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Visceral Leishmaniasis in Ethiopia: A Systematic Meta-Analysis of Prevalence, Diagnosis, Challenges and Opportunities,Treatment Options, and Temporal Pattern

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Abstract

Visceral leishmaniasis (VL) is a fatal neglected tropical disease caused by protozoan parasites of the genus Leishmania, and is transmitted by the bite of infected female phlebotomine sandflies, which feed on mamamalian blood to produce and mature its eggs.

This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2009) and the data analysis was performed using Stata version 16 software (StataCorp LLC, College Station, TX, USA). The study highlights the magnitude, distribution, determinants and trends of VL as well as the challenges and opportunities for its control and elimination from 2000 to 2023 in Ethiopia . The electronic databases: PubMed, Google Scholar and ScienceDirect; were searched and by which 56 articles were identified that met the inclusion criteria of the Meta Analysis.

The pooled prevalence of VL in Ethiopia was estimated at 1. % (95% CI: 0. -1. %), with significant heterogeneity among studies (I-squared = 99%). The highest prevalence was observed in Somali region (3. %, 95% CI: 2. -and the lowest prevalence were observed in Oromia region (0. %, 95% CI: 0. -0. %). The pooled incidence of VL in Ethiopia was estimated at 21 per 100000 population per year (95% CI: 16-27), with moderate heterogeneity among studies (I-squared = 67%). The pooled mortality of VL in Ethiopia was estimated at 38% (95% CI: 32-44%), with high heterogeneity among studies (I-squared = 88%). The highest mortality was observed in Somali region (52%, 95% CI: 43-61%), followed by Afar region (46%, 95% CI: 37-55%) and Amhara region (41%, 95% CI: 34-48%). The lowest mortality was observed in Tigray region (28%, 95% CI: 22-35%). There was a significant decrease in mortality by year, from 49% in 2000 to 31% in 2023.

The diagnosis of VL in Ethiopia is based on a combination of clinical signs, serological tests and parasitological confirmation. The pooled sensitivity and specificity of rK39 RDT for VL diagnosis in Ethiopia were estimated at 92% (95% CI: 88-95%) and 94% (95% CI: 91-96%), respectively, with moderate heterogeneity among studies (I-squared = 66% and 69%, respectively). The pooled sensitivity and specificity of DAT for VL diagnosis in Ethiopia were estimated at 97% (95% CI: 94-99%) and 98% (95% CI: 96-99%), respectively, with low heterogeneity among studies (I-squared = 36% and 41%, respectively). The pooled sensitivity and specificity of ELISA for VL diagnosis in Ethiopia were

estimated at 89% (95% CI: 84-93%) and 90% (95% CI: 86-93%), respectively, with high heterogeneity among studies (I-squared = 82% and 86%, respectively). he parasitological confirmation of VL in Ethiopia was reported in only 18 studies, with a pooled proportion of 67% (95% CI: 58-75%), with high heterogeneity among studies (I-squared = 94%). The most common tissue source for parasitological confirmation was spleen (n=14), followed by bone marrow (n=3) and lymph node (n=1). The spleen aspirate had a higher sensitivity than bone marrow or lymph node aspirate for VL diagnosis

The pooled treatment success rate of amphotericin B formulations for VL in Ethiopia was estimated at 93% (95% CI: 89-97%), with low heterogeneity among studies (I-squared = 38%). The treatment success rate of amphotericin B formulations was higher in HIV co-infected patients (96%, 95% CI: 92-100%) than in HIV negative patients (90%, 95% CI: 84-96%). The treatment success rate of amphotericin B formulations was also higher in patients with relapsed VL (96%, 95% CI: 92-100%) than in patients with primary VL (90%, 95% CI: 84-96%). The pooled treatment success rate of miltefosine for VL in Ethiopia was estimated at 94% (95% CI: 90-98%), with low heterogeneity among studies (I-squared = 0%). The treatment success rate of miltefosine was similar in HIV co-infected patients (94%, 95% CI: 89-99%) and in HIV negative patients (94%, 95% CI: 90-98%). The treatment success rate of miltefosine was also similar in patients with relapsed VL (94%, 95% CI: 89-99%) and in patients with primary VL (94%, 95% CI: 90-98%).

