

# Epidemiological Trends of Cutaneous Leishmaniasis in Al-Madinah Al-Munawarah Province, Western Region of Saudi Arabia

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## Abstract

**Objective:** To investigate the epidemiological trends of cutaneous leishmaniasis (CL) in Al-Madinah Al-Munawarah, western region of KSA. **Materials and Methods:** Four hundred and sixty-seven parasitologically confirmed CL cases attending Al-Meeqat Hospital, Al-Madinah, during 2012–2015, were included in this study. **Results:** Both Saudi and non-Saudi nationals were infected, with the highest infection rate being among Saudis (68.7%). Males were more affected than females as 86.9% of the total CL cases were males. Moreover, CL was prevalent in all age groups with higher frequency among young adults and adolescents (23.1% and 22.7%, respectively). Interestingly, almost all the patients in the adolescent and child age groups were Saudis (96.2% and 93.5%, respectively). Considering geographical distribution, the highest percentage of the cases (40.5%) were from the northern parts of Al-Madinah province while the eastern parts reported the least infection rate (7.3%). Few cases (2.5%) were supposed to encounter the infection abroad. Additionally, the frequency of infection was found to follow a seasonal distribution. Regarding treatment, pentostam, ketoconazole, or cryotherapy were the treatment options usually used. **Conclusion:** CL is prevalent in Al-Madinah Al-Munawarah area and new foci are being introduced. Thus, detailed studies with large surveillances regarding vector and reservoir hosts in and around the area are needed.

**Keywords:** Al-Madinah Al-Munawarah, cutaneous leishmaniasis, epidemiology

## INTRODUCTION

Old-world cutaneous leishmaniasis (CL), which occurs in Africa, Europe, Middle East, and Asia, is caused by *Leishmania major*, *Leishmania tropica*, and *Leishmania infantum* and is zoonotic with wild rodent/gerbil colonies representing the reservoir host. The estimated annual world incidence is around 1–1.5 million cases with over 100,000 new cases in the eastern Mediterranean region.<sup>[1]</sup> Some reports proved that *L. tropica* can also cause an anthroponotic form of CL.<sup>[2]</sup>

The transmission of leishmaniasis was observed to be focally associated with the parasite and the reservoir host distribution, which is in turn dependent on the ecology.<sup>[3]</sup> Domestication of the transmission cycle, urbanization, as well as introduction of agricultural projects into new areas are part of the environmental changes that can increase leishmaniasis incidence.<sup>[3,4]</sup>

Phlebotomine sandflies, with over fifty species of genus *Phlebotomus* in the old world, and genus *Lutzomyia* in the new world, are the vector of leishmania that transmit disease to humans.<sup>[4]</sup>

Depending on the type and duration of the lesion, there is a variability of the clinical and histological spectrum in CL<sup>[5,6]</sup> with the strain of parasite organism, host immunity, and other environmental factors contributing to this variation.<sup>[6,7]</sup>

Regarding host immune response in CL, macrophages, although are the major site of parasite replication, are also

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responsible for parasites' killing.<sup>[8]</sup> However, it is well known in leishmaniasis that Th1 development through IL-12 leads to resistance, while the early production of IL-4 results in susceptibility.<sup>[9,10]</sup>

Classical diagnosis of CL depends on the clinical features, microscopic examination of aspirate, skin biopsy, or scraping to identify the amastigotes (Leishman–Donovan [LD] bodies) or to culture the promastigote stage on specific media. However, all these methods are of low sensitivity.<sup>[11,12]</sup> New methods with higher sensitivity and specificity have been introduced in the diagnosis field including serological and molecular techniques.<sup>[13-15]</sup>

Treatment of the most forms of CL is mainly by one of the pentavalent antimonials; sodium stibogluconate or meglumine antimonate. CL is mostly self-healing; however, treatment is needed in cases of severe disseminated lesions and in antrophilic transmission as in *L. tropica* infections. Reports included different regimens with several drugs. Stibocaptate, chloroquine, niridazole, rifampicin, and streptomycin<sup>[16]</sup> as well as cryotherapy or cryosurgery<sup>[17]</sup> were used. Some combination therapies were also tried.<sup>[18,19]</sup> However, several studies regarding treatment were uncontrolled and not randomized, not taking into consideration all the factors and thus are not highly recommended.<sup>[20]</sup>

