



Original Research Article

Epidemiological Situation of Mucocutaneous Leishmaniasis in Yemen: A Descriptive Study in the Period from January 2017 to December 2022

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Background: Cutaneous leishmaniasis (CL) is endemic in all regions of Yemen, but the true incidence of the disease is not well known. Its burden is underestimated because many cases are not registered. The disease needs careful diagnosis as its manifestations overlap with many other conditions.

Objective: To determine the epidemiological situation of mucocutaneous leishmania in Yemen during the period from January 2017 to December 2022.

Results: The study included 3306 cases of CL. Males represented 60% (n=1984). Patients under 5-year-old accounted for 13% (n=430), those between 5 and 15 years accounted for 31% (n=1024), and those above 15 years represented 56% (n=1852).

Regarding annual rate of cases registered through 6 years; from 2017 to 2022, they were distributed as follows: 17.2% (n=567), 19.9% (n=657), 14.2% (n=470), 12.9% (n=425), 18% (n=597), and 17.8% (n=590) respectively. The load of cases was concentrated in Sana'a Governorate (28.2%) and the Secretariat (21.7%), followed by Thamar (8.9%), Amran (7.8%), Ibb (5%), Hajjah (4.2%), Almahweet (4%), Taiz (3.4%), Albaidaha (3.1%), Raymah (3.1%), Aljawf (2.9%), and Aldhale'a (2.5%). Most patients (97.5%; n=3225) presented by cutaneous lesions while 2.5% (n=81) had mucocutaneous lesions. In regard to phenotype, 52% (n=1719) of cases presented with ulcerative crusty lesions, 20.4% (n=675) presented as papulonodular, 12.2% (n=402) presented as plaques, 9.4% (n=311) presented as impetigo form, and 2.5% (n=81) presented as mucocutaneous.

Conclusion: Cutaneous leishmaniasis have been registered in almost all governorates and concentrated in northwest and central region of Yemen. An effective strategy for the control of leishmaniasis should be adopted by the national health authorities.

Key word: Cutaneous Leishmania, Sand fly, Neglected disease, Skin disease, Yemen

Introduction

Cutaneous leishmaniasis (CL) is a complex entity representing a significant public health problem in many countries including the WHO Eastern Mediterranean Region. Several epidemiological, parasitological and clinical aspects pose a challenge for the management and control of the disease [1,2]. It is a potentially severe and disfiguring disease and stems for psychological problems and stigmatization [3,4]. Globally, CL is currently endemic in 88 countries. An estimated 500000-1000000 new cases occur annually, but only a small fraction of cases (19%-37%) is actually reported to health authorities. CL principally affects poor populations. Outbreaks can occur anywhere, in both urban and rural areas, and is sometimes seen in refugee camps or among internally displaced populations. It predominates in the Eastern Mediterranean region, which accounts for 80% of the CL cases reported worldwide [1,5,6]. Leishmaniasis is caused by a protozoa parasite from over 20 Leishmania species. Over 90 sandfly species are known to transmit Leishmania parasites. Mucocutaneous is the most disfiguring form which invades the mucous membranes of the upper respiratory tract, causing gross mutilation as it destroys the soft tissues of the nose, mouth and throat. Patients with this form of the disease may also suffer from discrimination and prejudice [6]. Early diagnosis and effective prompt treatment reduce the prevalence of the disease and prevent disabilities and death. Studies from Yemen proved that the disease is endemic in all regions [7-15].

Majority of CL patients in Yemen are reported from rural areas [9]. The environmental and housing conditions in these areas are the important risk factors for Leishmania spread [7,12,13,15]. In Yemen, CL is a major public health problem that leaves a mutilating scar triggered by untreated disease or corrosive chemicals practiced by some traditional healers [9]. Although some studies were conducted, the subject has not received enough investigation, and there is still a wide area for more epidemiological and clinical studies on this subject. This gap makes a reasonable rationale to conduct this study to determine epidemiological situation of mucocutaneous leishmania in Yemen during the period from January 2017 to December 2022.

Materials and Methods

This retrospective, registry-based, and cross-sectional descriptive study was conducted in Yemen during the period from January 2017 to December 2022. The data were obtained from the National Program of Leishmania Control in Al-Gomhouri Teaching Hospital in Sana'a. Al-Gomhouri Teaching Hospital is one of the accredited centers for board training. Additional data were obtained from the National Center of Disease Control and Surveillance in the Ministry of Public Health and Population.