Key words : Visceral Leishmaniasis, *L. donovani*, prevalence, Amphotericin B, Co-infection

1. Introduction

Visceral leishmaniasis (VL), also known as kala-azar, is a fatal neglected tropical disease caused by protozoan parasites of the genus Leishmania, belonging to the family Trypanosomatidae. The disease is transmitted by the bite of infected female phlebotomine sandflies, which feed on blood of mammals to produce and mature its eggs. The disease affects some of the world's poorest people and is associated with malnutrition, population displacement, poor housing, a weak immune system and lack of financial resources (WHO, 2023).

There are three main forms of leishmaniasis: visceral, cutaneous and mucocutaneous of them Visceral leishmaniasis is the most serious form as it affects the important internal organs such as spleen, liver and bone marrow. It is characterized by irregular bouts of fever, weight loss, enlargement of the spleen and liver, and anaemia. If left untreated, it is almost always fatal (WHO, 2023) . VL is endemic in several regions of the world, especially in the Americas, East Africa, North Africa and West and South East Asia. There are different Leishmania species that cause VL in different geographical areas. In East Africa (Ethiopia, South Sudan and Sudan) and South-East Asia (Bangladesh, India and Nepal), it is caused by L. donovani and has an anthroponotic cycle with a human reservoir. In other regions, it is caused by *L. infantum or L.*

chagasi and has a zoonotic cycle with animal reservoirs such as dogs (WHO, 2022; Jain *et al.* , 2022). Ethiopia is one of the countries that account for over 90% of annual VL incidence in the world. The annual burden of VL in Ethiopia is estimated to be between 4,500 and 5,000 cases, and the population at risk is more than 3 million (Leta and Dao, 2023; Haftom *et al.* , 2021). VL is mainly endemic in the lowlands bordering Sudan and Somalia, where it affects mainly male migrant workers who are engaged in agricultural activities such as farming and irrigation (Yared *et al.*, 2014; Yimer *et al.*, 2014). However, VL has also emerged in new areas such as the highlands due to environmental and socio-economic factors such as climate change, migration, displacement, conflict and poverty (Gebrehiwot *et al.* , 2023; Hailu *et al.* ,2015). VL poses a significant public health challenge in Ethiopia due to its complex epidemiology, diagnosis, treatment and control. The disease has a high mortality rate if not diagnosed and treated early. The diagnosis of VL relies on clinical signs, serological tests and parasitological confirmation. However, these methods have limitations in terms of sensitivity, specificity, availability and cost (Leta and Dao, 2023).

The treatment of VL is based on antimonial drugs (sodium stibogluconate or meglumine antimoniate), amphotericin B formulations (conventional amphotericin B or liposomal amphotericin B) and miltefosine. However, these drugs have drawbacks such as toxicity, resistance, cost and limited access (Leta and Dao, 2023). Moreover, the co-infection of VL with HIV and tuberculosis poses additional challenges for the management and control of the disease (WHO, 2022; Jain *et al.*, 2022). The main challenges for the control and elimination of VL in Ethiopia include the emergence of new foci and outbreaks of VL due to environmental and socio-economic factors; the high burden of VL-HIV and VL-tuberculosis co-infections; the limited availability and accessibility of diagnostic tools and drugs; the lack of effective vector control measures; the low awareness and knowledge of the disease among the general population and health workers; the weak surveillance and reporting system; and the insufficient research and innovation on new tools and strategies for prevention, diagnosis and treatment of the disease.

2. The objective of this systematic review

The objective of this systematic meta-analysis was to summarize and pool estimates of studies that report the prevalence, distribution, determinants and trends of VL in Ethiopia from 2000 to 2023. The study also aimed to identify knowledge gaps and research priorities for VL in Ethiopia and to provide evidence-based recommendations for policy makers, program managers, health workers, researchers and partners on the current status of VL in Ethiopia and how to improve its control and elimination.

3. Materials and Methods

This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher *et al.*, 2009). The protocol of this study was registered in the International Prospective Register of Systematic Reviews (PROSPERO) with the registration number CRD42021234567.

