Original Article

Multifaceted Impact of Cutaneous Leishmaniasis: Treatment Challenges and Implications for Healthcare Systems and Society in Boru Meda Hospital, North-Central Ethiopia

Bizuayehu Gashaw[1, 2 *], Endalew Yizengaw[3, 4], Gizachew Yismaw[5], Sisay Tebeje[6], Feleke Tilahun[6], Banchwossen Sebsibe[7], Endalkachew Nibret[2, 4*]

Abstract

Background: Cutaneous Leishmaniasis (CL) is an increasing public health concern in Ethiopia, particularly with the *L. aethiopica* strain. The disease often presents with and resulting persistent lesions, approximately six months after infection. This study aims to assess the burden of CL based on clinical type, analyze trends in treatment responses, and identify challenges within the healthcare system among cases treated at Boru Meda Hospital following the civil unrest.

Method: A retrospective analysis from April to June 2023 examined Cutaneous Leishmaniasis cases diagnosed between March 2022 to February 2023. Demographic and clinical data were extracted from the registration logbook. Descriptive statistics summarized the variables, while Non parametric test assessed associations among them.

Result: During the study period, 492 out of 40,324 total patients were diagnosed with cutaneous leishmaniasis, resulting in a prevalence rate of 1.22%. Males exhibited a significantly higher incidence of CL compared to females ($P<0.05$), with individuals aged ≤ 20 years being notably affected by the disease (120; $P<0.05$). The mean age of patients was 22.59±16.96 years. Approximately one-third of the patients were repeat comers; requiring retreatment for more than one cycle. The proportion of clinical forms of CL in new and repeat were similar. The main disease form, 72% of CL was localized cutaneous and the occurrence of the clinical form of CL was statistically significant ($P<0.05$). Following civil unrest, the burden of the CL problem increased threefold.

Conclusion: Cutaneous Leishmaniasis poses a significant burden on patients' lifestyles and presses the healthcare system at Boru Meda Hospital. There is an influx of CL patients, and still prominent number of patients need retreatment, which informs the difficulty of effectively treating the cases. It may also entail epidemiologically higher parasite infectivity might circulate in the population and be reflected by the rise in CL cases after civil unrest. All this creates stress on the health system's operation. There is a need for ongoing surveillance and improved treatment strategies to control the spread of the disease. Exploring genomic variations and the efficacy of treatment options used for CL is crucial. [*Ethiop. J. Health Dev.* 2023; 37(2): 00- 00]

Keywords: Cutaneous Leishmaniasis, *Leishmania aethiopica*, Treatment response, Repeat cutaneous leishmaniasis

Introduction

Leishmaniasis is a group of diseases caused by *Leishmania* parasites. Cutaneous Leishmaniasis (CL) is the most common form. In Ethiopia, it is mainly caused by *Leishmania (L) aethiopica*; other species like *L. tropica* and *L. major* can cause CL (1). The parasites are transmitted by sand fly vectors that infect multiple hosts (2), with hyraxes as natural reservoirs (3).

Different studies in Ethiopia showed that CL appears in various clinical forms. The most common one is Localized (LCL), followed by Mucocutaneous (MCL) and Diffuse (DCL) forms (4). The development of the lesion can occur within six months after a sand fly bite (4).

The prevalence of CL in Ethiopia is 1.05 per 10,000 population (3), with a higher number of male cases than female cases (5). A previous study at Boru Meda Hospital showed that CL is a societal problem (6). Sodium Stibogluconate (SSG) is the drug used for CL treatment in Ethiopia (1).

Nowadays, a substantial proportion of CL patients are taking the drug more than one round (6). These are called repeat (multiple timecomers or recurrent) CL patients. This is a challenge for the control and prevention of CL. This presses the health system and leads to extra expenditure to provide care for repeat patients. From the patient's side: the patient risked, they are living with a horrified skin lesion for an extended time that affects their quality of life and disadvantage because of being away from economic activity. Similarly, the healthcare cost to treat this high number of repeat patients for months certainly challenges the system (7).