Inclusion criteria: All patients who have been diagnosed and documented in the registry book as cases of cutaneous or mucocutaneous leishmaniasis, of both genders, at any age encountered during the period of data collection.

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Exclusion Criteria: Pure visceral leishmania cases and cases with incomplete data were excluded from the study.

Tool of Data Collection: For data capture, a checklist was developed by the researchers relying on study objectives and on data availability in the registry of leishmania. The list included demographic data (age, gender, and resident governorate), year of registration, duration of lesions, clinical phenotype, anatomical sites of lesions, result of smear examination, and treatment method.

Data Analysis: SPSS version 23, IBM Corp. was used for data processing and analysis. Data were described by frequencies and percentages. Tables and graphs were used to display data. Chi square test was applied to find association between variables, and the test was considered to be significant when alpha error (p value) less than 0.05.

Results

This study included 3306 cases of CL. Males represented 60% (n=1984), while females represented 40% (n=1322), with males to females ratio (1.5:1) as shown in Table 1.

Table 1: Distribution of the cases according to gender

Gender	Number	Percent
Males	1984	60%
Females	1322	40%

Figure 1 shows that many of the cases, (n=1852), were in the age group more than 15 years, 31% (n=1024) were in the age group between 5 and 15 years, while the cases under 5 year-old accounted for (n=430) only.

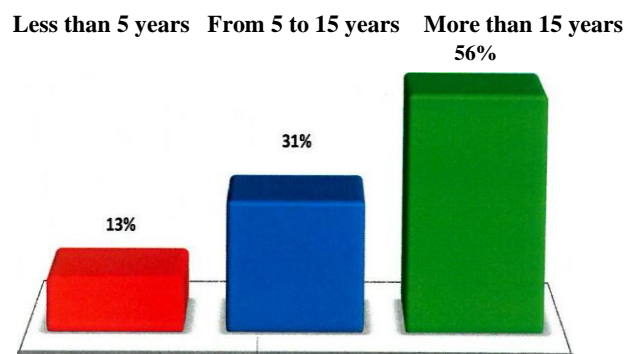


Figure 1: Distribution of the cases according to age

The percentage and number of registered cases through 6 years; from 2017 to 2022 was as follows: 17.2% (n=567), 19.9% (n=657), 14.2% (n=470), 12.9% (n=425) (n=597), and 17.8% (n=590) respectively. More specifically, the highest rate (19.9%) was registered in 2018, while the lowest rate (12.9%) was registered in 2020 Table (2).

Table (2): Distribution of the cases according to year of registration

Year	Number	Percent
2017	567	17.2%
2018	657	19.9%
2019	470	14.2%
2020	425	12.9%
2021	597	18%
2022	590	17.8%
Total	3306	100%

Table 3: Distribution of the cases according to governorate and gender

Governorate	Males	Females	Total
Sana'a Governorate	400 (20.2%)	533 (40.3%)	933 (28.2%)
Amanah (Sana'a Capital)	540 (27.2%)	179 (13.5%)	719 (21.7%)
Thamar	200 (10.1%)	94 (7.1)	294 (8.9%)
Amran	169 (8.5%)	89 (6.7%)	258 (7.8%)
Ibb	122 (6.1%)	44 (3.3%)	166 (5.0%)
Hajjah	55 (2.8%)	84 (6.4%)	139 (4.2%)
Almahweet	84 (4.2%)	47 (3.6%)	131 (4.0%)
Taiz	64 (3.2%)	50 (3.8%)	114 (3.4%)
Albaidaha	74 (3.7%)	30 (2.3%)	104 (3.1%)
Raymah	66 (3.3%)	36 (2.7%)	102 (3.1%)
Aljawf	51 (2.6%)	45 (3.4%)	96 (2.9%)
Aldhale'a	47 (2.4%)	35 (2.6%)	82 (2.5%)
Mareb	35 (1.8%)	21 (1.6%)	56 (1.7%)
Sa'adah	39 (2.0%)	12 (0.9%)	51 (1.5%)
Alhodaidah	19 (1.0%)	20 (1.5%)	39 (1.2%)
Hadramout	9 (0.5%)	2 (0.2%)	11 (0.3%)
Lahj	6 (0.3%)	0 (0.0%)	6 (0.2%)
Abyan	3 (0.2%)	0 (0.0%)	3 (0.1%)
Aden	1 (0.1%)	1 (0.1%)	2 (0.1%)