In Saudi Arabia, CL has been known for a long time and was considered of minor importance until 1975 when it was considered by the Saudi Ministry of Health as a disease that requires control.<sup>[21]</sup> Although declining of CL incidence in Al-Hassa in the eastern province of Saudi Arabia has been reported,<sup>[22]</sup> the disease is still endemic in different places of the kingdom,<sup>[22]</sup> and in the past 7 years, over 19,000 cases of CL have been reported. It is more common in males and appears to be more prevalent in adults.<sup>[23]</sup> Overall, it is found in equal percentages between Saudis and non-Saudis and is more prevalent in Al-Qassim area and least prevalent in Aljouf area.<sup>[23]</sup>

CL caused by *L. major* has been reported in many parts of Saudi Arabia, with *Phlebotomus papatasi* confirmed to be the vector, as in Al-Hasa area,<sup>[24]</sup> while CL caused by *L. tropica* is endemic in the southwestern part of the country<sup>[24,25]</sup> with *P. sergenti* identified as the vector.<sup>[26,27]</sup>

In Al-Madinah Al-Munawarah, both *L. major* and *L. tropica* were recently identified as the causative organisms of CL.<sup>[15]</sup>

## MATERIALS AND METHODS

### Study area and population

Al-Madinah Al-Munawarah is a region of Saudi Arabia, located on the country's west side, along the Red Sea coast. It coordinates a latitude of 25°0'N, a longitude of 39°30'E, and with an altitude of 1995 ft. It has an area of 151,990 km<sup>2</sup> and a population of 1,777,973 (2010 census), subdivided into seven governorates which include Medina, Al Hunakiyah, Mahd Al Thahab, Al-'Ula, Badr, Khaybar, and Yanbu Al Bahar. Medina has a hot desert climate; summers are extremely hot

with daytime temperatures averaging about 40°C (104°F) with nights about 28°C (82°F). Temperatures above 45°C (113°F) are not unusual between June and September. Winters are milder, with temperatures from 12°C (54°F) at night to 24°C (75°F) in the day. There is very little rainfall, which falls almost entirely between November and May.

This descriptive, analytical, cross-sectional study was carried out by assessing all individuals who referred to the Meeqat Hospital (Al-Madinah Al-Munawarah, Saudi Arabia) due to suspected CL during 2012–2014.

Overall, 467 patients confirmed positive CL patients were included after being given their informed consents. The patients completed a special questionnaire for basic demographic data including age, sex, nationality, lesion type, time of incidence, diagnosis, and type of treatment prescribed.

### Specimen collection and smear preparation

After cleaning the lesions and the adjacent skin around them, they were sterilized with disinfectant. After that, ~0.1 mL of sterile 0.9% saline was drawn into a 1.0–3.0 mL syringe with 23- to 27-gauge needle and the needle was inserted into the nodule or ulcer's margin and rotated gently several times. A small amount of saline was injected under the skin into the tissue, the needle was rotated while gentle suction was applied, and some tissue aspirate and freed tissue were withdrawn. The needle was withdrawn from the lesion, and part of the aspirate was discharged onto a clean glass microscope slide for smear preparation. After smears had dried completely, they were fixed with 100% methanol for 20–30 s, allowed to dry, and then stained with Giemsa for 20–30 min, CL was confirmed by the presence of *Leishmania* amastigotes (LD bodies) under the microscope.<sup>[28]</sup> Those with negative smears were excluded.

### Statistical analysis

The SPSS statistical software package, version 16 (SPSS Inc., Chicago, IL, USA) was applied for the data analysis. Descriptive statistics were used to describe the basic features of the data in this study. Differences in categorical variables between groups were compared and analyzed using the Chi-square test. A two-sided  $P < 0.05$  was considered statistically significant.

## RESULTS

A total of 467 participants including both males and females and with different ages were diagnosed as smear positive for LD bodies between January 2012 and March 2015 [Table 1].

