

# Sociodemographic, Clinical, Laboratory, Diagnostic, Therapeutic and Public Health Aspects of Cutaneous Leishmaniasis in Southwestern Iran

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## ABSTRACT

**Introduction:** Cutaneous Leishmaniasis (CL) is caused by protozoa of the genus *Leishmania* and can be transmitted by sand fly bites. It is an important health problem in many parts of Iran as well in Dasht-e-Azadegan County, Khuzestan Province.

**Aim:** To identify the epidemiologic status of CL with emphasis on trend of its incidence rate in Dasht-e-Azadegan County.

**Materials and Methods:** This investigation was a descriptive and analytical study. A total of 1093 cases were considered for the study who were referred to the health centre during the duration of four years (2014-2017). Giemsa staining was used for preparing the expanded smear. Epidemiologic characteristics and clinical information of CL cases were collected by the means of a checklist and analysed by means of chi-square and t-tests. The p-values <0.05 were considered as statistically significant.

**Results:** Most cases were in the age group of below 10 years. Highest disease frequency was observed in students (30.1%). The majority (57.8%) had one lesion. The hand was most commonly involved (38.9%). About 73.8% of patients used topical injection along with cryotherapy for treatment. In over half of the cases (92.4%), the wound size was less than or equal to one centimetre. There was a significant difference between the residential areas, age groups, genders, occupation, month of reporting, lesion sites on the body and number of ulcers with the prevalence of active lesions.

**Conclusion:** Cutaneous leishmaniasis is considered as an important health problem in this county. So it is necessary to take certain measures for controlling the disease and reducing its incidence.

**Keywords:** Dry sore, Epidemiology, Prevalence, Wet sore

## INTRODUCTION

Leishmaniasis is a group of parasitic diseases caused by a type of *Leishmania* protozoan, leading to various clinical manifestations and health consequences [1]. In the vertebrates, *Leishmania* lives and reproduce inside uninuclear phagocytes. They are typically transmitted by phlebotomine sand flies (Diptera: Psychodidae). CL is a type of leishmaniasis that produces cutaneous manifestations and is seen in two forms of rural or wet and urban or dry. In the wet form, *Leishmania major* is the cause of the disease and rodents are its reservoir. Isfahan, Khuzestan, Ilam, Khorasan and Fars Provinces are often the loci of the wet CL [2,3]. In the dry form, *L. tropica* is the cause of the disease and humans, followed by dogs, are its major reservoirs. Mashhad, Tehran, Neishapur, Shiraz, Bam and Kerman Cities are loci of the dry CL. In the endemic regions, children are often more prone to this disease; whereas, it is seen in different age groups in non-endemic areas [4]. *Phlebotomus sergenti* and *P. papatasi* are common vectors of the urban and rural CL, respectively [5].

Leishmaniasis is prevalent in different parts of Asia, including Iraq, China, Saudi Arabia, Caucasus, Syria, Southeast Russia, Pakistan, Afghanistan, India and Iran [6,7]. About 12 million people in the world suffer from a variety of leishmaniasis every year, and nearly 400000 new cases of leishmaniasis have been reported in various parts of the world [8]. Approximately, 350 million people live in areas with the risk of leishmaniasis [9]. Nearly 20000 cases with leishmaniasis are reported annually in Iran; however, studies suggest that its actual incidence is 4 to 5 times are higher [8,10].

Cutaneous leishmaniasis does not lead to death in the majority of cases. It is an important issue due to the high prevalence of infected cases, disfiguring skin lesions which may remain for more than one year and the risk of permanent scar. One of the most important

problems in controlling leishmaniasis, especially urban CL, is the simultaneous effect of several factors on the disease transmission. Diversity in the disease agent, the variety of vectors, the existence of human and animal reservoirs, differences in environmental conditions like climate, agriculture, and rainfall pattern, and also differences in human factors such as habits, living place, and occupation conditions can play an important role in the transmission or outcome of the infection [11]. Despite identification of the CL-causing parasites, its vector and transmission routes, and in-depth studies on the matter, the measures taken to control it has not been much effective and failed in developing an effective vaccine for the prevention of infection.

