



ISSN No: 2319-5886

International Journal of Medical Research & Health Sciences, 2016, 5, 9S:384-393

Epidemiologic description and therapeutic outcomes of cutaneous leishmaniasis in Childhood in Isfahan, Iran (2011-2016)

Mujtaba Shuja^{1,2}, Javad Ramazanpour³, Hasan Ebrahimzade Parikhani⁴, Hamid Salehiniya⁵, Ali Asghar Valipour⁶, Mahdi Mohammadian⁷, Khadijah Allah Bakeshei⁸, Salman Norozi⁹, Mohammad Aryaie¹⁰, Pezhman Bagheri¹¹, Fatemeh Allah Bakeshei¹², Turan Taghizadeh¹³ and Abdollah Mohammadian-Hafshejani^{14,15*}

¹ Researcher, Health Promotion Research Center, Zahedan University of Medical Sciences, Zahedan, Iran

² Researcher, School of Public Health, Iran University of Medical Sciences, Tehran, Iran

³ Researcher, School of Public Health, Isfahan University of Medical Sciences, Isfahan, Iran

⁴ MSc Student, Department of Medical Parasitology and Mycology, school of public Health, Tehran University of Medical Sciences, Tehran, Iran

⁵ Zabol University of Medical Sciences, Zabol, Iran

⁶ MSc in Epidemiology, Abadan School of Medical Science, Abadan, Iran

⁷ Social Development & Health Promotion Research Center, Gonabad University of Medical Sciences, Gonabad, Iran

⁸ MSc in Midwifery, Faculty of Nursing and Midwifery, Dezful University of Medical Sciences, Dezful, Iran

⁹ Social Determinants of Health Research Center, Yasuj University of Medical Sciences, Yasuj, Iran

¹⁰ MSc in Epidemiology, Deputy of Research, Golestan University of Medical Sciences, Gorgan, Iran

¹¹ MSc in Epidemiology, Non Communicable Diseases Research Center, Fasa University of Medical Sciences, Fasa, Iran

¹² PhD Candidate, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran

¹³ Department of Social Medicine, School of Medicine, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

¹⁴ MSc in Epidemiology, Department of Epidemiology and Biostatistics, Isfahan University of Medical Sciences, Isfahan, Iran

¹⁵ PhD Candidate, Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

* Corresponding Email: amohamadii1361@gmail.com

ABSTRACT

Cutaneous leishmaniasis is a parasitic disease produced by *Leishmania* parasite and is transmitted by sandfly. The aim of this study was to investigate the epidemiology of Cutaneous leishmaniasis and different aspects of treatment in children with 10 years of age and under in Isfahan Province. This cross-sectional study was conducted on 3143 child cases of cutaneous leishmaniasis in Isfahan province during the March 2011 to March 2016. Descriptive statistics were used to describe demographic and clinical status of cutaneous leishmaniasis in children. The relationship between treatment regime with demographic and clinical variables were examined using Chi-square test. Data of the study was analyzed by using SPSS 18, software. The significance level of the tests was considered as $P < 0.05$. Of 3143 cases, 52.3% were boys, 51.6% were in rural areas and 91.6% were Iranian. *Leishmania major* with 91% of cases was the most common species of the cutaneous leishmaniasis. The relationship between treatment regime and age group, season, year of disease occurrence, *Leishmania* parasite, residential

area, nationality, travel history, travel location and simultaneous disease in other family members were statistically significant as ($P < 0.05$). Children in Isfahan Province are at high risk of disease occurrence. Cutaneous leishmaniasis treatment in Iranian children was consistent with cutaneous leishmaniasis treatment guideline and scientific evidence. However, the process for combating the animal reservoirs and mosquito vector should be considered as a priority to control disease. Furthermore, the facilities should be provided for accurate and timely diagnosis and treatment of patients.

Key words: Children, Cutaneous, Iran, Leishmaniasis.

INTRODUCTION

Cutaneous leishmaniasis is a parasitic disease produced by *Leishmania Tropica*, major and infantum and is transmitted by sandfly [1,2]. Clinical manifestations of cutaneous leishmaniasis are different depending on the type of parasite and the host immune system [1]. Over 90% of the burden of Cutaneous leishmaniasis is on the shoulders of Iran, Afghanistan, Iraq, Algeria, Saudi Arabia, Brazil and Peru [1]. It is estimated that annually about two million people worldwide are infected with leishmaniasis and over 1.5 million ones are suffering from cutaneous leishmaniasis [1,3]. Iran is among the endemic areas of this disease and despite the fact that approximately 20,000 cases of cutaneous leishmaniasis are annually reported in Iran, the actual cases of disease are more than 4 to 5 times. According to the report of the World Health Organization (WHO) in 2012, the annual cases of Iran are about 69000 to 113000 cases per year [1]. In Iran in 2008, over 26,000 cases of cutaneous leishmaniasis are reported with incidence rate of 37 per 100,000 people, this number reached 20593 cases with incidence rate of 28 per 100,000 people in 2010 [1]. More than 90% of cases have emerged in 88 cities of Iran and its transmission happened in 17 provinces [4]. In Iran most of the cutaneous leishmaniasis cases were reported from Isfahan and Shiraz provinces, and the lowest rate of disease reported from Mazandaran province [5]. Isfahan province is endemic region for cutaneous leishmaniasis [6,7]. According to the study of Nadim and Seyedi Rashti, main endemic areas of cutaneous leishmaniasis in Isfahan province were the east, north and northeast [7].

