Original Article

Epidemiological Survey of Cutaneous Leishmaniasis in Gonbad-e-Kavus, Northern Iran

Farzad Motevalli Haghi[1], Nasibeh Hosseini-Vasoukolaei[1], Ghorban Mohammad Ozbaki[2], Roohollah Siahsarvie[3,4], Mahmoud Fazeli-Dinan[1], Omid Dehghan[1]

[1]Department of Medical Entomology and Vector Control, Health Science Research Center, Faculty of Health, Mazandaran University of Medical Sciences, [2]Department of Medical Entomology and Vector Control, Faculty of Health, Mazandaran University of Medical Sciences, Sari, [3]Department of Biology, Faculty of Sciences, Ferdowsi University of Mashhad, [4]Rodentology Research Department, Faculty of Sciences, Institute of Applied Zoology, Ferdowsi University of Mashhad, Mashhad, Iran

ORCID:
Farzad Motevalli Haghi: 0000-0003-0204-6283
Nasibeh Hosseini-Vasoukolaei: 0000-0003-4780-7795

Abstract

Aims: Cutaneous leishmaniasis (CL) is one of the most important health problems in Iran. The aim of this study was to investigate all aspects of the epidemiology of the disease, including examination of patients, the rate and nature of the disease, and the development of different forms of disease during 2009–2018 in Gonbad-e-Kavus, Northern Iran. **Materials and Methods:** This descriptive study was performed using epidemiological data, including demographic and clinical features collected from 5638 patients diagnosed with leishmaniasis in health centers affiliated to the Deputy of Health Center of Golestan University of Medical Sciences during 2009–2018. **Results:** A total number of 5638 individuals were diagnosed with CL over a 10-year period. Considering the population of Golestan, the incidence rate was reported as 137 per 100,000 populations. It was also revealed that most of the cases of CL (86/23%) lived in the villages and the majority of patients (21/46%) were in the age group of 1–4. In addition, most ulcers were observed in the hand (37.7%) and foot (33.1%), respectively. Most of the patients had multiple wounds on the body. The highest incidence was reported in November and the lowest in May. **Conclusion:** The results of this study showed that the endemicity of disease in Gonbad-e-Kavus city during the 10-year study period 2009–2018 was high compared to the average incidence rate of CL in Iran. Therefore, monitoring and emphasizing disease control methods to eliminate leishmaniasis in this city are essential.

Keywords: Cutaneous leishmaniasis, epidemiology, Gonbad-e-Kavus city

INTRODUCTION

Leishmaniasis is a group of parasitic diseases caused by protozoan species belonging to the genus *Leishmania* and spread by sand fly bites.[1] The disease mainly manifests in three clinical forms: visceral leishmaniasis (VL), cutaneous leishmaniasis (CL), and mucocutaneous leishmaniasis, of which VL is the most severe form of the disease. CL usually has a milder course and affects the skin causing scars and eventually disfiguration.[2] CL is endemic in approximately 88 countries, and approximately 90% of the cases occur in 10 countries, namely Afghanistan, Algeria, Bolivia, Brazil, Colombia, Iran (Islamic Republic of), Iraq, Pakistan, the Syrian Arab Republic, and Tunisia.[3,4] Iran is one of the countries

where most CL cases occur. Almost more than 20,000 new cases of CL are reported annually in Iran.[5] CL is widely distributed in different regions of Iran and is reported from 25 out of 31 provinces of the country.[6] Two forms of CL have been reported in Iran, including zoonotic CL (ZCL) caused by *Leishmania major* and anthroponotic CL (ACL) caused by *Leishmania tropica*.[5] ZCL and ACL are observed in rural and urban areas, respectively, and cause wet and dry lesions at the wound site.[7] In Iran, the rural type is prevalent in 17

Address for correspondence: Dr. Nasibeh Hosseini-Vasoukolaei, Department of Medical Entomology and Vector Control, Faculty of Health, Mazandaran University of Medical Sciences, Sari, Iran.
E-mail: nasibeh.hoseini@gmail.com, nhosseini@mazums.ac.ir

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provinces of Iran, while the urban type is affecting almost all of the country's urban areas.[8] Rodents of the *Gerbillidae* family are the main reservoir of ZCL in Iran.[9]

Golestan Province in Northern Iran is one of the most important focuses of ZCL.[10] The prevalence of this disease in Golestan province has increased in recent years.[11] Gonbad-e-Kavus is the largest city in Golestan province. This city is located in the center of Turkmen Sahara where 4% of people have acute ulcers and 78% have scars.[10] Two species of rodents *Rhombomys opimus* and *Meriones libycus* play an important role as a reservoir of disease in this city.[11] The population control of these two species is done by the Ministry of Health to reduce CL in the city of Gonbad-e-Kavus.

