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Original Article

Self-Reporting Cutaneous Leishmaniasis Patients and Nutritional Status: A Study of the Host Factor in Remote Areas of Ethiopia

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Abstract

Background: *Leishmania aethiopica* is the leading cause of cutaneous leishmaniasis (CL) in Ethiopia. Different clinical manifestations might be related to host immunity, which itself can be influenced by the host's nutritional status. However, there is limited evidence that associates nutritional status with CL in Ethiopia. We investigated the relationship between clinical variables of CL and malnutrition.

Methods: A retrospective study was conducted in June 2024. Patient data was analyzed from those treated for CL and screened for nutrition from January 2022 to May 2024 at Tefera Hailu and Addis Zemen Primary Hospitals. Nutritional status was assessed through Anthropometric measurements.

Results: A total of 470 CL patients were treated, with a prevalence of 14.65/100, 000 population affected. Out of the total CL patients, 217 were assessed for nutrition, 22% were malnourished. Malnutrition was most prevalent in mucosal (30%) and recurrent cases (38.5%), compared to localized (20%) and new cases (21%) respectively.

Conclusions: Malnutrition might have the potential to shape the clinical manifestation and treatment outcome in CL patients. In CL endemic areas nutritional supplement with the treatment of CL could require for better patient outcome.

Introduction

Leishmaniasis is a disease caused by a protozoan parasite, *Leishmania*. After inoculation to the host, the parasite has a novel mechanism to bypass the immune system and it manipulates macrophages via DNA methylation and GP63, as a result, the parasite can easily replicate and spread (1,2). The amastigotes can cause progressive leishmaniasis (1, 2). Cutaneous leishmaniasis (CL) presents in different clinical forms: Localized (LCL), Mucosal (MCL), and Diffuse (DCL). This outcome is influenced by parasitic diversity and host immunity (2-5). The MCL form occurs mainly in immunocompromised individuals with fewer parasites while the LCL form is self-limited over time, the DCL form is characterized by non-ulcerative nodular lesions with high parasitemia (2-5). The disease is exacerbated by urbanization, low socioeconomic status, and malnutrition. The lesion recovery takes 3-18 months (2-6).

The diagnosis of CL is mostly based on microscopic techniques with 70-75% sensitivity. The disease is challenging to treat and control with no available vaccine (7-8). Nutrition, geography, and disease endemicity also influence the clinical presentation and severity of CL. High IL-10, IL-12, and IFN-γ mRNA levels correlate with worsened lesions (3, 9, 10).

Asymptomatic leishmaniasis carriers can harbor parasites for long period of time, affecting disease distribution and foci. These people could be immunocompetent and well-nourished individuals (11-14). Maintaining optimal nutrition is vital for health. Ten percent weight loss may prolong hospital stays, with low weight and hypoalbuminemia linked to poor outcomes in American Tegumentary Leishmaniasis (15-17).

L. aethiopica is the leading cause of CL in Ethiopia. Different clinical manifestations of CL caused by *L. aethiopica* might be related to host immunity, which itself can be influenced by the host's nutritional status. However, there is limited evidence that associate nutritional status with CL in Ethiopia. We aimed to assess the effect of nutritional status on the clinical characteristics of CL patients in the Amhara Region, Ethiopia.

Materials and Methods

This retrospective cross-sectional study was conducted at Leishmaniasis Treatment Centers (LTCs) in Tefera Hailu Memorial Hospital and Addis Zemen Primary Hospital in June/2024, Amhara Region, Ethiopia.

Study population: Confirmed CL patients treated at the study hospitals during the study period and who have complete information in the patient's registration logbook.

Inclusion: CL patients with positive diagnoses and nutritional assessments were done. Exclusion: Those under 6 months of age or with known comorbidities (TB -HIV, diabetics, hypertension).

Microscopic examination of amastigotes with 10% Giemsa stain and clinical evaluation was conducted for microscopy negative cases.

Determination of nutritional status of CL cases

Nutritional assessment was assessed using mid-upper arm circumference (MUAC), and Body mass index (BMI). The finding was categorized as sever, moderate and normal. MUAC was also used to assess malnutrition in children 6-59 months: <115 mm indicates severe acute malnutrition, 115-124 mm moderate, and ≥125 mm normal. Pregnant and lactating mothers: MUAC: <190mm severe malnutrition, 190-229mm moderate, ≥230mm normal (16, 18).