Cutaneous leishmaniasis is not a fatal disease, but it is difficult for patients to tolerate it for two reasons: first, in terms of aesthetics which leads to lesions especially in open areas of body and the scar of lesions remains after healing; and second, the spontaneous remission of this disease may take up to several years [8,9]. Despite the recognition of factor, vector and transmission of cutaneous leishmaniasis and conducted fundamental research on this disease, unfortunately, the control measures have not been very effective. Also, there has not been any effective vaccine against it so far [10,11].

There are normally four types of lesions in cutaneous leishmaniasis including the ulcer & secretions, ulcer (dry), Lupoid, and Sporotrichoid. Common treatment methods include topical antimony (injection into the lesion), systemic antimony (intramuscular injection), the combined method (topical antimony and cryotherapy), and finally the use of other methods (topical paromomycin, thermotherapy, etc.). The selection of these treatment regimens is different based on species of Parasite, geographical area and clinical manifestations [12], but there is not still a complete and certain cure for this disease. In this regard, the use of Pentavalent Antimonate (PA) is still the most important drug in treatment of cutaneous leishmaniasis. Based on the results of a systematic review by Khatami et al., the highest numbers of clinical trials have been conducted for determining the effectiveness of PA in treatment of cutaneous leishmaniasis [13]. The most common applied antimony compounds include Sodium Antimony Gluconate (SAG) and Meglumine Antimonate (MA) [13-14]. MA drug is a standard treatment for Iranian patients and requires several painful injections, and also has side effects [15-17]. In treatment of disease, the treatment failure occurs in the presence of active lesion 4 weeks after completion of treatment. Furthermore, the clinical resistance refers to relapse and treatment failure which lesion remains active until 4 weeks after at least two full systemic treatment [18]. According to reviewed domestic and international electronic resources by researchers of this study, it is found that a majority of studies, which have been conducted on treatment of cutaneous leishmaniasis in Iran, usually compare two special treatment techniques with a small sample size [12,14-16,19]. Consequently, we haven't adequate information about frequency of different treatment methods used in treating patients, relationship between the type of selected treatment by patients' demographic, clinical and laboratory characteristics as well as the frequency of complications and treatment failure especially in Iranian children. Therefore, this study has been conducted with the aim to investigating the epidemiology of cutaneous leishmaniasis and different aspects of treatment in children with 10 years of age and under during the March 2011 to March 2016 in Isfahan Province as an endemic area for cutaneous leishmaniasis in Iran.

Study Design and Population

In a cross-sectional study, all cutaneous leishmaniasis cases in children under 10 years old in Isfahan province were recruited. Isfahan province is one of the thirty-one provinces of Iran. The city of Isfahan is the provincial capital. The Isfahan province is located in the central part of the country and covers a region of approximately 107,027 square km (Map 1). This province has 25 counties as follow: Aran o Bidgol, Ardestan, Lanjan, Shahinshahr, Isfahan, Khansar, Meymeh, Khomeini Shahr, Nain, Semirom, Fereydan, Falavarjan, Fereydunshahr, Mobarakeh, Kashan, Golpayegan, Shahreza, Najaf Abad, Dehaghan, Khur and Biabanak, Borkhar, Tiran and Karvan, Buin and Miandasht, Chadegan and Natanz. In addition, this province has 67 cities and 2,470 villages in all. According to the census in the year 2011, the population of the province was 4,879,312 of which approximately 83.3% were residents in the urban areas and 16.7% in the rural areas. This province has a moderate and dry weather in total, ranging among 10.6 °C to 40.6 °C. Also, has annual rainfall on an average about 117 mm (figure 1).

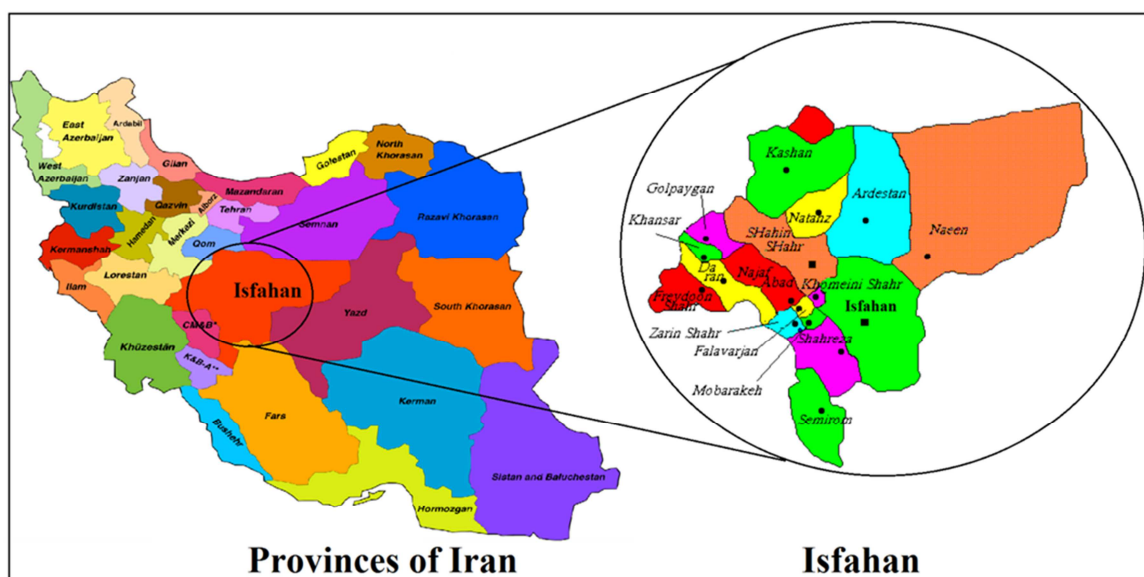


Fig.1: Location of Isfahan Province in Iran

MATERIALS AND METHODS

Cutaneous leishmaniasis is among the reportable diseases in disease-surveillance system of Iran. All private and governmental hospitals, laboratories and health centers are obliged to report leishmaniasis cases monthly based on the detection checklist which contains demographic, clinical and laboratory information. The detection checklists of leishmaniasis cases are sent to the health center of city at the end of each month. Health workers, experts and physicians in health centers should monitor the patients' recovery process until the full recovery and send the patients to higher levels of health care system to receive the specialized medical service if necessary.

