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Pediatric Cutaneous Leishmaniasis in Golestan Province, Iran: A Cross-Sectional Study of 8-years

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Abstract

Background: Cutaneous leishmaniasis (CL) is a main public health problem in Iran with a high incidence rate among children. According to numerous studies in Iranian society, the most commonly affected age group is 1–4 years. At present, we aimed to investigate the pediatric CL among children in Golestan Province in North of Iran.

Materials and Methods: A cross-sectional study was run on data existed for 3,371 cases with pediatric cutaneous leishmaniasis based on routinely collected data from the Health System of Golestan Province, Iran, between 2010 and 2017. Data of the study were gathered using two checklists about CL and demographic status from District Health Network. Data were analyzed using SPSS software (version 18.0).

Results: In general, 3371cases were investigated. The majority of cases were male 1495 (50.9%), lived in the rural area, while the least CL were female 155 (38.7 %), and lived in the urban area. Pediatric cutaneous leishmaniasis had the highest 883 (26.3%), and lowest 186 (5.5%) frequency in 2010 and 2013 years, accordingly. CL was increased from July and reached to maximum in October, then decreased considerably in January. In final, a significant relationship was found between CL cases and years of the survey (p= 0.001).

Conclusion: The most CL cases were found among males and aged 0-5 years. As indicated by different studies, CL in the endemic area of the country (Golestan Province) occurs more often in children, while it commonly happens among adolescents in the central area of the country. Thus, it points to the role of mothers in protecting children through dressing up and sleeping habits in the outdoor environments.

Key Words: Child, Cutaneous, Iran, Leishmaniasis, Public Health.

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1- INTRODUCTION

Cutaneous leishmaniasis (CL) is caused by different species of the parasite Leishmania, and is also spread by the bite of female Phlebotomine sand flies (1). Leishmaniasis is a widespread tropical infectious disease that manifests mainly in three types: visceral (L. donovani and L. infantum), cutaneous (L. tropica, L. major, L. aethiopica, L. mexicana, L. guyanensis, L. peruviana, and L. amazonensis), and mucocutaneous (L. subgenus Vianna braziliensis and L. subgenus Viannia guyanensis) (2). Being widespread in all continents in South Asia, Central and South America, the Horn of Africa and endemic in the Mediterranean region, this disease is introduced as a major public health problem (3).

Iran is considered one of the high risk countries for CL with more than 20,000 cases per year. The endemic foci of CL are found in 17 out of 31 provinces of the country while foci of Golestan, Yazd, Khorasan-e-Razavi, Isfahan, and Fars Provincs are more critical (4). CL is a remarkable tropical disease with lots of adverse effects on individuals' health in 98 countries as well as Iran (5). Annually, about 20,000 cases are reported across Iran; however, the real rate of the disease has been estimated to be five times higher (6, 7). Annually about 20–40/100,000 cases of CL are reported from the country (8). Children constitute 7-10% of CL cases in the endemic areas (9).

The most commonly affected age group in a study of 29 years conducted on Iranian society was 1–4 years (43 cases per 100,000), followed by 5–9 years (40 cases per 100,000) (10). In general, four epidemiological clinical manifestations of the disease have been diagnosed within the Eastern Mediterranean Region (EMR) (11). Four types of the disease – zoonotic/anthroponotic cutaneous leishmaniasis (ZCL/ACL), and zoonotic/anthroponotic visceral leishmaniasis (ZVL/AVL) are commonly observed in this region (10, 12). In general, cutaneous leishmaniasis has the highest prevalence in the Middle East (13). If left untreated, CL can lead to chronic ulcerative lesions. Despite low mortality or morbidity of the disease, the ugly appearance on the exposed organ of the body comprising face, neck, leg and hand can be unbearable for patients with permanent marks; thus, it likely causes social and psychiatric problems as well as a lower quality of life (14). In a study conducted by Norouzinezhad et al., between 2011 and 2013 years, 56,546 CL cases were found with the highest incidence in 2011. Also, Wet CL accounted for 43.7% of patients while 43.3% resulted from sporotrichoid leishmaniasis (15). Alavinia et al.'s study indicated that the highest incidence of disease was observed in 2005 (381.1 per 100,000). The disease was also observed in all months of the year with the highest incidence rate from September to November (16).

