



Human and Canine Leishmaniasis: Diagnosis and Risk Factors

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ABSTRACT

Leishmaniasis is a zoonosis disease caused by a parasite of the genus *Leishmania* transmitted by the sandflies. It is ranked among the 20 major neglected tropical diseases. Algeria is classified as one of the most affected countries by cutaneous leishmaniasis worldwide. This study was conducted in the Medea region, north-central Algeria, to investigate human and canine leishmaniasis. Diagnosis of human leishmaniasis was conducted on patients with symptoms suggestive of leishmaniasis. The presence of wet or dry lesions, number, location, duration, and travel history were recorded for each patient. Confirmation of the disease was performed by histopathological test. Canine leishmaniasis was diagnosed on the basis of clinical examination in 175 male Sloughi dogs. Symptoms included skin ulcerations, lymphadenopathy, dermatitis with alopecia, weight loss, and ocular or nasal lesions. A total of 1070 cases of human leishmaniasis were investigated, including 1067 (99.72%) cases of cutaneous leishmaniasis and 3 (0.28%) cases of visceral leishmaniasis. Of the 1067 human cutaneous leishmaniasis cases, 59.51% and 40.49% were male and female, respectively. For visceral leishmaniasis, all cases were male. Persons aged less than 10 years were more infected than those over 10 years of age. Chahbounia region was found to be the most infected area, compared to other regions. The highest number of human leishmaniasis cases was recorded during November (462 cases). Human cutaneous leishmaniasis was the most frequent (81.38%) among the other human pathologies in the study area; followed by pulmonary tuberculosis (14.8%). All Sloughi dogs were diagnosed with leishmaniasis of which the most common symptoms included lymph node hypertrophy, emaciation, skin lesions, fever, epistaxis, alopecia, ocular lesions, anemia, onychogryphosis, chemosis, and the less common symptoms are: fever, diarrhea, and splenomegaly. The *Psammomys obesus* and *Meriones shawi* were present especially in the periphery of the lands next to the valley of Chahbounia city. Leishmaniasis remains present in the region, constituting a public health menace. The union of veterinary and public services is necessary to eradicate the disease by controlling the vector and the reservoirs of the parasite.

Keywords: Diagnosis, Dogs, Human, Leishmaniasis, *Merione shawi*, *Psammomys obesus*

INTRODUCTION

Leishmaniasis is a zoonosis disease in the tropical and subtropical regions, caused by a parasite of the genus *Leishmania* transmitted by the sandflies (Tamiru et al., 2019). It is ranked among the 20 major neglected tropical diseases (WHO, 2021a).

Leishmaniasis can be observed in three forms of Visceral, Cutaneous, and Mucocutaneous Leishmaniasis (Desjeux, 2004; WHO, 2021b). Visceral leishmaniasis known as kala-azar is characterized by irregular fever outbreaks, weight losses, hypertrophy of the spleen and liver, and anemia (Al-Salem et al., 2016; WHO, 2021b). It is common in Brazil, East Africa, and India (Al-Salem et al., 2016; WHO, 2021b). Cutaneous leishmaniasis is the most common form. It causes skin lesions, mainly ulcers, on exposed parts of the body, and leaves lifelong scars (WHO, 2021b). It occurs in the Americas, the Mediterranean Basin, the Middle East, and Central Asia (WHO, 2021b). Mucocutaneous leishmaniasis results in the partial or total destruction of the mucous membranes of the nose, mouth, and throat (Desjeux, 2004). Occurs in Bolivia, Brazil, Ethiopia, and Peru (Desjeux, 2004; WHO, 2021b).

Dogs with clinical or subclinical leishmaniasis are a source of infection for the fly vectors that allow the transmission of the parasite to other dogs or humans (Solano-Gallego et al., 2011). Moreover, the proximity between man and dog favors the transmission cycle propagated by the insect vector (Dantas-Torres et al., 2012). It has been identified 21 species of *Leishmania* as pathogenic to humans (Sharma and Singh, 2008).