Any type of skin lesion coincident with clinical symptoms of cutaneous leishmaniasis which have lasted more than 14 days is suspected for cutaneous leishmaniasis. The suspected cases are referred to leishmaniasis laboratory of city for laboratory confirmation of disease.

Leishmaniasis can be diagnosed by laboratory methods such as the microscopic diagnosis, parasite Cultivation or PCR test.

Microscopic diagnosis

Three samples (smear) from different parts of lesion are prepared in the laboratory. The inflamed and swollen edges of lesion are the most important parts which have the highest density of Amastigotes (*Leishmania* parasite). Prepared smears are dried at room temperature without use of flame. Afterwards, methanol and diluted Giemsa solution are used for staining the smear.

Cultivation and PCR

If three smears are negative, but the patient is still suspected for disease based on clinical and epidemiological evidence, the patient is suitable for cultivation of smear, and the disease is diagnosed based on results of further tests such as PCR.

Inclusion criteria

Criteria for including people to study include the confirmed disease cases, residence in Isfahan province for at least a year before disease occurrence; and the patients with ages of 10 years or less.

Exclusion criteria

The failed registered or incomplete information about on studied variables is the only exclusion criterion.

Ethical considerations

With concealing information about name, surname and also residence address of patients, other data including age group, gender, history of disease, year of disease occurrence, season, type of leishmaniasis parasite causing disease, residential area, nationality, travel history, travel location, simultaneous disease in other family members, selected regimen therapy, size of ulcer, number of ulcers, shape of ulcer and location of ulcer were identified.

Data analyses

Descriptive and analytical statistics were used for analysis of the study data. In descriptive analysis, distribution of Demographic (gender, age, location , nationality, year of disease occurrence, season, history of travel, travel Locations, simultaneous disease in other family members), clinical and laboratory variables (Leishmania type, Leishmaniasis history, treatment regimen, wound size (cm), number of lesions, form of the lesion, location of the lesion) of the patients are presented with the number (%). In analytical analysis, we examined the relationship between treatment regimen with demographic variables and characteristics of the lesion using Chi-square test and Fisher's exact test. We used of the independent t-test for compare average age in two genders. Data were analyzed using SPSS version 19 software. $P \leq 0.05$ was considered as significant level of the tests.

RESULTS

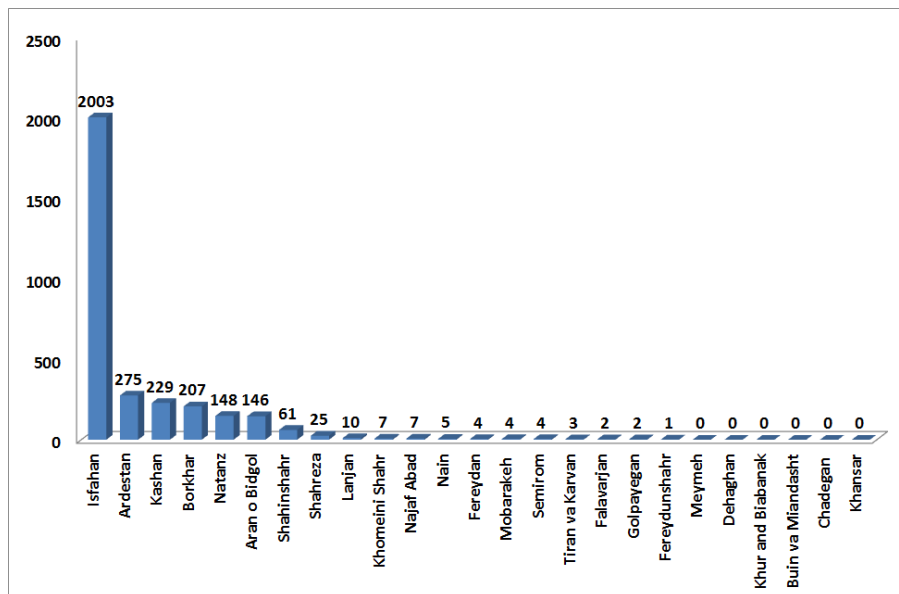


Fig.2: The frequency of leishmaniasis among children in Isfahan province, Iran (2011-2016)

In general, 3143 cases of leishmaniasis were reported in people with 10 years of age or lower in Isfahan province during March 2011 to March 2016. Among them, 1644 (52.3%) and 1499 (47.7%) were boys and girls, respectively. The gender ratio (male/female) was equal to 1.09. The patients' average age \pm SD was 2.45 ± 4.74 years. The average age was 4.67 ± 2.97 in girls and 4.8 ± 2.89 in boys, this difference was not statistically significant ($p = 0.135$). The disease symptoms occurred in most (61.69%) of the people in autumn. Leishmania Major was the cause of disease in 2860 (91%) of patients, and Leishmania Tropica in 283 (9%) of patients. Travel history during the past year was negative in 2579 (82.06%) cases of patients. Of total patients, 2881 (91.66%) cases were Iranian and 1622 (51.61%) cases were living in rural areas (Table .1).

