi, India 52.7% (38). This distinction in the results of thrombocytopenia between studies could be explained by variations in sample size, the cutoff point for the value used for the judgment of thrombocytopenia, and study design. In general, thrombocytopenia may be caused by bone marrow suppression and hepatomegaly as a result of disease progression (39

In this study, there is more or less no change in BUN findings as a consequence of antileishmanial treatment but there are some changes in creatinine levels in response to treatment low values; decreased from 39% to 29.7%, normal values increased by 32.2% to 42.3% and there was a decrement in high values from 4.6% to 1.3%. In our study; AST values in patients with

normal values at baseline, decreased from 52% to 37% during discharge whereas those with high AST values at admission increased from 22.3% to 35.7% at discharge. This could be due to the hepatotoxic nature of antileishmanial drugs. This study reveals that there is an insignificant change in ALT values in response to antileishmanial treatment.

7. STRENGTHS & LIMITATIONS.

Since we used secondary data, all the information was uprooted from the records of VL cases. There might be a lack of delicacy and there are incomplete records with missing data since the study was conducted retrospectively on pre-recorded data, and information on exposure may be inadequate as well there are patient charts with missing data and /or incomplete.

8. CONCLUSION AND RECOMMENDATIONS

8.1 CONCLUSION

In our study it revealed that almost all the hematological parameters of VL cases improved after treatment than before treatment.

Sepsis, ascites, lymphadenopathy, and prolonged duration of illness at presentation were among the independent predictors of poor treatment outcomes whereas treatment with SSG &PM combination as an antileishmanial treatment has inverse relation with poor treatment outcomes. So VL treatment outcomes would be improved if patients presented to the health care facilities as early as possible after the signs and symptom manifestations, and if attention during care were given to VL with septic infection and ascites as concomitant illness and those who presented with lymphadenopathy as clinical manifestation

8.2 RECOMMENDATIONS

Awareness creation in the community on signs and symptoms of VL and scaling up the health-seeking behavior to enhance early presentation to health facilities and training of health care providers on complications of VL patients and their treatment are some of the strategies to be promoted in improving patient outcomes in VL control programs. Special attention and care should be given to VL patients with sepsis, ascites, and lymphadenopathy.

9. References

1. Gidey K, Belay D, Hailu BY, Kassa TD, Niriayo YL. Visceral Leishmaniasis Treatment Outcome and Associated Factors in Northern Ethiopia. Biomed Res Int. 2019 Aug 21;2019:3513957. doi: 10.1155 /2019/3513957. PMID: 31531350; PMCID: PMC6719273.

2. Cunze S, Kochmann J, Koch LK, Hasselmann KJQ, Klimpel S. Leishmaniasis in Eurasia and Africa: geographical distribution of vector species and pathogens. R Soc Open Sci. 2019 May 22;6 (5):190334. doi: 10.1098/rsos.190334. PMID: 31218068; PMCID: PMC6549972.

3.Wamai RG, Kahn J, McGloin J, Ziaggi G. Visceral leishmaniasis: a global overview. Journal of Global Health Science. 2020;2(1).

4. Chowdhury IJK, Haque MF. Visceral Leishmaniasis Treatment and Its Challenges. South Asian Journal of Parasitology. 2020:1-16.

5. Mohebali M, Keshavarz H, Shirmohammad S, Akhoundi B, Borjian A, Hassanpour G, et al. The diagnostic accuracy of direct agglutination test for serodiagnosis of human visceral leishmaniasis: a systematic review with meta-analysis. BMC Infectious Diseases. 2020;20(1):1-12.

6. Pal M, Gutama KP, Steinmetz CHD, Dave P. Leishmaniasis: An Emerging and Re-emerging Disease of Global Public Health Concern. American Journal of Infectious Diseases. 2022;10(1):225.

7. Thakur S, Joshi J, Kaur S. Leishmaniasis diagnosis: An update on the use of parasitological, immunological and molecular methods. Journal of Parasitic Diseases. 2020;44(2):253-72.

