

Epidemiological Study of Cutaneous Leishmaniasis in Neyshabur County, East of Iran (2011-2017)

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Abstract

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BACKGROUND: Cutaneous Leishmaniasis (CL) isn't a lethal disease, but it has always been taken into consideration due to more involvement of patients with skin ulcers and its long-term treatment. Various factors can play an intervening role in increasing the rate of disease. The present study aimed to evaluate the prevalence and associated factors of disease from 2011-2017 and provide appropriate control strategies for reducing its incidence in Neyshabur county.

METHODS: All patients with CL, who had medical records in the health centres of Neyshabur from 2011 to 2017, were examined for conducting this cross-sectional analytical study. Data were analyzed by descriptive statistics and chi-square test at a 0.05 using Statistical Package for the Social Sciences (SPSS V.22).

RESULTS: Findings indicated that the highest annual incidence was in 2016 (229 patients), and the least incidence was in 2014 (100 patients). The majority of patients were under 10 years of age and 51.7% of patients were male. About 59.5% of patients were living in cities and 35% of them were living in North of Neyshabur city. Hands were the most affected part of the body (56.0%) followed by trunk (1.3%). Most patients (69.9%) were treated with topical regimens.

CONCLUSION: This study showed that CL was hypo-endemic in Neyshabur. Also, the disease was more prevalent in urban areas. Therefore, appropriate health measures to improve environmental conditions, public health educations, and the public awareness of the positive impact of early diagnosis of disease in the success of treatment (especially for inhabitation suburbanite) are essential.

Introduction

Leishmaniasis is a vector-borne and zoonotic disease [1] and is considered a neglected illness [2]. This disease is caused by a protozoan parasite called *Leishmania* from the Trypanosomatidae family and *Leishmania* genus [3]. This disease is transmitted to humans or animals by the bite of a female insect called sandflies from the Psychodidae family [4]. Dogs and rodents are the main reservoirs of this disease [5]. Leishmaniasis has three main clinical forms, namely Visceral leishmaniasis (VL) (Kala-azar), Cutaneous Leishmaniasis (CL) and Mucocutaneous leishmaniasis (MCL) [6], [7]. In this regard, the CL is a very common form and has the highest prevalence in the world [8], So that the World Health Organization (WHO) has introduced this disease as an important

neglected tropical disease. About 350 million people per year are exposed to this disease, and new cases are emerging annually [9]. In 2017, the WHO reported 94% of new cases from seven countries, Brazil, Ethiopia, India, Kenya, Somalia, Sudan, and South Sudan. The highest number of CL are also reported in Afghanistan, Algeria, Brazil, Colombia, Pakistan, Peru, Saudi Arabia, Syria and Iran [10]. In Iran, the CL is found in two types, namely Anthroponetic Cutaneous Leishmaniasis (ACL) and Zoonotic Cutaneous Leishmaniasis (ZCL) [9], [11] that are transmitted mainly by parasites, namely *Leishmania* (*L.*) major and *L. tropica*, *Phlebotomus* (*Ph.*) papatasi and *ph. sergenti* sandflies as the main vectors of this disease [12]. The main reservoirs of urban form are humans with CL and occasionally dogs; and rural form reservoirs are mainly desert rodents such as *Rombomis opimus*, *Meriones libycus*, and *tatera indica* [13]. CL which is popularly known as Salak in

Iran.

According to reports of the Center for Disease Control and Prevention, the number of people with Leishmaniasis in Iran is more than 20,000 per year [14]. CL is an important health problem in more than 15 provinces of Iran. Nearly 88 cities in Iran have been diagnosed with this disease, and the most frequent reports are related to ZCL [14]. The disease is endemic in many regions of Iran. Due to the increased prevalence of the disease in Iran, northeastern regions including Khorasan Razavi such as Neyshabur and Mashhad have had the emergence of new foci of this disease. The eastern regions of Iran, including the vast Neyshabur region with its numerous villages, have long been considered as a focus of the CL [15]. Although CL is no lethal disease, it has always been taken into consideration due to the more involvement of patients with skin lesions and its long-term treatment [16].

