



Original Article

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Epidemiological features of cutaneous leishmaniasis in North Khorasan Province in Iran: A cross-sectional study

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ABSTRACT

Objective: To investigate the trend and epidemiological status of cutaneous leishmaniasis in the North of Khorasan province, Iran from 2014 to 2022.

Methods: This a cross-sectional study collected and analyzed the information of 849 patients with cutaneous leishmaniasis (CL) through the health center portal from 2014 to 2022. The relationship between sex, number of lesions, and lesion shape was investigated.

Results: Totally 849 participants were included and their mean age was 23.0 ± 20.2 years. The most common parasite species found was *Leishmania major* ($n=714$, 84.1%). The number of CL in Esfarayen County increased from 2014 ($n=83$) to 2022 ($n=147$) and was more prevalent in men than in women. Furthermore, there was no significant difference in the number and shape of lesions between men and women.

Conclusions: As leishmania major is the predominant type in Esfarayen County of Iran and the number of cases is increasing, it is important to control the reservoir and disease vector in this area. Therefore, a more comprehensive surveillance is suggested.

KEYWORDS: Cutaneous leishmaniasis; Epidemiology; Prevalence; Zoonotic disease; Iran

1. Introduction

Leishmaniasis is a parasitic disease caused by intracellular protozoa of the genus *Leishmania* that infects vertebrate animals, including humans[1]. Leishmaniasis occurs in three clinical types: Cutaneous leishmaniasis (CL), visceral leishmaniasis, and mucocutaneous leishmaniasis, with the CL type being more common in the Middle East[2]. Clinical manifestations of CL

Significance

Cutaneous leishmaniasis is one of the most important zoonotic diseases and is endemic in Iran. Combating this disease requires accurate and complete information on its epidemiology. This study focuses on key demographic, behavioral, and clinical aspects of cutaneous leishmaniasis. Our results showed that the most common parasite species found was *Leishmania major*. This information will contribute to control and prevention programs.

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range from simple isolated lesions to widespread lesions that heal spontaneously, although facial scarring can have a psychological impact, especially in women[3]. Moreover, CL occurs in two forms in Iran: anthropogenic cutaneous leishmaniasis (urban or dry type) and zoonotic cutaneous leishmaniasis (rural or wet type)[4]. Every year, approximately 2 million people are infected with leishmaniasis, of which approximately 1.5 million are associated with CL[5]. The disease is considered a major public health problem in the Eastern Mediterranean and has been reported mainly in 14 countries in the region[4]. In Iran, the number of CL cases decreased from 23 202 in 2008 to 13 124 in 2019 (the incidence rate was 15.8 per 100 000 population in the same year)[6].

Host, vector, parasitic environment, and other conditions play a role in the development and progression of leishmaniasis, making disease control difficult[7]. The incidence of CL varies across regions of Iran[8,9]. In general, the northern and southern regions of Iran currently have a low prevalence of the disease. However, the western and southwestern regions have environmental conditions that allow the development of several vectors and reservoirs. Therefore, the prevalence is expected to decrease in the future[10].

In one study, the incidence of CL was highest in autumn and winter, which is one of the most important characteristics of zoonotic cutaneous leishmaniasis[9]. The control and prevention of this disease require accurate and complete information on its epidemiology. This study was carried out to investigate the epidemiological aspects of CL in Esfarayen county, Iran, since no new studies have been conducted in this area for years. Due to economic issues such as diagnosis and treatment of this disease, and non-economic impacts such as the psychological impact of scarring, the results may make a useful contribution to control and prevention programs.

2. Material and methods

2.1. Study setting

This cross-sectional study examined a total of 849 CL cases who attended the district CL treatment center in Esfarayen from the beginning of 2014 to the end of 2022. Eligibility criteria included cases with a positive direct microscopic sample prepared by the Leishmania Diagnostic Laboratory of the Cutaneous and Leishmania Research Center. Exclusion criteria were people not living in Esfarayen County. Sampling was done by census and all CL cases during this period were included in the study.

2.2. Inclusion criteria and exclusion criteria

There are 862 patients were diagnostic with cutaneous leishmaniasis while 13 of them were excluded as they were not residents in Esfarayen County. Totally 849 were included in the present study (Figure 1).