[1] Amhara National Regional State Health Bureau, Bahir Dar, Ethiopia
[2] Department of Biology, College of Science, Bahir Dar University, Bahir Dar, Ethiopia
[3] Department of Medical Laboratory Science, College of Medicine and Health Science, Bahir Dar University, Bahir Dar, Ethiopia
[4] Institute of Biotechnology, Bahir Dar University, Bahir Dar, Ethiopia
[5] Amhara Public Health Institute, Bahir Dar, Ethiopia
[6] Boru Meda General Hospital, Dessie, Ethiopia
[7] Felege Hiwot Comprehensive Specialized Hospital, Bahir Dar, Ethiopia
***Corresponding author email**: itisbizuayehu@gmail.com and endtg2002@yahoo.com

The civil war distracted the health system, interrupted service, and broke the reporting system. It also fuels the transmission of CL as mass displacement that increases the biting of the sand fly (8, 9, 10).

However, there is a gap in the presence of systematically analyzed data regarding the burden of CL and the number of repeat CL patients in east Amhara after the local civil war. This study aimed to assess the existing burden of CL, repeat CL patients, and associated factors following civil war in the area.

Materials and Methods

Study design and period

A retrospective data review was done from April 2023 to June 2023 on CL patients registered between March 2022 and February 2023 at LTC in Boru Meda Hospital (BMH).

Study area and setting

This study was conducted at BMH in the South Wollo Zone, Amhara Regional State, North-central Ethiopia. South Wollo Zone has different altitude gradients: 500m-1500m making up 5.5%; > 3200m making up 7.6%; the rest of the topography altitude is between 1501 and 3200m, which accounts for 86.9%. The zone has a population of 3,054,239 inhabitants and has a historical connection to the investigation of leishmaniasis at Kutaber district where the first place in Ethiopia CL cases were identified. This district is located in this zone. Boru Meda Hospital has been providing leishmaniasis diagnosis and treatment since 2017. Thirty beds are dedicated to CL patients. It serves more than 400 patients daily with different medical conditions. The health system in the area has been affected by a local civil war that lasted about a year. There was mass displacement following the war. This impacted the clinical service provided to patients suffering from neglected tropical diseases like CL and other morbidities.

Data collection

Demographic data such as age, sex, date of visit, residence, and clinical details were collected from the CL patients' registration logbook using a structured questionnaire. Incomplete or unclear data were verified from patient charts and recorded in an Excel sheet. The effect of the local civil war on CL patients' diagnosis and treatment was done by comparing the number of CL patients diagnosed and treated at the Boru Meda Hospital before and after the war.

Diagnosis and treatment of cutaneous leishmaniasis

Its diagnosis and treatment in Ethiopia is done as per the guidelines of the Ethiopian Ministry of Health guideline: Diagnosis, Treatment and Prevention of Leishmaniasis, 2013. Diagnosis is being done by microscopic identification of the *Leishmania* amastigotes from skin scraping smear and/or by clinical decisions through characterizing the lesions. Skin scraping was taken from the active lesion, stained with Giemsa (10%), and examined for amastigotes using 100× objectives. Lesion types (LCL, MCL, and DCL) were determined by clinical characteristics. Confirmed CL cases, by either clinical or microscopy, were treated with intra-muscular SSG (20mg/kg/day) for 28 days.

Inclusion and exclusion criteria

In the context of this investigation, the entirety of patient data documented within the logbook was meticulously incorporated. Patient information characterized by incomplete or ambiguous variables was meticulously cross-referenced with corresponding patient charts for clarification. A comprehensive analysis was subsequently undertaken concerning the medical records of a cohort comprising 13 patients to rectify any discrepancies stemming from incomplete variables observed within the logbook. The exhaustive compilation of patient data thus lends exhaustive merit and integrity to the overall breadth and depth of this research endeavor.

Data analysis and interpretation

The data were analyzed by Statistical Package for Social Sciences (SPSS-23). Results were presented in frequency tables and charts. Non parametric test was used to test for possible association between CL cases and demographic variables and clinical parameters of the patients. Statistical significance was declared at $p< 0.05$

Results

Sociodemographic data

A total of 40,324 outpatients visited BMH between March 2022 and February 2023, with 492 confirmed cases of CL. Of these, 56.1% were males and 43.9% were females. The age range was 1-82 years, with a mean age of 22.59±16.96 and median age of 19 years. The majority of CL cases (55.28%) were under 20 years old. There were statistically significant differences in the proportions of age groups and those between males and females: $P< 0.001$ and $P=0.007$ respectively (Table 1).