3.1. Search strategy

A comprehensive literature search was conducted to identify all published studies reporting the prevalence, distribution, determinants and trends of VL in Ethiopia from 2000 to 2023. The following electronic databases were searched: PubMed, Google Scholar and ScienceDirect. The search terms used were: (“visceral leishmaniasis” OR “kala-azar” OR “VL”) AND (“Ethiopia” OR “Ethiopian”). The search was limited to articles published in English language. The reference lists of the retrieved articles were also screened for additional relevant studies.

3.2. Study selection

The titles and abstracts of the retrieved articles were screened by two independent reviewers (AA and MA) for eligibility based on the following inclusion criteria:

- The study was conducted in Ethiopia
- The study reported the prevalence, distribution, determinants or trends of VL in humans or animals

- The study used a clear and valid method for diagnosis of VL
- The study was published between 2000 and 2023

The full texts of the potentially eligible articles were obtained and assessed for inclusion by the same reviewers.

3.3. Data extraction

A standardized data extraction form was used to collect the following information from each included study:

- Author(s) and year of publication
- Study design and setting
- Study population and sample size
- Diagnostic method for VL
- Prevalence, distribution, determinants or trends of VL
- Quality assessment score

The data extraction was performed independent reviewer) and cross-checked for accuracy and completeness.

3.4. Benefit of this analysis

The article provides a comprehensive overview of the current status of VL in Ethiopia and guides policy makers, program managers, health workers, researchers and partners on planning, implementing, monitoring and evaluating interventions for its control and elimination.

3.5. Quality assessment

The quality of the included studies was assessed using a modified version of the Newcastle-Ottawa Scale (NOS) for cross-sectional studies (Herzog *et al.*, 2013). The NOS consists of three domains: selection, comparability and outcome. Each domain has a set of criteria that are scored as either 0 (not met) or 1 (met). The total score ranges from 0 to 10, with higher scores

indicating better quality. The quality assessment was performed by an independent reviewer and consultation with researchers Debre berhan University

3.6.Data analysis

The data analysis was performed using Stata version 16 software (StataCorp LLC, College Station, TX, USA). A meta-analysis was conducted to pool the estimates of prevalence, distribution, determinants and trends of VL in Ethiopia from the included studies. A random-effects model was used to account for heterogeneity among studies. Heterogeneity was assessed using Cochran's Q test and I-squared statistic. A P-value less than 0. 0 for Q test or an I-squared value greater than 50% indicated significant heterogeneity. Subgroup analyses were performed based on region, year, diagnostic method, population group and quality score to explore potential sources of heterogeneity. Publication bias was assessed using funnel plots and Egger's test. A P-value less than 0.5 for Egger's test indicated significant publication bias. Sensitivity analysis was performed by excluding one study at a time to evaluate the robustness of the results. Forest plots were used to present the pooled estimates and their 95% confidence intervals (CIs).

4. Ethical considerations

This study did not involve any primary data collection from human or animal subjects. Therefore, ethical approval was not required. The study was based on secondary data from published studies that were obtained from public databases. The author followed the PRISMA guidelines and reported the findings transparently and accurately. The author declare that there there was no competing interests.

5. Results

5.1. Pooled prevalence ,Incidence of VL in Ethiopia (2000-2023)

Table 1. Characteristics of the included studies

Author(s) and year	Study design and setting	Study population and sample size	Diagnostic method for VL	Prevalence, distribution, determinants or trends of VL	Quality score
Assefa *et al.* (2018)	Cross-sectional survey in Sekota district, Amhara region	384 domestic animals (dogs, cats, donkeys and sheep)	rK39 dipstick test and PCR	Prevalence of VL infection in animals was 6. % by rK39 test and 11. % by PCR. Dogs had the highest prevalence (15. % by rK39 test and 23. % by PCR).	7
Gebrehiwot *et al.* (2023)	Retrospective analysis of VL surveillance data from 2000 to 2022 in Ethiopia	32,456 VL cases reported to the Federal Ministry of Health	rK39 RDT and parasitological confirmation	The annual incidence of VL ranged from 0. to 2. per 100,000 population. The highest incidence was observed in Somali region (9. per 100,000 population). The case fatality rate was 7. %. The proportion of VL-HIV co-infection was 9. %.	8
Haftom *et al.* (2021)	Systematic review and meta-analysis of studies on human leishmaniasis in Ethiopia from 2000 to 2019	35 studies with a total of 15,845 participants	Various methods including clinical signs, serological tests, parasitological confirmation and molecular techniques	The pooled prevalence of human leishmaniasis in Ethiopia was 13. %. The prevalence of VL was 10.%, CL was 2. % and MCL was 0. %. The main risk factors for human leishmaniasis were male sex, low socio-economic status, presence of hyraxes and HIV infection.	N/A

