International Journal of Dermatology

Report

Leishmaniasis in Yemen: a clinicoepidemiological study of leishmaniasis in central Yemen

Mohamed A. Al-Kamel, MD

Regional Leishmaniasis Control Center, Sana'a, Yemen

Correspondence
Mohamed A. Al-Kamel, MD
Regional Leishmaniasis Control Center
PO Box 12692
Sana'a
Yemen
E-mails: dralkamel@hotmail.com and www.RLCCye.org

Funding: None.

Conflicts of interest: None.

Abstract

Background Leishmaniasis is a serious public health problem in Yemen.

Objectives This study was designed to identify clinical and epidemiological features of leishmaniasis in Yemen.

Methods The study was conducted at the Regional Leishmaniasis Control Center in central Yemen. Data sourced from the medical records of 152 patients with confirmed active leishmaniasis, managed during April–August 2013, were analyzed.

Results A total of 94.1% of patients were rural residents. Al Bayda was the most endemic governorate (59.9%). Children represented the group at highest risk (57.2%), followed by adult females (32.9%); together these groups accounted for 90.1% of all patients. Mucocutaneous leishmaniasis was the most prevalent form (49.3%), followed by cutaneous leishmaniasis (47.4%), and visceral leishmaniasis (3.3%). The wet ulcer was the most common type of lesion (49.7%) and the single lesion (69.4%) represented the most common presentation. All patients were ignorant of the nature of the disease, and 55.9% had a history of using "popular" treatments.

Conclusions Cutaneous, mucocutaneous, and visceral leishmaniases have significant endemicity in Yemen, especially in central areas. Al Bayda is the governorate with the highest endemicity, and rural children and women represent the populations at highest risk. Mucocutaneous leishmaniasis seems to be the most prevalent form and a single wet ulcer is the most common presentation. Infected refugees may represent new foci for imported *Leishmania* species. Ecology, geography, climate change, cultural gender- and age-specific duties, urban night activities, and use of popular treatments are among proven risk factors.

Introduction

Leishmaniasis, a parasitic vector-borne disease caused by obligate intra-macrophage protozoa, is endemic in large areas of the tropics, subtropics, and the Mediterranean basin. It is caused by more than 20 *Leishmania* species and is transmitted to humans by sandflies.[1] Approximately, 600 species of sandfly are known, but only 10% of these act as disease vectors.[2] Infection by human protozoan parasites of the genus *Leishmania* can lead, depending primarily on *Leishmania* species, to cutaneous leishmaniasis (CL) or mucocutaneous leishmaniasis (MCL) lesions, or to fatal generalized visceral leishmaniasis (VL) infection.[3]

Leishmania was first identified in 1885 by Cunningham in India in a subject from Kala-azar. Donovani, Leishman, and Marchand confirmed its existence in 1903 with the discovery of this protozoan in a subject who died of kala-azar in Germany. World Health Organization (WHO) epidemiological data estimate that currently more than 12 million people suffer from leishmaniasis and that, in an at-risk population of about 350 million people, 1.5–2 million new cases will develop per year, of which 1–1.5 million cases will represent CL and 500,000 cases will represent VL.[4]

Although it is estimated to cause the ninth largest burden among individual infectious diseases, leishmaniasis is largely ignored in discussions of tropical disease priorities.[5,6] This consignment of the disease to critical oblivion results from its complex epidemiology and ecology, the lack of simple, easily applied tools for case management, and the paucity of current incidence data, and often results in a failure on the part of policymakers to recognize its importance.[7,8]

Climate change affects the distribution of leishmaniasis in three ways: (i) through the effects of temperature on parasite development and vector competence; (ii) through the effects of temperature and other environmental variables on the range and abundance of the sandfly species that act as vectors; and (iii) through socioeconomic

changes that affect the amount of human contact with transmission cycles.[9]

The burden of leishmaniasis falls disproportionately on the poorest segments of the global population. Within endemic areas, increased infection risk is mediated through poor housing conditions and inadequate environmental sanitation, lack of personal protective measures, and economically driven migration and employment that bring non-immune hosts into contact with infected sandflies.[7]