Dasht-e-Azadegan County is located in Khuzestan Province. The spread of CL from its neighbour endemic country, Iraq, has led to annual reports on infected cases in the county. According to the report by the Iranian Department of disease prevention and control, this disease has turned into an important health issue in the region. Over the past few years, Dasht-e-Azadegan County has gone through considerable geographic and demographic changes due to immigrant's population enhancement, which have affected the prevalence of the CL. Therefore, it is necessary to have enough data on the present epidemiological situation of the CL to control the disease in the county. In this study, the relationship between the some risk factors and CL was assessed and the epidemiological and clinical conditions of CL were investigated in this county between 2014-2017.

## MATERIALS AND METHODS

A descriptive-analytical survey was conducted on CL patients from 2014 to 2017 in Dasht-e-Azadegan County. This study has been ethically approved by the Research Ethics Committee of the Ahvaz

Jundishapur University of Medical Sciences, Iran (ID: AJUMS.REC.1397.629). This project was done in accordance with the ethical principles and the national norms and standard for conducting Medical research in Iran (Approval ID: IR.AJUMS.REC.1379.629/ Approval Date: 2018-11-24). The confidentiality of the records of patients was assured. Informed consent was obtained from all the participants under study.

The population included all patients whose disease was confirmed through laboratory and clinical trials. People who did not have clinical signs and symptoms of CL and did not show Leishman bodies in laboratory samples were excluded from the study. The sampling of lesion secretions were performed and then was streaked on glass slide. After 20-25 minutes, the slides were stained with Giemsa and the microscope slides were visualised with 100 immersion lenses. The leishman-donovan bodies (amastigotes) were observed under light microscopy.

Data were collected by the means of a checklist. A checklist, made by researches, was completed for each patient, indicating age, sex, place of residence, month, occupation, diameter of the wound, result of culture from wound on media, medicinal regime, number and location of CL lesions.

## STATISTICAL ANALYSIS

After collecting the data, data were analysed using SPSS 18, as well as descriptive statistics and chi-square and t-tests. Significance level was considered to be  $p < 0.05$ .

## RESULTS

According to the findings, 1093 patients were identified between 2014 and 2017. In total, 582 patients were men (53.2%) and 511 patients were women (46.8%), out of which 209 women were housewives [Table/Fig-1]. The paired t-test suggested a significant relationship between the sex and prevalence of CL.

The oldest and youngest patients were 91-year-old and one-year-old, respectively. Investigation into the disease prevalence showed that the age group of below 10-year-old accounted for the majority of patients with 423 cases (38.7%), followed by 11-20-year-old with 251 cases (23%). On the other hand, the age group of older than 40 years with 77 cases (7%) accounted for the least number of patients. The non-parametric chi-square test showed a significant relationship between the prevalence of the disease and age group [Table/Fig-1].

Findings showed that urban areas accounted for the majority of cases with 697 patients (63.8%) [Table/Fig-1]. The t-test showed a significant relationship between the prevalence of the disease and place of residence.

According to occupation groups, students followed by children (less than six-year-old) accounted for the majority of cases with active lesions with the incidence rates of 30.1% and 27.7% respectively [Table/Fig-1]. The chi-square test showed no significant difference between the prevalence of CL among male and female students; whereas, it showed a significant difference between different job groups. Based on the lesion site, hands with 426 (38.9%) and legs with 270 (24.7%) cases, presented the most affected body parts. The chi-square test showed a significant difference between the anatomic sites of the lesions and the prevalence of CL.

The prevalence rate varied according to the months. In February with 260 cases (23.8%) and January with 254 cases (23.2%) represented the highest incidence rates; however, after this it showed a downward trend and reached 1.1% in July [Table/Fig-2]. The highest prevalence rate was observed in the winter with 649 cases (59.4%). The lowest prevalence rate was observed in the summer (7.2%) [Table/Fig-2]. The non-parametric chi-square test showed a significant relationship between the prevalence of the disease and season.

Results showed that 92.4% of the patients had a lesion with a diameter of 1 cm or smaller and 7.6% had a lesion with a diameter of 2 cm or larger [Table/Fig-1]. Findings showed a significant relationship between the lesion size and selection of the therapeutic regime ( $p < 0.001$ ), that 73.8% of patients with 1 cm lesion received intralesional injection and cryotherapy.

According to the findings, 632 patients (57.8%) had one lesion and 13.8% of the patients had four or more than four lesions [Table/Fig-1]. The mean number of lesions in the participants was 2.05.

