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Original Article

Case Notification of Cutaneous Leishmaniasis at Different Elevations in the North-Central Ethiopia from 2018 To 2022

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Abstract

Background: We aimed to analyze a four-year trend of Cutaneous leishmaniasis (CL) to determine risk levels and hotspots in North-central Ethiopia.

Methods: This retrospective study was conducted at Boru Meda Hospital (BMH) from March to April 2023, focusing on CL patients treated at the leishmaniasis treatment center (LTC). Data collected included age, gender, CL type, and other clinical factors. Each patient's origin was traced and geographically mapped by elevation to assess CL risk levels.

Results: There were a total of 573 CL patients reported from 46 districts, with a higher number of male patients (n=356) compared to female patients (n=217) ($P < 0.001$). The median age of the patients was 21 years [15-30], with the highest number of CL cases observed among individuals aged 16 to 30 years. The majority of cases (69%) presented with localized CL (LCL). About 39% of patients had a previous treatment history for CL. A significant clustering of CL cases was observed at elevation of 2301-3300 meters above sea level ($\chi^2: 17.5$; $P < 0.001$), with the highest incidence (case notification) of 14.2/100,000 population.

Conclusion: Foci of CL, were burdened at higher elevations and no clinical variation were observed between elevation differences. The majority of cases were concentrated in an area covering approximately 21.4% of the total land mass. CL continues to be a significant issue in North-central Ethiopia and has the potential to spread to new areas.



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Introduction

Leishmaniasis is a disease that can range from a self-healing skin lesion to a fatal systemic infection if left untreated. The severity of the disease can be influenced by genetic variations in the parasite or the immune response of the host (1). In Ethiopia, the most common form of cutaneous leishmaniasis is caused by the parasite *Leishmania aethiopica* (2). Various small studies have examined the prevalence of Cutaneous Leishmaniasis (CL), with one community-based study in Tigray finding a prevalence of 2.3%. Children were found to be the most affected group, with nearly 21% of study subjects having scars from previous infections (3). Active CL prevalence varies from 0.01% to 10.8%. *L. aethiopica* in Ethiopia presents with crusty lesions, local edema, and color changes, indicating distinct severity compared to other species (4, 5). The incidence of leishmaniasis is closely linked to socio-economic challenges and environmental shifts (6). In Silti woreda, southern Ethiopia, an outbreak of cutaneous leishmaniasis was recorded with a prevalence rate of 4.8% (7). While there is no nationwide prevalence data available for cutaneous leishmaniasis in Ethiopia, a systematic review suggests a national pooled prevalence of 19% (8).

In Ethiopia, *Leishmania* RNA virus (LRV) might increase lesion severity CL (5), but recent findings reveal no notable LRV prevalence differences among clinical forms, including localized cutaneous leishmaniasis, diffuse cutaneous leishmaniasis, and mucocutaneous leishmaniasis (1).

In Ethiopia, localized CL is prevalent, while mucocutaneous and diffuse cutaneous forms occur less frequently and may have longer healing (4). Treatment failure is commonly observed in MCL and DCL cases (1, 9). The sand fly species of *Phlebotomus longipes* and *P. pedifer* transmit *Leishmania aethiopica*, primarily found at altitudes between 2326 and 2500 meters where the rock hyrax serves as the parasite's reservoir (4, 10).

In North-central Ethiopia, Boru Meda Hospital (BMH) serves as a treatment center for cutaneous leishmaniasis (CL), but the foci and risk areas for CL poorly understood. We aimed to identify

common CL areas by mapping endemic regions and assessing clinical features at various elevations. An accurate understanding of CL distribution will enhance disease transmission control efforts in the area.

Materials and Methods

Study design and period

In this retrospective study, data from the patient registration book at BMH were analyzed for CL cases registered at the hospital from July 30, 2018, to February 28, 2022. Data collection took place from March to April 2023.

Study area

The research occurred at BMH's LTC in South Wollo Zone, Ethiopia, at 11°8'N, 39°38'E, 2,470-2,550 meters elevation, providing general medical services and referrals within the region.

Data collection

Data were extracted from the CL patient registration logbook, encompassing age, gender, CL type, treatment history, lesion size, and disease onset. Environmental factors like elevation and population size were analyzed. To ensure accuracy, logbook information was photographed, entered into Excel, and verified with health workers at BMH.

Diagnosis of cutaneous leishmaniasis

At BMH, cutaneous leishmaniasis is diagnosed by examining skin scrapings under a microscope for amastigotes. Negative results lead to dermatologist evaluation to decide on treatment necessity.