The Republic of Yemen is a developing country with very poor healthcare conditions. Medical facilities and qualified personnel are limited, and the population, especially women and children, suffer from deficiencies in medical care.[10]

Leishmaniasis is a public health problem in Yemen, where it has a nationwide distribution.[11] A full epidemiological study of skin diseases from Yemen is not available, although some data have been published from nearby Arab countries.[12] However, although the disease is not well documented, it seems to be endemic in the country and is primarily widespread in arid and semi-arid areas.[10]

Sarnelli[13] reported five cases of MCL in Sanaa as early as 1933. Cutaneous leishmaniasis is widespread in Yemen, and its true incidence is not well reflected as only a few published documents are available.[14] The cutaneous form is caused by *Leishmania tropica* (anthroponotic CL [ACL]) and *Leishmania major* (zoonotic CL [ZCL]).[15]

Further, VL (kala-azar) is endemic in Yemen. This diagnosis is generally missed or delayed for months or years, and some patients are treated blindly.[16] Kala-azar was first reported in the northern part of Yemen over a century ago, but sporadic cases of the disease are now widely reported from all over the country.[17] Nearly 4047 cases of VL, mostly in young children, were reported by the Ministry of Health in the decade to 1988.[18]

The scanty information on VL epidemiology in Yemen shows that the causative organisms are species of the *Leishmania donovani* complex (anthroponotic VL [AVL]) and *Leishmania infantum* complex (zoonotic VL [ZVL]), and vectors are *Phlebotomus orientalis* and *Phlebotomus arbicus*.

Canine leishmaniasis was reported by Rioux *et al.*[19] from a human VL focus in the Taiz area of Yemen.

The present study was conducted to identify the clinical and epidemiological features of leishmaniasis disease in Yemen, particularly in the central areas of the country.

Materials and methods

This study was conducted at the Regional Leishmaniasis Control Center (RLCC), Yemen, through a retrospective review of the medical records of patients with confirmed leishmaniasis from three governorates in central Yemen, all of whom were managed during the 5 months of the study period (April–August 2013).

The study area (Fig. 1) involved Al Bayda (Al-Baida), Ibb, and Dhamar governorates. These areas typically reflect the morphology and landscape of the central (inner) highlands, which represent a plateau of 2000–3200 m a.s.l.[20]

The study involved all leishmaniasis patients registered at the RLCC and living in the study area, of both sexes and all age groups. Study subjects were required to have been diagnosed and managed during the study period at the RLCC offices or to have been actively detected and managed during remote field campaigns and to show active leishmaniasis lesion(s) or symptoms. All patients were required to have been given a clinical diagnosis of leishmaniasis, which had been confirmed in laboratory tests by cytology, histopathology, or immunology (enzyme-linked immunosorbent assay [ELISA]), and to have filled out the surveillance questionnaire.

The study sample was obtained by screening all patient records. Any patient who had been living outside the study area, had not been clinically and laboratory test-diagnosed with leishmaniasis, did not have active leishmaniasis lesion(s), had not completed the questionnaire, or had not been managed by the center's staff was excluded from this study.

A total of 152 valid records were found to be compliant with the study's inclusion and exclusion criteria, and thus those 152 confirmed leishmaniasis patients were considered as the study population.

In this study, individuals aged ≤17 years were classified as children. The differentiation between CL and MCL was based on clinical findings; lesions that involved mucous membranes of the eyelids, nose, or mouth with any degree of inflammation were considered to represent MCL.[21]

During RLCC field visits, center staff had walked around villages and looked for any possible risk factors. Surveillance visits covered disadvantaged areas that included refugee camps and marginalized camps in eight districts. Geographic

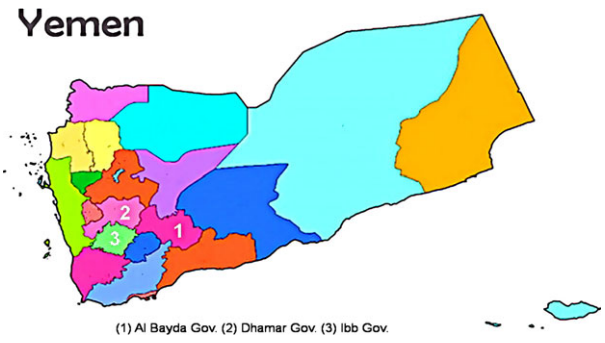

Figure 1 Map of Yemen showing the three governorates in the study area

and ecological surveillance data were also considered in this study.