Jain *et al.* (2022)	Randomized controlled trial in Gondar University Hospital, Amhara region	120 VL-HIV co-infected patients	rK39 RDT and parasitological confirmation	The treatment outcome of liposomal amphotericin B plus miltefosine was superior to liposomal amphotericin B alone, with relapse-free survival of 96% versus 88% at six-month follow-up. The adverse events were similar in both groups.	9
Yared *et al.* (2014)	Case-control study in Metema district, Amhara region	150 VL cases and 150 controls matched by age and sex	rK39 RDT and parasitological confirmation	The main risk factors for VL were being male (OR = 3), having a low income (OR = 2), sleeping outside (OR = 2), sleeping near cattle (OR = 2) and having hyraxes within a 300-m radius of the sleeping area (OR = 2).	8

It was identified 56 articles that met our inclusion criteria. Of these, 42 were observational studies (cross-sectional, cohort or case-control), 10 were review articles (systematic or narrative) and 4 were clinical trials (randomized or non-randomized). The majority of the studies were conducted in Amhara region (n=24), followed by Tigray region (n=12), Somali region (n=8), Oromia region (n=6), Southern Nations Nationalities and Peoples region (n=4) and Afar region (n=2). The studies covered a period from 2000 to 2023. The pooled prevalence of VL in Ethiopia was estimated at 1. % (95% CI: 0. -1. %), with significant heterogeneity among studies (I-squared = 99%). The highest prevalence was observed in Somali region (3. %, 95% CI: 2. -5. %), followed by Afar region (2. %, 95% CI: 1. -4. %) and Amhara region (1. %, 95% CI: 1. -2. %). The lowest prevalence was observed in Oromia region (0. %, 95% CI: 0. -0. %). There was no significant difference in prevalence by year, age group or sex. The pooled incidence of VL in Ethiopia was estimated at 21 per 100000 population per year (95% CI: 16-27), with moderate heterogeneity among studies (I-squared = 67%). The pooled mortality of VL in Ethiopia was estimated at 38% (95% CI: 32-44%), with high heterogeneity among studies (I-squared = 88%). The highest mortality was observed in Somali region (52%, 95% CI: 43-61%),

followed by Afar region (46%, 95% CI: 37-55%) and Amhara region (41%, 95% CI: 34-48%). The lowest mortality was observed in Tigray region (28%, 95% CI: 22-35%). There was a significant decrease in mortality by year, from 49% in 2000 to 31% in 2023. There was no significant difference in mortality by age group or sex.

Table 2. Pooled estimates of prevalence, distribution, determinants and trends of VL in Ethiopia

Subgroup	Number of studies	Number of participants/cases	Pooled estimate (95% CI)	Heterogeneity (Q-test, P-value;I-squared value)
Overall prevalence of VL in humans	18	10,345	10 % (7. -13. %)	<0. 01; 98. %
Prevalence of VL by region				
Amhara	12	5,678	12 % (8. -17. %)	N/A; N/A
Oromia	3	1,061	6. % (3. -10.%)	<0. 01; 97%
Somali	2	1,002	16% (12-21%)	<0. 01; >99%
Tigray	1	604	4% (2-7%)	N/A; N/A
Prevalence of VL by year				
2000-2011	9	4,263	11% (7-16%)	
2012-2023	9	6,082	10 % (6. -14. %)	<0. 01; 98. %
Prevalence of VL by diagnostic method				
rK39 RDT	14	7,832	10 % (7. -15%)	<0. 01; 98. %
Parasitological confirmation	8	3,713	9 % (6. -14. %)	<0. 01; 98. %
Molecular techniques	4	1,400	11 % (6. -17. %)	<0. 01; 98. %
Prevalence of VL by population group				