Treatment of cutaneous leishmaniasis

Treatment of CL cases at BMH typically involves intramuscular injection of Pentavalent Antimonials where Sodium Stibogluconate (SSG) is the most common drug. It is administered at a dosage of 20 mg/kg/day for 4 weeks. The management and duration of treatment for both new and relapsed cases of CL are based on the national guidelines of Ethiopia (11). Besides SSG, meglumine antimonate and liposomal amphotericin B are also alternatively used. Moreover, Liposomal amphotericin B, miltefosine, and paromomycin are used as second line options

with 20 mg/Kg/day depending on the disease severity and response for the first line drug. Topical treatments are used for CL patients with uncomplicated LCL lesions cryotherapy with liquid nitrogen is also used as treatment option at BMH. Systemic treatment with SSG and paromomycin are a treatment of choice for systemic treatment of MCL due to *L. aethiopica* (11).

Incidence rate of cutaneous leishmaniasis (Case notification)

The incidence of CL cases was calculated by dividing the total CL cases by the total number of people who live in the area. And, it was converted to 100,000 populations.

Category of elevation

According to the June 2022 report of plan commission, the Amhara National Regional State has five elevation categories and corresponding district population names.

1. <500 meters (1%): Bereha (Hot lowland)
2. 500-1500 meters (29%): Kolla (lowland)
3. 1501-2300 meter (43%): Woina Dega (mid lands)
4. 2301-3200 meters (24%): Dega (highlands)
5. >3200 meter (3%): Wurch+kur (highlands)

Data analysis

The data was analyzed with SPSS version 23 using the Pearson chi-square test to assess proportion differences across groups, with significance set at $P < 0.05$.

Operational definition

- Elevation: indicates height above above sea level where CL patients live
- New cases: Are first time LTC visitors
- Repeat cases: are individuals treated previously for cutaneous leishmaniasis
- Case notification: Number of CL cases from one district during the study period *100,000 population/total population of the district.

Ethical consideration

The Amhara Public Health Institute approved and conducted this study under protocol NoH/R/T/T/D/07/73. The privacy and confidentiality of the study participants were maintained by keeping them anonymous. No personal identifying information, such as names, was included in the data collection checklist.

Results

Demographic variables of CL cases

A retrospective study of 573 CL cases at LTC, BMH found 217 females (38%) and 354 males (62%), with significant sex differences ($P < 0.001$). The median age was 21 (IQR: 15-30 years), and the mean age was 24.8, with the highest prevalence in those aged 16-30 (Table 1)

Table 1: Demographic variables of CL patients

Variable	Classification	Frequency	χ^2 : (P-Value)
Age (yr)	≤15	159	5 (0.0001)
	16-30	280	
	31-45	64	
	46-60	49	
	61-75	17	
	>75	3	
	Total	572	
Sex	F	217	32.3 (0.0001)
	M	354	
	Total	571	

Clinical characteristics of cutaneous leishmaniasis

The great majority (69%) of CL patients were presented with LCL clinical forms. The remaining

CL cases were of MCL form. Most (61%) of the CL cases were new, diagnosed and treated for the

first time and 39% were repeats. Regarding the lesion size, 54.5% of CL cases have a lesion size of 4cm² (Table 2). There was a statistically significant

difference observed between the occurrence of CL forms ($P < 0.001$) (Table 2).

Table 2: Clinical characteristics of CL patients

<i>Characterized Variables</i>		<i>Frequency (%)</i>	<i>χ² (P -Value)</i>
CL type	LCL	390 (69)	387.5 (0.0001)
	MCL	177 (31)	
	Total	567(100)	
Treatment history	New	346 (61)	307.4 (0.0001)
	Repeat	220 (39)	
	Total	566 (100)	
Lesion size	≥4cm ²	226 (45.8)	101 (0.0001)
	<4cm ²	267 (54.2)	
	Total	493 (100)	
Diagnosis	Microscopy	201 (39)	175 (0.0001)
	Clinical	315 (61)	
	Total	516 (100)	

More MCL cases tend to be getting negative than LCL clinical form in a microscopic diag-

nosis and this difference was statistically significant (Table 3).

Table 3: Microscopic result in different clinical forms

<i>Microscopic result (%)</i>		<i>CL type and number (%)</i>			
		LCL	χ² (P -Value)	MCL	χ² (P -Value)
Negative	315 (61)	198 (55.5)	20.9 (0.0001)	117 (73.5)	65 (0.0001)
Positive	201 (39)	159 (44.5)		42 (26.5)	
Total	516 (100)	357 (100%)		159 (100)	

Yearly trend of CL patients

The number of recorded CL cases varied across different years. It shows that the most

cases belonged to the year 2019 with 280 numbers (Table 4).