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According to WHO, Algeria is one of the most affected countries by cutaneous leishmaniasis in the world (Alvar et al., 2012). It was in 1860 and 1911 that the first cases of cutaneous and visceral leishmaniasis were observed in Algeria. In 1921, it was indicated the role of sandflies as a vector (Louzir et al., 2013). In Algeria, cutaneous leishmaniasis is more frequent than visceral leishmaniasis. It is caused by *Leishmania major* (*L. major*), *Leishmania infantum* (*L. infantum*), and *Leishmania tropica* (*L. tropica*) (Eddaikra et al., 2018). *Leishmania major* is responsible for zoonotic cutaneous leishmaniasis of which the vector is *Phlebotomus papatasi* and the reservoir *Psammomys obesus* and *Meriones shawi* (Belazzoug, 1983; Belazzoug, 1986; Harrat et al., 1996). This zoonotic cutaneous leishmaniasis remains the dominant form in arid and semi-arid areas (Bachi et al., 2019). Anthroponotic cutaneous leishmaniasis, a rare chronic form, is caused by *L. tropica* and frequently occurs with *L. major* (Harrat et al., 2009; Garni et al., 2014). It is limited in Algeria to Annaba, Tipaza, Constantine, and Ghardaia (Mihoubi et al., 2008; Harrat et al., 2009; Izri et al., 2014). *Phlebotomus sergenti* is known as the vector of *L. tropica*, of which humans are the principal reservoir. However, *Massoutiera mzabi* (Mzab gundi, family Ctenodactylidae) is another suspected reservoir (Boubidi et al., 2011; Jaouadi et al., 2011).

Leishmania infantum vectorised by *Phlebotomus perfiliewi*, is responsible for sporadic cutaneous leishmaniasis (Bachi et al., 2019) which is found in the coastal regions of north Algeria (Eddaikra et al., 2018). Zoonotic visceral leishmaniasis is due to *L. infantum*. It is vectored by *Phlebotomus longicuspis* and *P. perniciosus* of which the dog is the main reservoir (Bachi et al., 2019). It is mostly found in humid and subhumid areas of northern Algeria (Eddaikra et al., 2018).

The control of human leishmaniasis is closely dependent on efficient control of canine leishmaniasis and the control strategy should be based on local epidemiological information (Gálvez et al., 2018). Therefore, the objective of this study is to fill the gaps in the current scientific knowledge about human and canine leishmaniasis in the Medea region, Algeria, by assessing the prevalence, associated risk factors, and symptoms of the disease.

MATERIALS AND METHODS

Ethical approval

No experiments were performed on humans or animals in this study. The results of this study were obtained during the routine examination of human or canine leishmaniasis.

Study area

The study was conducted between 2002 and 2012 in the Medea region (36°17'7.385"N 2°46'4.889"E), north-central Algeria (Figure 1). The Medea region is 981m above sea level. The surface area of the region is 8.775, 65 Km² and it is characterized by a warm Mediterranean climate with dry summer and cold and wet winters. The rainfall average is 676.3 mm per year. The temperature varies from -2.5°C to 40.5°C and humidity is between 50% and 83% with an average of 65%.

Data collection

Statistical data on cases of human leishmaniasis were provided to the researchers by the public health directions (DSPs) of four Daïras of the wilaya of Medea, including Chahbounia, Ksar El Boukhari, Aziz, and Ouled Antar. The word Daïra means an administrative division of a wilaya. These DSPs were responsible for the diagnosis and treatment of patients with laboratory-confirmed cases of leishmaniasis. All cases were declared on a mandatory basis. In the present investigation, data were collected for 11 years (from 2002 to 2012). The sex and age of the patient were recorded along with the date of diagnosis and the area of residence.