8.Kone AK, Niaré DS, Piarroux M, Izri A, Marty P, Laurens MB, Piarroux R, Thera MA, Doumbo OK. Visceral Leishmaniasis in West Africa: Clinical Characteristics, Vectors, and Reservoirs. J Parasitol Res. 2019 Sep 2; 2019:9282690. doi: 10.1155/2019/9282690. PMID: 31565426; PMCID: PMC6745142

9. Campos-Neto A, Abeijon C. Urine-Based Antigen (Protein) Detection Test for the Diagnosis of Visceral Leishmaniasis. Microorganisms. 2020;8(11):1676.

10. Bi K, Chen Y, Zhao S, Kuang Y, John Wu C-H. Current visceral leishmaniasis research: a research review to inspire future study. BioMed research international.

11.Amsalu Alagaw M, Tamiso A. Treatment outcome and determinants among patients with visceral leishmaniasis in Arba-minch General Hospital, Leishmaniasis Research and Treatment Center Gamo Gofa Zone, SNNPR, Ethiopia. Innovative Journal of Medical and Health Science. 2018;8(8):113-31.

12.Ahmed MAA, Ahmed AA, Omar SM, Adam GK, Abdallah TM, Ali AA. Epidemiology of visceral leishmaniasis among children in Gadarif hospital, eastern Sudan. BMC Public Health. 2016;16(1):1-4.

13.Grifferty G, Shirley H, McGloin J, Kahn J, Orriols A, Wamai R. Vulnerabilities to and the Socioeconomic and Psychosocial Impacts of the Leishmaniases: A Review. Research and Reports in Tropical Medicine. 2021; 12:135.

14.Eyayu T, Yasin M, Workineh L, Tiruneh T, Andualem H, Sema M, et al. Evaluation of urine sample for diagnosis of visceral leishmaniasis using rK-39 immunochromatographic test in Northwest Ethiopia. PloS ONE. 2022;17(2): e0263696.

15.Gebreyohannes EA, Bhagvathula AS, Abegaz TM, Seid MA. Treatment outcomes of visceral leishmaniasis in Ethiopia from 2001 to 2017: a systematic review and meta-analysis. Infectious diseases of poverty. 2018;7(1):1-9.

16.Gelaye KA, Demissie GD, Ayele TA, Wami SD, Sisay MM, Akalu TY, et al. Low Knowledge and Attitude Towards Visceral Leishmaniasis Among Migrants and Seasonal Farm Workers in Northwest Ethiopia. Research and reports in tropical medicine. 2020; 11:159.

17.Tekalign S, Adera C, Den Boer M, Miecha H, Zewde A, Mulugeta D, et al. Clinical features and treatment outcomes of visceral leishmaniasis patients admitted to three centers in Oromia, Ethiopia. The Journal of Infection in Developing Countries. 2020;14(06.1):42S-7S.

18.Fararouei M, Sarkari B, Khabisi SA, Rezaei Z. Diagnostic accuracy of urinary latex agglutination test (KAtex) for the diagnosis of visceral leishmaniasis: A meta-analysis. The Journal of Infection in Developing Countries. 2018;12(12):1045-51.

19.Sarkari B, Rezaei Z, Mohebali M. Immunodiagnosis of visceral leishmaniasis: current status and challenges: a review article. Iranian journal of parasitology. 2018;13(3):331.

20Al-Salem W, Herricks JR, Hotez PJ. A review of visceral leishmaniasis during the conflict in South Sudan and the consequences for East African countries. Parasites & vectors. 2016;9(1):1-11.

21. Tadese D, Hailu A, Bekele F, Belay S. An epidemiological study of visceral leishmaniasis in North East Ethiopia using serological and leishmanin skin tests. PLoS One. 2019 Dec 27;14(12):e0225083. doi: 10.1371/journal.pone.0225083. PMID: 31881021; PMCID: PMC6934302.

22. Tarekegn B, Tamene A. Clinical and laboratory profiles of visceral leishmaniasis among adult patients admitted to Felege Hiwot Hospital, Bahir Dar, Ethiopia. SAGE Open Med. 2021 Jul 31; 9:20503121211036787. doi: 10.1177/20503121211036787. PMID: 34377476; PMCID: PMC8326606.

23.Abeijon C, Alves F, Monnerat S, Mbui J, Viana AG, Almeida RM, et al. Urine-based antigen detection assay for diagnosis of visceral leishmaniasis using monoclonal antibodies specific for six protein biomarkers of Leishmania infantum/Leishmania donovani. PLoS Neglected Tropical Diseases. 2020;14(4):e0008246.