Various factors contribute to the incidence of disease, including climatic changes, environmental conditions, occupation, gender, and reduced vegetation cover. Furthermore, agricultural expansion, urban migration, and marginalisation contribute to the transmission of vector and parasitic of disease to new areas and increase the risk of this disease [17]. The incubation period of ACL is up to 8 months, and it is less than 4 months for ZCL. After the incubation period, painless red papules appear in the sandfly bite location; and the lesion grows after a few weeks to several months, and dimples at a depth of 1 mm appear with the secretion of liquids [18]. Treatment of leishmaniasis is based on the national protocol using Antimony (Sb5+) compounds such as Glucantime (intramuscular injection of 50 mg/kg of body weight, 10 ml per day for two to three weeks).

Patients should be examined and monitored by physicians for up to three weeks after the start of treatment to three months after healing. The injection of Glucantime into the lesion should be performed three times a week until the complete recovery [19]. Since CL treatment needs a lot of time and it is associated with several adverse effects such as arrhythmia, increasing of liver enzymes, anaemia, thrombocytopenia and leukopenia [20], Even if left untreated, the disease leads a fatality rate 95%-100% within 2 years [21], therefore the use of effective measures to prevent the disease is important and requires the identification of vulnerable groups and epidemiologic agents that are effective in the disease in these areas. Given the increased cases of the disease in northeastern villages of Iran, especially in Neyshabur and its villages, the present study sought to evaluate the incidence of disease in this county in recent years, so that more effective control strategies could be adopted to reduce disease by identifying related factors of disease.

Material and Methods

Geographical area

Neyshabur County is a city in the central part of Razavi Khorasan and is located between 58° 19' and 59° 30' longitude and 35° 40' to 36° and 39' latitude in the eastern margin of the central desert of Iran [22]. The vast majority of this city is located in a relatively large plain that is limited to Chenaran and Quchan counties from the north (by the Binalud Mountains); Mashhad County from the east; Torbat Heydariyeh and Kashmar from the south; Sabzevar from the west; and Farooj County from the northwest in North Khorasan province. Neyshabur is located 110 kilometres west of Mashhad (Center of the Khorasan Razavi province) and 768 kilometres east of Tehran (Capital of Iran). The size of Neyshabur county is 8,722 square kilometres, which is equal to 2.9 percent of the area of Khorasan and 53 percent of the total area of Iran. Due to the population of Neyshabur with 451,780 people in the last census in 2016, it is the second-most populous city in Khorasan Razavi province [23].



Figure 1: Geographical location of Neyshabur county, Khorasan Razavi province, East Iran

Data collection and analysis

In this cross-sectional analytical study, the statistical population consisted of all individuals (971 cases of CL) who had medical records in the health centers of Neyshabur and were diagnosed with CL according to the laboratory confirmation in Neyshabur county and its villages during 2011-2017; and their data were recorded in a health record by health care workers. Diagnostic methods were smear, culture. The necessary data including age, sex, place of residence (urban and rural), month and season of disease, incidence, number and location of lesions and some other important factors were extracted from their cases and then centres. The records that did not have the necessary data such as age, sex, job, diagnosis date and place of residence were removed from the study. To observe ethics in research, their full name and, father name and national code of all patients were removed from information files. For data analysis, data were first categorised into appropriate

groups. After grouping and preparing data, the whole data was analysed using SPSS V.22. Chi-square test was used to analyse data, and the alpha value less than 0.05 was considered as the significance level.

Results

The research results indicated that during the 7 years (2011-2017), a total of 971 cases of CL were reported. The highest incidence of CL was estimated in 2017 (44.7 per 100,000) and the least in 2015 (19.5 per 100,000) according to the population of Neyshabur in 2016 census (Fig. 2).

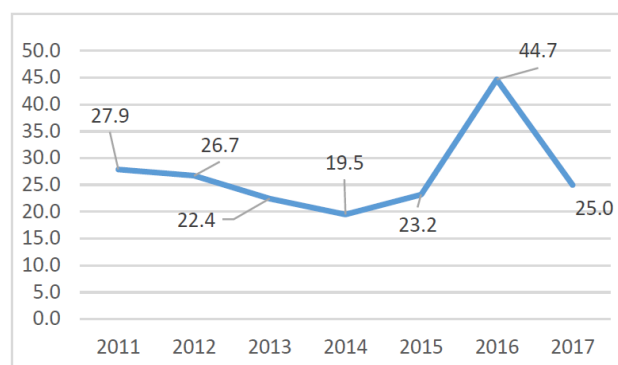


Figure 2: Time trend of incidence of CL per 100,000 populations in Neyshabur from 2011-2017 according to 2016 census

Of these, 469 (48.3%) were female, and 502 (51.7%) were male. The chi-square test showed that there was no significant association between sex and the disease ($P > 0.05$). In Neyshabur villages, the CL was more common among men 246 (56.7%) versus 188 (43.3%) females but unlike villages, more women were affected in Neyshabur city 281 (52.3%) women versus 256 (47.7%) males, however, there was no significant difference between men and women in the incidence of CL in the city ($P > 0.05$), while the difference was statistically significant in the village ($P < 0.001$).