The patient data used in this study were anonymized. These data were studied according to the temporal (annual and monthly), demographic (age and sex), and spatial (origin of patients) distribution of the cases. Data on canine leishmaniasis cases were obtained from the direction of veterinary inspection and the veterinary clinics of the four Daïras mentioned above. Information regarding the presence of *Psammomys obesus* and *Meriones shawi* in the different Daïras was obtained from the direction of the agricultural services of Medea.

Environmental variables

Information on environmental parameters was also collected during this study, including the presence of dogs in the proximity of the patients' residences, ponds, rivers, field rats, *Psammomys obesus*, and *Meriones shawi*.

Diagnosis of leishmaniasis

In dogs

175 male Sloughi dogs aged 1 to 3 years and weighing between 18 and 25 kg were reported with the leishmaniasis infection. The breeders gave importance only to Sloughi dogs, and other breeds were not considered. The Sloughi dogs were examined following systematic procedures in different veterinary clinics in the region of Medea, Algeria. The clinical investigations were conducted without affecting animal welfare. Dogs were clinically examined, including a history of their habits and previous health conditions. A physical examination was performed to evaluate the dog's clinical signs. Symptoms or lesions suggestive of leishmaniasis were dermatitis, cutaneous ulcerations, alopecia, weight loss, and ocular or nasal lesions. The total number of examined Sloughi dogs was not recorded by the veterinarians, and so the measurement of canine leishmaniasis prevalence was not possible.

In humans

The survey included patients with suspected leishmaniasis. The personal information of each patient was recorded with the type of lesions observed (wet or dry) and their location on the body. The travel history of the patients was also recorded. Confirmation of leishmaniasis was conducted by histopathological examination. Skin biopsies, collected according to the procedures of Evans et al. (1989), were spread on a slide, air-dried, and fixed with absolute methanol, followed by staining by 10% Giemsa. Direct examination was performed under a light microscope (Olympus, Japan, at $\times 500$ / $\times 1000$ magnification). Data concerning most frequent pathologies, including pulmonary tuberculosis and extrapulmonary tuberculosis were recorded.

Data analysis

R 3.0.2 for Windows was the statistical program used. ANOVA and Chi-square tests were used for the statistical analysis. Tukey's post-hoc test was used to explore differences between multiple means. $P < 0.05$ was considered statistically significant.

RESULTS

A total of 1070 cases of human leishmaniasis were investigated, including 1067 (99.72%) cases of Cutaneous Leishmaniasis (CL) and 3 (0.28%) cases of Visceral Leishmaniasis (VL) only ($p < 0.05$). Of the 1067 human CL cases, 59.51% and 40.49% were male and female, respectively ($p < 0.05$, Table 1). For visceral leishmaniasis, all cases were male. People under 10 years of age were more infected than those aged over 10 years ($p < 0.05$, Table 1). The Chahbounia region was found to be the most infected area, compared to other regions ($p < 0.05$, Table 1). The highest number of human leishmaniasis cases were recorded during November (462 cases, $p < 0.05$) after which the number of recorded cases gradually decreased (Figure 2). In humans, the signs observed were a painful and pruritic insect bite sensation, which developed into a button. This button then turns into a cratered ulcer, which does not respond to antibiotic treatment.

The comparison between the number of human leishmaniasis cases and the number of pulmonary and extrapulmonary tuberculosis cases during the 11 years of the study (2002-2012), showed that CL (81.38%) was the most frequent one followed by pulmonary tuberculosis (14.8%, $p < 0.05$, Table 2). All Sloughi dogs ($n=175$) were diagnosed with leishmaniasis of which the most common signs encountered in almost all dogs included lymph node hypertrophy, emaciation, skin lesions, fever, epistaxis, alopecia, ocular lesions, anemia, onychogryphosis, chemosis. On the other hand, the less common symptoms were fever, digestive disorder, and splenomegaly which were seen in less than 10 dogs (Figure 3).

The *Psammomys obesus* and *Meriones shawi* were present especially in the periphery of the lands next to the valley of Chahbounia.