24. Dulacha D, Mwatha S, Lomurukai P, Owiny MO, Matini W, Irura Z, et al. Epidemiological characteristics and factors associated with Visceral Leishmaniasis in Marsabit County, Northern Kenya. Journal of Interventional Epidemiology and Public Health. 2019;2(3).

25.Farahani LZ, Saghafipour A, Mohebali M, Akhoundi B, Raufi H. Visceral leishmaniasis (Kala-azar) in Qom Province, Iran: Report of two cases. F1000Research. 2019;7(1371):1371.

26.Tsegaw T, Gadisa E, Seid A, Abera A, Teshome A, Mulugeta A, et al. Identification of environmental parameters and risk mapping of visceral leishmaniasis in Ethiopia by using geographical information systems and a statistical approach. Geospatial health. 2013;7(2):299-308.

27.Alebie G, Worku A, Yohannes S, Urga B, Hailu A, Tadesse D. Epidemiology of visceral leishmaniasis in Shebelle Zone of Somali Region, eastern Ethiopia. Parasites & vectors. 2019;12(1):1-10.

28.mondiale de la Santé O, World Health O. Global leishmaniasis surveillance, 2017–2018, and first report on 5 additional indicators–Surveillance mondiale de la leishmaniose, 2017-2018, et premier rapport sur 5 indicateurs supplémentaires. Weekly Epidemiological Record= Relevé épidémiologique hebdomadaire. 2020;95(25):265-79.

29.Chapman LAC, Morgan ALK, Adams ER, Bern C, Medley GF, Hollingsworth TD. Age trends in asymptomatic and symptomatic Leishmania donovani infection in the Indian subcontinent: A review and analysis of data from diagnostic and epidemiological studies. PLoS neglected tropical diseases. 2018;12(12):e0006803.

30.Pedrosa MSC. Clinical manifestations of visceral leishmaniasis (American visceral leishmaniasis). The Epidemiology and Ecology of Leishmaniasis; IntechOpen Limited: London, UK. 2017:17-30.

31.Gize A, Workineh A, Hailu T. A trend prevalence of visceral Leishmaniasis in West Armachiho District, Amhara Region, Northwest Ethiopia. Tropical Diseases, Travel Medicine and Vaccines. 2020;6(1):1-5.

32.Amanya JK, Peng HJ. Visceral leishmaniasis: evaluation of diagnostic tools, therapeutic regimens, and associated risk factors in areas with frequent outbreaks in South Sudan and Sudan: case reports and review of literature. J Trop Dis. 2018;7(1):293.

33.Ayelign B, Jemal M, Negash M, Genetu M, Wondmagegn T, Zeleke AJ, et al. Validation of in- house liquid direct agglutination test antigen: the potential diagnostic test in visceral Leishimaniasis endemic areas of Northwest Ethiopia. BMC microbiology. 2020;20(1):1-7.

34.Sundar S, Singh OP. Molecular diagnosis of visceral leishmaniasis. Molecular diagnosis & therapy. 2018;22(4):443-57.

35.Lévêque MF, Battery É, Delaunay P, Lmimouni BE, Aoun K, L'ollivier C, et al. Evaluation of six commercial kits for the serological diagnosis of Mediterranean visceral leishmaniasis. PLoS Neglected Tropical Diseases. 2020;14(3):e0008139.

36.Herrera G, Castillo A, Ayala MS, Flórez C, Cantillo-Barraza O, Ramirez JD. Evaluation of four rapid diagnostic tests for canine and human visceral Leishmaniasis in Colombia. BMC Infectious Diseases. 2019;19(1):1-9.

37.Hagos DG, Schallig HDFH, Kiros YK, Abdulkadir M, Wolday D. Performance of rapid rk39 tests for the diagnosis of visceral leishmaniasis in Ethiopia: a systematic review and meta-analysis. BMC Infectious Diseases. 2021;21(1):1-11.

38.Gupta N, Kamla K, Mirdha BR. Clinical and laboratory analysis of patients with leishmaniasis: a retrospective study from a tertiary care center in New Delhi. Iranian Journal of Parasitology. 2017;12(4):632.