Both Saudi and different non-Saudi nationals were infected; 321 (68.7%) were Saudis and 146 (31.35) were residents of different Asian, African, and Arabian nationals who live in Al-Madinah Al-Munawarah area [Table 1]. This difference in percentage was statistically significant ( $P < 0.000$ ).

Out of the 467 patients with confirmed CL, 406 (86.9%) were male and 61 (13.1%) were female with a difference that was statistically significant ( $P < 0.0001$ ).

**Table 1: Frequency of cutaneous leishmaniasis among Saudi and non-Saudi males and females in different age groups of patients in Al-Madinah Al-Munawarah, Saudi Arabia, during 2012-2015**

Age groups	Male, n (%)	Female, n (%)	Saudis			Non-Saudis			Grand total, n (%)
			Male	Female	Total, n (%)	Male	Female	Total, n (%)	
≤10	41 (66.1)	21 (33.9)	38	20	58 (93.5)	3	1	4 (6.5)	62 (13.3)
11-20	89 (84)	17 (16)	86	16	102 (96.2)	3	1	4 (3.8)	106 (22.7)
21-30	100 (92.6)	8 (7.4)	46	6	52 (48.1)	54	2	56 (51.9)	108 (23.1)
31-40	84 (92.3)	7 (7.7)	49	5	54 (59.3)	35	2	37 (40.7)	91 (19.5)
41-50	50 (90.9)	5 (9.1)	19	4	23 (41.8)	31	1	32 (58.2)	55 (11.8)
>50	42 (93.3)	3 (6.7)	29	3	32 (71.1)	13	0	13 (28.9)	45 (9.6)
Total	406 (86.9)	61 (13.1)	267	54	321 (68.7)	139	7	146 (31.3)	467 (100)

The 21–30 years' age group composed of the highest frequency ( $n = 108$ , 23.1%) of patients with CL while the lowest frequency of the infection was recorded in individuals with >50 years of age. The difference between age groups is highly statistically significant ( $P < 0.0001$ ). Regarding gender and age distribution among Saudis and non-Saudis, the highest percentage of infected females was among Saudis (54/61, 88.5%) which is significantly higher than that in non-Saudis. Interestingly, 20/54 (37%) of the infected Saudi females are of the age group of 10 years and less and 36/54 (66.7%) are between 11 to 20 years of age. This is similar to previous findings from the KSA<sup>[22,29]</sup> and from other parts of the world.<sup>[30-33]</sup> Moreover, almost all the children (both males and females) in the two age groups mentioned above are Saudis (93.5% and 96.2%, respectively).

The surroundings of Al-Madinah Al-Munawarah region were divided into North, South, East, and West while the central part of the study area was considered as the city of Al-Madinah. Assessment of the prevalence of CL in the different parts around Al-Madinah Al-Munawarah revealed that, while the northern area had the highest number of infected individuals ( $n = 189$ ; 40.5%), the lowest rate was observed in the eastern areas ( $n = 34$ ; 7.3%) [Table 2]. The different towns, villages, and country sides where the patients were resident are shown in Table 2. Few patients, who were non-Saudis, and who were from known CL-endemic countries, were supposed to encounter the infection outside the KSA [Table 2]. The difference in the prevalence of CL between different geographical zones was highly statistically significant ( $P < 0.0001$ ).

When the month of encountering the infection was taken into consideration, the highest frequency was observed from January to May [Figure 1], with another elevation in September.

Regarding treatment, most of the cases were treated with standard dose (20 mg/kg/day for 21 days) of pentostam ( $n = 268$ , 57.4%) or ketoconazole with an oral dose of 10 mg/kg/day for 28 days ( $n = 191$ , 40.9%) while few ( $n = 8$ , 1.7%) with cryotherapy [Figure 2]. Treatment methods are dependent on the number and severity of the lesions, with the more severe lesions requiring systemic treatment and the mild ones can be

**Table 2: Distribution of cutaneous leishmaniasis according to residence in Al-Madinah Al-Munawarah, Saudi Arabia, during 2012-2015**