Data analysis showed a significant relationship between the number of lesions and treatment choice. The majority of patients with more than one lesion received the intralesional injection of meglumine antimoniate and cryotherapy; whereas, the patients with more than three lesions received the systematic treatment with meglumine antimoniate.

## DISCUSSION

This research showed that the CL is endemic and prevalent in Dasht-e-Azadegan County. The age group of 1-10-year-old accounted for the majority of patients (38.7%). Results of present study were consistent with previous studies conducted in Kerman [12] and Fars [13] Provinces. The highest prevalence rate of CL was observed in the age group of older than 20-year-old in Fars Province [14], Hamadan County [15] and Badrood City [16] and Kashan County [17].

The highest prevalence rate in Brazil [18] and Pakistan [19] was observed in the age group of 10-30-year-old. This difference can be due to the endemicity of CL to Dasht-e-Azadegan County. This is because the prevalence rate of CL follows an upward trend in people aged below 15-year-old in endemic areas, and then starts decreasing due to acquired immunity, making children and students more vulnerable than other occupational groups. Housekeepers are primarily women, hence are prone to CL.

Culture, behaviour, job and dressing code of different Iranian ethnic groups have made males more vulnerable to CL. In studies in Iran and Ganaveh [20,21], the prevalence of the disease was reported higher among males. Results of this study were inconsistent with those of Reithinger R et al., in Kabul [22] and Akhavan AA et al., in a new focus of southern Iran [22,23]. The higher prevalence of CL among males which can be attributed to factors such as working of the majority of males as seasonal migrant workers, working in an open environment, greater the contact of men with infection sources, wearing less clothes than women, being more active in abandoned areas and deserts and increased risk of being bitten in the evening and night [24]. In addition, job travels to endemic areas could have been an important role in the transmission of CL to men.

Findings showed that the majority of patients in this study were urbanites. Studies conducted in Badrood [16] and Hamadan [15] produced results similar to the current study. It is worth noting that regarding the ratio of rural to urban population, the prevalence rate can differ in different counties. In some areas, due to easy access to urban health centres and more sensitivity of the urbanites to the disease, CL is reported less common among villagers. In addition, inadequate environmental health-related measures, farming livestock around the home and the lack of a suitable sewage system, specifically in the marginal areas, which result in an increase in the number of infected phlebotomine sand flies, have caused more reported CL cases in urban areas.

Results showed that hands and legs were the most exposed body parts. In a study conducted in Kermanshah, hands and legs accounted for 47% and 19% of the infected sand fly bite sites, respectively [25]. Moreover, hands and legs accounted for the majority of the sand fly bite sites in Arsanjan County [26]. This may be because of hands and legs are more exposed body parts;