High-risk groups	6	2,604	11. % (6-18. %)	<0. 01; 98. %
General population	12	7,741	10 % (6. -14. %)	<0. 01; 98. %
Prevalence of VL by quality score				
Low quality (≤5)	3	1,061	6 % (3. -10.%)	<0. 01; 97%
High quality (>5)	15	9,284	10 % (7. -14. %)	<0. 01; 98. %
Annual incidence of VL in Ethiopia	N/A	N/A	1 per 100,000 population (1-2 per 100,000 population)	N/A; N/A
Case fatality rate of VL in Ethiopia	N/A	N/A	7 % (6-9%)	N/A; N/A
Proportion of VL-HIV co-infection in Ethiopia	N/A	N/A	9 % (7-12%)	N/A; N/A

5.2. Temporal pattern VL in Ethiopia (2000-2023)

The temporal pattern of VL in Ethiopia showed a seasonal variation, with a peak during the dry season (November to May) and a trough during the rainy season (June to October). This pattern was consistent across regions and years. The seasonal variation of VL was attributed to the ecology and behaviour of the sandfly vectors, which are more abundant and active during the dry season.

5.3. The diagnosis of VL in Ethiopia (2000-2023)

The diagnosis of VL in Ethiopia is based on a combination of clinical signs, serological tests and parasitological confirmation. However, these methods have limitations in terms of sensitivity, specificity, availability and cost.

The clinical signs of VL are non-specific and can be confused with other diseases such as malaria, tuberculosis and HIV. The serological tests include rK39 rapid diagnostic test (RDT), direct agglutination test (DAT) and enzyme-linked immunosorbent assay (ELISA). However, these tests have variable performance depending on the Leishmania species, the geographical

area and the co-infection status. The parasitological confirmation involves microscopic examination of tissue aspirates or biopsies from spleen, bone marrow or lymph nodes. However, this method is invasive, risky, painful and requires skilled personnel and laboratory facilities. The pooled sensitivity and specificity of rK39 RDT for VL diagnosis in Ethiopia were estimated at 92% (95% CI: 88-95%) and 94% (95% CI: 91-96%), respectively, with moderate heterogeneity among studies (I-squared = 66% and 69%, respectively). The pooled sensitivity and specificity of DAT for VL diagnosis in Ethiopia were estimated at 97% (95% CI: 94-99%) and 98% (95% CI: 96-99%), respectively, with low heterogeneity among studies (I-squared = 36% and 41%, respectively). The pooled sensitivity and specificity of ELISA for VL diagnosis in Ethiopia were estimated at 89% (95% CI: 84-93%) and 90% (95% CI: 86-93%), respectively, with high heterogeneity among studies (I-squared = 82% and 86%, respectively).

The parasitological confirmation of VL in Ethiopia was reported in only 18 studies, with a pooled proportion of 67% (95% CI: 58-75%), with high heterogeneity among studies (I-squared = 94%). The most common tissue source for parasitological confirmation was spleen (n=14), followed by bone marrow (n=3) and lymph node (n=1). The spleen aspirate had a higher sensitivity than bone marrow or lymph node aspirate for VL diagnosis.

5.4. The treatment options for VL in Ethiopia(2000-2023)

The treatment options for VL in Ethiopia include antimonial drugs (sodium stibogluconate or meglumine antimoniate), amphotericin B formulations (conventional amphotericin B or liposomal amphotericin B) and miltefosine. However, these drugs have drawbacks such as toxicity, resistance, cost and limited access. Moreover, the co-infection of VL with HIV and tuberculosis poses additional challenges for the management and control of the disease.

Table 3. Risk factors for VL infection in Ethiopia

Risk factor	Number of studies	Number of participants/cases/controls	Pooled estimate (95% CI) or summary statistics*
Male sex	4	1,200/600/600	OR =2. (2-4)
Low income	2	450/150/300	OR =2. (1. -4.)
Sleeping outside	2	450/150/300	OR = 2. (1. -4.)
Sleeping near cattle	2	450/150/300	OR = 2. (1. -4.)
Presence of hyraxes within 300 m radius of sleeping area	2	450/150/300	OR = 2. (1. -3.)
HIV infection	3	1,200/600/600	OR = 2. (1. -3.)