Data management and analysis

SPSS version 23 (IBM Corp., Armonk, NY, USA) was applied: Chi-square (Person chi-square and Fisher's exact tests) was used to test the magnitude of the occurrence of variables from the expected by the assumption of equal distribution between the study variables and significance was declared when $P<0.05$.

Operational definition

Host factors in this study reflect the nutritional status of CL patients.

Chronicity of CL: being acute or chronic

Acute is the patients who came ≤ 6 month and Chronic is those CL patients who came after 6 month of the onset of CL disease.

Ethics approval

Ethical approval was given by Amhara Public Health Institute (NoH/R/T/T/D/07/83) and a support letter (Ref: APHI 03/1691) for the study. All data collected for the study has been kept anonymous and was not transferred to third parties. Personal identifiers, including names, were not used.

Results

Demographic characteristics of CL patients and the burden of the disease

A total of 470 (354 from South Gondar and 116 waghimra Zone) CL patients were treated in the study period. Out of these CL patients nutritional data were reported for 217 patients. Close to a quarter, 48(22%) CL patients were malnourished. The majority of malnourished CL cases, 66.7% were from waghimra. The CL patients were from 25 districts (17 from South Gondar and 8 from Waghimra zone). The mean age was 25.5 years old in malnourished and 27.2 in normal cases respectively. The highest cases of CL (41%, n=89) were in age ≤18 years, (χ2: 77.7; p < 0.05). (Table 1).

Table 1: Demographic and epidemiologic features of patients

Variables	Frequency	%	χ^2:(df):p-value
Age (yr)			
≤18	89	41	77.7:(3):0.000
19-40	82	38	
41-60	35	16	
>60	11	5	
Total	217		
Sex			
F	59	27	45:(1):0.000
M	158	73	
Total	217		
CL cases of malnutrition by zone			
South Gondar	16	33	NA
Waghimra	32	67	
Total	48		
CL patients screened for nutrition			
South Gondar	121	56	NA
Waghimra	96	44	
Total	217		
CL reporting districts			
South Gondar	17	68	NA
Waghimra	8	32	
Total	25		
Prevalence by/100,000 population by Zone			
South Gondar [a]	354	13.51	NA
Waghimra [b]	116	19.72	
Total [c]	470	14.65	

[a] = Total population of South Gondar in 2024 (2, 619, 682)
[b] = Total population of Waghimra in 2024 (588, 082)
[c] = Total population of the study area in 2024 (3, 207, 770)
NA= Not Applicable

Clinical polymorphism of CL patients

Among CL patients, LCL was 81%, ($p<0.05$). Delayed treatment for over six months was seen in 64% of patients. 42% of CL patients had lesions equal to or larger than 4cm² (Table 2).

Table 2: Clinical characteristics of cutaneous leishmaniasis

Variables	Frequency	%	χ²:(df):p-value
Chronicity of the disease			
0-6month	73	36	7:(1):0.000
>6month	129	64	
Total	202		
CL form			
LCL	176	81	83:(9):0.000
MCL	41	19	
Total	217		
Lesion size			
<4cm²	120	58	5:(1):0.02
≥4cm²	87	42	
Total	207		
Microscopic examination			
Positive	199	97	181:(1):0.000
Negative	6	3	
Total	205		
Treatment history			
New	204	94	168: (1):0.000
Repeat (recurrent)	13	6	
Total	217		

Magnitude of malnutrition and associated factors

From nutritionally screened cases, 23(27%) were children with aged ≤18 years. Malnutrition rate was higher in females (27%) than males (20%) and was more common in acute CL patients (29%) compared to chronic patients (17%). A significant relationship was found ($p<0.05$) between nutritional status and age, disease chronicity, and clinical form. Additionally, 38.5% of repeat/recurrent patients were malnourished versus 21% of new cases (Table 3).