The largest number of the leishmaniasis patients reported from Isfahan, Ardestan and Kashan County and the lowest number of Khansar, Meymeh, Dehaghan, Khur and Biabanak, Buin and Miandasht, Chadegan and Natanz County (Figure.2).

In 503 (16%) cases lesion size was more than 2 cm. Furthermore, the number of lesion in 344 (10.94%) cases was 4 or higher. In most of the patients (68.6%), the wounds had ulcer and secretion types. The most common sites of lesion in these patients were as follows: face in 912 (29.02%), hand and forearm in 703 (22.37%), several different body parts in 667 (21.22%), feet in 603 (19.19 %), middle of body in 140 (4.45%) and head and neck in 118 (3.75%) cases. During the study period, all patients received appropriate treatment and there was not any case of death caused by disease. Of 3143 cases, 3112 (99%) were treated completely without any complications (Table. 2).

Table-1: Demographic characteristics of the children with cutaneous leishmaniasis

Variables		Number	Percent
Gender	Female	1499	47.69
	Male	1644	52.31
Age group	0-2	903	28.73
	2.1-4	706	22.46
	4.1-6	578	18.39
	6.1-8	501	15.94
	8.1-10	455	14.48
Year of disease occurrence	2011	555	17.66
	2012	602	19.15
	2013	800	25.45
	2014	752	23.93
	2015	434	13.81
Season	Spring	78	2.48
	Summer	907	28.86
	Autumn	1939	61.69
	Winter	219	6.97
Leishmaniasis history	Negative	3119	99.24
	Positive	24	0.76
Leishmania type	Major	2860	91
	Tropica	283	9
Area	Urban	1521	48.39
	Rural	1622	51.61
Nationality	Iranian	2881	91.66
	Afghan	262	8.34
History of travel	No	2579	82.06
	yes	564	17.94
Travel Locations	Rural	76	2.42
	Urban	426	13.55
	both	62	1.97
Simultaneous disease in other family members	No	2420	77
	yes	723	23
Treatment regimen	Cryotherapy and Local antimony	814	25.9
	System antimony	1692	53.8
	Local antimony	368	11.7
	Cryotherapy	195	6.2
	Other treatments	74	02.4

In the assessment of the relationship between treatment regimen with demographic, clinical and epidemiological records, significant relationship between treatment regime and age group ($P \leq 0.001$), year of disease occurrence ($P \leq 0.001$), season ($P \leq 0.001$), the type of leishmaniasis parasite causing disease ($P \leq 0.001$), residential area ($P \leq 0.001$), nationality ($P \leq 0.001$), travel history ($P \leq 0.001$), travel location ($P = 0.039$) and simultaneous disease in other family members ($P \leq 0.001$) were observed. In other words, most of the people who received the systemic antimony were in age group of 0-2 years with occurrence of symptoms in spring, due to Leishmania Tropica species, living in urban areas, with Afghan nationality, and history of travel to rural areas, and had other family members with simultaneous disease. However, there was not any statistical significant relationship between treatment regime with gender ($P=0.226$) and history of disease ($P=0.263$) (Table.3).

Table 2: The characteristics of the lesion in children with cutaneous leishmaniasis

Variables		Number	Percent
Wound size (cm)	0-1	1294	41.17
	1.1-2	1346	42.83
	2.1 \geq	503	16.00

The number of lesions	1	1639	52.15
	2	801	25.49
	3	359	11.42
	4≥	344	10.94
Form of the lesion	ulcer	980	31.18
	ulcer & secretions	2156	68.60
	Lupoid	7	0.22
Location of the lesion	Hand and Forearm	703	22.37
	Leg	603	19.19
	Face	912	29.02
	Trunk	140	4.45
	Head and Neck	118	3.75
	Several body parts	667	21.22

In the evaluation of the relationship between treatment regime and features of lesion, there was a statistical significant relationship between treatment regime and size of lesion ($P \leq 0.001$), number of lesions ($P \leq 0.001$), shape of lesion ($P \leq 0.001$) and location of lesion ($P \leq 0.001$). Consequently, patients with 4 or more Lupoid lesion on face with sizes of 2 cm or more received more systemic antimony therapy (Table.4).

Table 3: The relationship between demographic characteristics and treatment regimen in patients with cutaneous leishmaniasis