Table 3 show that The load of cases was concentrated in Sana'a Governorate (28.2%) and the Secretariat (21.7%), followed by Thamar (8.9%), Amran (7.8%), Ibb (5%), Hajjah (4.2%), Almahweet (4%), Taiz (3.4%), Albaidaha (3.1%), Raymah (3.1 Aljawf (2.9%), and Aldhale'a (2.5%). Lower rates of cases were registered in the governorates of Mareb, Sa'adah, Alhodaidah, Hadramout, Lahj, Abyan, and Aden (less than 2%

each). Males have higher rates than females in all governorates except in Sana'a Governorate, Hajjah, and Aljawf where females outnumbered males (p value <0.0001).

Clinical form of leishmania in this study showed that 97.5% (n=3225) were cutaneous, while 2.5% (n=81) were mucocutaneous lesions Figure 2.

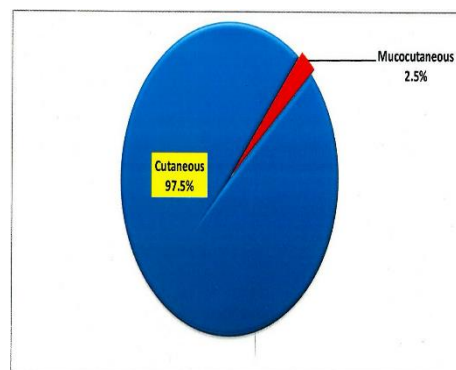


Figure 2: Distribution of the cases according to clinical form Phenotype of the lesion showed that 52% (n=1719) of cases presented with ulcerative crusty lesions, 20.4% (n=675) presented as papulonodular, 12.2% (n=402) presented as plaques, 9.4% (n=311) presented as impetigoform, and 2.5% (n=81) presented as mucocutaneous. Other less common types were eczematiformerysipeloid, Verrucous, psoriasiform, and pseudotumoral Figure 3.

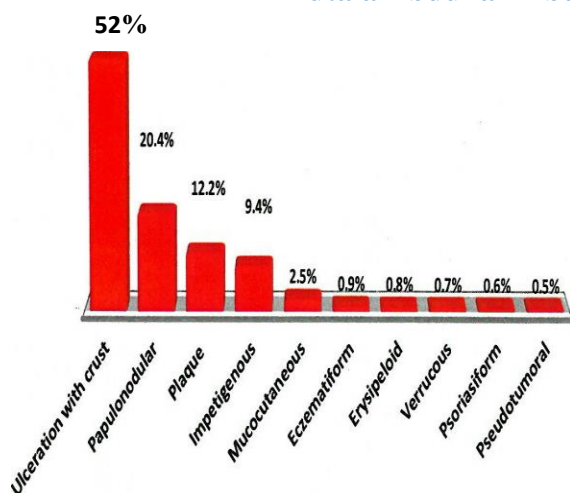


Figure 3: Distribution of the cases according to phenotype of the lesion

Duration of the lesion showed that 63.9% (n=2113) of cases presented to seek for medical help around 6 months of disease onset, and 31.3% (n=1034) of cases presented between 6 - 12 months. However, minority of the cases, which represented 4.8% (n=159), came after one year from disease onset.

Table 4: Distribution of the cases according to duration of the lesion

Duration	Number	Percent
Less than 6 Months	2113	63.9%
From 6 months to 12 months	1034	31.3%
More than 1 year	159	4.8%
Total	3306	100%

Face was the common site for lesions in a rate of 72.6% (n=2402), followed by upper limb, then by lower limbs in rates of 14.7% (n=485), and 8% (n=263) respectively. Lesions in multiple sites occurred only in 2% (n=156) of Cases Figure 4.