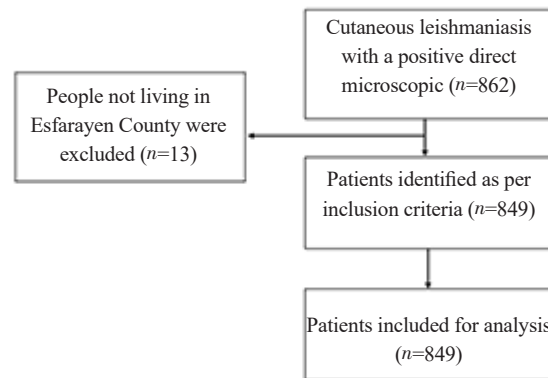


Figure 1. Flowchart of cutaneous leishmaniasis cases who attended the district cutaneous leishmaniasis treatment centers in Esfarayen County.

2.3. Data collection

In this study, demographic characteristics (*e.g.*, age, sex, occupation, place of residence, nationality) and clinical characteristics (*e.g.*, number of lesions, shape of lesions, etc.) of all CL cases referred for treatment and referred for follow-up care were collected. Information on CL patients was collected through the county health center portal. In this study, to control the information bias due to the reading of case files, subjects were contacted randomly and information was collected about the location and characteristics of the wound due to sand fly bites.

2.4. Statistical analysis

Frequencies and percentages were used to describe categorical variables, and means and standard deviations were used for continuous variables. The *Chi*-square tests were used to determine the relationship between sex, number of lesions, and shape of lesions. Due to the descriptive and cross-sectional nature of this study, there were no confounding or interaction variables, and since all people were included in the study by the census, there was no missing. STATA version 16.0 (Stata Corp, College Station, Texas, USA) was used for data analysis.

2.5. Ethical approval

This study was approved by the Ethics Committee of Esfarayen Faculty of Medical Sciences with approval No. of IR.ESFARAYENUMS.REC.1402.001.

3. Results

3.1. Demographic characteristics

Descriptive results showed that of the 849 cases, 499 (58.8%) were men, 240 (28.3%) were aged between 6 and 17 years, and 600 (70.7%) lived in villages. The mean age of the subjects was 23.0 ± 20.2 years. In terms of occupation, 257 (30.3%) were children, 202 (23.8%) were students, and 141 (16.6%) were householders (Table 1).

Table 1. Demographic characteristics of cutaneous leishmaniasis patients in Esfarayen County ($n=849$).

Characteristics	Frequency
Sex	
Male	499 (58.8)
Female	350 (41.2)
Age group (years)	
0-5	188 (22.1)
6-17	240 (28.3)
18-29	145 (17.1)
30-59	214 (25.2)
≥ 60	62 (7.3)
Residence place	
Urban	249 (29.3)
Rural	600 (70.7)
Nationality	
Iranian	847 (99.8)
other	2 (0.2)
Occupation	
Child	257 (30.3)
Student	202 (23.8)
Householder	141 (16.6)
Others	249 (29.3)

Data were expressed as $n(\%)$.

Of all cases, 620 (73.0%) had no travel history in the past year, whereas 229 (27.0%) had a travel history. Of the travelers, 173 (20.4%) had visited rural areas. The most common parasite species found was *Leishmania major* 714 (84.1%). Of the 849 people, 456 (53.9%) were self-ill, and other family members were healthy, while 107 (12.6%) had other family members infected and 33 (3.9%) had neighbors infected. Furthermore, treatment failed in 36 patients (4.2%), relapse occurred in 5 patients (0.6%), and treatment was discontinued in 9 patients (1.1%).

3.2. Clinical features of cutaneous leishmaniasis patients

Clinical observation showed that 372 cases (43.8%) had a solitary lesion, while 272 cases (32.0%) had three or more lesions. In addition, 783 patients (92.2%) had wounds with skin discharge. Overall, there was no significant difference between men and women in the number and shape of lesions. (Table 2).