Treatment variables		Cryotherapy and Local antimony	System antimony	Local antimony	Cryotherapy	Other treatments	Total	P.value
Sex	Female	407(27.2)	780(52)	182(12.1)	99(06.6)	31(02.1)	1499(100)	0.226
	Male	407(24.8)	912(55.5)	186(11.3)	96(05.8)	43(02.6)	1644(100)	
Age group	0-2	202(22.4)	525(58.1)	106(11.7)	44(04.9)	26(02.9)	903(100)	0.001*
	2.1-4	192(27.2)	391(55.4)	78(11)	39(05.5)	6(0.8)	706(100)	
	4.1-6	148(25.6)	297(51.4)	63(10.9)	49(08.5)	21(03.6)	578(100)	
	6.1-8	145(28.9)	250(49.9)	63(12.6)	33(06.6)	10(02)	501(100)	
Year of disease occurrence	8.1-10	127(27.9)	229(50.3)	58(12.7)	30(06.6)	11(02.4)	455(100)	0.001
	2011	127(22.9)	356(64.1)	49(08.8)	12(02.2)	11(02)	555(100)	
	2012	117(19.4)	370(61.5)	64(10.6)	37(06.1)	14(02.3)	602(100)	
	2013	155(19.4)	325(40.6)	255(31.9)	41(05.1)	24(3)	800(100)	
	2014	231(30.7)	445(59.2)	0(0)	59(07.8)	17(02.3)	752(100)	
Season	2015	184(42.4)	196(45.2)	0(0)	46(10.6)	8(01.8)	434(100)	0.001
	Spring	16(20.5)	51(65.4)	1(01.3)	10(12.8)	0(0)	78(100)	
	Summer	223(24.6)	481(53)	117(12.9)	68(07.5)	18(02)	907(100)	
	Autumn	540(27.8)	1019(52.6)	231(11.9)	99(05.1)	50(02.6)	1939(100)	
Leishmaniasis history	Winter	35(16)	141(64.4)	19(08.7)	18(08.2)	6(02.7)	219(100)	0.263*
	Negative	806(25.8)	1678(53.8)	368(11.8)	194(06.2)	73(02.3)	3119(100)	
Leishmania type	Positive	8(33.3)	14(58.3)	0(0)	1(04.2)	1(04.2)	24(100)	0.001*
	Major	785(27.4)	1507(52.7)	348(12.2)	157(05.5)	63(02.2)	2860(100)	
Area	Tropica	29(10.2)	185(65.4)	20(07.1)	38(13.4)	11(03.9)	283(100)	0.001
	Urban	425(27.9)	822(54)	97(06.4)	128(08.4)	49(03.2)	1521(100)	
Nationality	Rural	389(24)	870(53.6)	271(06.7)	67(04.1)	25(01.5)	1622(100)	0.001
	Iranian	775(26.9)	1499(52.1)	359(12.5)	179(06.2)	69(02.4)	2881(100)	
History of travel	Afghan	39(14.9)	1931(73.7)	9(03.4)	16(06.1)	5(01.9)	262(100)	0.001
	No	719(27.9)	1353(52.2)	292(11.3)	151(05.9)	64(02.5)	2579(100)	
Travel Locations	yes	95(16.8)	339(60.1)	76(13.5)	44(07.8)	10(01.8)	564(100)	0.039*
	Rural	5(06.6)	54(71.1)	10(13.2)	6(07.9)	1(01.3)	76(100)	
	Urban	82(19.2)	248(58.2)	60(14.1)	28(06.6)	8(01.9)	426(100)	
Other infected family members	both	8(12.9)	37(59.1)	6(09.7)	10(16.1)	1(01.6)	62(100)	0.001
	No	710(29.3)	1325(54.8)	145(06)	173(07.1)	67(02.8)	2420(100)	
	yes	104(14.4)	367(50.8)	223(30.8)	22(03)	7(01)	723(100)	

*fisher exact test

Table 4: The relationship between characteristics of the lesion and treatment regimen in patients with cutaneous leishmaniasis

Treatment variables		Cryotherapy and Local antimony	System antimony	Local antimony	Cryotherapy	Other treatments	Total	P.value
Wound size (cm)	0-1	309(23.9)	664(51.3)	212(16.4)	65(5)	44(03.40)	1294(100)	0.001
	1.1-2	367(27.3)	738(54.8)	138(10.3)	86(06.4)	17(01.3)	1346(100)	
	2.1≥	138(27.4)	290(57.7)	18(03.6)	44(08.7)	13(02.6)	503(100)	
The number of lesions	1	443(27)	828(50.5)	229(14)	102(06.2)	37(02.3)	1639(100)	0.001
	2	219(27.3)	423(52.8)	93(11.6)	49(06.1)	17(02.1)	801(100)	
	3	89(24.8)	202(56.3)	33(09.2)	22(06.1)	1(03.6)	359(100)	
	4≥	63(18.3)	239(69.5)	13(03.8)	22(06.4)	7(02)	344(100)	
Form of the lesion	ulcer	328(33.5)	500(51)	42(04.3)	82(08.4)	28(02.9)	980(100)	0.001*
	ulcer & secretions	483(22.4)	1188(55.1)	326(15.1)	113(05.2)	46(02.1)	2156(100)	
	Lupoid	3(42.9)	4(57.1)	0(0)	0(0)	0(0)	7(100)	
Location of the	Hand and Forearm	235(33.4)	293(41.7)	107(15.2)	52(07.4)	16(07.4)	703(100)	0.001

lesion	Leg	203(33.7)	263(43.6)	80(13.3)	36(06)	21(03.5)	603(100)
	Face	155(17)	595(65.2)	95(10.4)	51(05.6)	16(01.8)	912(100)
	Trunk	52(37.1)	54(38.6)	20(14.3)	11(07.9)	3(02.1)	140(100)
	Head and Neck	20(16.9)	75(63.6)	11(09.3)	6(05.1)	6(05.1)	118(100)
	Several body parts	149(22.3)	412(61.8)	55(08.2)	39(05.8)	12(01.8)	667(100)

*fisher exact test

DISCUSSION

During the March 2011 to March 2016 in Isfahan province, 3143 cases of cutaneous leishmaniasis in 10- year- old children and younger were observed. Cutaneous leishmaniasis was more common in boys and rural inhabitants and in Isfahan County. Most of cases occurred during autumn and the lowest in spring. *Leishmania Major* was the most common causes of cutaneous leishmaniasis in Isfahan. Most of Iranian patients have suffered from serious wounds, because 47% of patients had more than one lesion, in 59% of patients the size of wound was more than one cm, and 68% of the wounds were ulcer & secretions types. Also, 29% of wounds were occurred in the face of patients. Most of the people who were in age group of 0-2 years with occurrence of symptoms in spring, with *Leishmania Tropic* species, living in urban areas, with Afghan nationality, and history of travel to rural areas, and had other family members with simultaneous disease and with serious wounds more received the systemic antimony regimen therapy. All patients received appropriate treatment and there was not any case of death caused by disease. Also, 99% of cases were treated completely without any complications.