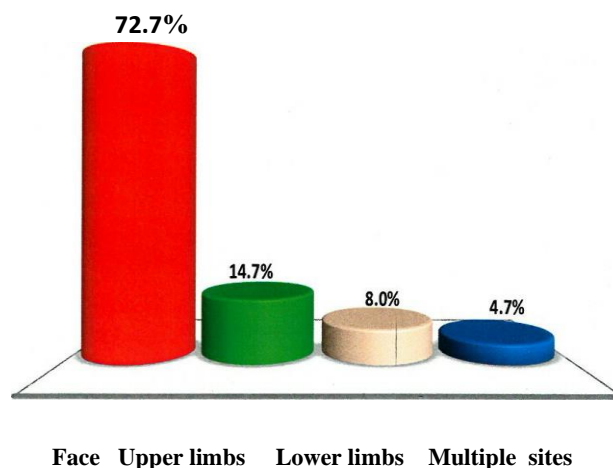


Figure 4: Distribution of cases according to anatomical site

Smear results showed that smear is positive for leishmania parasite. The histopathological examination was done for 2964 (89.7%) of cases. For the remaining cases, no confirming smear was performed and the diagnosis was made only clinically.

Table 5: Distribution of cases according to smear results

Smear results	Number	Percent
Positive	2964	89.7%
Not done	342	10.3%
Total	3306	100%

In terms of the type of treatment the results disclosed that treatment was mainly systemic for 91.6% (n=3029) of cases, while local treatment was given for only 8.4% (n=277) of them. The most frequently drug used is pentostam. Other drugs are itraconazole and ketoconazole, in addition to cryotherapy.

Table 6: Distribution of cases according to type of treatment

Type of treatment	Number	Percent
Systemic	3029	91.6%
Local	277	8.4%
Total	3306	100%

Regarding the association between gender and other variables (clinical forms, and year of registration), the results revealed no significant association (each p value >0.05).

Table 7: Association between gender, age, duration, clinical form, and year of lesions

Variable	Gender	Males	Females	P value*
Ears				
	Less than 5 ears	232 (11.7%)	198 (15.0%)	<0.001 **
	From 5 to 15 ears	589 (29.7%)	435 (32.9%)	
	More than 15 ears	1163 (58.6%)	689 (52.1%)	
	Total	1984 (100%)	1322 (100%)	
Duration				
	Less than 6 months	1299 (65.5%)	814 (61.6%)	<0.001 **
	From 6 months to 12 months	575 (29.0%)	459 (34.7%)	
	More than 1 year	110 (5.5%)	49 (3.7%)	
	Total	1984 (100%)	1322 (100%)	
Clinical form				
	Cutaneous	1940 (97.8%)	1285 (97.2%)	0.290
	Mucocutaneous	44 (2.2%)	37 (2.8%)	
	Total	1984 (100%)	1322 (100%)	
Years				
	2017	331 (16.7%)	236 (17.9%)	0.339
	2018	392 (19.8%)	265 (20.0%)	
	2019	280 (14.1%)	190 (14.4%)	
	2020	268 (13.5%)	157 (11.9%)	
	2021	374 (18.9%)	223 (16.9%)	
	2022	339 (17.1%)	251 (19.0%)	
	Total	1984 (100%)	1322 (100%)	

* Pearson Chi square was applied.

** Significant p value at level of <0.001.

Discussion

CL is endemic in many regions, including central Asia, the Middle East, southern Europe, and Africa. It also appears to be endemic in all regions in Yemen [7]. This study was carried out to determine epidemiological situation of mucocutaneous leishmania in Yemen over a period of 6 years; from January 2017 to December 2022. It included 3306 cases of CL. Males represented the majority (60%), with males to female's ratio 1.5:1. This rate is close to that reported by Khatri et al., as 63.1% of their patients were males and 36.9% were females [8]. Some other studies also reported male predominance, which may be explained by their higher exposure to vector when working outside [6,9]. Nonetheless, some studies like the one by Muthanna et al. reported that both males and females were infected at a similar rate (51% vs. 49%) respectively. On the other hand, Al-Kamel reported a female predominance of CL (32.9% of adult females vs. 9.9% of adult males) [10]. It has been also speculated that much of the observed excess risk in adult females may derive from habitual gender-specific occupational roles as most of women work in agriculture and animal care, and are responsible for procuring water, especially at dusk and in the early morning, which increases their exposure to sandfly bites [10]. The results of this study revealed that majority of the cases (56%) were in the age group more than 15 years, 31% were in the age group between 5 and 15 years, while the cases under 5 year-old accounted for 13% only. These findings are consistent with previous studies findings [11,12,13].