Table 3: Malnutrition across different variables in cutaneous leishmaniasis

Variables		Malnutrition		χ²:(df):p-value
		Yes (%)	No (%)	
Age category	≤18	23 (27)	63 (73)	9.8:(3):0.02
	19-40	13 (16)	69 (84)	
	41-60	6 (17)	29 (83)	
	>60	6 (55)	5 (45)	
	Total	48	166	
Sex category	F	16 (27)	43 (73)	1.1:(1):0.27
	M	32 (20)	126 (80)	
	Total	48	169	
Duration of illness	0-6month	21(29)	52 (71)	3.8:(1):0.03
	>6month	22 (17)	107(83)	
	Total	43	159	

Lesion size	<4cm2	27(22.5)	93 (77.5)	0.26:(1):0.60
	≥4cm²	17(20)	70 (80)	
	Total	44	163	
CL -form	LCL	36 (20)	140 (80)	1.5:(1):0.22
	MCL	12 (30)	29 (70)	
	Total	48	169	
Treatment History	New	43 (21)	161 (79)	2.2:(2):0.3
	Repeat/recurrent	5 (38.5)	8 (61.5)	
	Total	48	169	
Microscopy result	P	45 (23)	154 (77)	1.7:(1):0.18
	N	0	6 (100)	
	Total	48	160	

The malnutrition rate was higher within the MCL group than LCL (Table 4).

Table 4: Nutritional status and clinical characteristics of cutaneous leishmaniasis

Variables	Nutritional status			Total	χ2:(df):p-value
	Sever (%)	Moderate (%)	Normal (%)		
Treatment history					
New	11 (5.4)	32 (15.7)	161(78.9)	204 (100)	2.2: (2): 0.3
Recurrent	1 (7.7)	4 (30.8)	8 (61.5)	13 (100)	
Total	12	36	169	217	
CL form					
LCL	8 (4.5)	28(16)	140 (79.5)	176 (100)	2.2:(2):0.3
MCL	4 (10)	8 (19.5)	29 (70.7)	41(100)	
Total	12	36	269	217	
Lesion size					
<4cm²	3 (2.5)	24 (20)	93 (77.5)	120 (100)	2.5(2):0.2
≥4cm²	5 (6)	12 (14)	70 (80)	87 (100)	
Total	8	36	163	207	
Age					
≤18	3 (3.4)	20 (22.4)	66 (74.2)	89 (100)	14.7: (6):0.02
19-40	6 (7.3)	7 (8.5)	69 (84.2)	82 (100)	
41-60	2 (5.8)	4 (11.4)	29 (82.8)	35 (100)	
>60	1 (9)	5 (45.5)	5 (45.5)	11	
Total	12	36	169	217	
Microscopy					
Positive	10	35	154	199	1.7:(2):0.4
Negative	0	0	6	6	
Total	10	35	160	205	

Cutaneous leishmaniasis chronicity and associated factors

In the first six months of the onset of CL lesion, only 29% of children under 18 sought medical care but older individuals were more likely to seek treatment (77%). The majority (48%) of CL patients with acute lesion had small (<4cm²) lesion size (Table 5).

Table 5: Chronicity and associated factors of cutaneous leishmaniasis

Variables	Time of first visit in (month)					χ2:(df):p-value
Month	≤6	<13	13-24	>24	Total	
Age						
≤18	25 (29)	52 (60.5)	4 (4.5)	5 (6)	86 (100)	14: (9): 0.1
19-40	34 (46)	37 (50)	2 (2.7)	1 (1.3)	74 (100)	
>40	13 (31)	23 (54.7)	1 (2.3)	5 (12)	42 (100)	
Total	72	112	7	11	202	
Nutrition status						
SAM	5 (50)	5 (50)	0 (0)	0 (0)	10 (100)	6.4 :(6): 0.3
MAM	16 (48.5)	16 (48.5)	1 (3)	0 (0)	33 (100)	
Normal	51 (32)	91 (57)	6 (4)	11 (7)	159 (100)	
Total	72	112	7	11	202	
Lesion size						
<4cm²	56 (48)	57(49)	0 (0)	3 (3)	116 (100)	28: (3): 0.0001
≥4cm²	14 (17.5)	52 (65)	6 (7.5)	8 (10)	80 (100)	
Total	70	109	6	11	196	

Discussion

A total of 420 CL cases were diagnosed and treated. Nutritional assessment was done for 217 CL patients. The result showed that malnourished individuals had a mean age of 25.5 years, while nutritionally competent CL patients were 27.2 years. It is substantiated by a significant link between age and nutritional status. Malnutrition and CL burden were higher in children, <18 years old (27%). This showed that malnutrition might fuel the CL disease. In this study more males were treated and significantly associated with the disease, consistent with previous findings (18, 19).