Similar to other studies [20-22], cutaneous leishmaniasis is more common in boys in Isfahan province. Probably this is due to differences in type and rate of clothes to cover body, so because of cultural and religious reasons, in Iranian the rate of body cover is higher in women than men. This difference is also true in children. On the other hand, the boys are outside the home more than girls, and thus have higher risk of exposure to vector-borne diseases. In other studies in Iran on cutaneous leishmaniasis in adults [23-25], also observed that disease is higher in men than women and this is probably because of males' greater exposure to vector of diseases due to their jobs.

Similar to other studies in Iran [23,24], in Isfahan Province a higher percentage of patients are Iranians and the Afghan patients allocate a lower (8.34%) proportion of patients. According to studies in Iran, Khorasan and Kerman Provinces have the highest number of cutaneous leishmaniasis cases in Iran. However, the large numbers of people migrate from Afghanistan to Iran; have residence in these provinces [24,26]. Cutaneous leishmaniasis is endemic in Afghanistan and lots of Afghans legally and illegally migrate to Iran and their arrival may be a factor for spread of disease in these areas. Therefore, the diagnosis and treatment of this group can prevent the occurrence of disease in non-endemic areas of Iran.

In this study, most of the patients (51.61%) are living in rural areas. The study results are consistent with findings of study by Postigo in Eastern Mediterranean Region of WHO in 2008 [27], but were inconsistent with the result of study that conducted with Saatchi *et al.*, in 2015 in Iran, that observed that majority of patients (62%) are living in urban areas [23]. These results showed that individuals in rural regions were infected in the childhood and would have acquired immunity in their youth.

Similar to other studies [7,23], the largest number of diseases was observed in autumn. In a study by Yaghoobi Ershadi *et al* in rural areas of Sabzevar in 2003, the highest frequency of *Phlebotomus* (vector of disease) was observed in autumn [25]. Therefore, the larger number of diseases in autumn was probably due to an increase in the number of vector of diseases, and thus the increased exposure to them in this season.

According to obtained results of this study, most of the patients (52%) have an lesion and this is consistent with research by Saatchi *et al* [23], while according to studies in Afghanistan, and Turkey, 70%, 60% and 80% of patients have an lesion respectively [22,28,29]. Consequently, a greater proportion of patients have multiple lesions caused by leishmaniasis at the same time in Iran. Therefore, it is essential to identify different types of vectors and pay attention to their bite habits in endemic areas to avoid creating multiple lesions in patients. In this regard, it should be noted that the increased number of lesions enhances the need for systemic therapy, and thus increases the incidence of complications and treatment failure which are more in systemic method than other methods [23].

In this study, there was a significant relationship between size of lesion and treatment regimen, so that most (57.7%) of the patients who had lesions of 2 cm or larger, were treated by systemic therapy. According to study by Saatchi *et al*, about 40% of patients with lesions of 3 cm and more received systemic therapy [23]. These results are consistent with findings of our study. According to the Leishmaniasis treatment guideline of Iran Ministry of Health and Medical Education and also the clinical trials, the systemic therapy should be used for facial lesions and lesions with diameters higher than 3 cm and 5 or more lesions [30]. This study also indicates that the patients with lesion size

over 2 cm and 4 or more lesions and lesions on the face received more systemic treatment regime. These results indicate that cutaneous leishmaniasis treatment in Iranian children was consistent with Leishmaniasis treatment guideline. In other word, Iranian physicians doing the treatment of cutaneous leishmaniasis based on scientific evidence.

According to numerous studies in the world and Iran, it is found that the use of combined therapy has more effects than the treatment methods which use only a treatment [31,32]. According to review study by Khatami et al., on 50 clinical trial studies, the combined treatment methods have more effects than monotherapy method [13]. Based on clinical trials, the recovery rate is from 85% to 100% in combined treatment methods [13]. Based on the conducted studies in Iran, it is found that the recovery rate is higher in combined method (92.3%) than monotherapy method (50%) [33,34]. Furthermore, according to a clinical trial on children in Iran, the effect of cryotherapy treatment is higher than topical therapy and it is suggested using the cryotherapy in children treatment due to its lower complications [35]. Therefore, according to results of mentioned studies, it is suggested using the combined therapy in treatment of large lesions. Moreover, cryotherapy method should be possibly used for treating children according to the type of lesion. It should be noted that the choice of appropriate regimen therapy depends on the type of factor, genetic characteristics and host immunity, cost-effectiveness and cost-benefit, drug availability, cultural factors and patients' knowledge [36].

Similar to other studies [22,37], the treatment of cutaneous leishmaniasis has been effective in complete and uncomplicated remission of more than 99% of patients in this study. However, the complete remission is seen in 77% of patients according to study conducted with Thiel et al., on Dutch troops in Afghanistan [28]. Similarly, according to a research in Turkey, the side effects of treatment have been reported in 5% of patients [29]. In another study conducted in Brazil, the complications of treatment (Arthralgia, nausea and vomiting, skin rash) have been observed in 58% of patients [37]. The comparison of these results on the one hand can show the good quality of treatment and lower incidence of side effects in Iranian patients, and on the other hand, indicates that despite these side effects caused by topical and systemic treatment of antimony compounds, the side effects of this drug have not fully registered and reported in Iranian surveillance system of cutaneous leishmaniasis.

Limitations of the study

Present study had some limitations that must be considered; this study was carry out based on information from Leishmaniasis surveillance system. Therefore patients that for whom Leishmaniasis detection checklist has been completed, registered and reported, consider in study. Consequently patients that their information is not recorded, by reason of lack of access to them data's, are not considered in the study. In addition, actual numbers of cases and side effects of treatment were higher than reported cases. In fact, we have information bias. Furthermore, this data has been gathered for an objective other than research plan.

