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Ten Years Investigation on Situation Analysis of Cutaneous Leishmaniasis in an Endemic Area, Southwestern Iran

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ABSTRACT

Epidemiologically, Cutaneous Leishmaniasis (CL) is presently endemic in 98 countries worldwide, including Iran. Both forms of CL, Anthroponotic CL and Zoonotic CL are seen in many parts of the country. Because of the importance of CL in Khorramshahr county (30°26′23″N 48°09′59″E) and slightly increasing of disease in recent years, this study was designed to assess the status of CL from 2007 to 2016. In this analytical-descriptive study, all of the patients suspected to CL were identified by passive case detection. With the help of the health experts, uncovered parts of the body of all cases were examined regarding active lesion (s). Patients with active lesions were examined using parasitological method and according to the physician diagnosis based on the shape of the lesion and the patient's history. Some information including the number of lesions, location of lesions in different parts of the body, gender , age of the patients , month, season, residential area (city or village) were recorded in questionnaires. Statistical analysis of the epidemiological data was performed in the SPSS -21 software, to determine any significant difference between above mentioned factors and disease incidence. From 2007 to 2016, at least 745 new cases of CL were considered in Khorramshahr County. The highest frequency of CL was seen in the age groups of 21-30 years old (25.9%). In the past ten years, most of the patients were males (51.8%). There was not any significant difference between males and females according to their infection with CL. In the last ten years, most of the patients were citizens of urban areas. There were significant difference between frequency of CL in urban and rural residents. Review on occupation of patients with CL indicates that approximately 36.1% of them were housewives. There was significant difference between seasons and number of patients. The highest frequency of CL was seen in winter (53.9%) and fall (19.5%). Lesions of patients in more than 97.7% of the cases were between 1-3 numbers. Distribution of lesions in the body showed that hands were the most affected location (35.2%). It is necessary to take strong steps to control the CL and prevent its extension. Furthermore, It is critical to provide rapid treatment of cases. The control of CL needs to close cooperation between the universities of medical sciences, the government and health services centers.

Keywords: Cutaneous Leishmaniasis, Incidence Rate, Epidemiology, Demography, Iran

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INTRODUCTION

Leishmaniasis is a parasitic disease caused by a unicellular parasite belonging to the genus *Leishmania. This parasite develops a* group of diseases with a variety of clinical manifestations and outcomes, including cutaneous leishmaniasis (CL), a benign skin ulcer caused by *Leishmania major* (rural, wet or zoonotic type) and *L. tropica* (urban, dry or anthroponotic type) [1].

It is not a fatal disease, but difficult for patients to cope with it due to three important reasons: first, aesthetic implications (especially in open areas of the body such as the face); second, lengthening of the self-healing process of ulcer; and third, the scar formation after healing [2, 3].

Despite having enough knowledge about the CL-inducing parasite, vector, means of transmission, as well as substantial research on the disease, the measures taken to control the CL have, unfortunately, not been pivotal and no effective vaccine has been produced to prevent it so far [4, 5].

This disease imposes a heavy economic burden on families, societies and countries, especially developing countries [6]. Pentavalent antimony (glucantime) is used to treat the disease, which is expensive and requires several injections. Drug resistance is also a common phenomenon. Local administration of drug around the ulcer is also painful [7].

About two million people are affected annually, of which 1,5 million cases are CL and 500,000 are visceral leishmaniasis or Kala-azar. Approximately 90% of the CL cases are living in Afghanistan, Brazil, Iran, Peru, Saudi Arabia and Syria [8-11]. Leishmaniasis is a major health problem in Iran [12].