Most lesions were located on the hands ($n=266$, 20.6%), face ($n=258$, 20.1%), feet ($n=210$, 16.2%), and forearms ($n=199$, 39.2%). Totally, 630 (73.3%) wounds were 1-2 cm in size, and 790 (92.0%)

wounds had skin discharge. Regarding the presence or absence of underlying diseases, only 18 patients (2.1%) had underlying diseases, the most common of which were heart failure ($n=11$), hypertension ($n=11$), and diabetes ($n=5$). Drug complications were also reported in only 6 patients (0.7%). Five patients had local complications such as pain, inflammation, and blisters at the injection site, and seven patients had systemic complications such as hypotension, dizziness, nausea, and sporadic hives (Table 2).

Table 2. Clinical features of cutaneous leishmaniasis patients in Esfarayen County ($n=849$).

Parameters	Men	Women	Total	<i>P</i>
Number of lesions				
1	207 (41.5)	165 (47.1)	372 (43.8)	0.285
2	129 (25.9)	76 (21.7)	205 (24.1)	
3	68 (13.6)	51 (14.6)	119 (14.0)	
≥ 4	95 (19.0)	58 (16.6)	153 (18.0)	
Total	499 (100)	350 (100)	849 (100)	
Shape of the lesion				
Ulcers without secretions	44 (8.8)	22 (6.3)	66 (7.8)	0.175
Ulcers with skin secretions	455 (91.2)	328 (93.7)	783 (92.2)	
Total	499 (100)	350 (100)	849 (100)	
Wound size				
1-2 cm	365 (72.1)	265 (74.3)	630 (73.1)	0.345
>2 cm	134 (27.9)	85 (25.7)	219 (26.9)	
Total	499 (100)	350 (100)	849 (100)	
Site of wound				
Hands	135 (32.6)	111 (25.9)	246 (29.2)	0.4
Face	101 (24.3)	133 (31.1)	234 (27.8)	
Feet	83 (20.0)	103 (24.1)	186 (22.1)	
Forearms	95 (22.9)	80 (18.7)	175 (20.8)	
Total	414 (99.8)	427 (99.8)	841 (99.9)	
Underlying disease				
No	491 (98.4)	340 (97.1)	831 (97.9)	0.212
Yes	8 (1.6)	10 (2.9)	18 (2.1)	
Total	499 (100)	350 (100)	849 (100)	
Type of underlying disease				
Heart failure	2 (0.4)	9 (2.6)	11 (3)	0.087
Hypertension	2 (0.4)	9 (2.6)	11 (3)	
Diabetes	3 (0.6)	2 (0.6)	5 (1.2)	
Total	7 (1.4)	20 (5.8)	27 (7.2)	
Drug complication				
No	496 (99.4)	347 (99.1)	843 (99.3)	0.661
Yes	3 (0.6)	3 (0.9)	6 (0.7)	
Total	499 (100)	350 (100)	849 (100)	

Data were expressed as $n(\%)$.

3.3. Distribution of cutaneous leishmaniasis cases by months of the years from 2014 to 2022

In terms of month, most of the CL cases occurred in November (271 cases, 31.9%), October (266 cases, 31.3%), September (111 cases, 13.1%), and December (108 cases, 12.7%), and the lowest cases were reported in spring including April, May and June (9 cases, 1.1%) (Figure 2).

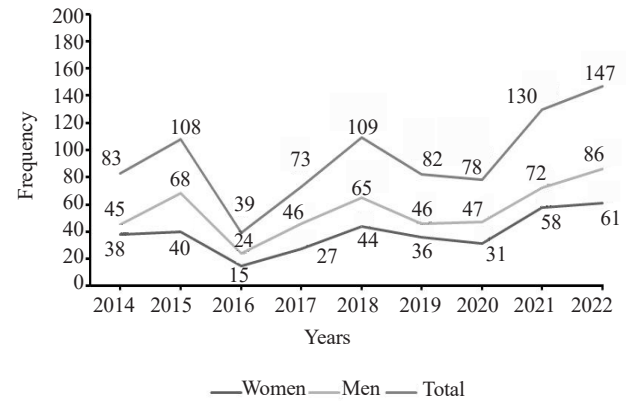
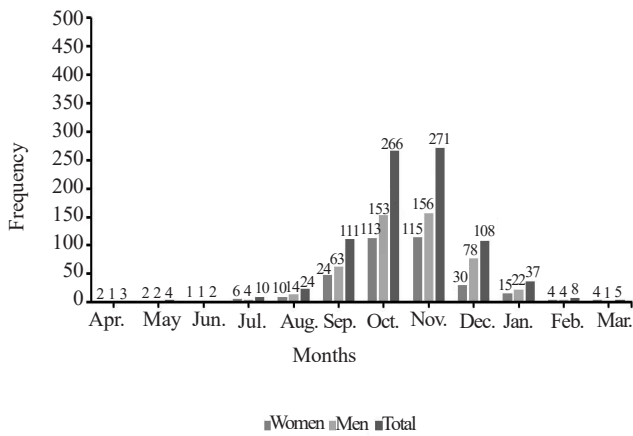