39.Shiferaw E, Murad F, Tigabie M, Abebaw M, Alemu T, Abate S, et al. Hematological profiles of visceral leishmaniasis patients before and after treatment of anti-leishmanial drugs at University of Gondar Hospital; Leishmania Research and Treatment Center Northwest, Ethiopia. BMC Infectious Diseases. 2021;21(1):1-7.

40.Tadese D, Hailu A, Bekele F, Belay S. An epidemiological study of visceral leishmaniasis in North East Ethiopia using serological and leishmanin skin tests. PloS ONE. 2019;14(12):e0225083.

41. Welay GM, Alene KA, Dachew BA. Visceral leishmaniasis treatment outcome and its determinants in northwest Ethiopia. Epidemiol Health. 2016 Dec 28;39:e2017001. doi: 10.4178/epih.e2017001. PMID: 28092934; PMCID: PMC5343104.

42.Kimutai R, Musa AM, Njoroge S, Omollo R, Alves F, Hailu A, Khalil EA, Diro E, Soipei P, Musa B, Salman K. Safety and effectiveness of sodium stibogluconate and paromomycin combination for the treatment of visceral leishmaniasis in eastern Africa: results from a pharmacovigilance programme. Clinical Drug Investigation. 2017 Mar;37:259-72.

43.Ademe M, Osorio Y, Howe R, Atnafu S, Mulaw T, Fikre H, Travi BL, Hailu A, Melby PC, Abebe T. Hematological and Clinical Features Associated with Initial Poor Treatment Outcomes

in Visceral Leishmaniasis Patients with and without HIV Coinfection in Gondar, Northwest Ethiopia. Tropical Medicine and Infectious Disease. 2023 Jan;8(1):36.

44.Tesfaye E, Fissehatsion K, Terefe B, Enawgaw B. Haematological Abnormalities in Visceral Leishmaniasis Patients Attending Gondar UniversityHospital; Retrospective Study. IJHPEBS. 2017;3(5):48–53

45. Saurabh K, Ranjan S, Prasad RR. Clinical and haematological parameters associated with patients of visceral leishmaniasis in a district of North Bihar. 2017;4(6):1957–60

46 .Mulaw T, Tariku A, Tsegaye AT, Abebe Z. Efect of iron-folic acid sup plementation on change of hemoglobin among visceral Leishmaniasis patients in northwest Ethiopia: a retrospective follow up study. BMC Hematol. 2018;18(29):2

Annex: Questionnaire

1. Socio-demographic characteristics of patients with VL

1.1 What is the gender of the patient?	1 Male 2.Female
1.2 Age of the patient?	
1.3 What is the religion of the patient?	1. Protestant 2.Orthodox 3. Muslim 4. Other specify……
1.4 Level of education of the patient?	1. Illiterate 2. Can read & write 3. Primary (1-8G) 4. Secondary (9-12G)and above
1.5 Occupation of the patient?	1. Employed 2. Student 3. Farmer 4.No information
1.6 What is the marital status of the patient?	1. Single 2 Married 3. Divorced 4. Widowed 5. Others specify……
1.7 What is the ethnic group of the patient?	1. Konso 2. Oromo 3. Hamer 4. Others specify……..

Geographic distribution of the patient with VL

2.1. Where is the address of the patient?	1. Zone……2. Woreda 3. Kebele(village)……..4.Gote……..
2.2. Where is the place of residence?	1/Rural 2/Urban
3. What is the duration of illness duringa presentation? Write the actual figure in	1.Years…..2.months……. 3.Weeks…… 3.days……..
4. Have the patient had a similar illness inthe past?	1. Yes 2.No
4.1 If the above answer is yes, how longago?	1.years……2Months…… 3.weeks…..4. Days…….