The mean and standard deviation of patients' age was 29.4 ± 19.3 . The youngest patient was under the age of one, and the oldest was 90 years old. Less than a quarter of patients were above 42 years of age, and more than half of the patients were under the age of 28. The prevalence of CL was statistically significant in different age groups ($P < 0.001$) (Table 1).

Exactly 393 (40.5%) and 578 (59.5%) patients were rural and urban, respectively. There was a decreasing trend in the number of people with CL in villages and the increasing trend in the city from 2011 to 2017, and numbers of patients in the city and village were significantly different ($p < 0.001$) in all years except for 2013 and 2014; and number of

patients in cities was always higher than the villages. Considering the number of the rural population ($N = 201,492$) and the urban population ($N = 311,256$) in Neyshabur in 2017, the prevalence of the disease in the city (31 per hundred thousand) was about twice as high as the village (16.6 per hundred thousand).

In terms of geological division, people living in the north of the city ($n = 340$ patients) and southern villages ($n = 195$ patients), were more susceptible to CL, but those living in Northern villages ($n = 35$ patients) and southern city ($n = 42$) were less prone to CL (Fig. 3).

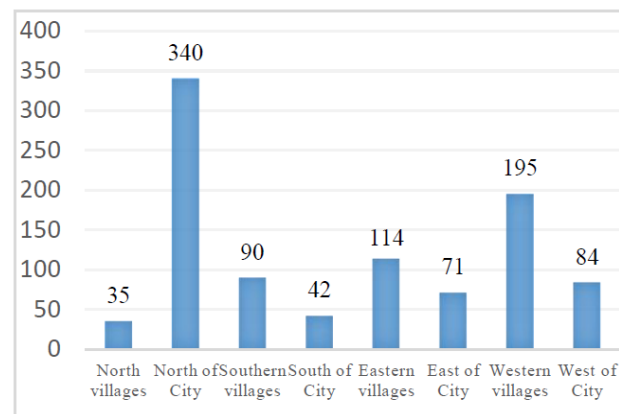


Figure 3: Distribution of CL disease in the city of Neyshabur according of Geographical Area from 2011-2017

Regarding the seasonal tendency, the highest and lowest number of patients with CL belonged to autumn 308 (31.7%) and summer 183 (18.8%), and there was a significant different incidence in different seasons during 2011, 2012 and 2015, but no difference was seen in the rest of years, but generally there was a significant difference in the incidence of disease in different seasons ($P < 0.001$). The highest prevalence was seen in April, October, November, and December in rural areas, and November, December, January, and February in urban areas.

According to research findings, in all examined years, the incidence of CL among those, who had travelled to other cities during the last year, was 510 (52.5%) compared to those who had not traveled 461 (47.5%) and they were not significantly different ($P = 0.062$), while the incidence of disease was greater and significantly different among non-travellers in 2011, 2013, 2016 and 2017.

Most of the patients with CL were housewives 287 (29.6%), children 193 (19.9%) and the least of them had military occupation 18 (2.0%). There was a statistically significant difference between the incidence of disease and multiple occupations in all years ($P < 0.001$).

In this study, the location of the lesion was different in patients' bodies. The most common place of the lesion was on hands (56.0%), legs (22.0%), face (20.7%) and trunk (1.3%). The size of lesions

was 2.7 ± 1.6 centimetres on average, and 47.0% were less than 1 cm, and 38.9% (1-4 cm); and only 14.0% of lesions were greater than 4 cm. The greatest lesion size was 11 cm (2.0%).