CONCLUSION

In current study, cutaneous leishmaniasis occurred more in boys who were lived in rural areas of Isfahan. Leishmania major was the most important cause of disease. Most of the patients were observed in Isfahan, Ardestan, Kashan county, respectively. Most of the wounds were occurred in the face of patients. Most of the people who were in age group of 0-2 years, with occurrence of symptoms in spring, with Leishmania tropica species, living in urban areas, with Afghan nationality, and history of travel to rural areas, and had other family members with simultaneous disease received the systemic antimony regimen therapy. All patients that described in this study received suitable medical treatment. All patients recovered from the disease and there was no case of death as a result of leishmaniasis. Iranian physicians doing the treatment of leishmaniasis based on scientific evidence. However, children in Isfahan province are at high risk of disease occurrence. So the process for combating the animal reservoirs and mosquito vector should be considered as a priority to control disease. Furthermore, the facilities should be provided for accurate and timely diagnosis and treatment of patients.

Conflict of interest

All the authors declare that they have no conflict of interest.

REFERENCES

- [1]Alvar J, Velez ID, Bern C, Herrero M, Desjeux P, Cano J, et al. Leishmaniasis worldwide and global estimates of its incidence. PloS one. 2012;7(5):e35671.
- [2] Kishore K, Kumar V, Kesari S, Dinesh D. Vector control in leishmaniasis. Indian Journal of Medical Research. 2006;123(3):467.

- [3] Desjeux P. Leishmaniasis: current situation and new perspectives. *Comparative immunology, microbiology and infectious diseases.* 2004;27(5):305-18.
- [4] Mohebali M, Edrissian GH, Shirzadi MR, Akhoundi B, Hajjarian H, Zarei Z ,et al. An observational study on the current distribution of visceral leishmaniasis in different geographical zones of Iran and implication to health policy. *Travel medicine and infectious disease.* 2011;9(2):67-74.
- [5] Mesgarian F, Rahbarian N, Hajarani H ,Shahbaz F, Mesgarian Z, Taghipour N. Identification of Leishmania species isolated from human cutaneous Leishmaniasis in Gonbad-e-Qabus city using a PCR method during 2006-2007. *Tehran University of Medical Sciences.* 2010;68(4):25-32.
- [6] Yaghoobi-Ershadi M, Javadian E. [Zoonotic cutaneous leishmaniasis to the north of Isfahan. *Human infection in 1991.* *Bulletin de la Societe de pathologie exotique (1990).* 1994;88(1):42-5.
- [7] Nilforoushzadeh MA, Bidabadi LS, Hosseini SM, Nobari RF, Jaffary F. Cutaneous Leishmaniasis in Isfahan Province, Iran, During 2001-2011. *Journal of Skin and Stem Cell.* 2014; 1(2):89-96.
- [8] Masmoudi A, Hariz W, Marrekchi S, Amouri M, Turki H. Old World cutaneous leishmaniasis: diagnosis and treatment. *Journal of dermatological case reports.* 2013.(2)7;
- [9] Reithinger R, Aakil K, Kolaczinski J, Mohsen M, Hami S. Social impact of leishmaniasis, Afghanistan. *Emerg Infect Dis.* 2005;11(4):634-6.
- [10] Noazin S, Khamesipour A, Moulton LH, Tanner M, Nasser K, Modabber F, et al. Efficacy of killed whole-parasite vaccines in the prevention of leishmaniasis—A meta-analysis. *Vaccine.* 2009;27(35):4747-53.
- [11] Noazin S, Modabber F, Khamesipour A, Smith PG, Moulton LH, Nasser K, et al. First generation leishmaniasis vaccines: a review of field efficacy trials. *Vaccine.* 2008;26(52):6759-67.
- [12] Asilian A, Jalayer T, Whitworth J, Ghasemi R, Nilforoushzadeh M, Olliaro P. A randomized, placebo-controlled trial of a two-week regimen of aminosidine (paromomycin) ointment for treatment of cutaneous leishmaniasis in Iran. *The American journal of tropical medicine and hygiene.* 1995;53(6):648-51.
- [13] Khatami A, Firooz A, Gorouhi F, Dowlati Y. Treatment of acute Old World cutaneous leishmaniasis: a systematic review of the randomized controlled trials. *Journal of the American Academy of Dermatology.* 2007;57(2):335. e1-. e29.
- [14] Nilforoushzadeh MA, Jaffary F, Moradi S, Derakhshan R, Haftbaradaran E. Effect of topical honey application along with intralesional injection of glucantime in the treatment of cutaneous leishmaniasis. *BMC complementary and alternative medicine.* 2007;7(1):1.
- [15] Mohebali M, Fotouhi A, Hooshmand B, Zarei Z, Akhoundi B, Rahnama A, et al. Comparison of miltefosine and meglumine antimoniate for the treatment of zoonotic cutaneous leishmaniasis (ZCL) by a randomized clinical trial in Iran. *Acta tropica.* 2007;103(1):33-40.
- [16] Zerehsaz F, Salmanpour R, Handjani F, Ardehali S, Panjehshahin MR, Tabei SZ, et al. A double-blind randomized clinical trial of a topical herbal extract (Z-HE) vs. systemic meglumine antimoniate for the treatment of cutaneous leishmaniasis in Iran. *International journal of dermatology.* 1999;38(8):610-2.
- [17] Shazad B, Abbaszadeh B, Khamesipour A. Comparison of topical paromomycin sulfate (twice/day) with intralesional meglumine antimoniate for the treatment of cutaneous leishmaniasis caused by *L. major*. *European Journal of Dermatology.* 2005;15(2):85-7.
- [18] Hadighi R, Mohebali M, Boucher P, Hajjarian H, Khamesipour A, Ouellette M. Unresponsiveness to Glucantime treatment in Iranian cutaneous leishmaniasis due to drug-resistant *Leishmania tropica* parasites. *PLoS Med.* 2006;3(5):e162.
- [19] Asilian A, Davami M. Comparison between the efficacy of photodynamic therapy and topical paromomycin in the treatment of Old World cutaneous leishmaniasis: a placebo-controlled, randomized clinical trial. *Clinical and experimental dermatology.* 2006;31(5):634-7.
- [20] Reithinger R, Mohsen M, Leslie T. Risk factors for anthroponotic cutaneous leishmaniasis at the household level in Kabul, Afghanistan. *PLoS Negl Trop Dis.* 2010;4(3):e639.
- [21] de Araújo Pedrosa F, de Alencar Ximenes RA. Sociodemographic and environmental risk factors for American cutaneous leishmaniasis (ACL) in the State of Alagoas, Brazil. *The American journal of tropical medicine and hygiene.* 2009;81(2):195-201.
- [22] Pontello Junior R, Gon AdS, Ogama A. American cutaneous leishmaniasis: epidemiological profile of patients treated in Londrina from 1998 to 2009. *Anais brasileiros de dermatologia.* 2013;88(5):748-53.
- [23] Saatchi M, Salehinia H ,Khazaei S, Mohammadian M, Mohammadian-Hafshejani A. Cutaneous leishmaniasis in Iran: Demographic description and therapeutic outcomes. *Journal of Dermatology and Cosmetic.* 2015;6(2):108-18.
- [24] Khazaei S, Hafshejani AM, Saatchi M, Salehiniya H, Nematollahi S. Epidemiological Aspects of Cutaneous Leishmaniasis in Iran. *Archives of Clinical Infectious Diseases.* 2015;10(3):7-17.
- [25] Yaghoobi Ershadi M, Akhavan A, Zahraei Ramazani A, Abai M, Ebrahimi B, Vafaei Nezhad R, et al. Epidemiological study in a new focus of cutaneous leishmaniasis in the Islamic Republic of Iran. 2003.