Figure 2. Distribution of cutaneous leishmaniasis cases by months of the years. **Figure 3.** Trend of cutaneous leishmaniasis by years.

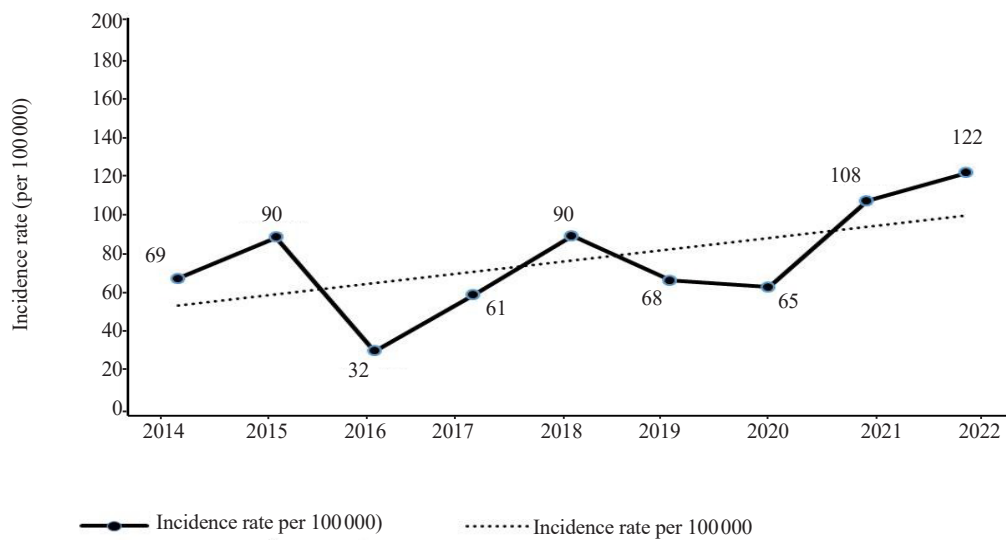


Figure 4. The incidence of cutaneous leishmaniasis in Esfarayen and the trending linear by years.

3.4. Trend of cutaneous leishmaniasis by years

The number of CL in Esfarayen County increased from 2014 ($n=83$) to 2022 ($n=147$), with more men than women. The highest number of cases was in 2022 ($n=147$) and the lowest in 2016 ($n=39$) (Figure 3).

According to the Cochran-Armitage test, the trend of cutaneous leishmaniasis in Esfarayen County has not been stable in nine years, and it has increased from 69 per 100000 in 2014 to 122 per 100000 in 2022 (Figure 4) ($P<0.001$).

4. Discussion

This study provides a comprehensive overview of cutaneous leishmaniasis in Esfarayen County in Iran, and offers valuable insights into various demographic and behavioral aspects of the disease.

The two common species that cause CL are *Leishmania tropica* and *Leishmania major*[11]. The two principal CL species overlap

in their geographical distribution. *Leishmania major* extends from West Africa to Central Asia and *Leishmania tropica* is common in the Eastern Mediterranean, Middle East, North India, Afghanistan, and northeast and South Africa[12]. In this study, most patients were found to be infected with *Leishmania major*, which is consistent with other studies conducted in Iran[13,14]. Understanding the predominant parasite species is important to implement effective control and treatment strategies.