CL is one of the most important health problems in Gonbad-e-Kavus city. The aim of this study was to investigate all aspects of the epidemiology of the disease, including examination of patients, prevalence and nature of the disease, and disease burden and endemicity during the years 2009–2018 in Gonbad-e-Kavus, Northern Iran.

MATERIALS AND METHODS
Study area
This cross-sectional study was conducted from 37°3.6′ to 38°6.3′N latitude and 54°31.7′ to 55°39.1′E longitude in Gonbad-e Kāvus City, which is located in the northern and central part of Golestan province in the border of Iran and Turkmenistan, with an approximate area of 5071 km² [Figure 1].

Sample collection
This descriptive study was performed on 5638 patients with CL referred to health centers in Gonbad-e-Kavus during 2009–2018. Smears were obtained from all patients, fixed in methanol for 5 min, and then stained with Giemsa for 30 min. The prepared smears were examined microscopically for the presence of the amastigote form of *Leishmania*. After diagnosis, patients' epidemiological information was recorded in a specific patient form and then treated for CL according to the national guidelines

Figure 1: Location map of the study area and sampling site

for CL case management. The required demographic and clinical information was recorded, and the relationship between these factors and the incidence of the disease was analyzed.

These factors include sex, age, occupation, place of residence, nationality, appearance and location of the lesion on the body, number of lesions, and month of infection. The burden of disease in the city was assessed based on the number of patients with CL in a 10-year period. The frequency of patients was analyzed and reported based on age, gender, occupation, lesion location, nationality, and CL form. Before the study, approval was obtained from the Ethics Committee of Mazandaran University of Medical Sciences, Mazandaran, Iran (IR. MAZUMS.REC.1398.1114). The patients' data were analyzed and reported privately. Then, SPSS software (version 20) was used for data analysis. The differences were considered statistically significant when $P \leq 0.01$.

RESULTS
In the present study, the demographic and clinical data obtained from 5638 patients with CL were recorded in Gonbad-e-Kavus health centers from 2009 to 2018. The CL incidence rate varied in different years of the study. The average incidence of the disease during 10 years was 159.8 per 100,000 people. It was 190 in 2009, 347 in 2010, 104 in 2011, 100 in 2012, 98.6 in 2013, 116.4 in 2014, 127 in 2015, 176 in 2016, 96 in 2017, and 243 in 2018 per 100,000 people. As shown in Table 1, the gender distribution of cases is statistically significant. Of 5638 cases with lesions, 2962 (52.5%) were males and 2675 (47.5%) were females ($P = 0.0001$). In addition, the frequency of the cases of CL was different based on the age groups. Most cases were diagnosed in the age group of 1–4 years ($n = 1210$; 21.46%), while the least [95, 1.68%; $P = 0.0001$; Table 1] were in the 55–59 years of age group. The number of 4862 cases (86.23%) lived in the villages and 776 cases (13.76%) lived in the city ($P = 0.0001$). In the present study, the CL patient's frequency varied in different occupations. The group with the highest frequency was children ($n = 1913$; 33.93%), while the least frequency was observed in farmers and ranchers [0.42%; $P = 0.0001$; Graph 1]. The results of the current study showed differences in the location of the lesions on the body. Most lesions were observed on patients hands ($n = 2862$; 50.7%), while the least were on the trunk [$n = 512$; 9.1%; $P = 0.0001$; Table 2]. Furthermore, 2488 patients had only one lesion, while 1319, 692, and 1139 patients had two, three, and more than three lesions, respectively [$P = 0.0001$; Table 1].

The frequency of CL patients in Gonbad-e-Kavus varied in different months. The highest frequency was in November ($n = 1844$; 32/70%), while the lowest was in June ($n = 13$; 0/23%) [$P = 0.0001$; Graph 2].