- [26] Sharifi F, Sharifi I, Zarean M, Parizi MH, Aflatoonian M, Harandi MF, et al. Spatial distribution and molecular identification of *Leishmania* species from endemic foci of south-eastern Iran. *Iranian journal of parasitology*. 2012;7(1):45.
- [27] Postigo JAR. Leishmaniasis in the world health organization eastern mediterranean region. *International journal of antimicrobial agents*. 2010;36:S62-S5.
- [28] van Thiel P-P, Leenstra T, de Vries HJ, van der Sluis A, van Gool T, Krull AC, et al. Cutaneous leishmaniasis (*Leishmania major* infection) in Dutch troops deployed in northern Afghanistan: epidemiology, clinical aspects, and treatment. *The American journal of tropical medicine and hygiene*. 2010;83(6):1295-300.
- [29] Uzun S, Durdu M, Culha G, Allahverdiyev AM, Memisoglu HR. Clinical features, epidemiology, and efficacy and safety of intralesional antimony treatment of cutaneous leishmaniasis: recent experience in Turkey. *Journal of Parasitology*. 2004; 90(4):853-9.
- [30] Palacios R, Osorio LE, Grajalaw L, Ochoa MT. Treatment failure in children in a randomized clinical trial with 10 and 20 days of meglumine antimonate for cutaneous leishmaniasis due to *Leishmania viannia* species. *The American journal of tropical medicine and hygiene*. 2001;64(3):187-93.
- [31] Sundar S, Sinha PK, Rai M, Verma DK, Nawin K, Alam S, et al. Comparison of short-course multidrug treatment with standard therapy for visceral leishmaniasis in India: an open-label, non-inferiority, randomised controlled trial. *The Lancet*. 2011;377(9764):477-86.
- [32] Reddy M, Gill SS, Kalkar SR, Wu W, Anderson PJ, Rochon PA. Oral drug therapy for multiple neglected tropical diseases: a systematic review. *Jama*. 2007;298(16):1911-24.
- [33] Salmanpour R, Razmavar MR, Abtahi N. Comparison of intralesional meglumine antimonate, cryotherapy and their combination in the treatment of cutaneous leishmaniasis. *International journal of dermatology*. 2006;45(9):1115-6.
- [34] Asilian A, Sadeghinia A, Faghihi G, Momeni A, Harandi AA. The efficacy of treatment with intralesional meglumine antimonate alone, compared with that of cryotherapy combined with the meglumine antimonate or intralesional sodium stibogluconate, in the treatment of cutaneous leishmaniasis. *Annals of tropical medicine and parasitology*. 2013.
- [35] Layegh P, Pezeshkpoor F, Soruri AH, Naviafar P, Moghiman T. Efficacy of cryotherapy versus intralesional meglumine antimonate (glucantime) for treatment of cutaneous leishmaniasis in children. *The American journal of tropical medicine and hygiene*. 2009;80(2):172-5.
- [36] Minodier P, Parola P. Cutaneous leishmaniasis treatment. *Travel medicine and infectious disease*. 2007;5(3):150-8.
- [37] Passos V, Barreto SM, Romanha AJ, Krettli AU, Volpini ÂC, Costa MFF. American cutaneous leishmaniasis: use of a skin test as a predictor of relapse after treatment. *Bulletin of the World Health Organization*. 2000;78(8):968-74.