Table 1: Distribution of CL disease characters in 971 patients in the city of Neyshabur, in 2011-2017

Characters/Years	2011	2012	2013	2014	2015	2016	2017	Total (%)
Age								
0-10 Year	18	19	18	10	34	64	38	201 (20.7)
11-20 Year	26	25	18	22	14	26	20	151 (15.6)
21-30 Year	36	33	42	15	17	25	17	185 (19.1)
31-40 Year	26	22	22	17	23	47	22	179 (18.4)
41-50 Year	12	18	9	13	16	37	7	112 (11.5)
>50 Year	25	20	6	23	15	30	24	143 (14.7)
Total	143	137	115	100	119	229	128	971 (100)
P-Value	0.016	0.237	0.000	0.170	0.012	0.000	0.000	0.000
Sex								
Male	76	75	75	49	62	105	60	502 (51.7)
Female	67	62	40	51	57	124	68	469 (48.3)
P-Value	0.452	0.267	0.001	0.841	0.647	0.209	0.480	0.290
Habitat								
Rural	92	77	61	60	30	39	34	393 (40.5)
Urban	51	60	54	40	89	190	94	578 (59.5)
P-Value	0.001	0.146	0.514	0.057	0.001	0.001	0.001	0.000
Session								
Spring	29	26	27	25	13	65	30	215 (22.1)
Summer	28	28	20	26	12	43	26	183 (18.8)
Autumn	54	59	41	29	30	56	39	308 (31.7)
Winter	32	24	27	20	64	65	33	265 (27.3)
P-Value	0.005	0.000	0.044	0.641	0.001	0.129	0.421	0.000
Treatment Type								
Systemic	43	39	15	0	0	0	0	97 (10.0)
Glucantime								
Topical	99	69	38	0	0	0	0	206 (21.2)
Glucantime								
Topical	1	9	48	0	0	0	0	58 (6.0)
Glucantime & Cryotherapy								
Cryotherapy	0	20	14	2	1	4	1	42 (4.3)
Cryotherapy & Topical								
Antimoniate	0	0	0	63	52	122	60	297 (30.6)
Antimoniate								
Topical	0	0	0	10	48	71	47	176 (18.1)
Systemic								
Antimoniate	0	0	0	25	18	32	20	95 (9.8)
Duration of systemic treatment								
7-10	10	10	1	2	0	0	1	24 (2.5)
11-14	5	6	2	4	2	0	6	25 (2.6)
15-18	1	3	5	14	3	0	1	27 (2.8)
19-21	27	20	7	5	13	32	11	115 (11.8)
Duration of Topical & Cryotherapy treatment								
1-4	2	12	4	27	31	46	2	124 (12.8)
5-8	85	75	81	48	45	81	60	454 (46.9)
9-12	13	11	15	0	25	70	47	154 (15.8)
Occupation								
Driver	4	2	1	4	1	4	3	19 (2.0)
Worker	14	7	11	6	4	6	4	52 (5.4)
Employer	3	7	5	2	5	23	11	56 (5.8)
Farmer	22	20	17	10	5	6	7	87 (9.0)
Student	24	21	19	19	26	46	33	188 (19.4)
Military	1	1	10	0	0	0	6	18 (1.9)
housewife	49	46	21	38	34	64	35	287 (29.6)
Baby	13	14	10	19	42	74	21	193 (19.9)
self-Employment	13	19	21	2	2	6	8	71 (7.3)
P-Value	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Lesion Site								
Hand	95	88	80	76	78	146	71	634 (65.6)
Feet	30	35	31	23	37	73	20	249 (25.6)
Face	36	29	15	17	28	68	41	234 (24.0)
Trunk	5	1	3	0	2	0	4	15 (1.5)
Total	166	153	129	116	145	258	136	1132 (100)
Travel history								
Haven't	89	62	40	42	60	133	84	510 (52.5)
Have	54	75	75	58	59	96	44	461 (47.5)
P-Value	0.003	0.087	0.000	0.450	0.929	0.002	0.000	0.062

Most of the patients (80.2%) were treated by topical method, and 192 (19.8%) patients were treated using the systemic method. The duration of treatment in 608 (62.7%) of patients, who were treated by topical and combination of cryotherapy and topical methods, was 5-8 weeks or more. Patients treated with systemic methods had a shorter duration of treatment (Table 1).

Discussion

The present study aimed to provide and analyse epidemiological information about CL in Neyshabur county during the last 7 years (2011-2017). During this period, a total of 971 cases of CL referred to health centres of the Neyshabur and were treated. Over the years, the overall incidence of CL did not change significantly in Neyshabur, and it also

seemed to be a public health problem. Medium prevalence of CL in Neyshabur county (27.05 per 100,000) was almost equal to the average prevalence in Iran (27.5 per 100,000) based on the results of studies [24].