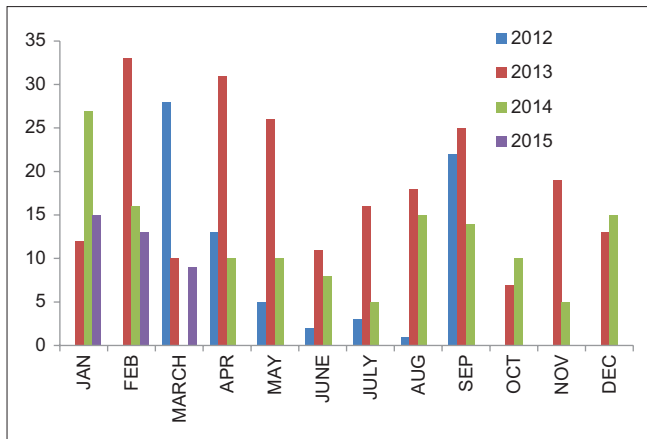
Location	Places	n (%)
North	Almeleleh, Almondassa, Alsalsala, Khaybar, Aljazeera, Taymaa, Albeyda, Alola, Alsaleela, Shgwa, Almoraba'a, Alboweir, Keteifa, Almaramea, Alshabha, Matan, Aldile'a, Alkhaleel, Tura'a, Alzabae'r	189 (40.5)
South	Abar Ali, Abyar Almashi, Alesheira, Wadi Reem, Alyotama, Mahd Aldahab, Wadi Alfara'a, Alranona'a, Shoran, Alhalaba, Althama	77 (16.5)
Center	Al-Oyoon, Alharra Alshrqiah, Aldeytha, King Fahd Garden, Al Azhari, Al Hijra	116 (24.8)
East	Alhanakeia, Alnakheel, Weaira, Alagoon, AlQasim, Alogra, Dea'a, Aldamereia, Alo'wina, Alfogara, Dea'a, Weaira	34 (7.3)
West	Yanbu'a, Alfaga'ali, Alfaraa, Aleis, Madsoos, Alsowig, Alrayes, Alforeish, Almiseigeid, Alhamra, Hizra, Abo mirkha, Khuls Altaragma, Melal, Beir Alsayegh, Fara'a Alraddadi	39 (8.4)
Abroad	Syria, Sudan, Bangladesh, Yemen	12 (2.5)
Total		467 (100)

treated with simple cryotherapy. In this study, the differences between frequencies of lesions, as reflected by methods of treatment, are highly statistically significant ( $P < 0.000$ ).

## DISCUSSION

CL is well known in the old world since ancient times. In the KSA, CL was first reported in 1973 in the eastern province. However, in Al-Madinah Al-Munawarah, although many cases are annually reported, the epidemiology of CL has not been well studied.

The total number of patients was 467, 86.9% of them were male and 13.1% were female. The significant increase in infection among males could be explained by the nature of social life in the KSA. The men are responsible for work in the farms and outdoors while the women are not. Moreover, women are traditionally covering most parts of their bodies, thus being protected from sand flies; the parasite vector. This possibility is strengthened by the fact that 34% of the total infected females are young children of <10 years of age who are not wearing a



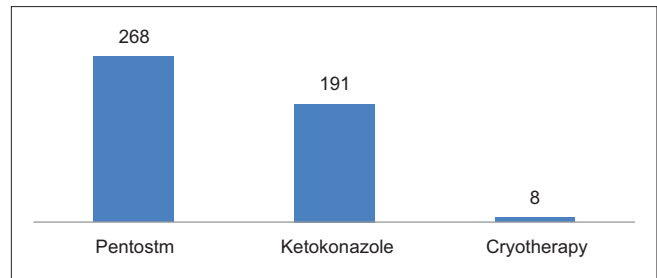
**Figure 1:** Frequency distribution of patients with cutaneous leishmaniasis based on months of occurrence (Al-Madinah Al-Munawarah, Saudi Arabia, 2012–2014)

whole body covering and more than 50% of the total infected females are <20 years old. Our results come into agreement with the results of a previous study by Amin *et al.*, 2013<sup>[22]</sup> in Al Hassa, eastern region of KSA, who found dominance in CL cases among males. Moreover, a recent review study revealed a 77.5% infection rate of CL among males in the KSA.<sup>[29]</sup> Different studies from Ethiopia, Iran, Afghanistan, and Pakistan showed similar results.<sup>[30–33]</sup> However, other studies from the KSA<sup>[34]</sup> and Africa<sup>[35]</sup> showed similar infection rate among males and females.