As an important point, CL has already been sporadic in some parts of Iran, but today the disease appears to be endemic and has even spread to areas with no previous cases of CL [13]. Fighting this disease has always been considered in Iran's national plans. Despite the extensive efforts as well as national and international investments, not only this disease has not been eradicated, but it has also become more prevalent with the emergence of new focal points of the disease around the country. It has attracted an important part of social and health activities as a major problem and imposed irreparable losses on the community through creating social and psychosocial problems. The national CL control program emphasizes the need for determining the epidemiological characteristics of CL in its focal points [14]. Due to its proximity to Saudi Arabia and Iraq, the county of Khorramshahr is affected by hot dry winds flowing from these

countries. On the other hand, the relative humidity of this area is high in all seasons due to its proximity to Arvand river and the Persian Gulf. Therefore, the region is ecologically favorable for the growth and reproduction of sandflies. Since epidemiological studies are effective in controlling the disease and taking preventive measures, this study aimed to determine the epidemiologic status of CL in Khorramshahr during a 10-year period (2007-2016).

MATERIALS AND METHODS:

Khorramshahr (30°26′23″N 48°09′59″E) is located on the south-west end of Khuzestan plain on the confluence of Karun and Arvand rivers near the border with Iraq. The county's population is reported 170000 at 2016 census. Khorramshahr's altitude is 4 m above sea level with warm and dry climates. This study has been approved by the research ethics committe of the Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran. This project was in accordance to the ethical principles and the national norms and standards for conducting medical research in Iran. The confidentiality of the records of patients was assured. Also, agreement of patients to participate in this study was acquired.

In this cross-sectional descriptive – analytical study, cases with suspicious lesions referred to health center in Khorramshahr city. Then demography and epidemiological data such as gender, age, occupation, location of wound on the body, geographical area (city or village), month , season and number of wounds on the body were recorded in data collection forms. For each case, a questionnaire was completed by face-to-face interview along with clinical observation of the ulcer(s). Samples were obtained using a sterile blade by scraping from the edge of the lesion on the microscopic glass slides. Then, the smears of the serous fluids of their lesions were dried in the air, fixed with methanol, stained with Giemsa and examined to view Lishman bodies (amastigotes) by light microscope with 100 immersion lenses. Each patient was defined by clinical evaluation and observation of amastigotes. Collected data were later analyzed using SPSS version 19, the chi-square and T tests. Meanwhile, p-values <0.05 were considered statistically significant.

RESULTS:

In the present study, the information of about 745 patients with CL in Khorramshahr was collected during 2007-2016. The average incidence of this disease during the 10-year

period in Khorramshahr was 45 out of 100000 people. The number of patients with CL was 10 in the first year, but in 2009, the number of people suffering from this disease reached a peak of 327 cases, especially during February and January of that year (Table 1).

Of the total number of patients, 359 (48.2%) were female and 386 (51.8%) were male (Table 1). The results showed no significant relationship between gender and catching of CL. The study of the prevalence of CL in terms of the age groups showed that the highest prevalence of the disease was respectively observed in the 21-30 age group with 193 cases (25.9%) and under 10 age group with 179 cases (24%). The lowest incidence was also observed in the age group of more than 40 years with 56 cases of disease (7.6%) (Table 1). The nonparametric chi-square test showed a significant relationship between the incidence of CL and the age groups (p<0.05).

The findings of this study showed that the incidence of CL in the urban areas, with 506 cases (67.9%), was more than rural areas; so that the incidence of the disease in urban areas was more than twice as high as in rural areas. T-test showed a significant relationship between the incidence of the disease and the patients residence area (p<0.05). The highest incidence of CL in terms of occupation was observed in housewives (36.1%) and then the students (20.0%) (Table 1). The nonparametric chi-square analytical test showed a significant relationship between occupation and catching of CL (p<0.05).

In terms of number of lesions, 82.4%, 10.9%, 4.4% and 2.3% of patients had one, two, three , four lesions and more, respectively (table 1). The nonparametric chi-square analytical test showed a significant relationship between the two variables (p<0.05). Based on the location of lesions on the body, cutaneous lesions were most commonly formed on the hands with 262 cases (35.2%) and the feet with 249 cases (33.4%), and least commonly formed on the neck with 11 cases (1.5%) (Table 1). The nonparametric chi-square test showed a significant relationship between number of lesions and the incidence of lesions (p<0.05).