Since majority of cases occur among children, therefore many children's lives may be affected. Epidemiological survey could be important for controlling and managing the leishmaniasis in endemic areas such as Iran such that it can support policy-makers and health authorities to diagnose the parasite cycle, Phlebotomine sand flies characteristics and its ecological and clinical features (11). Since few studies have been conducted on children's leishmaniasis in Iran, the current study was aimed to find pediatric cutaneous leishmaniasis status in Golestan Province, Iran.

2- MATERIALS AND METHODS

2-1. Study Design and Procedure

The current study was conducted on data existed in the Health System of Golestan Province (North of Iran) between 2010 and 2017. The study protocol was

approved by the Ethic Committee of Golestan University of Medical Sciences with number of IR.GOUMS.REC.1396.32. All new cases of CL for children aged ≤ 15 years that registered in the Iranian Health System from different cities of Golestan province were included in the study. Online forms of patients were completed to investigate the extent of the problem, diagnose at risk populations, and provide disease information for authorities.

2-2. Data Instrument

Two checklists were used to collect data. CL form was used to extract data existed online in the Provincial Health System including information about centers for diagnosis, number, type and size of lesion, duration of the treatment, and history of the scar. In addition, a patient sheet was run to collect demographic status such as age, gender, job, and residence (city and village).

2-3. Inclusion and Exclusion Criteria

The inclusion criteria were as follows: 1) CL cases diagnosed by a physician, or 2) patients presented to the Rural and Urban Health Centers that are supervised by the District Health Center in Golestan Province. Laboratory diagnosis was employed for all patients based on the direct observation of Leishmania parasites using sampling skin lesions, and prepared and stained with Giemsa, and observing the form of Amastigote parasite. In total, 6873 subjects participated. Incomplete questionnaires were excluded.

2-4. Data Analysis

The mean and standard deviation (SD) were used to report descriptive statistics. The Chi-square test was employed to analyze the relationship between gender and years of the disease and difference between centers of the diagnosis. Data were analyzed using SPSS software (version.18). A p-value less than 0.05 was considered significant. A diagram was used to present the Health System structure in Iran.

3- RESULTS

In total, 3371 cases were studied, including 1432 (48.9%) females and 1495 (50.9%) males living in the rural area; while 244 (60.8%), and 155 (38.7) were male and female respectively. Although information of female 18 (56.2%) and male 14 (43.8%) cases were recorded as other. The mean age of CL cases was 5.64 ± 4.56 years such that most of them 1959 (58.5%) were in the age group of 0-5 year. Moreover, CL patients 2919 (87.2%) were mostly found in the rural areas. The vast majority of CL cases 1,467 (43.9%) reported one lesion on their body. In final, only 26 (0.8%) had a history of scar (**Table.1**).

Table-1: Baseline characteristics of cases with pediatric cutaneous leishmaniasis.

Variables		Number	Percentage	Mean± SD
Gender	Male	1753	52.2	---
	Female	1605	47.8	
Age (year)	0-5	1959	58.5	5.64 ± 4.56
	6-10	771	23	
	11-15	616	18.4	
Residence	Rural	2919	87.2	---
	Urban	427	12.8	
Duration of treatment (week)	0-5	4071	98.4	1.42 ± 0.9
	6-10	41	1	
	10<	26	0.6	

Number of lesions	1	1467	43.9	2.62 ± 2.55
	2	789	23.6	
	3	427	12.8	
	4	223	6.7	
	5<	438	13.1	
Size of lesion (centimeter)				1.90 ± 1.42
Type of lesion	Sporotrichoid	2	0.1	------
	Dry	113	3.9	
	Wet	2767	95.9	
	Lupoid	2	0.1	
History of scar	Yes	26	0.8	------
	No	3089	99.2	

SD: Standard deviation.