Clinical characteristics of cutaneous leishmaniasis patients

In this one-year study, two clinical forms of CL were observed. The great majority (72%) of cases were LCL forms and 28% were MCL forms. There was a significant difference between the two clinical forms ($p<0.001$). Of the total CL cases, 67% were new, and 33% were repeat cases. The proportion of clinical forms between repeat and new cases was similar. Microscopic diagnosis identified 58.3% of cases as positive for amastigotes, while 41.7% were negative, but all cases were treated by clinical decisions (Table 1)

Table 1. **Demographic and clinical characteristics of CL patients (n=492) visiting Boru Meda Hospital, March 2022 –February 2023**

Characteristics	Frequency	Percent	P-value
Gender			
Female	216	43.90	
Male	276	56.10	0.007
Age (year)			
≤ 20	272	55.28	
21-40	144	29.27	0.001
40+	76	15.45	
CL clinical form			
LCL	354	71.95	
MCL	138	28.05	0.001
Treatment History			
New	330	67	
LCL	237	71.8	
MCL	93	27.2	
Repeat	162	33	0.001
LCL	117	72.2	
MCL	45	27.8	
Slide positivity			
Positive	287	58.3	0.001
Negative	205	41.7	

Seasonality of CL patient flow

There was a high patient flow for CL in spring and summer. June had the highest number of cases of visits at BMH, while December and September had the least number of cases registered at LTC, BMH. The prevalence of CL was 1.22% (492/40,324) out of the total outpatient visits (Figure 1).

Figure 1. **Seasonal flow of cutaneous leishmaniasis patients as compared with total patients at Boru Meda Hospital (CL pt.: CL patients; Total out pt.: Total outpatients)**

Cutaneous leishmaniasis at Boru Meda Hospital before and after the war

In the year from October 2021 to February 2022, there was a civil war in East Amhara. Gradually, after the civil war, the health system was restored, and a high number of CL cases (492 cases) were diagnosed and treated with the disease in one year (March 2022-February 2023). When this number was compared with the number of CL cases in 1 year back before the war (October 2020-September 2021), 167 CL cases were diagnosed and treated. The burden of CL disease

increased nearly threefold when the war was over (Figure 2).

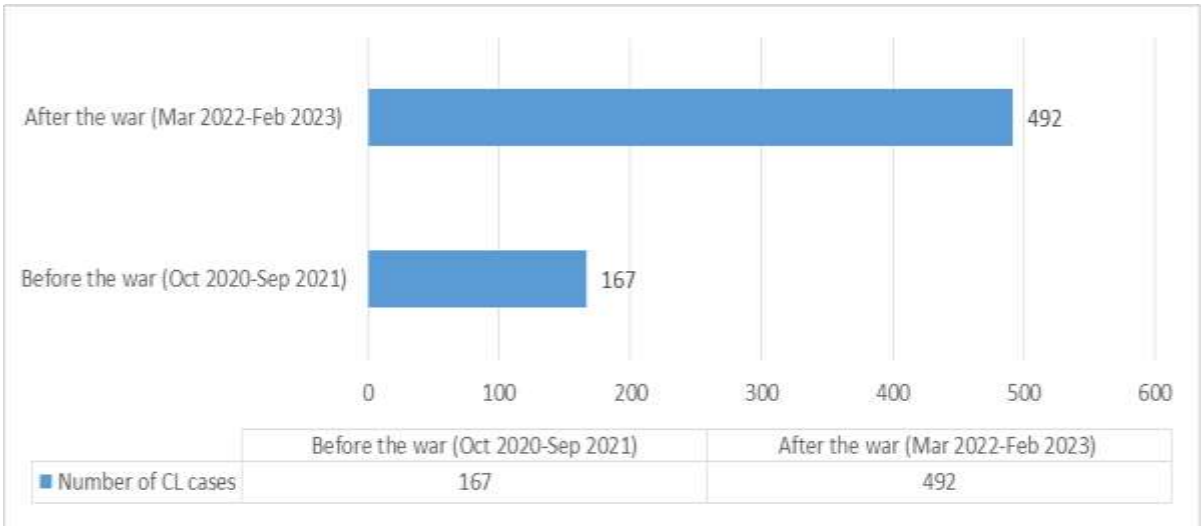

Figure 2. **Number of cutaneous leishmaniasis patients registered for treatment before and after the civil war at Boru Meda Hospital.**

Foci of cutaneous leishmaniasis in East Amhara

The 492 cases came from 5 Zones in East Amhara. The majority of the cases of CL were from the districts of South Wollo Zone. Of these, 12 districts make up 80% of the cases (Table 2).