The incidence of CL varied according to the months of the year, so that the maximum number of patients was observed in February with 158 cases (21.1%) and in January with 129 cases (17.3%) . Then, the number of patients fell down and reached to 19 cases (2.6%) in August (Table 2). The highest incidence of disease during winter was 402 cases (53.9%) (Table 1). The nonparametric chi-square test showed a significant relationship between the incidence of CL and the months of the year (p<0.05).

Table 1: Distribution of cutaneous leishmaniasis cases based on age group, gender, job, season, lesion frequency, residential area and lesion site in Khorramshahr County, southwestern Iran (2007-2016)

Variables	2007 No (%)	2008 (%)	2009 No (%)	2010 No (%)	2011 No (%)	2012 No (%)	2013 No (%)	2014 No (%)	2015 No (%)	2016 No (%)	Total No (%)
Age Group											
0-10	3 (30.0)	5 (83.3)	76(23.2)	68(26.1)	4(15.4)	3(60.0)	2(18.2)	7(14.9)	8(23.5)	3(15.8)	179(24.0)
11-20	3 (30.0)	1(16.7)	84(25.7)	52(20.0)	6(23.1)	0(0.0)	0(0.0)	9(19.2)	3(8.8)	5(26.3)	163(21.8)
21-30	1(10.0)	0(0.0)	76(23.2)	77(29.6)	5(19.2)	1(20.0)	4(36.4)	18 (38.3)	8(23.5)	3(15.8)	193(25.9)
31-40	2(20.0)	0(0.0)	60(18.4)	54(20.8)	7(26.9)	1(20.0)	4(36.4)	8(17.0)	15(44.2)	3(15.8)	154(20.7)
≥40	1(10.0)	0(0.00	31(9.5)	9(3.5)	4(15.4)	0(0.0)	1(9.0)	5(10.6)	0(0.0)	5(26.3)	56(7.6)
Gender											
Male	6(60.0)	3(50.0)	123(37.6)	180(69.2)	12(46.1)	1(20.0)	1(9.1)	35(74.5)	16(47.1)	9(47.4)	386(51.8)
Female	4(40.0)	3(50.0)	204(62.4)	80(30.8)	14(53.9)	4(80.0)	10(90.9)	12(25.5)	18(52.9)	10(52.6)	359(48.2)
Job											
Student	3(30.0)	1(16.7)	64(19.6)	51(19.6)	8(30.8)	2(40)	0(0.0)	11(23.4)	7(20.6)	2(10.5)	149(20.0)
Housewife	1(10.0)	2(32.3)	123(37.6)	105(40.4)	6(23.1)	1(20.0)	1(9.1)	12(25.5)	9(26.4)	9(47.4)	269(36.1)
Farmer	0(0.0)	0(0.0)	9(2.8)	3(1.2)	1(3.8)	0(0.0)	0(0.0)	1(2.1)	2(5.9)	1(5.3)	17(2.3)
Child	2(20.0)	2(32.3)	77(23.5)	49(18.8)	3(11.5)	1(20.0)	8(72.7)	6(12.8)	7(20.6)	2(10.5)	161(21.6)
Others	4(40.0)	1(16.7)	54(16.5)	52(20.0)	8(30.8)	1(20.0)	2(18.2)	17(36.2)	5(14.7)	5(26.3)	149(20.0)
Season											
Spring	5(50.0)	4(64.7)	1(0.3)	94(36.1)	10(38.5)	1(20.0)	4(36.4)	0(0.0)	6(17.7)	4(21.1)	129(17.3)
Summer	0(0.0)	0(0.0)	0(0.0)	61(23.5)	2(7.7)	0(0.0)	0(0.0)	0(0.0)	2(5.9)	4(21.1)	69(9.3)
Autumn	3(30.0)	0(0.0)	53(16.2)	55(21.2)	6(23.0)	1(20.0)	1(9.1)	12(25.5)	13(38.2)	1(5.2)	145(19.5)