Table 1. Prevalence of human cutaneous leishmaniasis according to different risk factors

Risk factors		Number of cases (%)	p-value
Sex	Males	635 (59.51)	0.01
	Females	432 (40.49)	
	Total	1067	
Age	1-10 years	640 (59.98)	0.01
	11-20 years	320 (29.99)	
	21-89 years	107 (10.02)	
Regions	Chahbounia	594 (55.67)	0.01
	Ksar El Boukhari	251 (23.52)	
	Aziz	209 (19.58)	
	Ouled Antar	13 (1.21)	
Location of lesions			
Superior limb	Hand	90 (8.43)	0.01
	Forearm	220 (20.62)	
Inferior limb	Knee	23 (2.16)	
	Foot	102 (9.56)	
	Leg	48 (4.50)	
Head	Face	41 (3.84)	
	Neck	20 (1.87)	
	Scalp	28 (2.62)	
	lip	10 (0.94)	
	Mandibular	12 (1.12)	
	Nose	50 (4.69)	
	Ear	12 (1.12)	
	Eyelid	20 (1.87)	
	Forehead	74 (6.94)	
	Cheek	182 (17.06)	
Body	Temporal	28 (2.62)	
	Lumbar	13 (1.22)	
	Back	28 (2.62)	
	Multiple injuries	17 (1.59)	
	Umbilical	14 (1.31)	
	Skin	13 (1.22)	
	Chest	12 (1.12)	
Belly	10 (0.94)		

Table 2. Comparison of the number of human cutaneous and visceral leishmaniasis cases with pulmonary and extrapulmonary tuberculosis in Medea region, Algeria from 2002 to 2012

Years	Cutaneous Leishmaniasis	Visceral Leishmaniasis	Pulmonary Tuberculosis	Extra-Pulmonary Tuberculosis
2012	67	2	31	2
2011	54	0	35	2
2010	4	0	7	2
2009	22	0	38	15
2008	75	0	25	10
2007	56	0	17	2
2006	184	1	11	3
2005	544	0	17	3
2004	41	0	9	7
2003	12	0	3	1
2002	3	0	1	0
Total	1067 (81.38%)*	3 (0.22%)	194 (14.80%)	47 (3.58%)

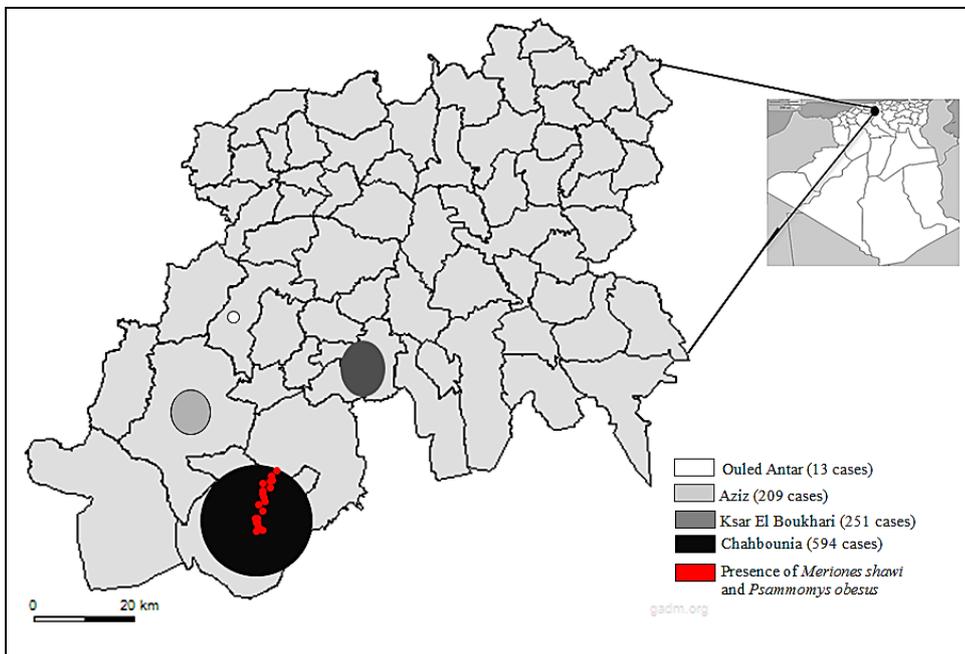


Figure 1. Presentation of the study area and the number of human cutaneous leishmaniasis cases