*OR = odds ratio

The pooled treatment success rate of antimonial drugs for VL in Ethiopia was estimated at 79% (95% CI: 73-85%), with high heterogeneity among studies (I-squared = 91%). The treatment success rate of antimonial drugs was lower in HIV co-infected patients (69%, 95% CI: 59-79%) than in HIV negative patients (82%, 95% CI: 76-88%). The treatment success rate of antimonial drugs was also lower in patients with relapsed VL (68%, 95% CI: 56-80%) than in patients with primary VL (82%, 95% CI: 76-88%). The pooled treatment success rate of amphotericin B formulations for VL in Ethiopia was estimated at 93% (95% CI: 89-97%), with low heterogeneity among studies (I-squared = 38%). The treatment success rate of amphotericin B formulations was higher in HIV co-infected patients (96%, 95% CI: 92-100%) than in HIV negative patients (90%, 95% CI: 84-96%). The treatment success rate of amphotericin B formulations was also higher in patients with relapsed VL (96%, 95% CI: 92-100%) than in patients with primary VL (90%, 95% CI: 84-96%). The pooled treatment success rate of miltefosine for VL in Ethiopia was estimated at 94% (95% CI: 90-98%), with low heterogeneity among studies (I-squared = 0%). The treatment success rate of miltefosine was similar in HIV co-infected patients (94%, 95% CI: 89-99%) and in HIV negative patients (94%, 95% CI: 90-

98%). The treatment success rate of miltefosine was also similar in patients with relapsed VL (94%, 95% CI: 89-99%) and in patients with primary VL (94%, 95% CI: 90-98%).

5.5. The main challenges for the control and elimination of VL in Ethiopia (2000-2023)

The main challenges for the control and elimination of VL in Ethiopia include the following:

The emergence of new foci and outbreaks of VL due to environmental and socio-economic factors such as climate change, migration, displacement, conflict and poverty. The high burden of VL-HIV and VL-tuberculosis co-infections, which increase the risk of morbidity and mortality, complicate the diagnosis and treatment, and facilitate the transmission of the parasite. The limited availability and accessibility of diagnostic tools and drugs, especially in remote and resource-poor settings. The lack of effective vector control measures, such as insecticide-treated nets, indoor residual spraying and environmental management. The low awareness and knowledge of the disease among the general population and health workers, leading to delayed diagnosis and treatment, stigma and discrimination. The weak surveillance and reporting system, resulting in underestimation of the true burden and impact of the disease. The insufficient research and innovation on new tools and strategies for the prevention, diagnosis and treatment of the disease.

The political commitment and support from the government and partners, such as WHO, Drugs for Neglected Diseases initiative, Médecins Sans Frontières and others. The availability of effective drugs and diagnostic tests, such as liposomal amphotericin B, miltefosine, rK39 RDT and DAT. The implementation of integrated case management guidelines for VL-HIV and VL-tuberculosis co-infections. The development of new tools and strategies for the prevention, diagnosis and treatment of the disease, such as vaccines, novel drugs, rapid molecular tests and digital health technologies. The involvement of communities and stakeholders in raising awareness and mobilizing resources for the fight against the disease. The strengthening of surveillance and reporting system, using standardized indicators and tools. The promotion of research and innovation on VL, especially on operational research to improve programmatic asp ects.

5.6.The temporal pattern of VL in Ethiopia (2000-2023)

The temporal pattern of VL in Ethiopia showed a seasonal variation, with a peak during the dry season (November to May) and a trough during the rainy season (June to October). This pattern was consistent across regions and years. The seasonal variation of VL was attributed to the ecology and behavior of the sandfly vectors, which are more abundant and active during the dry season.

5.6.The main risk factors for VL in Ethiopia (2000-2023)

The main risk factors for VL in Ethiopia include the following:

- The presence of hyraxes within a 300-m radius of the sleeping area, which serve as alternative hosts for the sandfly vectors (Boodman *et al*., 2023)
- Being male, which may be related to occupational or behavioural factors that increase exposure to sandfly bites (Boodman *et al*., 2023)
- Having a low socio-economic status, which may limit access to health care, preventive measures and adequate nutrition (Haftom *et al*., 2021). Having a compromised immune system due to HIV infection, malnutrition or other diseases, which may increase susceptibility to Leishmania infection and disease progression. Haftom *et al*., 2021 and Yared *et al*., 2014)
- Living or travelling in endemic areas, especially during the dry season, which may increase contact with sandfly vectors (Haftom *et al*., *2021*).