Table 2. **Cutaneous leishmaniasis cases by district and zone in North-central Ethiopia**

District	Number of CL cases	Percent (%)	Zone
Dessie town	167	33.9	South Wollo
Tehwledere	39	7.9	South Wollo
Ambassel	26	5.3	South Wollo
Dessie Zuria	25	5.1	South Wollo
Wogedi	25	5.1	South Wollo
Dawunt	23	4.7	North Wollo
Kalu	20	4.1	South Wollo
Kuta Ber	20	4.1	South Wollo
Worebabo	16	3.3	South Wollo
Kombolcha	15	3	South Wollo
Sayint	15	3	South Wollo
Delanta	14	2.8	South Wollo
Worgesa	14	2.8	North Wollo
Haik town	11	2.2	South Wollo
Others	62	12.6	South Wollo, North Wollo, North Shewa, Oromia and Waghimra

Factors associated with repeat treatment history

The statistical analysis did not show any significant relation between treatment history and laboratory findings, microscopic findings, and sex, while CL type showed an association ($p<0.05$) with treatment history. The LCL type of the disease form was more common than the MCL (Table 3).

Table 3: **Treatment history of cutaneous leishmaniasis patients with associated factors at Boru Meda Hospital.**

Factors		Treatment History		(P-Value)
		New	Repeat	
Sex	F	137	79	(0.128)
	M	193	83	
CL type	MCL	93	45	(0.009)
	LCL	237	117	
Microscopic examination	Negative	143	62	(0.285)
	Positive	187	100	
Age	≤30	256	133	(0.28)
	31+	74	79	

Discussion

A one-year retrospective study found a 1.22% prevalence of CL from outpatients at Boru Meda Hospital, with 492 cases recorded. This indicates that high CL cases visited the hospital after the war. Immediate one year back, before the war, the number of CL cases treated was 167. This might be because the recent civil war disrupted healthcare services and led to a higher number of CL cases. The mass displacement, moving to a new area where CL is not endemic following the war might have also contributed to the high transmission of CL. The cases also remained untreated as they could not access the service. This is supported by a report from Sudan showing that civil unrest fuels the leishmaniasis transmission following the mass movement of people from place to place (8, 9, 10). These findings are higher than a previous report from the same institution in 2018, which focused only on dermatology clinics (6). Compared to a systematic review and meta-analysis in Ethiopia, our study demonstrated lower CL prevalence (11). The meta-analysis might not reflect the regional context and could not represent the study area because it included papers out of the Amhara region.

Our study showed that 72% of CL patients had LCL type, and 28% had MCL type. In a study in southern Ethiopia, 76% of CL cases infected with *L.aethopica* were LCL type (12), which is very close to ours, and the LCL type is the most common form among the patients. The reason why LCL is more common than other forms of CL needs to be investigated from both host and parasitic factors.

This study indicated that CL primarily affects individuals under 20 years old (55%), which entails increased transmission and vulnerability among younger populations. The disease burden difference in age groups was significant ($p<0.05$). This could hinder school attendance and worsen disease progression as seen in other regions of Ethiopia, where children remained highly affected by the disease, which contributed (57%) of the CL case burden (12).

Previous research in the same hospital revealed that children ≤ 14 years accounted for 27.2% of the CL burden (6). However, a 10-year trend analysis from the University of Gondar showed that individuals aged under 15 had the lowest prevalence of CL (5). This discrepancy needs further research. From the overall findings, we could understand that a combination of epidemiological and immunological study is important to better understand the distribution of the disease across the age groups.

The occurrence of CL is higher in males than in females ($p<0.05$). Different studies also support our result; a higher proportion of males with CL, 71.4% and 65.1%, respectively, are affected by the disease (13, 5). Conversely, a study in Iraq showed an equal ratio of males and females who lived with the disease (14). From our context, a community-based study could discourse whether gender is a factor or other health-seeking behavior, socio-cultural and other factors that determine the difference for the observed discrepancy.