Table 4: The patient flow of CL cases at LTC and trend in 4 years

<i>Year</i>	<i>2018*</i>	<i>2019</i>	<i>2020</i>	<i>2021</i>	<i>2022#</i>	<i>Total</i>
Case Number	42	280	42	168	37	569

*5 month data
#2 month data

Mapping of CL patients by district

A total of 561 CL cases were reported across 46 districts in East Amhara, primarily at elevations of 2,301 to 3,300 meters, covering over

21% of the land mass. Cases varied by district, with Dessie city reporting the highest number. Eight cases were unclassified, while three were reported from Tigray, Semera, and Addis Ab-

aba, and one was unassigned (Data not shown).

CL case notification and risk mapping by elevation

The study examined case notification and disease burden by elevation and district. The

lowest elevation was 1358 meters in Artumafursi and Jiletimuga districts, each with one case. Case burden varied in areas with similar elevations (Table 5).

Table 5: Case notification and risk mapping of CL in different elevations: North-central Ethiopia, 2023

<i>Weather</i>	<i>Elevation</i>	<i>CL case number</i>	<i>Districts where cases reported</i>	<i>Number of people who live in the area/ district</i>	<i>Case notification/ 100,000</i>	<i>χ²(P - value)</i>
Bereha (Hot low land)	<500	0	0	0	0	17(0.0001)
Kolla (low land)	500-1500	2	2	204,241	0.97	
Woina Dega (mid lands)	1501-2300	149	20	2,897,502	5.14	
Dega (highlands)	2301-3300	419	24	2,937,931	14.2	
Wurch+kur (highlands)	>3300	0	0	0	0	
Total		570	46	6,039,674	9.4	

Discussion

The mean age of CL patients at the LTC in BMH was 24.8 years, with a median of 21 and a standard deviation of ±16.2. In contrast, a prior study reported a mean age of 31.9 years and a standard deviation of ±14.29, indicating a shift towards younger patients over time. The disease prevalence peaked among those aged 16-45, with 70% of cases in this group (2). Notably, our study found the 16-30 age group most affected, aligning with other research showing the highest burden among individuals aged 15-29 (12) and a median age of 23 in CL cases (13).

A study conducted at the University of Gondar reported a slightly higher mean age, 28.72 years for CL cases (14), with an age range of 1 month to 88 years. In contrast, our study found a mean age of 24.8 years with cases spanning from 1 to 90 years old. A community-based survey in Silti Woreda, southern Ethiopia revealed that the age group most affected was 11-20 years old (7). This difference could be due to the study design

and the CL endemicity of the area, the CL case notification in Silti Woreda where a new epidemic may have exposed immunologically incompetent children to the disease. The CL has been present in the BMH area for a long time and is considered endemic (9). The first cases of CL in Ethiopia were identified in Kutaber, near BMH. In Ethiopia, younger children are more susceptible to *Leishmania* recidivans, the chronic and relapsing form of CL (15). This form of the disease affects both the skin and mucous membranes in these patients, indicating that their macrophages and T-cells may not be effectively killing the parasite.

More (68%) males were affected by the CL disease in our study. This gender disparity was statistically significant ($P<0.05$). A similar trend was observed in Israel, where CL incidence was higher in males than females (16). The difference in gender distribution in cases of leishmaniasis may be due to variations in health-seeking behaviors. For example, one study found a higher prevalence of the disease in males (13.7%) compared to females (8.8%)

(2). In another study, a majority of cases were found in males 543(61.1%), indicating potential disparities in access to healthcare services (9). While in a community-based study on the prevalence of CL, both sexes showed almost an equal burden of infection by CL (3). This highlights the impact of gender inequality on the treatment and management of Leishmaniasis. Additionally, low health-seeking behavior among certain populations may also play a role in the gender disparities observed in Leishmaniasis cases.

In a study of 491 CL cases, 265 (54%) had lesions under 4cm² and 226 (46%) were 4 cm² or larger. While *L. aethiopicus* lesions are thought to present more severely (4) as *LRV*, while recent findings suggest that *LRV* prevalence in *L. aethiopicus* is comparable to other strains, questioning the virus's role in disease severity (5).

In terms of treatment history, our study revealed that 61% of the CL cases were new cases, while 39% were repeat cases (41.3% females and 58.7% males). These results are in line with a previous study at BMH that showed 41% of CL patients were repeat cases (38.7% females and 61.3% males) (9). Likewise, in a study (13) the CL patients who need retreatment accounted 38%. All the findings reflect a need for wise choices for the treatment of CL and a need for assessment before treatment.