Study variables included age, sex, clinical form, number and nature of lesion(s), distribution, residence, and awareness status.

Results

Data analysis of the selected records showed that the majority of patients were Yemenis (59.9% of them were Al Bayda inhabitants), and two were Ethiopian refugees. Most patients lived in rural areas. Age at presentation ranged from 2 months to 120 years. The delay before first presentation ranged from 2 weeks to 16 months. Four families in which all members were infected were identified (Fig. 2). Four patients reported a history of visits to other endemic districts in the governorates of Raymah, Hudeidah, and Taiz in the west and south of the country.

Overall, the prevalence of leishmaniasis was higher among children than adults, higher among male than female children, and higher among female than male adults. Children and women accounted for 90.1% of identified cases (n = 137 patients) (Table 1, Fig. 3).

Mucocutaneous disease was the most prevalent form of leishmaniasis (49.3%). Children were more affected than adults by all forms of the disease (Table 2, Fig. 4).

All VL patients were children. Principal presentations included high intermittent fever, marked loss of weight, abdominal distension, malaise, and xerosis.

Figure 2 Diffuse nodulo-ulcerative lesions of cutaneous leishmaniasis infecting a mother and both her children

Most patients (69.4%) presented with a single lesion on an exposed part of the body; two patients had lesions on the abdomen and back. The wet form was the most common clinical presentation (49.7%).

A total of 128 patients were treated successfully using available topical and systemic regimens. Treatment in these patients achieved no or minimal scarring, except in

Table 1 Characteristics of patients with leishmaniasis (n = 152) in central Yemen

Variable	Group	*n*	Percentage
Sex	Male	85	55.9
	Female	67	44.1
Age	Children	87	57.2
	Male	70	46.1
	Female	17	11.2
	Adults	65	42.8
	Male	15	9.9
	Female	50	32.9
Clinical form	CL	72	47.4
	MCL	75	49.3
	VL	5	3.3
Number of lesion(s) (CL and MCL)	Single	102	69.4
	Multiple	45	30.6
Nature of lesion(s) (CL and MCL)	Dry	65	44.2
	Wet	73	49.7
	Mixed	9	6.1
Site of presentation (CL and MCL)	Exposed areas	144	98.0
	Hidden areas	3	2.0
Residence	Rural	143	94.1
	Urban/suburban	9	5.9
Geographic distribution	Al Bayda governorate	91	59.9
	Ibb governorate	33	21.7
	Dhamar governorate	28	18.4

CL, cutaneous leishmaniasis; MCL, mucocutaneous leishmaniasis; VL, visceral leishmaniasis.

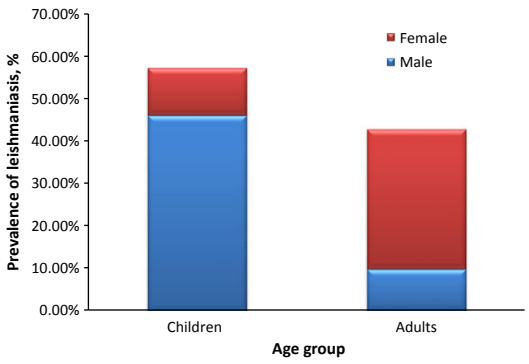

Figure 3 Overall prevalences of leishmaniasis by sex and age group

Table 2 Prevalences of different forms of leishmaniasis by age group (n = 152)

Age group	CL *n* (%)	MCL *n* (%)	VL *n* (%)
Children	42 (27.6)	40 (26.3)	5 (3.3)
Adults	30 (19.7)	35 (23.0)	0

CL, cutaneous leishmaniasis; MCL, mucocutaneous leishmaniasis; VL, visceral leishmaniasis.