Winter	2(20.0)	2(32.3)	273(83.5)	50(19.2)	8(30.8)	3(60.0)	6(54.5)	35(74.5)	13(38.2)	10(52.6)	402(53.9)
Lesion Frequency											
1	6(60.0)	6(100.0)	271(82.8)	230(88.5)	14(53.9)	5(100.0)	8(72.7)	36(76.6)	22(64.7)	16(84.2)	614(82.4)
2	3(30.0)	0(0.0)	32(9.8)	19(7.3)	7(26.9)	0(0.0)	3(27.3)	9(19.1)	6(17.6)	2(10.5)	81 (10.9)
3	1(10.0)	0(0.0)	15(4.6)	6(2.3)	3(11.5)	0(0.0)	0(0.0)	2(4.3)	5(14.7)	1(5.3)	33(4.4)
≥4	0(0.0)	0(0.0)	9(2.8)	5(1.9)	2(7.7)	0(0.0)	0(0.0)	0(0.0)	1(3.0)	0(0.0)	17(2.3)
Residential Area											
Urban	8(80.0)	6(100.0)	215(65.7)	180(69.2)	21(80.8)	2(40.0)	8(72.7)	37(78.7)	20(58.8)	9(47.4)	506(67.9)
Village	2(20.0)	0(0.0)	112(34.3)	80(30.8)	5(19.2)	3(60.0)	3(27.3)	10(21.3)	14(41.2)	10(52.6)	239(32.1)
Lesion Site											
Hand	4(40.0)	5(83.3)	115(32.5)	75(28.9)	12(46.2)	3(60.0)	6(54.5)	21(44.7)	13(38.2)	8(42.1)	262(35.2)
Foot	2(20.0)	1(16.7)	102(31.2)	96(36.9)	12(46.2)	2(40.0)	5(45.5)	15(31.9)	9(26.5)	5(26.3)	249(33.4)
Face	1(10.0)	0(0.0)	46(14.1)	40(15.4)	1(3.8)	0(0.0)	0(0.0)	4(8.5)	5(14.7)	1(5.3)	98(13.2)
Hand & Foot	1(10.0)	0(0.0)	39(11.9)	9(3.5)	1(3.8)	0(0.0)	0(0.0)	4(8.5)	4(11.8)	2(10.5)	60(8.0)
Hand & Face	0(0.0)	0(0.0)	17(5.2)	5(1.9)	0(0.0)	0(0.0)	0(0.0)	3(6.4)	2(5.9)	2(10.5)	29(3.9)
Neck	0(0.0)	0(0.0)	0(0.0)	10(3.8)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(2.9)	0(0.0)	11(1.5)
Trunk	2(20.0)	0(0.0)	8(2.4)	25(9.6)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(5.3)	36(4.8)
Total	10(100)	6(100)	327(100)	260(100)	26(100)	5(100)	11(100)	47(100)	34(100)	19(100)	745(100)

Table 2: Distribution of cutaneous leishmaniasis cases based on month in Khorramshahr County, southwestern Iran (2007-2016)