In this study, the most susceptible age group is the age group of 21–30 years, this finding is explained by the fact that this age group is the most active population in the community and that most of the labors are of this age group. This agrees with previous studies in Iran,<sup>[30]</sup> Kuwait,<sup>[36]</sup> and other parts of the world<sup>[37]</sup> that showed that this age group is exactly the one with the highest rate of infection. A review study from the KSA reported by the Saudi Ministry of Health during 2006–2011<sup>[29]</sup> also showed higher prevalence rate of CL among adults. However, another longitudinal study from the endemic area of Al Hassa, eastern region of KSA, revealed a trend of higher prevalence of infection among children <15 years of age, who were supposed to be with low immunity to CL.<sup>[34]</sup>

Regarding the regional distribution, the highest rate of infection was recorded in the northern region of Al-Madinah Al-Munawarah. The geography of Al-Madinah Al-Munawarah is composed of three big valleys that join at the northwestern part of the holy city, resulting in provision of good ecological cover for the vector-breeding sites. Moreover, the northern provinces are composed of the major farming areas and most of the expatriates there are farmers who spend most of their time outdoors.

Regarding the distribution of CL according to the nationality, the majority of the cases was among Saudi nationals. However, the interesting fact was that most of the infected Saudis were in young age of <20 years. A recent study showed that CL in the KSA occurs almost equally in Saudis and non-Saudis.<sup>[29]</sup>



**Figure 2:** The types and frequency of treatment of cutaneous leishmaniasis in Al Meqat Hospitals, Al-Madinah Al-Munawarah

However, a previous study reported higher ratio of infection among Saudis during 2000–2002 which was later on reversed by a higher ratio for non-Saudi nationals, most of which were expatriates.<sup>[22]</sup> In an epidemiological study over a long period of time (more than 40 years) in 2004, Al-Tawfiq and AbuKhamis<sup>[34]</sup> reported that almost all the CL cases were among Saudis (more than 98%). Hence, our results come into agreement with this study, although the infection rate among males and females was not equal as reported in that study and with a difference in the percentage of affected Saudi population which was 68.7% in this study. However, the difference from the other studies may be due to the fact that the vector has been found in new foci around the city, so increasing the infection rate among the original Saudi residents of Al-Madinah Al-Munawarah. In a study in Iran, the majority of CL patients were found to be Iranian in a known endemic area.<sup>[30]</sup>

Regarding the season of the highest frequency of infection, it was from February to May. This agrees with previous studies from the KSA<sup>[22,34]</sup> and is thought to be dependent on the vector activity in this period of the year. Similar results of seasonal increased frequency were reported from Iran<sup>[30]</sup> and more recently reported from the nearby northwestern part of the kingdom.<sup>[38]</sup>

Most of the lesions were of the classic form and occur in the lower extremities and the majority of patients had more than one lesion on their bodies (312/467; 66.8%) and it is prevalent in both Saudi and non-Saudi patients. This finding agrees with the results of a longitudinal study from an endemic area of eastern region of the KSA.<sup>[22]</sup> Treatment options included pentostam as the drug of choice, ketoconazole, and cryotherapy, all of which are the usual prescription for CL treatment.<sup>[1]</sup>

## CONCLUSION

Both males and females in all age groups are susceptible to CL; however, most of the infected children are Saudis; this confirms a previous finding from the region.<sup>[20]</sup> Moreover, CL is not only prevalent in Al-Madinah Al-Munawarah, but is also emerging into new foci of the province which were not previously described as endemic, such as Almeleleh in the North, Yanbua' in the West, Alhanakeia in the East, and Abar Ali in the South. Thus, large-scale studies regarding vector

and reservoir host are deeply needed, putting into account the seasonal distribution of the disease.

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### Conflicts of interest

There are no conflicts of interest.

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