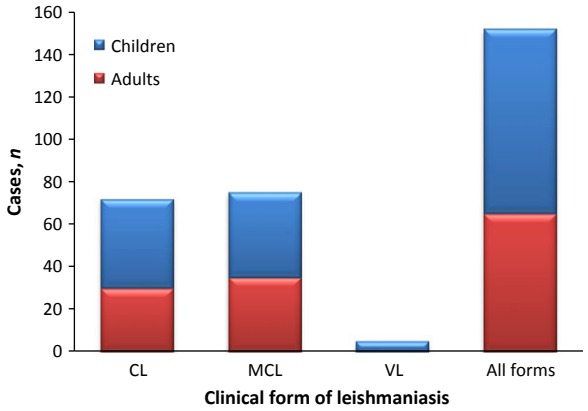

Figure 4 Prevalences of different clinical forms of leishmaniasis by age group

four patients with late presentations who developed nasal deformity (three adult women) and nasal perforation (one female child) (Fig. 5). Of the remaining patients, five were referred for further management, and 19 were lost from follow-up. The most commonly used treatment comprised pentavalent antimonial-containing compounds.

Most patients presented at later than 4 months after disease onset. Some late patients presented with advanced symptoms such as huge ulcers, dissemination, diffuse facial erythema (Fig. 6), mucosal involvement, and mutilation.

Eighty-five patients (55.9%) had tried popular forms of treatment before their first presentation, and some of these had developed unnecessary complications. Substances such as animal saliva (e.g. chameleon), herbal (e.g. cactus) recipes, corrosive chemicals, and topical steroids had been used.

The majority of patients belonged to farming families living in remote villages and working in agriculture. Common practices included keeping livestock within 100 m of human habitations and sleeping on the ground. Most patients did not adhere to proper hygiene practices.

Constant growth in populations of dogs, cats, and rodents was reported. All patients displayed a lack of

Figure 5 Destructive mucocutaneous leishmaniasis ulcer complicated by nasal perforation in a female child

essential knowledge about the nature of the disease, its etiology, vectors, and reservoirs, and primary protective measures; some of them described the disease as attributable to air or water pollution. Badah, Ofiah, and Atharah were identified as local synonyms for leishmaniasis in the study areas. All of these terms mean stigma and refer to both esthetic and social stigmatization.

During field campaigns, RLCC staff noticed that tribal and rural populations prefer to live in houses that are close together, which lie in unplanned slums or settlements, near to uncovered water sources, and often lack adequate water supplies and sanitation facilities. In villages (particularly around Radaa), children and young adults were seen working in khat (a stimulant plant which accounts for about 50% of the gross domestic product of the agricultural sector in Yemen[22]) cultivation. Hundreds of African refugees were seen working in these farms, and sandflies were also seen in many locations, especially in domestic animal shelters and mud houses.

Discussion

There are no solid data on the incidence of *Leishmania* infections in Yemen, but the disease is certainly underreported, especially in women and children, and may exceed 10,000 cases per year.[10]

From the current study, CL, MCL, and VL seem to be endemic in central Yemen, and Al Bayda governorate seems to be the area with the highest endemicity. Other reports from Yemen have described the occurrence of CL

Figure 6 Diffuse form of leishmaniasis in a 120-year-old woman

in Hajjah, Amran, Sadah, Sanaa, Al-Hudeidah, Taiz, Ibb, Mahweet, Raimah, and Al-Jouf governorates in northern, western, and southern Yemen, of both zoonotic and anthroponotic types, and caused mainly by *L. tropica* and *L. major*.[10,15,19,23–25] Others that cited the endemicity of VL reported most cases as registered in southeast and northern Yemen and as caused mainly by *L. infantum* and *L. donovani*.[19,24]

Overall, the prevalence of leishmaniasis was higher among children than adults and was markedly higher in male than in female children and in female than in male adults; a comparable situation was reported from Afghanistan.[26] Children and women can be considered as one comparator group as they represent the sector suffering from the greatest deficiencies of medical care in Yemen.[10]

It is useful to compare incidences of leishmaniasis in Yemen with those in Afghanistan because these countries have comparable geographic and socioeconomic features; similar comparisons have been made with reference to malaria.[27]

It has been speculated that much of the observed excess risk in male children and adult females may derive from habitual gender- and age-specific occupational roles: most boys and 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. In addition, male children (57.4% of working children in Yemen are agricultural workers[28]) often spend several hours of the night guarding khat farms.