In this study, both sexes were susceptible to CL disease; and the results of the study did not show any significant relationship between gender and disease ($P = 0.29$). Studies in Iran in cities, such as Kermanshah, Kashan, and Fars province reported similar findings [25], [26], [27] but studies in Fasa city of Fars province and Jahrom different reports [28], [29].

Based on findings of the study in terms of age, the minimum age of 7 months and the highest age of 90 years had CL; the highest frequency (20.7%) was observed in the age group of 0-10 years probably due to the higher prevalence among the students. Our findings were inconsistent with studies in Kashan, Kermanshah and Fars [25], [26], [27]. Based on analyses, prevalence in age groups depended on the residence ($p < 0.04$, ρ (Spearman Correlation) = -0.031), gender ($p < 0.001$, $\rho = 0.105$) and occupation ($p < 0.001$, $\rho = -0.091$).

The incidence of disease in urban regions (59.5%) was higher than in rural regions (40.5%), and a significant difference was found between habitat in terms of the prevalence of CL ($P < 0.001$). Results of our study were inconsistent with a study by Doroodgar in Kashan [26] and Mohammadi's study in Marvdasht [30] and a study by Rahmanian in Jahrom; there was a higher prevalence in villages [29]. Due to its increasing prevalence in urban areas relative to rural areas, there was a need for health and education measures in these regions.

In terms of geographical division, the majority of patients lived in the north of the city (35%) and western villages (20%) of Neyshabur; and rates of CL were in statistically different in various geographical regions ($p < 0.001$), probably due to amounts of building waste and public health conditions in those areas. Since the rate of disease increased in the north of the city and western villages during 2011-2017, it indicated the source of infection and appropriate growth conditions for cause of CL.

Seasonal trend study indicated that the highest prevalence of the disease was in autumn, especially November/December in Neyshabur and its villages. It seems that the incubation period of disease begins due to cool weather in autumn, and sandflies' peak activities and sucking the victims' blood reach their peak in the winter, and then their activity is slowly decreasing. Our results were consistent with findings in Kashan, Qom, Fars, and Yazd in terms of more prevalence in autumn [26], [31], [32], but they were inconsistent with findings of Kermanshah in terms of more prevalence of the disease in winter [25].

In the field of occupational groups, the

highest prevalence was seen in housewives (27.1%), students (18.9%) and infants (19.3) due to staying more at home and their clothing styles, and more activity of sandflies in wet places [33]. Also it may be due to higher number of housewives group in population. In men, the prevalence of disease was higher in farmers (8.5%), workers (5.4%) and self-employment (7.3%) due to their location in endemic regions, inadequate health information, and a significant difference in the incidence of disease and type of occupation ($P < 0.001$). In a study by Doroodgar et al., (2018), the prevalence of disease was higher in housewives [26] and in a research by Rahmanian et al., [2018] in the southwest of Iran, the highest prevalence was seen in students (28.8%), and there was a significant statistical difference between occupations in terms of prevalence of CL ($p < 0.001$) [29].

Based on findings of the present study, 95% of lesions were dry and without secretion, and were seen in all organs of the body such as (hands, arms, feet, trunk, face, forearm, legs, head and neck). In this study, hands (56%) had the highest bite reporting; and the location of the lesion was probably associated with the body cover. Face (32%) in women and hands and arms (31%) in men were the most involved locations. The average size of lesions was (2.2 ± 1.6 cm), and the smallest one was 1 cm, and the biggest one was 11 cm, and the average number of lesions was 2 ± 1.9 and the highest was 18. Rahmanian et al., (2018) reported the maximum number of lesions as 30 lesions in their study in Jahrom, southwestern Iran. This finding may be different due to the types and behaviour of insect blood-feeding, the number of bites feeding by sandflies per feeding time, and the frequency of infectious sandflies in that region [29].

In conclusion, according to the results of the present study, the incidence of CL in Neyshabur was higher in north and west regions; and autumn was a more suitable season for the prevalence of CL in the region. Most patients were housewives, children under the age of ten, and people living in the city. Therefore, measures should be taken to improve environmental health, public health education, and making people aware of the positive impact of early diagnosis to achieve successful treatment by public health authorities and control the disease. Due to multiple lesions with different sizes in this disease, the likelihood of scar is higher, and thus the future studies should investigate the status of these scars and their causes. As the incidence of disease increased in the county in 2017, further studies should be conducted to clarify its causes.

Ethical considerations

This study was approved by the Research

Ethics Committee Neyshabur University of Medical Sciences under Opinion number IR.NUMS.REC.1397.020.

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