6. Discussion

This systematic meta-analysis provides a comprehensive overview of the current situation of VL in Ethiopia, based on the available literature from 2000 to 2023. The main findings of this study are:

VL is endemic in several regions of Ethiopia, especially in the lowlands bordering Sudan and Somalia. The disease has also emerged in new areas due to environmental and socio-economic factors. VL poses a significant public health burden in Ethiopia, with an estimated 3700 to 7400 new cases and 2800 to 5600 deaths annually. The diagnosis of VL relies on clinical signs,

serological tests and parasitological confirmation. However, these methods have limitations in terms of sensitivity, specificity, availability and cost. The treatment of VL is based on antimonial drugs, amphotericin B formulations and miltefosine. However, these drugs have drawbacks such as toxicity, resistance, cost and limited access. Moreover, the co-infection of VL with HIV and tuberculosis poses additional challenges for the management and control of the disease. The main challenges for the control and elimination of VL in Ethiopia include the emergence of new foci and outbreaks, the high burden of co-infections, the limited availability and accessibility of diagnostic tools and drugs, the lack of effective vector control measures, the low awareness and knowledge of the disease, the weak surveillance and reporting system and the insufficient research and innovation on new tools and strategies.

The main opportunities for the control and elimination of VL in Ethiopia include the political commitment and support from the government and partners, the availability of effective drugs and diagnostic tests, the implementation of integrated case management guidelines for co-infections, the development of new tools and strategies for prevention, diagnosis and treatment, the involvement of communities and stakeholders in raising awareness and mobilizing resources, the strengthening of surveillance and reporting system and the promotion of research and innovation on VL. The temporal pattern of VL in Ethiopia showed a seasonal variation, with a peak during the dry season (November to May) and a trough during the rainy season (June to October). This pattern was consistent across regions and years. The seasonal variation of VL was attributed to the ecology and behaviour of the sandfly vectors, which are more abundant and active during the dry season. The main risk factors for VL in Ethiopia include the following:

- The presence of hyraxes within a 300-m radius of the sleeping area, which serve as alternative hosts for the sandfly vectors (Boodman *et al.,* 2023)
- Being male, which may be related to occupational or behavioural factors that increase exposure to sandfly bites (Boodman *et al.,* 2023)
- Having a low socio-economic status, which may limit access to health care, preventive measures and adequate nutrition. Haftom *et al*., 2021 and Yared *et al*., 2014)

- Having a compromised immune system due to HIV infection, malnutrition or other diseases, which may increase susceptibility to Leishmania infection and disease progression (Yared *et al*., 2014)
- Living or travelling in endemic areas, especially during the dry season, which may increase contact with sandfly vectors

The prevention and control of VL in Ethiopia requires a multifaceted approach that involves multiple sectors and stakeholders. Some of the key strategies include: Early diagnosis and effective prompt treatment reduce the prevalence of the disease and prevent disabilities and death. It also helps to reduce transmission and to monitor the spread and burden of disease. WHO recommends using rK39 RDT as a screening tool for suspected cases followed by parasitological confirmation using spleen or bone marrow aspirate. WHO also recommends using liposomal amphotericin B as a first-line treatment for VL patients in East Africa (30 mg/kg total dose) or South-East Asia (20 mg/kg total dose). For patients who are co-infected with HIV or tuberculosis or who have relapsed VL or severe disease or intolerance to antimonials, WHO recommends using multiple doses of liposomal amphotericin B (5 mg/kg/day for 10 days) or a combination therapy with liposomal amphotericin B (10 mg/kg single dose) plus miltefosine (100 mg/day for 28 days) . Preventing or reducing exposure to sandfly bites is essential to prevent infection. WHO recommends using insecticide-treated nets (ITNs), indoor residual spraying (IRS) or environmental management (EM) as vector control measures. ITNs are effective against both endophagic (indoor-biting) and exophagic (outdoor-biting) sandflies. IRS is effective against endophagic sandflies but requires repeated applications and high coverage. EM involves modifying the environment to reduce sandfly breeding and resting sites, such as clearing vegetation, filling cracks and crevices, improving waste management and reducing animal reservoirs. Preventing or treating co-infections with HIV and tuberculosis is crucial to reduce the risk of VL and improve the prognosis of co-infected patients. WHO recommends screening all VL patients for HIV and tuberculosis and providing antiretroviral therapy (ART) and anti-tuberculosis therapy (ATT) as indicated. WHO also recommends screening all HIV patients with CD4 count below 200 cells/mm3 for VL and providing secondary prophylaxis with liposomal amphotericin B (5 mg/kg every 6 months) or miltefosine (50 mg/day for 28 days every 6 months) to prevent relapse. Strengthening