Months	2007 No (%)	2008 No (%)	2009 No (%)	2010 No (%)	2011 No (%)	2012 No (%)	2013 No (%)	2014 No (%)	2015 No (%)	2016 No (%)	Total No (%)
April	2(20.0)	2(33.3)	1(0.3)	27(10.4)	7(26.9)	0(0.0)	3(27.3)	0(0.0)	4(11.8)	3(15.8)	49(6.6)
May	2(20.0)1	2(33.3)	0(0.0)	35(13.5)	2(7.7)	0(0.0)	1(9.1)	0(0.0)	2(5.9)	1(5.3)	45(6.0)
June	1(10.0)	0(0.0)	0(0.0)	32(12.3)	1(3.8)	1(20.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	35(4.7)
July	0(0.0)	0(0.0)	0(0.0)	25(9.6)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(2.9)	2(10.5)	28(3.8)
August	0(0.0)	0(0.0)	0(0.0)	16(6.2)	1(3.8)	0(0.0)	0(0.0)	0(0.0)	1(2.9)	1(5.3)	19(2.6)
September	3(30.0)	0(0.0)	0(0.0)	20(7.7)	1(3.8)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(5.3)	22(3.0)
October	0(0.0)	0(0.0)	0(0.0)	15(5.8)	0(0.0)	1(20.0)	0(0.0)	0(0.0)	2(5.9)	0(0.0)	21(2.8)
November	(0.0)0	0(0.0)	1(0.3)	22(8.5)	2(7.7)	0(0.0)	0(0.0)	1(2.1)	3(8.8)	0(0.0)	29(3.9)
December	1(1.0)	0(0.0)	52(15.9)	18(6.9)	4(15.4)	0(0.0)	1(9.1)	11(23.4)	8(23.5)	1(5.3)	95(12.8)
January	1(10.0)	1(16.7)	87(26.6)	18(6.9)	3(11.5)	1(20.0)	2(18.2)	8(17.0)	4(11.8)	4(21,1)	129(17.3)
February	0(0.0)	1(16.7)	104(31.8)	15(5.8)	2(7.7)	2(40.0)	1(9.1)	22(46.8)	6(17.6)	4(21.1)	158(21.2)
March	0(0.0)	0(0.0)	82(25.1)	17(6.5)	3(11.5)	1(20.0)	3(27.3)	510.6)	3(8.8)	2(1.5)	115(15.4)
Total	10(100)	6(100)	327(100)	260(100)	26(100)	5(100)	11(100)	47(100)	34(100)	19(100)	745(100)

DISCUSSION:

The results of this study showed that the mean incidence of CL in Khorramshahr during this 10-year period was 45 per 100000 people. The incidence rate in other parts of Iran was 103 per 100000 in Aran va Bidgol County [15], 312 per 100000 people in Damghan County [1], and 39 per 100000 people in Kermanshah [16]. The prevalence of this disease is high in Khorasan, Fars, Isfahan, Khuzestan and Kerman provinces. Provinces such as Ilam, Yazd and Bushehr were recognized to have the highest incidence of new cases in recent years. In general, with an average incidence of 166 per 100000 people, provinces such as Yazd, Bushehr, Khorasan, Fars, Ilam, Khuzestan and Isfahan have the highest incidence of CL in Iran, and the western and northwestern provinces have the lowest incidence of this disease in the country, *i.e.* less than 10 cases per 100000 people [17-22]. Based on this categorization of the Ministry of Health and Medical Education, Khorramshahr has a moderate prevalence in Iran. Traveling to areas where the disease is endemic is a risk factor. The incidence of the disease will be increased due to the exposure of people, especially non-natives, to the disease vectors. In this regard, military personnel and seasonal migrant workers may be at the risk of CL due to their occupational status and settlement in suburban areas or because of business trips [23]. Migration and population changes caused by the war and disasters have led to changes in the disease trend in the distressed areas. As a matter of fact, population displacement is a very important factor in causing CL, especially its urban type [24].

In this study, the number of male patients (51.8%) was higher than female patients, which is consistent with the results of the study of Barati in Khatam County (61% male, 39% female) [25], Abbasi in Gorgan County (31.4% female and 68.6% male) [26], Kassiri in Shushtar County (68.9% male, 31.1% female) [27], Feyz- Haddad in Shadegan County [28] and Kassiri in Genaveh County (54% male and 46% female) [29]. However, in the study of Dehghan in Larestan County [30]and in a study conducted in Abarkuh County, the incidence was reported to be more among females [31]. In different areas, the prevalence of CL varies according to the occupation that women are most likely to have. For example, in areas where women are more likely engaged in carpet weaving in low-light and underground rooms, the incidence of CL is higher, as the sandflies continue to bite them throughout the day [32]. The higher incidence of CL among men in Khorramshahr is due to reasons such as the engagement of the majority of men as seasonal migrant laborers in the Khorramshahr port, resting or working at the beginning of the night outside the working or residential places, employment of military forces in the border areas of Khorramshahr and their work in open areas, the lower coverage of men than women, the greater traffic in the abandoned areas and around the wetlands, which are good places for the growth and reproduction of sandflies, thus causing more contact with the sandflies during the night.