Pediatric cutaneous leishmaniasis had the highest 883 (26.3%) and lowest 186 (5.5%) frequency in 2011 and 2014 years, accordingly. In addition, pediatric CL cases were increased in the three recent years from 320 (9.5%) in 2015 to 386 (11.5%) and 539 (16.1%) in 2016 and 2017 years. Also, there was a significant statistical relationship between CL cases and years of the survey (p= 0.001) (**Table.2**).

Table-2: Frequency of pediatric cutaneous leishmaniasis during 2010 to 2017 in Golestan province, Iran.

Variables		2010	2011	2012	2013	2014	2015	2016	2017	Total	P-value
Gender, Number, (%)	Female	223 (13.9)	404 (25.2)	124 (7.7)	143 (8.9)	77 (4.8)	172 (10.7)	166 (10.3)	296 (18.4)	1605 (100)	0.001*
	Male	231 (13.2)	479 (27.3)	159 (9.1)	164 (9.4)	109 (6.2)	148 (8.4)	220 (12.5)	243 (13.9)	1753 (100)	
Total		454 (13.5)	883 (26.3)	283 (8.4)	307 (9.1)	186 (5.5)	320 (9.5)	386 (11.5)	539 (16.1)	3358 (100)	

* Chi-square test.

According to diagnosis center of pediatric CL, the vast majority of patients 3003 (92.1%) was found in the Health Centers compared to hospitals with the lowest 3 (0.1%) diagnosis. A remarkable difference was found between the centers for diagnosing CL cases (p=0.001) (**Table.3**).

Table-3: Centers for diagnosis of pediatric cutaneous leishmaniasis.

Variables	Number	Percentage	P-value
Private laboratory	11	0.3	0.001*
Governmental laboratory	155	4.8	
Hospital	3	0.1	
Private clinic	64	2	
Health center	3003	92.1	
Other	23	0.7	
Total	3259	100	

* Chi-square test.

As delineated by **Table.4**, most of the CL cases were major 2553 (77.4%) compared to immigrated in cases 3 (0.1%) as the lowest cases. As indicated by **Figure.1**, CL was increased from July and reached to maximum in October, then decreased considerably in January. The Iranian Health System actively diagnoses and follows-up the CL in the rural area compared to inactive screening in the urban area. All patients finally refer to units and rural health centers, health post and health supervised by the District Health Center, including urban houses.

Table-4: Frequency distribution of pediatric cutaneous leishmaniasis stratified based on months and seasons of occurrence and type of CL.

Season	Month	Type of pediatric cutaneous leishmaniasis, Number (%)				Total Number (%)
		Major	Tropica	Immigrated in	Unknown	
Spring	April	15 (100)	0 (0)	0 (0)	0 (0)	15 (100)
	May	19 (76)	4 (16)	0 (8)	2 (0)	25 (100)
	June	9 (75)	2 (16.7)	0 (0)	1 (8.3)	12 (100)
Summer	July	9 (47.4)	8 (42.1)	0 (0)	2 (10.5)	19 (100)
	August	38 (52.1)	29 (39.7)	0 (0)	6 (8.2)	73 (100)
	September	166 (63.1)	90 (34.2)	0 (0)	7 (2.7)	263 (100)
Autumn	October	622 (83)	111 (14.8)	0 (0)	16 (2.1)	749 (100)
	November	874 (80)	208 (19)	0 (0)	11 (1)	1093 (100)
	December	506 (77.3)	140 (21.4)	0 (0)	9 (1.4)	655 (100)
Winter	January	229 (76.1)	64 (21.3)	3 (1)	5 (1.7)	301 (100)
	February	50 (71.4)	19 (27.1)	0 (0)	1 (1.4)	70 (100)
	March	16 (64)	8 (32)	0 (0)	1 (4)	25 (100)
Total		2553 (77.4)	683 (20.7)	3 (0.1)	61 (1.8)	3300 (100)