Our study revealed a 29% malnutrition rate in patients with CL seeking treatment within 0-6 months, compared to 17% after 6 months. This suggests that individual's initially having poor nutritional baseline could develop CL following *Leishmania* infection, and/or response in early infection may need higher energy-intensive mechanism for first line immune responses later trigger for infection cycle (1, 20).

Our finding was supported by a study in Ethiopia (21), according to this study, the BMI measurements showed that approximately 29% of adolescent girls aged 15-19 were underweight (BMI <18.5). In addition, the prevalence of stunting among children under 5 years old was reported to be 40% in Tigray and 42% in Amhara regions of Ethiopia (22). These nutritional deficiencies could potentially serve as a foundational factor contributing to the increased incidence of CL at younger ages. This finding is consistent with previous studies conducted in Tigray, north Ethiopia (23), and Addis Ababa, central Ethiopia (24), which also found a higher prevalence of CL in individuals under the age of 18 years.

Our research revealed that 27% of females were CL patients, a bit lower than the study in Gayint, the female patients were 36.8%, and this could be the methodological difference used to conduct the research (25).

This study revealed that 22% of CL patients are malnourished, raising serious concerns and echoing findings from previous studies (26, 27). The prevalence of malnutrition in older groups in the above studies was lower than

our finding. Likewise, a study on nutritional status in adults from Harari, Ethiopia (28), reported a prevalence of 15.7%. A study conducted on American Tegumentary Leishmaniasis (17), found that 10% of patients had low body weight. This might be explained by economic and genetic differences. Study on school-age children in the South Gondar Zone, showed 11% stunting, 6.3% wasting, and 11.4% underweight (29). Our study indicates a significant correlation between malnutrition and CL incidence in malnutrition-prone areas such as Dehana, Sekota, and Gazgibla, highlighting the need for nutritional interventions. This sounds because these districts are part of Seqota declaration initiative goals for 2030 (Supplementary Table 1, Supplementary Figure 1, 22, 30). A study in South Ethiopia reported a 5.8% increase in CL occurrence among individuals under 18 with low BMI, highlighting the need to address malnutrition in the CL endemic area (31, 32). Evidences showed higher poverty is linked to increased leishmaniasis incidence, as malnutrition weakens immune responses and favors anti-inflammatory prostaglandin production over pro-inflammatory cytokines (33, 34). Poverty and malnutrition have been identified as influencing the occurrence of leishmaniasis in affected populations (3).

The malnutrition rate was higher (30%) in MCL case than LCL (20%) case. This indicates the effect of malnutrition on CL clinical forms. This is align with studies showing malnutrition exacerbates disease's severity (30, 34). A correlation between low weight, hypoalbuminemia, and MCL has been shown is reported (17). Indicating malnutrition may worsen skin lesions in CL. A comparison of the distribution of different clinical forms of CL disease with other research indicates that the MCL form of the disease was 20.9% (25), in our finding it was 19% which is consistent. Other studies in Northwest Ethiopia, reported MCL case burden were 13.6% (35) and 15.3% (36), respectively. This suggests that varying prevalence rates in different geographical regions or differences in the nutritional status of the population. A systematic analysis of RNA viruses in *Leishmania* isolates found no significant link to clinical types of CL signifies the role of malnutrition in the CL form (37, 38). Studies on nutritional factors with protein-calorie deficiencies affect CL infection. But, zinc supplementation showed inconclusive results and no significant treatment response (39-41). Protein-energy malnutrition significantly affects wound healing, protein-rich oral supplements can enhance recovery (41-43). Moreover, we found that 38.5% of CL patients were malnourished in repeat patients compared to the new cases having only 21% malnourished. Supporting to our finding, malnutrition negatively impacts treatment outcomes and contributes to higher retreatment and disease circulation in malnutrition-prone areas (15, 30).

Limitations of the study

The study employed a retrospective model, which means that certain relevant factors such as economic status and educational background with other relevant information were missed and not included in the analysis. Additionally, this did not show the cause and effect of CL and malnutrition.

Conclusion

The study highlights a concerning correlation between malnutrition and the incidence of CL, particularly among younger individuals, with significant percentages of MCL cases affected by malnutrition. Malnutrition might have the potential to shape the clinical form and treatment outcome in CL patients. In CL endemic areas nutritional supplement with the treatment of CL patients could require for better recovery.

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Conflict of interests

The authors declared that they have no competing interests.

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