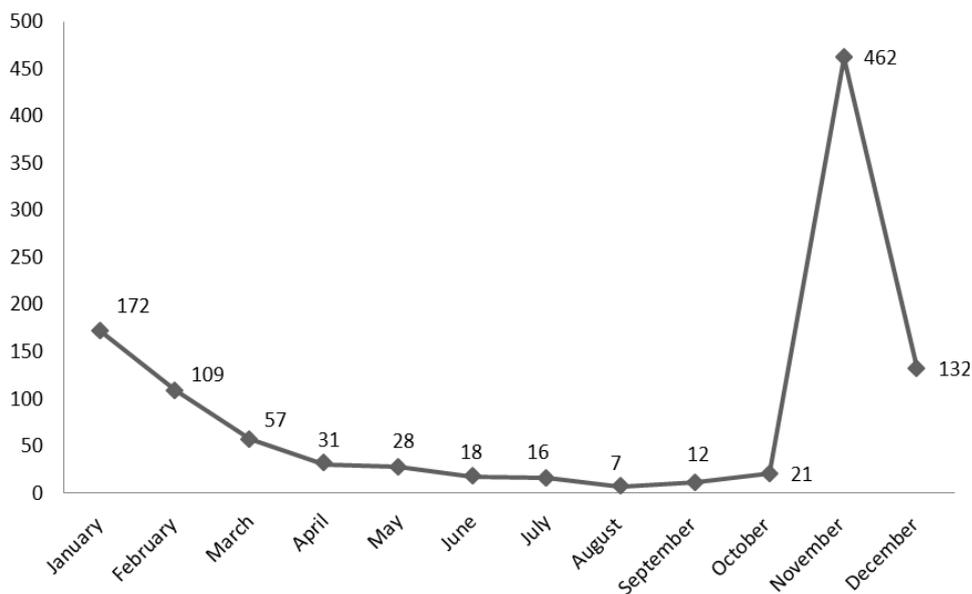


Figure 2. Monthly distribution of the number of human cutaneous leishmaniasis cases in Medea region, Algeria from 2002 to 2012



Figure 3. Cutaneous leishmaniasis in a Sloughi dog with a typical ulcer on the shoulder (photos on the left) and diffuse cutaneous leishmaniasis in the back with cachexia (Chahbounia region, Medea, 2010)

DISCUSSION

Human CL is the most widespread form in Algeria. It is distinct in three forms of zoonotic CL, formerly called clou de Biskra, sporadic CL known as northern CL, initially described as clou de Mila, and chronic CL caused by *Leishmania tropica* (syn *Leishmania killicki*, Harrat et al., 2009; Bachi et al., 2019). The present study represents a large-scale epidemiological investigation of human and canine leishmaniasis in the Medea region, Algeria. This survey provides for the first time a picture of the current epidemiological scenario of human and canine leishmaniasis in Medea, including the main clinical signs and associated risk factors.