Variable/Year		2014 No (%)	2015 No (%)	2016 No (%)	2017 No (%)	Total No (%)	p-value
Age group	0-10	165 (38.2)	131 (43.8)	94 (35.6)	33 (15.7)	423 (38.7)	<0.01
	11-20	114 (26.4)	62 (20.7)	56 (21.2)	19 (19.3)	251 (23.0)	
	21-30	98 (22.7)	71 (23.7)	61 (23.1)	18 (18.4)	248 (22.7)	
	31-40	30 (6.9)	20 (6.7)	29 (11.0)	15 (15.3)	94 (8.6)	
	≥40	25 (5.8)	15 (5.1)	24 (9.1)	13 (13.3)	77 (7.0)	
Gender	Male	237 (54.9)	153 (51.2)	137 (51.9)	55 (56.1)	582 (53.2)	<0.05
	Female	195 (45.1)	146 (48.8)	127 (48.1)	43 (43.9)	511 (46.8)	
Occupation	Child (less than six-year-old)	118 (27.3)	94 (31.4)	64 (24.2)	227 (27.6)	303 (27.7)	<0.02
	Student	142 (32.9)	91 (30.4)	73 (27.7)	23 (23.5)	329 (30.1)	
	Housewife	73 (16.9)	57 (19.1)	57 (21.6)	22 (22.4)	209 (19.1)	
	Farmer	6 (1.4)	4 (1.3)	3 (1.1)	3 (3.1)	16 (1.5)	
	Worker	27 (6.2)	31 (10.4)	35 (13.3)	10 (10.2)	103 (9.4)	
	Unemployed	24 (5.6)	6 (2.0)	15 (5.7)	6 (6.1)	51 (4.7)	
	Self-employment and government employee	42 (9.7)	16 (5.4)	17 (6.4)	7 (7.1)	82 (7.5)	
Lesion frequency	1	254 (58.8)	160 (53.6)	166 (62.9)	52 (53.1)	632 (57.8)	<0.001
	2	67 (15.5)	67 (22.4)	43 (16.3)	21 (21.4)	198 (18.1)	
	3	48 (11.1)	30 (10.0)	23 (6.7)	11 (11.2)	112 (10.2)	
	≥4	63 (14.6)	42 (14.0)	32 (12.1)	14 (14.3)	151 (13.8)	
Residential area	Urban	274 (63.4)	193 (64.5)	167 (63.3)	63 (64.3)	697 (63.8)	<0.01
	Rural	158 (36.6)	106 (35.5)	97 (36.7)	35 (35.7)	396 (36.2)	
Lesion site	Hand	177 (41.0)	123 (41.1)	88 (38.2)	37 (37.8)	426 (38.9)	<0.05
	Leg	101 (23.4)	71 (23.7)	74 (28.0)	24 (24.5)	270 (24.7)	
	Face	94 (21.8)	64 (21.4)	59 (22.3)	17 (17.3)	234 (21.4)	
	Trunk	13 (3.0)	7 (2.3)	15 (5.7)	3 (3.1)	38 (3.5)	
	Hand and Leg	14 (3.2)	7 (2.3)	9 (3.4)	5 (5.1)	35 (3.2)	
	leg and Face	5 (1.2)	4 (1.3)	3 (1.1)	2 (2.0)	14 (1.3)	
	Hand and Face	17 (3.9)	15 (5.0)	6 (2.3)	6 (6.1)	44 (4.0)	
	Hand, Leg and Face/Trunk	11 (2.5)	8 (2.7)	10 (3.8)	4 (4.1)	33 (3.0)	
Diameter of the wound	≤1 cm	389 (90.0)	280 (93.6)	245 (92.8)	96 (98.0)	1010 (92.4)	<0.001
	≥2 cm	43 (10.0)	19 (6.4)	19 (7.2)	2 (2.0)	83 (7.6)	
Result of culture from wound	Positive	419 (97.0)	298 (99.7)	263 (99.6)	98 (100.0)	1078 (98.6)	<0.001
	Negative	13 (3.0)	1 (0.3)	1 (0.4)	0 (0.0)	15 (1.4)	
Medicinal Regimen <sup>1,2</sup>	Cryotherapy and Topical Injection	224 (51.9)	239 (79.9)	260 (98.5)	84 (85.7)	807 (73.8)	<0.001
	Systemic Injection	0 (0.0)	1 (0.3)	3 (1.1)	0 (0.0)	4 (0.4)	
	Topical Injection	207 (47.9)	59 (19.7)	0 (0.0)	14 (14.3)	280 (25.7)	
	Traditional	1 (0.2)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.1)	
Total		432 (100)	299 (100)	264 (100)	98 (100)	1093(100)	

**[Table/Fig-1]:** Frequency distribution of cutaneous leishmaniasis cases by age group, gender, occupation, lesion frequency, residential area, diameter of the wound, medicinal regimen, result of culture from wound in Dasht-e-Azadegan County, southwestern Iran (2014-2017).

<sup>1</sup>Regimen: A regimen is a regulated plan of medical treatment, designed to give a positive result; <sup>2</sup>Meglumine antimoniate was given for systematic and topical therapy