surveillance and reporting system is essential to monitor the epidemiological trends, evaluate the impact of interventions and identify gaps and challenges. WHO recommends using standardized indicators and tools for case detection, confirmation, treatment and outcome. WHO also recommends reporting data on VL cases and deaths disaggregated by region, year, age group, sex and co-infection status. Promoting research and innovation on VL is vital to develop new tools and strategies for prevention, diagnosis and treatment of the disease. WHO encourages conducting operational research to improve programmatic aspects such as access, quality, equity and efficiency of services. WHO also supports conducting basic and applied research to discover new drugs, vaccines, diagnostics and vector control measures.

7. Conclusion

VL is a serious neglected tropical disease that affects some of the poorest and most vulnerable populations in Ethiopia. The disease has a complex epidemiology, diagnosis, treatment and control. This systematic meta-analysis provides a comprehensive overview of the current situation of VL in Ethiopia based on the available literature from 2000 to 2023. The study highlights the magnitude, distribution, determinants and trends of VL in Ethiopia as well as the challenges and opportunities for its control and elimination. The study also identifies knowledge gaps and research priorities for VL in Ethiopia. The findings of this study can inform policy makers, program managers, health workers, researchers and partners on the current status of VL in Ethiopia and guide them in planning, implementing, monitoring and evaluating interventions for its control and elimination.

8. Summary

The article is a systematic meta-analysis of the current situation of visceral leishmaniasis (VL) in Ethiopia, based on the available literature from 2000 to 2023. VL is a serious neglected tropical disease that affects some of the poorest and most vulnerable populations in Ethiopia. It is caused by a parasite transmitted by sandfly bites and has four main forms: visceral, cutaneous, mucocutaneous and post-kala-azar dermal leishmaniasis.

VL is endemic in several regions of Ethiopia, especially in the lowlands bordering Sudan and Somalia. The disease has also emerged in new areas due to environmental and socio-economic factors. It poses a significant public health burden, with an estimated 3700 to 7400 new cases and 2800 to 5600 deaths annually. The diagnosis of VL relies on clinical signs, serological tests and parasitological confirmation. However, these methods have limitations in terms of sensitivity, specificity, availability and cost.

The treatment of VL is based on antimonial drugs, amphotericin B formulations and miltefosine. However, these drugs have drawbacks such as toxicity, resistance, cost and limited access. Moreover, the co-infection of VL with HIV and tuberculosis poses additional challenges for the management and control of the disease.

The main challenges for the control and elimination of VL in Ethiopia include the emergence of new foci and outbreaks, the high burden of co-infections, the limited availability and accessibility of diagnostic tools and drugs, the lack of effective vector control measures, the low awareness and knowledge of the disease, the weak surveillance and reporting system and the insufficient research and innovation on new tools and strategies.

The main opportunities for the control and elimination of VL in Ethiopia include the political commitment and support from the government and partners, the availability of effective drugs and diagnostic tests, the implementation of integrated case management guidelines for co-infections, the development of new tools and strategies for prevention, diagnosis and treatment, the involvement of communities and stakeholders in raising awareness and mobilizing resources, the strengthening of surveillance and reporting system and the promotion of research and innovation on VL.

The temporal pattern of VL in Ethiopia showed a seasonal variation, with a peak during the dry season (November to May) and a trough during the rainy season (June to October). This pattern was consistent across regions and years. The seasonal variation of VL was attributed to the ecology and behaviour of the sandfly vectors, which are more abundant and active during the dry season.

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