Leishmania major is responsible for zoonotic CL of which the vector is *Phlebotomus papatasi* known for its frequent use of rodent burrows for resting and reproduction during the day (Harrat et al., 1996; Aoun and Bouratbine, 2014). The reservoir hosts are *Psammomys obesus* and *Meriones shawi* (Belazzoug, 1986; Harrat et al., 1996; Aoun and Bouratbine, 2014). Zoonotic CL remains the dominant form in Algerian (including Tunisia, and Lybia) arid and semi-arid areas (Aoun and Bouratbine, 2014; Bachi et al., 2019). This is in concordance with present results. Two outbreaks of zoonotic CL were recorded in Algeria. In 1982, M'sila has known an epidemic where 8000 cases were diagnosed, followed in 1985 by another epidemic in Ksar Chellala with 700 cases (Bachi et al., 2019). This explains the highest incidence of CL observed in the present study in Chahbounia. The presence of *Psammomys obesus* and *Meriones shawi* (reservoir) around the Chahbounia valley also has a large role in this higher prevalence.

Indeed, *Psammomys obesus* is distributed in the semi-desert areas of the northern fringe of the Sahara (Ashford, 2000) where the study area is located. It is found in highly populated saline burrows, especially in the succulent halophilic steppes, or on the edge of wadis where it finds its main food (Ashford, 2000), such as that of Chahbounia in present study.

In Algeria, there are several species of forestry rodents, however, the most damaging species to agriculture is the shaw merione (*Meriones shawi*) (Belazzoug, 1986). This rodent has been declared as an agricultural plague by the decree n° 95 387 of November 28, 1995 (Aoun and Bouratbine, 2014). An over-population of *Meriones shawi* has been associated with CL epidemics in humans in southern Morocco (Rioux et al., 1982). *Meriones shawi* inhabits the arid and semi-arid regions of the northern Algerian Sahara. It is considered an agricultural pest and a natural reservoir of *L. major* in Algeria, Tunisia, and Morocco (Rioux et al., 1982; Ghawar et al., 2011; Boudrissa et al., 2012). *Meriones libycus* was also found infected with *L. major* in Tunisia and Libya, and *Meriones crassus* in Egypt (Ben-Ismaïl et al., 1987; Morsy et al., 1991). Cutaneous leishmaniasis outbreaks are also due to ecological and environmental changes that have occurred in the North African region (Aoun and Bouratbine, 2014). The dromedary is the main competitor of *Psammomys obesus* for the halophilic plants on which it feeds. Their replacement by vehicles is responsible for the increase in the number of rats and consequently of CL (Ashford, 2000).

Cutaneous leishmaniasis lesions usually appear at the site of the sandfly bite as a non-suppurative papule (Berman, 1997). Lesions develop in a few months into painless ulcers with bulging edges, which may heal spontaneously in a few months or years, or cause scarring and disfigurement (Berman, 1997). All this was observed in this survey. Moreover, it is important to note that all CL patients should be evaluated for mucosal damage (Aronson et al., 2017).

Visceral leishmaniasis is caused by *L. infantum* and causes leishmaniasis in humans, domestic dogs, and some wild animals (Ferroglia et al., 2018; Mohebbi et al., 2018; Tabbabi, 2019). It is vectored by *Phlebotomus longicuspis* and *Phlebotomus perniciosus* of which the dog is the main reservoir (Bachi et al., 2019). It is present mainly in humid and subhumid regions of northern Algeria (Tizi-Ouzou, Bejaïa, Blida, Chlef, and Tipaza, Eddaïkra et al., 2018). The annual incidence is low, varies between 0.36 and 0.73 cases per 100,000 inhabitants (Belazzoug et al., 1985; Harrat et al., 1992) which is in agreement with the result of the current study where VL was observed only in three subjects representing a prevalence of 0.28%.

Cutaneous leishmaniasis is observed from October and peaks in December followed by a gradual decrease and is characterized by characteristic ulcerative-crust lesions on the face and limbs particularly (Bachi, 2006). All of these findings are in agreement with the current survey.