In the present study, VL was found to affect mainly children; similar findings were reported from southern Yemen by Hamid and Gobah.[29]

The current study shows that MCL was the most predominant form, a finding that may be unique to the central areas of the country and which represents a matter of serious concern; no similar situation has been previously addressed in Yemen.

The prevalence of CL was higher among children than adults; similar data were reported by Ullah *et al.* from Pakistan.[30] There are no comparable reports from other regions of Yemen.

The majority of patients presented with single lesions. Comparable findings were obtained by Khatri *et al.* in northern Yemen, who also described most patients as being from rural areas.[25] Single lesions are usually detected in *L. tropica* infection.[31,32]

Multiple lesions are seen in *L. major* infection.[33,34] In the Old World, this form is caused by *Leishmania ethiopica*.[33] In the current study, the presence of multiple

lesions in 30.6% of patients may indicate the endemicity of these species in the study areas.

Dissemination in CL may derive from a lack of cell-mediated immunity to *Leishmania* antigen, which then results in the uncontrolled growth of the parasite.[34] This may have relevance to the current study population.

The wet form was the most common clinical presentation; comparable findings were reported from Iraq by Al-Mafraji *et al.*[35]

Based on the findings of the current study, refugees infected with disseminated CL or MCL may represent new foci for imported *Leishmania* species; refugees living in Yemen are predominantly from endemic countries such as Iraq, Somalia, Ethiopia,[36] and Syria.[37]

Leishmania species, vectors, and reservoirs in central Yemen have not been studied. However, the relative similarity between the spectrum of clinical presentations found in this study and those described in other reports from Yemen and comparable countries may imply the presence of the same strains; specifically, *L. major* may be the most prevalent strain in central Yemen.

Inherited habits, poverty, and a perceived inability to obtain a proper diagnosis and treatment were among the risk factors identified in this study. The last of these may encourage patients to use hazardous methods of popular treatment; the WHO has reported that 75% of rural populations in Yemen do not have easy access to local health services.[38]

Findings in the current study indicate that the incidence of leishmaniasis infection peaks in August (autumn). In the semi-arid highlands that comprise the area covered by the present study, mean temperatures range from <15 °C in winter to 25 °C in summer, and rainfall is heavier in autumn.[20] The rate of warming is projected to be more rapid in these areas than in areas closer to the coast, which is consistent with the higher rates of warming projected for the Arabian peninsula and East Africa.[20] In 2011, the Global Facility for Disaster Reduction and Recovery (GFDRR) reported that Yemen is highly vulnerable to the adverse impacts of climate change.[39]

Conclusions

Many risk factors have been proven to increase the disease burden imposed by leishmaniasis and the overall risk to the public in Yemen. Ecology, geography, climate change, cultural gender- and age-specific duties, urban night activities, popular treatment methods, illiteracy, overcrowding, the practice of keeping domestic animals indoors, constant increases in rodent and dog populations, and improper diagnosis, treatment, housing, hygiene, and sanitation are among these factors.

This study is expected to aid the RLCC and health authorities in estimating incidences of infection and identifying major risk factors that can be used to inform the development and implementation of initiatives to raise awareness and knowledge of leishmaniasis and to support early diagnosis and control strategies.

Recommendations

Yemen is often missed out of maps of the worldwide distribution of leishmaniasis. These maps should be redrawn regularly and should consider Yemen as one of the most endemic countries.

Because CL can develop to MCL, especially in poor and immunocompromised individuals, I would like to suggest that leishmaniasis disease should be reclassified as consisting of only two major clinical entities, CL and VL, and that all other forms should be considered as complications.

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