Some studies found that younger individuals are affected more than others, such as the study by Khatri et al. that reported a ranged of patients' age from 8 months to 80 years with a median of 15 years [8], which is in agreement with the findings of the current study. The results of the present study also disclosed a stable trend with some fluctuations in annual number of CL cases registered in the period of 6 years; from 2017 to 2022 as follows: 17.2%, 19.9%, 14.2%, 12.9%, 18%, and 17.8% respectively. The highest rate (19.9%) was registered in 2018, while the lowest rate (12.9%) was registered in 2020.

According to results of this study, the load of registered cases was concentrated in Sana'a governorate (28.2%) and the Amanah (21.7%), followed by the governorates of Thamar (8.9%), Amran (7.8%), Ibb (5%), Hajjah (4.2%), Almahweet (4%), Taiz (3.4%), Albaidaha (3.1%), Raymah (3.1%), Aljawf (2.9%), and Aldhale'a (2.5%). The lower rates of cases were registered in the governorates of Mareb, Sa'adah, Alhodaidah, Hadramout, Lahj, Abyan, and Aden (less than 2% each). In a study in northwestern Yemen by Khatri et al. the cases were distributed between Hajjah (83.0%), Amran (9.3%), Sa'adah (3.4%), Sana'a (1.2%), Alhodaidah (1.0%), Taiz (0.6%), Almahweet (0.5%), Raymah (0.3%), Ibb (0.3%), Thamar (0.2%), Aljawf (0.1%), and Lahj (0.1%). The study conducted by Al-Qubati et al. in a private clinic in Taiz reported somewhat different distribution as more than half of the patients (69.5%) were residing in highlands in the southwest and central governorates: Taiz (48%), Ibb

(21.5%), Lahj (24.3%), Aldhale'a (2.1%), Abyan (0.7%). Less patients, (3.5%), were from the northern governorates: Sana'a (0.7%), Thamar (1.4%) and Raymah (1.4%) [11].

The results of this study revealed that 97.5% of lesions were cutaneous, while only 2.5% were mucocutaneous lesions, which is consistent with results of Khatri M. et al., who observed mucosal lesions in 3.1% of their patients [8]. Other studies reported a minority of mucosal lesions. Muthanna, for example, observed that 10.6% of lesions developed in lips, nose, eyelids and ear. Lesions on lips resulted in diffuse lip swelling, localized lip swelling, and localized erosions and ulcerations. CL on ear and eyelid resembled a furuncle. On the nose, lesions caused extensive erosions with dry a serous crusting resembling lupus pernio or impetigo contagiosum [11]. Lesions on mucous membrane may have wide mimickers as chronic actinic cheilitis, chronic granulomatous cheilitis and squamous cell carcinoma [11]. Unexpectedly, Al-Kamel reported that MCL was the most predominant form (49.3%) in the central areas of the country, which is a matter of serious concern; no similar situation has been previously addressed in Yemen [10]. The results of this study demonstrated that in 52% of the cases presented with ulcerative crusty lesions, 20.4% presented as papulonodular, 12.2% presented as plaques, 9.4% presented as impetigoform, and 2.5% presented as mucocutaneous. Other less common types were eczematiform, erysipeloid, verrucous, psoriasiform, and pseudo tumoral.

Phenotypic appearance is varying from a study to another. Khatri et al. found that 58.5% of the cases were noduloulcerative lesions, 16.9% ulcerative plaques, 13.6% indurated plaques, 7.3% nodular lesions, 4.2% papular lesions, 0.7% diffuse induration, 0.1% diffuse induration with ulceration, 0.5% induration of the whole face, 0.7% thick verrucous plaque, 0.5 scaly plaque, 0.1% large lichenoid plaque, and 0.3% subcutaneous nodular dissemination lesions. Besides, they classified lesions as dry (97.9%) and wet (2.1%). Muthanna et al. reported that CL displayed a wide spectrum of clinical phenotypes which included centrally ulcerated nodules in 35%, in which some patients had slightly eroded papules and nodules, while ulcers were recognized in 21.4% [11]. They also reported that atypical phenotypes constituted 12%. These were in the form of well-defined and large ulcerative plaques which were primary lesions in some cases, but were sometimes secondary to corrosive substances commonly applied by traditional healers to treat leishmania in rural areas, resulting in large ulcers with thick adherent crusts [11]. Diagnosis is challenging in atypical and unusual forms which need a skin biopsy to confirm the diagnosis and ruled out other diseases [14].