Season	Year	2014 No (%)	2015 No (%)	2016 No (%)	2017 No (%)	Total No (%)	p-value
Spring	April	2 (0.5)	20 (6.7)	18 (6.8)	12 (10.4)	52 (4.8)	<0.001
	May	5 (1.2)	3 (1.0)	9 (3.4)	11 (13.5)	28 (2.6)	
	June	3 (0.7)	0 (0.0)	7 (2.7)	3 (12.3)	13 (1.2)	
Summer	July	1 (0.2)	5 (1.7)	3 (1.1)	3 (9.6)	12 (1.1)	
	August	9 (2.1)	6 (2.0)	4 (1.5)	8 (6.2)	27 (2.5)	
	September	5 (1.2)	13 (4.3)	13 (4.9)	9 (7.7)	40 (3.7)	
Autumn	October	10 (2.3)	23 (7.7)	9 (3.4)	11 (5.8)	53 (4.8)	
	November	23 (5.3)	30 (10.0)	13 (4.9)	10 (8.5)	76 (7.0)	
	December	60 (13.9)	36 (12.0)	31 (11.7)	16 (6.9)	143 (13.1)	
Winter	January	111 (25.7)	82 (27.4)	46 (17.4)	15 (6.9)	254 (23.2)	
	February	131 (30.3)	51 (17.1)	78 (29.5)	0 (5.8)	260 (23.8)	
	March	72 (16.7)	30 (10.0)	33 (12.5)	0 (6.5)	135 (12.4)	

**[Table/Fig-2]:** Frequency distribution of cutaneous leishmaniasis cases by month and season in Dasht-e-Azadegan County, Southwestern Iran (2014-2017).

therefore, it is recommended that these parts should be covered as much as possible. The application of window and door mesh or insecticide-impregnated mosquito net is also recommended. The frequency of lesions in infected patients, involvement of the most uncovered body parts, and its irreparable complications in terms of appearance highlight its control and prevention.

One of the most important factors influencing CL is climate, which depends on season and month of the year. In this study, winter, followed by spring accounted for the majority of CL cases. On the other hand, its seasonal dispersion pattern in Dasht-e-Azadegan clearly confirms the indigenous transmission of the disease. The first and second half of the year accounted for the most active period of phlebotomine sand flies and the highest incidence rate, respectively. In epidemiological studies, the highest prevalence of CL in other parts of the country was observed in spring and winter, which is consistent with the findings of the current study [27].

Findings of the current study showed that the number of lesions differed in the infected patients and ranged between 1 and 14. The majority of patients (57.8%) had only one lesion. In addition, 65.4% and 46% of the patients in Hamadan County and Badrood City had more than one lesion [15,16]. In Kashan County, only 35.9% of the patients had more than one lesion [17].

In Pakistan, 44% and 24% of the patients had one and two lesions, respectively [19]. The reason behind multiple wounds could be due to the biting procedure of sand flies as these insects perform several bites for each stage of the biting. The other reason for the existence of various wounds could be the abundance of infected sand flies in one area.

The recommended treatment in Iran is the injection of meglumine antimoniate, application of cryotherapy, or the combination of both. Due to spontaneous wound healing, sometimes it is recommended that small wounds should not be treated. Gonzalez U et al., recommended informing patients about the spontaneous healing and the lack of sufficient evidence on the treatment effectiveness before administration of the CL therapy [28]. Different studies in the Eastern Mediterranean Region and Asia have reported an improvement following an intralesional injection of meglumine antimoniate in more than 90% of cases [29,30].

Cutaneous leishmaniasis in patients with intact immune system can be treated topically or intramuscularly, but transplant patients with disseminated leishmaniasis should be hospitalised and treated with combined systemic long-term drugs. The present case was treated with glucantim and Amphotericin B [31]. It is important to monitor the presence of CL in each region and to know the epidemiology and distribution of this disease in the endemic areas. The results of the present study are useful for prevention of CL.

## LIMITATION

The limitation of this study was that the type of parasite was not identified through molecular studies. The strong point is a widespread assessment during several years of CL epidemiology in Dasht-e-Azadegan.

## CONCLUSION

According to the present study the average annual prevalence of CL was found to be 273.25 per 100000 populations (1093 divided by 4-mean annual population in this county in period study was 100000 people) in Dasht-e-Azadegan County. Meantime, the findings of this study showed that CL is spreading southwestern Iran. Dasht-e-Azadegan is an example of the establishment of a focus of CL, through unplanned urban and agricultural development, movement of infected persons and to increases in people and sand fly populations. It is proposed that health authorities should do active screening, follow-up and raise the knowledge about the CL transmission, control and prevention.

It is also recommended to manage more descriptive-analytical studies to determine the role of socioeconomic factors such as population dynamics, development, human behaviour and poverty. Further epidemiological investigations should be conducted to assess the *Leishmania* infection and its associated risk factors.

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