In our study, of 516 CL cases, and only 39% of skin scrape were positive for amastigotes, in Tigray also, 31.4% of the screened cases were positive (17). In our study, microscopic positivity of LCL were (44.5%) than MCL (26.5%). Findings contrast with (6), showed (60.8% positivity), highlighting the challenges of microscopic identification of the parasite in our study hospital.

The clinical types presented in BMH showed that the majorities (69%) of cases were of LCL type and 31% were MCL. Unlike our finding in the study conducted in Tigray (17), indicated that 51.4% were LCL and 22.9% of them were DCL. A study conducted in Gondar

showed that 52% of them had LCL and 4.5% were DCL (13). The difference in the CL frequency of clinical forms could be a geographical matter that needs in-depth study and is open for research. In addition, the technical competency to define CL cases to different clinical types might also contribute for the inconsistency. Based on our study, we noticed that the number of CL cases was different across the reported years. This is likely due to the impact of the COVID-19 pandemic in 2019, in 2021. However, as the year progressed, the patient flow decreased again, this was likely due to the civil unrest in the study area in 2022.

Our study in North-central Ethiopia highlighted endemic cutaneous leishmaniasis (CL) cases predominantly clustered in highland areas (2301-3300 meters). In contrast, Sri Lanka's Moran's I Index of 0.0321 suggests random case distribution (18). Our finding was also supported by other study in Ethiopia (19). This is associated with distribution of the vector, *P. longipes* (The major vector of CL in Ethiopia) (19). Our study showed that while CL cases increased with elevation, case numbers varied significantly even at similar altitudes; Dessie recorded 133 cases at 2525 meters, while Wuchale had only 2 at 2526. This indicates that factors like sandfly species and environmental conditions also influence CL distribution (10, 20-22)

Our study identified CL cases at altitudes of 1358 to 3017 meters. *P. longipes* was positively linked to altitude, while *P. pedifer* was absent above 2000 meters (19), In Nepal, for the first time CL due to *L. donovani*, was confirmed by PCR found at an elevation 2000 meters above sea level (23). Likewise, a study on the vector of leishmaniasis in Northwest Ethiopia showed that *P. longipes* were found in Tikil Dingay (1950 meter-2100 meter) and Gondar Town (2200 meter-2300 meter) (19). In our study, CL cases appeared at varied elevations, suggesting that vectors may circulate widely. Factors such as environmental changes, population mobility, and projects like irrigation and

dam construction may contribute to the broader spread of sandflies and the disease. A similar study (24), that focused on altitude and CL showed that *P. pedifer*, a vector for *L. aethiopica*, was found at altitudes ranging from 1685m to 2892m. Due to all these the survival of the vector at wider altitude ranges and the presence of the disease in the wider area is globally recognized as an emerging disease and public health problem (25).

In contrast to our study, a study conducted in Iran revealed a high prevalence of CL at altitudes ranging from 600 to 1800 meters (26). Additionally, a study conducted by Sang et al (21) indicated the presence of promastigote in the guts of female sandflies (*P. pedifer*) at altitudes below 1900 meters.

The case notification in Israel had an incidence of 5/100,000 in males vs. 3.5/100,000 in females (16). In our study the highest case notification in low land was 0.97/100,000 people but in high lands, it was 14.2/100,000 and the average incidence was 9.4/100,000 population. Similarly, in Iran the case occurrence was clustered in a defined area but the incidence of CL cases was 19.9/100,000 (27). Collectively, these studies highlights that CL cases in North-central Ethiopia are predominantly concentrated in highland areas as compared to other countries.

Related studies in CL and VL showed the establishment of a laboratory surveillance system for the detection of CL in the endemic areas of the disease. This will help for early detection and management of cases. This will again help to control the disease transmission and improves treatment response (28, 29).

The main limitation of this study is lack of detail clinical features of CL cases.

Conclusion

In North-central Ethiopia, high CL cases cluster at elevations of 2301-3300 meters, exposing over 3 million residents to risk and the existence of the disease in varied elevations complicating the control efforts.

The widespread distribution of CL cases across various districts highlights the urgent need for comprehensive surveillance and control measures to combat the increasing burden of the disease. A comprehensive laboratory based periodic surveillance of CL cases in the community is essential to control the disease. Awareness creation about prevention mechanisms especially sandfly bite protection is also crucial in different seasons of the year to combat the disease. It is recommended to conduct a large-scale community-based study to address the issues identified in this study and effectively control CL in the region. Moreover, training of laboratory personnel about skin scrapping and parasite identification is quite important as significant number of CL patients are diagnosed clinically.

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Conflict of interest

The authors declare that they have no competing interests

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