Based on the current study findings, 63.9% of the cases presented to seek for medical help around 6 months of disease onset, and 31.3% of the cases presented between 6-12 months. However, in a minority of the cases (4.8%), the patients came after one year of disease onset. Similarly, Al-Kamel reported that most patients presented later than 4 months after

disease onset [10]. Another study reported a quite similar duration for the disease which ranged from 3 weeks to 12 years (median duration: 4 months), in which 4.6% of the patients reported disease duration exceeded one year [8].

The results of the present study revealed that face was the common site for lesions in a rate of 72.6%, followed by upper limb, then by lower limbs in rates of 14.7% and 8%, respectively. Lesions in multiple sites occurred only in 2% of cases. These findings are consistent with the findings of Muthanna et al. in the sense that most lesions were on the face (58%), followed by upper limbs (22.6%), lower limbs (18%) and lastly on the trunk [11]. Similarly, Al-Kamel [10], Khatri et al. [8], and Alharazi et al. [9] reported that most of patients had a single lesion which usually appears in the face.

According to the results of this study, all confirming smears taken from lesions were positive for leishmania parasite. The histopathological examination was done for 89.7% of the cases. For the remaining cases, no confirming smear was performed and the diagnosis depended only on clinical suspicion. No data was available in the registry on types of leishmania species. According to Khatri et al. *L. tropica* was the dominant causative species accounting for 95% of the cases, while *L. donovani* and *L. infantum* represented 4.1%, and 1.9% for atypical molecular patterns [8]. In

Conclusion

CL is endemic in Yemen, and its incidence has increased recently because of the lack of vector control attributable to the unstable sociopolitical situation and devastated health

the southwestern highlands at Lahj and Taiz governorates, Mogalli et al. [15] and Alharazi et al. [9] reported that CL was endemic disease mainly in the rural regions. However, in 1989, Rioux et al. reported that *L. donovani* and *L. infantum* were the causative species for VL and *L. tropica* was the causative agent for CL in Tehama city in Yemen [16].

The results of this study unveiled that treatment was mainly systemic for 91.6% of the cases, while local treatment was given for only 8.4% of the cases. The most common available drug used by the program of leishmania control was pentostam, and the other less commonly used drugs were ketoconazole and itraconazole. In a previous study, 55.9% of patients had tried traditional and herbal forms of treatment before seeking medical advice, and some of them had developed unnecessary complications [10]. Substances such as animal saliva (e.g. chameleon), herbal (e.g. cactus) recipes, corrosive chemicals, and topical steroids had been used [10]. Inherited customs, poverty, and a perceived inability to obtain a proper diagnosis and treatment were among the risk factors described [10]. Most of Yemeni people, especially in rural areas, do not have easy access to local health services which encourage patients to use hazardous methods of traditional treatment [17].

system. The disease is distributed in all ages with predilection to younger individuals and male gender. Cases have been registered in

almost all governorates and concentrated in northwest and central region of the country.

The disease is mainly manifested as cutaneous lesions but, in some cases, it involves mucosal areas in mouth and nose. Lesions take a chronic course and mostly appear as a single lesion in face and other exposed parts.

It is recommended to increase awareness among medical personnel to be highly suspicious on this neglected disease which may be confused with a wide variety of skin lesions. General practitioners and health workers in primary health centers should have the ability to identify of the common presentations of CL since the majority of patients, especially in rural areas, do not have access to dermatologists.

It is also recommended to increase community awareness about the importance of early seeking for medical help to avoid unwanted sequelae as disfigurement and stigma.

An effective strategy for the control of leishmaniasis should be adopted by the national health authorities.

Further studies are recommended for updating epidemiological aspects and for identifying causative species and new genotypes to provide the necessary information for control programs.

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