DISCUSSION
CL is one of the most important endemic diseases in Iran and is the second parasitic disease transmitted by arthropods after

Table 1: Distribution of leishmaniasis patients according to demographic features of sex, age groups, location, nationality, travel history, lesion number, and appearance in Gonbad-e-Kavus city, 2009-2018, *n* (%)
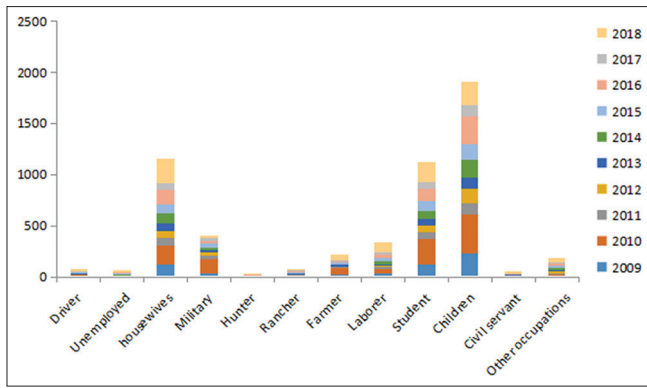
	Years									
	2009	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**
Sex										
Male	304 (5.4)	647 (11.5)	195 (3.4)	195 (3.4)	197 (3.5)	222 (3.9)	221 (3.9)	307 (5.4)	190 (3.4)	484 (8.6)
Female	303 (5.4)	464 (8.3)	145 (2.6)	145 (2.6)	151 (2.7)	214 (3.8)	271 (4.8)	365 (6.5)	176 (3.1)	441 (7.8)
Age groups										
<1	37 (0.6)	40 (0.7)	13 (0.2)	25 (0.4)	31 (0.5)	32 (0.6)	23 (0.4)	39 (0.7)	24 (0.4)	25 (0.4)
1-4	131 (2.3)	231 (4.1)	56 (0.1)	84 (1.5)	80 (1.4)	109 (1.9)	97 (1.7)	190 (3.4)	78 (1.4)	154 (2.7)
5-9	98 (1.7)	177 (3.1)	52 (0.9)	57 (0.1)	39 (0.7)	65 (1.1)	77 (1.4)	106 (1.9)	56 (0.1)	128 (2.3)
10-19	121 (2.1)	241 (4.3)	62 (1.1)	43 (0.8)	64 (1.1)	76 (1.3)	85 (1.5)	87 (1.5)	44 (0.8)	144 (2.5)
20-29	121 (2.1)	232 (4.1)	77 (1.4)	62 (1.1)	81 (1.4)	64 (1.1)	95 (1.7)	103 (1.8)	71 (1.2)	151 (2.7)
30-39	53 (0.9)	79 (1.4)	23 (0.4)	35 (0.6)	24 (0.4)	38 (0.7)	54 (0.9)	59 (1)	42 (0.7)	117 (2.1)
40-49	19 (0.3)	60 (1.1)	24 (0.4)	16 (0.3)	13 (0.2)	25 (0.4)	30 (0.5)	42 (0.7)	33 (0.6)	84 (1.5)
50-59	13 (0.2)	29 (0.5)	26 (0.5)	11 (0.2)	11 (0.2)	13 (0.2)	20 (0.3)	25 (0.4)	12 (0.2)	62 (1.1)
>60	14 (0.2)	21 (0.4)	7 (0.1)	8 (0.1)	4 (0.1)	14 (0.2)	11 (0.2)	21 (0.4)	6 (0.1)	50 (0.9)
Location										
City	63 (1.1)	80 (1.4)	60 (1.1)	67 (1.2)	86 (1.5)	49 (0.9)	63 (1.1)	115 (2)	58 (1)	135 (2.4)
Village	544 (9.7)	1031 (18.3)	280 (5)	274 (4.9)	262 (4.7)	387 (6.9)	429 (7.6)	557 (9.9)	308 (5.5)	790 (14)
Lesion number										
1	328 (5.9)	417 (7.4)	164 (2.9)	167 (3)	148 (2.6)	178 (3.1)	223 (3.9)	289 (5.1)	161 (2.8)	414 (7.3)
2	133 (2.3)	245 (4.3)	68 (1.2)	84 (1.5)	87 (1.5)	103 (1.8)	127 (2.2)	161 (2.8)	88 (1.5)	223 (3.9)
3	25 (0.4)	143 (2.5)	48 (0.8)	37 (0.6)	52 (0.9)	57 (1)	58 (1)	91 (1.6)	65 (1.1)	116 (2)
>3	121 (2.1)	306 (5.4)	60 (1)	53 (0.9)	61 (1)	98 (1.7)	85 (1.5)	131 (2.3)	52 (0.9)	172 (3)
Lesion appearance										
Dry	12 (0.2)	38 (0.7)	6 (0.1)	3 (0.05)	7 (0.1)	23 (0.4)	4 (0.05)	12 (0.2)	3 (0.05)	228 (4)
Wet	592 (10.5)	1068 (18.9)	332 (5.8)	334 (5.9)	338 (6)	409 (7.2)	485 (8.6)	656 (11.6)	329 (5.8)	694 (12.3)
Lupoid	-	-	-	-	-	2	-	-	-	-
Sporotrichoid	3 (0.05)	5 (0.1)	2 (0.05)	3 (0.05)	3 (0.05)	2 (0.05)	3 (0.05)	4 (0.05)	4 (0.05)	3 (0.05)