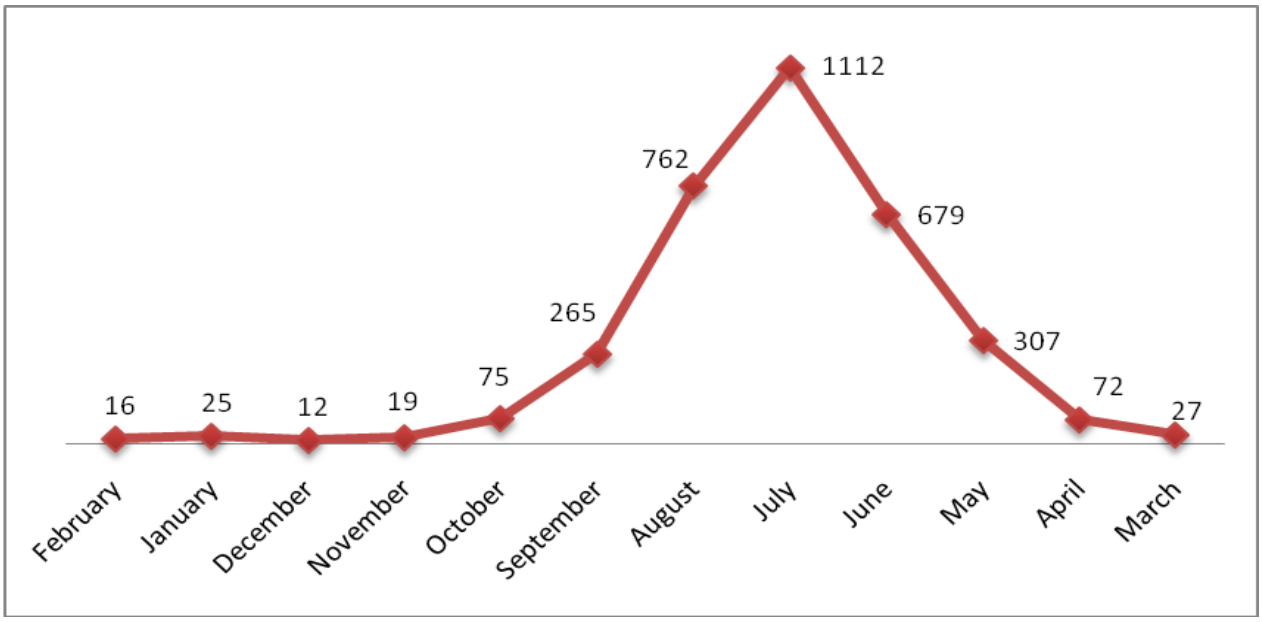

Fig.1: Trend of pediatric cutaneous leishmaniasis based on months during (2010 to 2017).

4- DISCUSSION

Iran is introduced as one of the high risk countries for CL with more than 20,000 cases per year. CL is also a main public health problem in Iran with a high incidence rate among children presently, we sought to investigate the pediatric CL among children in Golestan Province in North of Iran for eight years (2010 to 2017). The results of this study confirmed that the disease is endemic in the Golestan Province and that it infects many individuals, annually. The mean age of subjects was 5.64 ± 4.56 years. In the present study, most CL cases were aged 0-5 years. According to a study conducted by Karami et al., adults were more infected (17); while, Doroodgar et al. showed that CL had the highest prevalence among housewives in Kashan (18). In a study implemented in Turkey, the mean age of pediatrics was 7.52 years (range 0-15 years) (1). In total, the incidence of CL is very low in the elderly (19).

The most likely cause for the greater incidence in children is the lack immunity to CL. Finally, it can be hypothesized that rates of infection in different age groups might be changed based on the study location. In Delgado et al.'s survey (2008), the mean age of cases was 35 years that is different with the current study (20). The possible reason for these differences might be the high incidence of CL in the Golestan Province. As an endemic disease in the province, immaturity of the immune system, malnutrition, and abundant reservoirs are hypothesized as factors that may highlight the increased prevalence among young children (13, 21). A slight male predominance was currently observed. In two other studies implemented in Qom and Shiraz cities (Iran), 59.3% of patients were male. In agreement with our findings, Talari et al., made similar observations, with a boy-to-girl ratio of 1.2 in Iranian society (22). Similar findings have been found in other studies, supporting this explanation (13, 23-25). Gender differences can be caused by the fact that males wear fewer pieces of clothing than females, play in open environments and probably have more exposure to sandflies, especially in the rural areas. Although a female majority was found in Tunisian and Moroccan studies that might be caused by the cultural differences affecting people's clothing (26, 27). Given the residence, majority of CL patients were found in the rural area. It has been well-documented that Golestan Province is an endemic area of rural CL in Iran, with Leishmania major as dominant parasite species in the infected areas (28).