The demographic distribution in our study highlights the predominance of men patients. A study conducted in Iran showed that 56.4% of CL patients over a three-year period were men[14]. Another study conducted in Nepal and India showed that the male-to-female ratio of visceral leishmaniasis cases reported by the health system was 1.4[15]. These gender differences may reflect differences in sex hormone levels between men and women, genetic factors, behavioral and social factors such as exposure to certain pathogens, and occupational and lifestyle preferences[16].

In this study, most patients were villagers, which may be related to the more common reservoir and rural breeding sites of sandflies[8]. However, another study found that the infection rate in urban areas of Iran was higher than in rural areas[14]. The current study shows that most cases in the past year were not accompanied by travel, highlighting the dynamics of localized transmission of the disease in this region. However, a significant proportion of those with a travel history had traveled to rural areas, which is consistent with the higher prevalence of CL among villagers and suggests an association between travel to rural areas and increased infection rates.

The age distribution is particularly noteworthy. The majority of the affected population are young people, and those most affected occupationally are children, students and householders. The increased susceptibility of children and adolescents may be due to the development of their immune system, certain lifestyles and behaviors such as outdoor activities[14,17,18]. This information provides information on possible routes of infection within the community. The low incidence of coinfections among individuals, family members, and neighbors indicates limited person-to-person transmission and may highlight the role of vector-borne transmission.

Regarding treatment outcomes, there have been few reports of treatment failure, recurrence or treatment discontinuation, indicating a relatively good response to the treatment protocol, although ongoing challenges such as treatment failure and relapse require continued attention in the management of leishmaniasis cases.

A nationwide survey conducted in Iran from 2011 to 2020 showed a seasonal pattern in the number of CL cases, with the number peaking in autumn and decreasing in spring. Notably, the incidence of CL was highest in October and November, suggesting an increase in the incidence of CL after summer. This trend continued during the winter, with a gradual decrease in CL cases [19]. Also, most of the *Leishmania* cases were observed in autumn, apparently from September to December. The number of cases observed in autumn may indicate increased mosquito activity, probably leading to more frequent human bites during the warmer months, which may result in an increased number of human bites in the following season. While the number of cases in Iran decreased from 2011 to 2020, the number of cases in Esfarayen County from 2014 to 2022 has not had a constant incidence rate in different years, but it is generally increasing.

In the present study, most CL lesions occurred on the hands, face, legs, and forearms, which are the area's most susceptible to the sandfly vector that transmits the disease. A survey conducted in

Kerman province from 1994 to 2014 found that most CL lesions occurred on the hands (46.3%), face (34.1%), legs (14.3%), and other body sites (5.3%), with an average number of lesions of 1.5 per patient [18]. Most wounds were found to be 1–2 cm in size, and most wounds had skin secretions. The number of lesions ranged from 1 to 3. Similar results were observed in other studies, where most cases of CL had 1–3 lesions [14].

A study in Iran showed that patients with diabetes, cardiovascular disease, and hypertension were significantly more likely to develop non-reactive CL compared to those without chronic diseases[20]. Although the study reported that a minority of people suffered from diseases such as diabetes, hypertension, and heart disease, understanding and treating comorbidities in patients with CL may improve treatment outcomes, which is important in reducing the risk of recurrence and improving the overall health and wellness of patients.

5. Conclusions

In conclusion, the epidemiological profile presented in this study highlights important aspects of the demographic, behavioral and clinical aspects of CL in Esfarayen of North of Khorasan province. These findings are important for the development of targeted interventions, improved prevention measures and optimization of treatment strategies to reduce the disease burden in this specific geographical region.

Conflict of interest statement

The authors claim there is no conflict of interest.

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Data availability statement

The data supporting the findings of this study are available from the corresponding author upon request.

Authors' contributions

Lakzaei M contributed to interpreting the findings and drafting the manuscript. Jafari F provided guidance in conducting the study,

analyzed the data, and wrote the manuscript. Pasokh Z contributed to interpreting the findings and wrote the manuscript. Mohammadi Abnavi M analyzed the data, and wrote the manuscript. Keshvari S compiled and prepared the final data for analysis reviewed the analysis, and wrote the manuscript. Karami H provided guidance in conducting the study, conceptualized the study plan, and edited the manuscript. All authors read and approved the final manuscript for publication.

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