In the present study, the highest incidence rate was observed in the age groups of 21-30 (25.9%) and under 10 (24%). In the study of Fazaeli *et al.*, most cases of ulcers and scars were observed in the under 10 age group [11]. In a study conducted after the Bam earthquake in Dehbakri located in southeastern Iran, Sharifi *et al.* (2003) observed the most cases of CL in the under 10 age group [33]. Sufizadeh *et al.* conducted a study in Gonbad-Kavous County and reported the highest incidence of CL in the under 10 age group [34]. In other studies conducted in endemic areas, the childhood has been reported as the most common age for the onset of CL; and subsequently, the incidence of this disease is likely to be reduced due to acquired immunity [35]. The prevalence of CL at young age can be due to the fact that youths are usually at outdoor areas at the beginning of the night and are therefore more likely to be exposed to the bites of sandflies.

The results of this study showed that most patients had cutaneous ulcers in their hands and feet. In a study conducted in Kermanshah, 47% of patients had ulcers in their hands and 19% in their feet [36]. The studies conducted in Larestan [30], Mirjavah [37] and Gorgan [26] Counties indicated that most of the lesions were observed in the hands and feet which was consistent with the results of the present study; while in the studies of Ebadi in Borkhar County [38] and Karimi Zarchi in Sarakhs County [39], the face was the most affected organ of the body. As the face has no coverage, but other organs are usually covered, it is more likely that the hands, feet and face are bitten, and consequently the chance of ulcers in these organs increases. Therefore, it is recommended that people cover these organs to the possible extent. During the night, the bed nets impregnated to insecticides must be used to prevent the sandflies from entering the home. The prevalence of lesions in affected individuals, the involvement of more open and uncovered areas of the body with this disease as well as the irreversible complications of CL, especially in terms of beauty highlight the importance of controlling and preventing this disease.

The number of ulcers is an effective factor in choosing the injection method of glucantime ampoule, *i.e.* intramuscular or topical. In people with the high number of ulcers, daily and intramuscular injections are administered. The findings showed that the number of ulcers in the infected individuals were different. In the present study, most people (82.4%) had an ulcer on their body. In the studies of Hamzawi *et al.* [36] and Yaghoobi - Ershadi *et al.* [40], 55% and 52% of patients had an ulcer on the body, respectively. In the study of Rafati *et al.*, about 60% of people had more than one ulcer on their body [1] while in the study of Dehghan *et al.*, 62.38% of patients had one ulcer on their body [30]. The number of bites can be due to the way the blood feeding by sandflies, because sandflies perform numerous bites for once filling the ab-domen with blood, or it can be caused by the high number of infected sandflies in the area.

Findings of the present study showed that 70.8% of the patients were living in the cities. Studies in the counties of Damghan [1] and Hamadan [41] showed similar results. It is necessary to note that due to the proportion of rural and urban population, the rate of infection in urban or rural areas in different cities can vary, so that in the study of Dehghan, the incidence rate of CL in the rural areas was almost three times that of the urban areas [30]. In the present study, due to the ease of visiting the urban health centers by the patients and more susceptibility of urban residents to CL, the number of cases among the townspeople was more than villagers. Inadequate environmental health measures, including poor collection of waste and construction debris, livestock storage near the houses (in the outskirts of the cities), and lack of proper sewage systems, especially in the outskirts of the cities, which in turn, increased the number of sandflies and consequently the prevalence of CL in the urban areas, are among the causes of this disease [17].

CONCLUSIONS:

Results can provide serious guidelines for initiating control strategies for policy makers to monitor CL. Moreover, further researches are needed to determine the reservoirs, vectors and species of disease and to plan suitable strategies to control CL.

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