5. What type of clinical manifestation the patient had during the presentation?

Type of clinical feature onpresentation	Result	Incomplete information /missing data.
Fever	1. Yes	
	2. No	
Weight loss	1. Yes	
	2.No	
Abdominal swelling/Ascites	1. Yes	
	2.No	
Loss of appetite	1. Yes	
	2.No	
Diarrhea/Vomiting	1. Yes	
	2.No	
Cough	1. Yes	
	2.No	
Bleeding /Epistaxis	1. Yes	
	2.No	
Skin lesion /petechiae	1.Yes	
	2.No	
Lymph node enlargement	1. Yes	
	2.No	
Edema	1. Yes	
	2.No	
Abnormal respiratory sound	1. Yes	
	2.No	
Fatigue	1.Yes	
	2.No	
Jaundice	1. Yes	
	2.No	
Splenomegaly	1.Yes	
	2.No	
Hepatomegaly	1. Yes	
	2.No	
Headache	1. Yes	
	2.No	
Joint pain	1. Yes	
	2.No	
Chills	1. Yes	
	2.No	

6.. What other concomitant illness the patient had?

Type of illness	Result	Incomplete information /missing data
Intestinal Parasite	1.Yes	
	2.No	
Malaria	1.Yes	
	2.No	
Pneumonia	1.Yes	
	2.No	
Tuberculosis	1.Yes	
	2.No	
Sepsis	1.Yes	
	2.No	
Urinary tract infections	1. Yes	
	2.No	
Diabetes mellitus	1. Yes	
	2.No	
Acute Kidney Injury	1. Yes	
	2.No	
	2.No	
HBV infection	1. Yes	
	2.No	
HCV infection	1. Yes	
	2.No	
Acute gastroenteritis	1. Yes	
	2.No	
Otitis Media	1.Yes	
	2.No	
Hyper-reactive malarialsplenomegaly	1. Yes	
	2.No	
Asthma	1. Yes	
	2.No	
Pneumocystis pneumonia	1. Yes	
	2.No	
Bacillary dysentery	1. Yes	
	2.No	
HIV	1. Yes	
	No	

7. Type of laboratory investigations.

Type of investigation done	Result	Incomplete information /missing data.
7.1 Serologic investigations.		
Rk39	1 Positive	
	2 Negative	
	3 Not done	
DAT	1 Positive	
	2 Negative	
	3 Not done	
7.2 Parasite microscopy test		
Spleen aspiration	1 Positive	
	2 Negative	
	3 Not done	
Bone marrowaspiration	1 Positive	
	2 Negative	
	3 Not done	
Lymph nodeaspiration	1 Positive	
	2 Negative	
	3 Not done	

7.3 Was CBC done? 1. Yes 2. No

If the above answer is yes, write the entire actual figure for the following, at admission and on discharge

CBC component	Result		Incomplete information /missing data
	At admission	On discharge	
WBC			
RBC			
HCT			
HGB g/dl			
Platelet count ×103/μL			

7.4 Was liver Enzymes done? 1. Yes 2.No

7.5 If the above answer is yes, what is the result of the liver enzymes? Write the figure

Liver Enzyme type	Result		Incomplete information /Missing data
	At admission	At discharge	
AST			
ALT			

7.6 Was a renal function test done? 1. Yes 2. No

7.7 If the above answer is yes, what is the result of the following?

Type of renal function test	Result		Incomplete information /Missing data
	At Adm	On disc	
BUN			
Creatinine			

7.8 Type of Treatment prescribed among the VL patients. Tick √ mark in front of the medication/ combination of medications prescribed

Type of Anti-Leishmaniasis	
AmBisome (6 dose of 5mg/kg/day)	
AmBisome and miltefosine(100-150mg/day) for 28 or 56 days	
SSG (20mg/kg/day) and paromomycin(11mg/kg/day) for 17 days	
PM and MF for 14 to 28 days	
SSG (20mg/kg) for 28 days	
SSG and PM then switch to AmBisome	

7.9 Additional antibiotics/ other medications were prescribed among the VL patients. Tick √ mark in front of the medication prescribed

Type of anti-biotic/medication s	
Ceftriaxone	
Tinidazole	
Azithromycin	
Anti-tuberculosis drugs	
Vancomycin	
Ceftazidime	
Cotrimoxazole	
Fluconazole	
Ciprofloxacin	
Augmentin	
artemether-lumefantrine (Coartem)	

8.1 When the client was diagnosed as a VL patient? Write the DD/MM/YYYY

8.2 When anti-leishmaniasis was initiated? Write DD/MM/YYYY

8.3 What is the outcome of the patient?

1. Cured 2. Dead 3. Relapse 4. Failure 5 Defaulter 6.Referred

7. Other specify……

8.4 If the outcome was death what was the immediate cause for the death?