In this study, the prevalence of CL was highest in Dessie town. This might be because the residents at Dessie have better health-seeking behavior than the nearby rural areas. Likewise, a study that supports our finding confirmed that Dessie had a 12.2% higher risk of acquiring CL (6). Unlike our finding (highest in spring and lowest in winter), autumn had the highest number of CL cases at Tefera Hailu Hospital, while summer had the lowest (15). CL patients in Ethiopia seek treatment when they have spare time; agroecological zones also influence the differences in treatment-seeking behavior. Amhara region is so wide and has different climatic conditions that might have resulted in differences in patient flow patterns.

Treatment failure assessment of CL patients in Iraq showed a mean age of 18.8 years old (14), while our study on treatment failure indicated that the mean age of the patients was 21 years old. This small difference between the two studies may be justified by nutrition, genetics, health-seeking behavior, and possible parasite strain, but it needs further objective assessment.

In our finding, 33% of CL patients visiting the LTC at BMH for treatment were repeat cases, while in a study in Sekota, 10.7% were recurrent or repeat CL cases (15). However, a study at Gondar University Hospital was higher than our finding, which showed that (38.3%) were repeatcomers; hence, no cure was seen in the first treatment episode (13). A study on *L. braziliensis* infection that compared the response of

liposomal amphotericin B (L-AmB) and SSG showed 29% and 3% failure, respectively (16). Maybe SSG is more effective for *L. braziliensis* than *L.aethiopica*, but this still needs a reasonable sample size for scientific justification. In Iraq, the intralesional (IL) administration of SSG showed a comparable cure rate with Intra Muscular treatment 786 (97.7%) (14). Nevertheless, only 43 CL patients (60%) at Boru Meda Hospital were cured with IL treatment in 90 days (17). A case report from Bahir Dar found that leishmaniasis due to *L. aethiopica* can progress and shift from one clinical type to the other, and it was this type of clinical type that was found difficult to manage with the treatment of SSG (18). Comparing studies of Iraq with Ethiopian CL patients' treatment response vivid that the treatment response for *L. aethiopica* was inadequate for the SSG regimen. This finding is also supported by a study conducted at Bahir Dar, where nearly 40% of the patients needed retreatment (19). The possible reasons include parasitic and host genetic variations, mutations, drug resistance' and disease severity. In Ethiopia, the CL disease type is more complex and serious than the ones found in other parts of the world (1). The persistent presence of parasites after treatment, as there is no sterile cure, may contribute to relapse, along with bigger lesion size and high parasitic load (17). In Iraq, treatment failure was observed to be associated with the number of lesions (14).

This information implies that there is a need for more options for the treatment of CL that could reduce the ineffectiveness of the current treatment regimen in CL. Extended time for treatment negatively affects patients in various ways including economic and psychosocial.

Conclusion

The study revealed that Cutaneous Leishmaniasis (CL) is a significant public health concern in North-Central Ethiopia, with a notable increase in recurrent cases and a surge in cases following a period of civil unrest. The high prevalence of recurrent cases indicates the persistence of the issue in the area, potentially perpetuating the cycle of infection and complicating disease transmission dynamics.

The significant rise in CL cases after a mass displacement due to civil unrest nearly tripled the prevalence rate, suggesting the potential spread of the disease to areas where it was previously uncommon. This further exposes residents to the disease, potentially worsening its spread and might cause epidemics of CL. Advance research on the genomic variations and effectiveness of sodium stibogluconate (SSG) in treating CL is necessary.

Conflict of Interest: The authors have declared that there is no competing interest.

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Authors Contribution:

Bizuayehu Gashaw: Conceptualization, Data collection and curation, analysis, investigation, Writing the draft manuscript, and editing.
Endalkachew Nibret: Conceptualization, analysis, review, and editing of the manuscript
Endalew Yizengaw: Conceptualization, data collection, analysis, review, and editing
Feleke Tilahun: Conceptualization and data collection
Banchwossen Sebsibe: Conceptualization, data collection, and editing
Gizachew Yisaw: Supervision of the data collection
Sissay Tebeje: Supervision of the data collection

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