Table 2: Distribution of leishmaniasis patients according to anatomic location of lesion in Gonbad-e-Kavus city, 2009-2018, *n* (%)

Years	Lesion location								
	Head and neck	**Trunk**	**Face**	**Leg**			**Hand**		
				Thigh	**Foot**	**Leg**	**Forearm**	**Arm**	**Hand**
2009	42 (0.7)	58 (1)	139 (2.5)	24 (0.4)	118 (2.1)	148 (2.6)	134 (2.4)	54 (0.9)	118 (2.1)
2010	74 (1.3)	68 (1.2)	164 (2.9)	34 (0.6)	241 (4.2)	212 (3.8)	210 (3.7)	125 (2.2)	221 (3.9)
2011	50 (0.9)	35 (0.6)	59 (1)	10 (0.2)	52 (0.9)	62 (1.1)	86 (1.5)	26 (0.5)	54 (0.9)
2012	48 (0.8)	38 (0.7)	66 (1.2)	8 (0.1)	62 (1.1)	68 (1.2)	82 (1.4)	28 (0.5)	62 (1.1)
2013	54 (0.9)	45 (0.8)	78 (1.4)	12 (0.2)	65 (1.1)	72 (1.3)	92 (1.6)	34 (0.6)	65 (1.1)
2014	68 (1.2)	53 (0.9)	116 (2)	14 (0.2)	76 (1.3)	88 (1.6)	104 (1.8)	40 (0.7)	71 (1.2)
2015	48 (0.8)	40 (0.7)	98 (1.7)	20 (0.3)	95 (1.7)	97 (1.7)	103 (1.8)	58 (1)	108 (1.9)
2016	68 (1.2)	63 (1.1)	167 (3)	28 (0.5)	129 (2.3)	162 (2.9)	144 (2.5)	58 (1)	122 (2.2)
2017	34 (0.6)	33 (0.6)	77 (1.4)	12 (0.2)	75 (1.3)	76 (1.3)	81 (1.4)	24 (0.4)	64 (1.1)
2018	76 (1.3)	79 (1.4)	179 (3.1)	26 (0.5)	230 (4.1)	198 (3.5)	181 (3.2)	110 (1.9)	203 (3.6)

malaria. Gonbad Kavous is one of the most important endemic areas of this disease in Northern Iran.[12] Based on the results of this study, the incidence of this disease in Gonbad Kavous city was estimated 159.8 per 100,000 people during the study period of 2009–2018. The average annual incidence of CL over 30-year period was reported 32/100,000 people in Iran.[13] Over the past 10 years in the current study, the incidence of the disease shows two peaks of activity in 2010 and 2018. Previous studies in this city also showed the highest incidence of the disease in 2010.[14] In a 10-year study in the neighboring province of Mazandaran, an increase in cases of leishmaniasis in 2010 was also observed.[15] Although the number of cases of leishmaniasis in Iran has been declining since 1990 and decreased to one-third in 2010, a sudden increase in the number

Graph 1: Distribution of leishmaniasis patients according to occupation in Gonbad-e-Kavus city, 2009–2017