Climatic changes have a great influence on the incidence of CL, notably expressed by the appearance of certain epidemics observed in North African countries (Bounoua et al., 2013; Aoun and Bouratbine, 2014). In fact, in the present study, a very high number of CL cases were diagnosed (544 cases) in Ksar El Boukhari in 2005. Regarding the age distribution of CL cases, young children (less than 10 years) were the most infected ones in the present investigation. This result was in agreement with that of Zait and Hamrioui (2009) in Algeria and other Mediterranean countries (Burza et al., 2018; Tzani et al., 2021). The majority of cases of CL were male (59.51% versus 40.49%), which is probably due to the greater exposure of men to sandflies during agricultural work or other outdoor activities (Tzani et al., 2021). The same observation has been reported in other vector-borne diseases (Cozzarolo et al., 2019).

The presence of sandflies in the proximity of the residence was reported by a large proportion of persons with leishmaniasis (Tsirigotakis et al., 2018; Tzani et al., 2021). This is due to the climatic conditions of the region which are favorable to the development of sandflies. The same was reported elsewhere (Tsirigotakis et al., 2018; Tzani et al.,

2021).

Canine leishmaniasis is an endemic disease in many countries worldwide (Dantas-Torres et al., 2012). It is mainly caused by *L. infantum* and the infected dogs are clinically healthy or develop variable clinical signs (Solano-Gallego et al., 2009). The dog is very sensitive to leishmaniasis which has a very high parasitic charge (Magalhães-Junior et al., 2016). Since it is very close to humans, it constitutes a dangerous domestic reservoir (Magalhães-Junior et al., 2016). Dogs may develop both VL and CL, while CL occurs in some cases of human leishmaniasis (Sasani et al., 2016). The majority of human leishmaniasis cases have been reported in the presence of domestic dogs or the proximity of their residence (Tzani et al., 2021). The same observations were noticed in the present investigation.

In this study, Sloughi dogs' breed was only received at the veterinary clinic due to their high importance in hunting. The other breeds of dogs are not considered and are not declared by the breeders. For this reason, it is difficult to establish a prevalence of canine leishmaniasis in this region. In addition, clinical diagnosis of canine leishmaniasis remains a challenge for practicing veterinarians because infected dogs may remain asymptomatic for months or even their entire lives (Solano-Gallego et al., 2009). Some dogs manifest clinical disease, others develop a subclinical infection, and protozoan-resistant dogs can overcome the infection and self-heal (Solano-Gallego et al., 2011).

However, most cases of canine leishmaniasis occur far from cities and veterinary services making it a neglected disease (Sasani et al., 2016). Moreover, in some cases, the symptoms are vague ranging from mild local skin lesions to fatal systemic syndromes (Solano-Gallego et al., 2011). Therefore, laboratory examination is essential because asymptomatic dogs can transmit *L. infantum* to the vector sandflies (Laurenti et al., 2013). Algeria is highly endemic and important prevalence was reported (36%) by Medkour et al. (2019) and (18%) by Bellatreche et al. (2021). However, in other investigations, it is important to study the prevalence of dogs' leishmaniasis in Medea region and to perform serological diagnoses on dogs even in case they are asymptomatic.

CONCLUSION

This study indicates that CL is more predominant than VL in Algeria. Symptoms are predominantly localized on the face and hands. Males and children aged under 10 years are the most affected. Most cases have been reported in the presence of dogs, *Psammomys obesus* and *Merione shawi*. The disease is still a danger for public health as breeders do not take into consideration the disease in dogs except in precious dogs, such as the Sloughi while it is the main source of contamination of sandflies. The union of veterinary, agricultural, and public services is necessary to eradicate the disease by controlling the vector and the reservoir (dogs, *Psammomys obesus* and *Merione shawi*) and limiting human contamination.

DECLARATIONS

Authors' contribution

Ali Dahmani conceived and designed the research. Nassim Ouchene analyzed data. Nadjat Amina Ouchene-Khelifi wrote the manuscript. All authors checked and approved the final draft of the manuscript before submission to the journal.

Competing interests

The authors declare that they have no competing interests.

Ethical consideration

Ethical issues (including plagiarism, consent to publish, misconduct, data fabrication and/or falsification, double publication and/or submission, and redundancy) have been checked by all the authors.

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