Alavinia et al.'s (2009) study yielded the same result (16). Soofizadeh et al. (2016) also cited that the highest incidence of CL cases was observed in the rural district of Korand in Gonbad-e- Kavoos (a city in Golestan Province) (29). CL remains yet an important public health concern in many rural areas of Iran due to increase in the number of rodents as the most prominent reservoir hosts (30). Moreover, rural CL has increased in the last decade in the Golestan Province due to development of colony of gerbils, structure of residential houses in the vicinity of them, increasing carriers, vulnerable individuals entering contaminated areas, and in brief, disposal of unhealthy waste (29).

The incidence of the disease has risen in the last three years from 2014 to 2016. A slight increase was observed in Hamzavi and Khademi's study (2015) that is in line with our results (31). Climate changes due to gradual warming of the planet might be the reason of this trend which is profitable to the growth of sand flies. Low attention to CL by the Iranian Health System may be another reason of increase in the incidence and prevalence rate. Additionally, a remarkable increase was found in 2011 that might be caused by the climate change and some health actions

such as rodent control that is usually done at a radius of 500 meters in the villages. Interestingly, pediatric CL subjects reached maximum in the month of October. Soofizadeh et al.'s investigation (2016) run in Golestan Province found exactly the same findings such that the greatest number of CL cases were seen in the months of October and November (29). Some conditions are necessary to reproduce sandfly, which include temperature of 23-28 centigrade and moisture of 70-100 percent that usually happen in the last months of summer and early autumn. Thus, the incubation period varies from 1 to 2 months (32); therefore, CL is expected to happen in the autumn season in the Golestan Province.

Given the number of lesions, most of the cases reported having one lesion followed by two and more than five lesions, respectively. Norouzinezhad et al.'s, study reported the same results (15). Previous studies have found that patients presented more than one lesion (33, 34). Moreover, the most frequent lesion was the wet form (95.9%), while the sporotrichoid and the lupoid forms were the least (0.1%), which was supported by Norouzinezhad et al.'s findings (15). L. major is endemic in Iran and routinely observed in many rural areas, particularly in the northeastern plains near the Russian border. Almost 80% of the rural population is exposured to the disease before the age of 10 and mostly all non-immune newcomers become infected (35).

Alavinia et al., carried out a study in the Northern Khorasan Province and found approximately similar results; although the prevalence of CL is high in other Provinces of Iran, including Isfahan, Shiraz, Khorasan, Khuzestan and Kerman (16). The study protocol benefits from an adequate sample size such that all CL cases were investigated in a time trend of eight years from 2010 to 2017. Given the importance of CL in the Golestan Province, all centers (governmental and private) are required to report and refer cases to the Health Centers; therefore, all CL cases are finally registered in the governmental centers. In the present study, we mostly investigated some of the epidemiologic and demographic data in a long term of eight years. Thus, measuring the clinical forms and the incidence rate of the CL as well as the quality of life of the children as a major outcome is recommended.

4-1. Study Limitations

Given that we used the second hand data, some of the information was lost. In addition, some cases may be referred to the private clinics that can underestimate the results of CL cases, partly. Finally, we were not able to calculate the characteristics such as cumulative incidence because there was no at risk population information in detail.

5- CONCLUSION

In the present study, 3371 cases were investigated during (2010 to 2017). CL mostly happened among children aged 0-5 years, which points to the role of mothers in protecting children through dressing up and sleeping habits in the outdoor environments. In final, the most observed type of CL was major (in the rural area) and in the autumn season (especially in November), that made it necessary to implement environmental health actions such as rodent control, environmental reform, and proper disposal of garbage and sewage.

6- CONFLICT OF INTEREST: None.

7- ACKNOWLEDGMENT

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