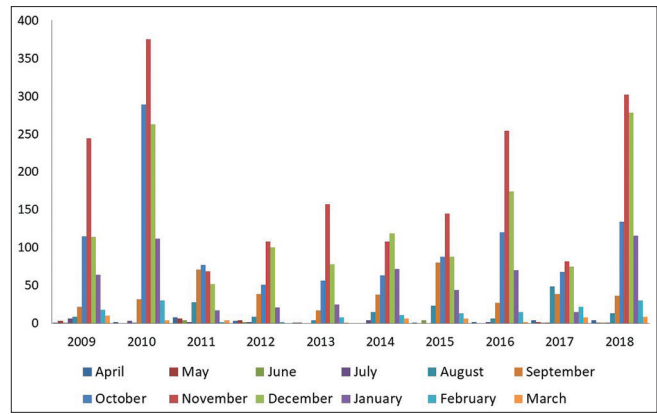**Graph 2:** Distribution of leishmaniasis patients in different months in Gonbad-e-Kavus city, 2009–2018

of leishmaniasis cases has been observed every few years.[16] Various factors such as not paying attention to screening and treating patients and controlling vectors and reservoirs of disease and climate change increase the incidence of leishmaniasis in the endemic areas.[17]

In the present study, the majority of patients were male which is consistent with other studies.[12,18,19] The higher incidence of leishmaniasis in men can be due to more outdoor activities and their light clothing which is more exposed to sand fly bites than women.[20]

In this study, most cases of leishmaniasis were reported from villages. The activity of two rodents, *R. opimus* and *M. libycus* and sand fly *Phlebotomus papatasi*, as the main reservoir and vector of the disease in rural areas, has increased the incidence of leishmaniasis in rural areas, and Gonbad-e-Kavus has become an endemic center of leishmaniasis.[14] Most cases of leishmaniasis in this province are ZCL.[21] Relocation and travel of residents from city to village have led to the spread of ZCL in urban areas.

Regarding patients' occupation, the highest and lowest prevalence was observed in children and farmers–ranchers, respectively. In the previous study conducted in Khorasan Razavi, the highest rate of disease was observed in the student's group (40.4%).[20] The activity of the disease vector and the reservoir in this city has caused high endemicity of leishmaniasis in students under 15 years old. Older people with livestock and agricultural occupations have been infected in recent years and are immune to the disease, so most cases of infection have occurred in the age group of children.[12,22]

In the present study, the peak of disease distribution was observed in autumn. The highest rate was reported in November and the lowest in June. Considering the incubation period of the disease, the increase in the incidence of the disease in November indicates an increase in the number of bites in summer, especially in August and September. The activity of sand flies in the central regions of Iran with temperate climate begins in April or May and continues to October or November with two peaks of activities: one in June or July and the other in August or September.[23] Various factors such as natural

disasters, climate change, and seasonal changes affect the physiological parameters of the vector and cause changes in the peak activity of *P. papatasi*.[24-26]

Given that the anatomical location of the lesions on the patients' body is concerned, most of the lesions were found on the hand (37.7%) and then the feet (31.1%), which is consistent with a previous study conducted in this city.[12] The most exposed areas for leishmaniasis were the hands and face.[27] The manner of dressing and the tradition of each region have a great influence on the anatomical location of leishmaniasis lesions.

The presence of more than one wound in infected individuals indicates that sand flies bite more than one site at a time, and most infected bites contain enriched doses of metacyclics. Increasing the vector *Leishmania* load can lead to an increase in the number of bites and the transmission of more parasites to the host. However, *Leishmania* transmission is more efficient from sand flies that have low-intermediary parasite burdens, which transmit lower doses.[28]

The majority of patients had wet wounds, indicating the zoonotic type of CL in the area; however, in 2018, the number of dry wounds has increased exponentially. Therefore, due to the endemicity of the disease in Gonbad-e-Kavus, it is necessary to use differential diagnosis methods to determine the parasitic trend in the region.

In expressing the limitations of the present study, since CL usually has a spontaneous healing process, a number of patients do not refer to health centers, so the number is less than the actual number of patients. As a result, it is better to analyze the study data based on active patient diagnosis or door-to-door visits.

CONCLUSION

Gonbad-e-Kavus is considered as an endemic focus of CL in Golestan Province in Northern Iran. Based on the results of the current study, the incidence rate in Gonbad-e-Kavus during the 10-year study period 2009–2018 was on average 159.8/100,000 people, which was more than four times higher than the average

incidence rate of CL in Iran. Therefore, continuous monitoring and surveillance of disease control methods are essential to eliminate leishmaniasis in this area.

Conflicts of interest

There are no conflicts of interest.

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