

## Brief Original Article

# A Retrospective Study of Cutaneous and Visceral Leishmaniasis in Istanbul, Turkey

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### Abstract

**Introduction:** Leishmaniasis is a vector-borne disease caused by flagellated protozoans of the genus *Leishmania*. This study aimed to evaluate the epidemiological status of Visceral Leishmaniasis (VL) and Cutaneous Leishmaniasis (CL) among patients admitted to a university hospital in Istanbul, located in western Turkey.

**Methodology:** This study included 160 and 77 patients with a pre-diagnosis of VL and CL, respectively, between January 2001 and December 2017. Detailed demographic data, including age, gender, nationality and the number and location of lesions were collected and recorded from the patient registries.

**Results:** Among 160 bone marrow specimens that suspected as VL, 22 (13.7%) of the specimens that were evaluated with both culture and Giemsa staining detected as positive. Furthermore, 29 (37.7%) of the 77 patients suspected for CL showed evidence of *Leishmania*.

**Conclusions:** The increase in human immigration from neighbouring countries (with a high incidence of leishmaniasis) to Turkey might increase the risk of spreading the disease. This situation could result in a higher prevalence in metropolitan cities like Istanbul, where the country's population is concentrated.

**Key words:** Cutaneous leishmaniasis; human; Istanbul; *Leishmania*; Turkey; visceral leishmaniasis.

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### Introduction

Leishmaniasis may result in a life-threatening visceral disease, visceral leishmaniasis (VL), if the self-limiting infection cutaneous leishmaniasis (CL) is untreated. *Phlebotomus* and *Lutzomyia* act as vectors for the disease, which is recognised as one of the seven most important tropical diseases by the World Health Organisation (WHO) and is observed as an endemic disease in 98 countries around the world [1,2]. Leishmaniasis is endemic to Turkey, with the majority of cases reported in the southeastern cities of the country. In Turkey, leishmaniasis is clinically observed in two ways: CL and VL. Approximately 2000 CL and 26 VL cases are reported annually, on average [3,4]. The dominant species in the country is reported as *Leishmania tropica* in CL cases, and *Leishmania infantum* in VL cases [5,6]. However, some studies over recent years have reported that *L. infantum* and *L. major* were also detected in CL cases, and *L. tropica* was detected in VL cases [5,7-9]. Leishmaniasis has become

a national problem in Turkey (particularly in some endemic regions) and has started to be detected all over the country. This could be due to migrants entering the country from Syria to escape the ongoing civil war; their numbers have reached approximately 4 million, which has necessitated the revision of possible measures [10,11]. The aim of this retrospective study was to evaluate the epidemiological situation of VL and CL among the patients admitted to the university hospital in Istanbul located in northwest Turkey.

### Methodology

#### *Study area and timescale*

This study includes a retrospective evaluation of the prospectively collected data. It was conducted between January 2002 and December 2017 in Istanbul in northwest Turkey. Results were sent to a medical microbiology laboratory for diagnosis purposes over a period of 15 years and were reviewed and included in this study.

**Table 1.** Comparison of the direct microscopy and culture methods employed in leishmaniasis diagnosis.

Direct microscopy	Visceral leishmaniasis			Cutaneous leishmaniasis		
	Culture			Culture		
	Positive	Negative	Total	Positive	Negative	Total
Positive	14	7	21	6	23	29
Negative	1	138	139	-	48	48
Total	15	145	160	6	71	77

*Sample size and data collection*

The study included a total of 160 patients who underwent bone marrow aspiration and were suspected for having VL, and 3 patients were suspected of having CL and their biopsies were sent to the laboratory. Additionally, skin exudate materials taken from 74 patients who were pre-diagnosed with CL were also used. Detailed demographic data, including age, gender, nationality and the number and location of lesions were collected and recorded from the patient registries. This study was conducted in accordance with the World Medical Association’s Declaration of Helsinki: ‘Ethical Principles for Medical Research Involving Human Subjects’. This research did not require an ethics committee approval because of its retrospective nature.

*Leishmania diagnosis*

Smears were prepared from the specimens and stained with Giemsa for microscopic examination in terms of *Leishmania* amastigote forms at 1000× magnification. Additionally, *Leishmania*-suspected

samples were cultured in Novy-Nicolle-McNeal (NNN) and RPMI 1640 broth medium. The samples were incubated at 27°C and were assessed for 40 days by weekly checks at 400× microscopic magnification. Under microscopic examination, the samples with amastigote and promastigote forms of *Leishmania* in the culture were considered positive.

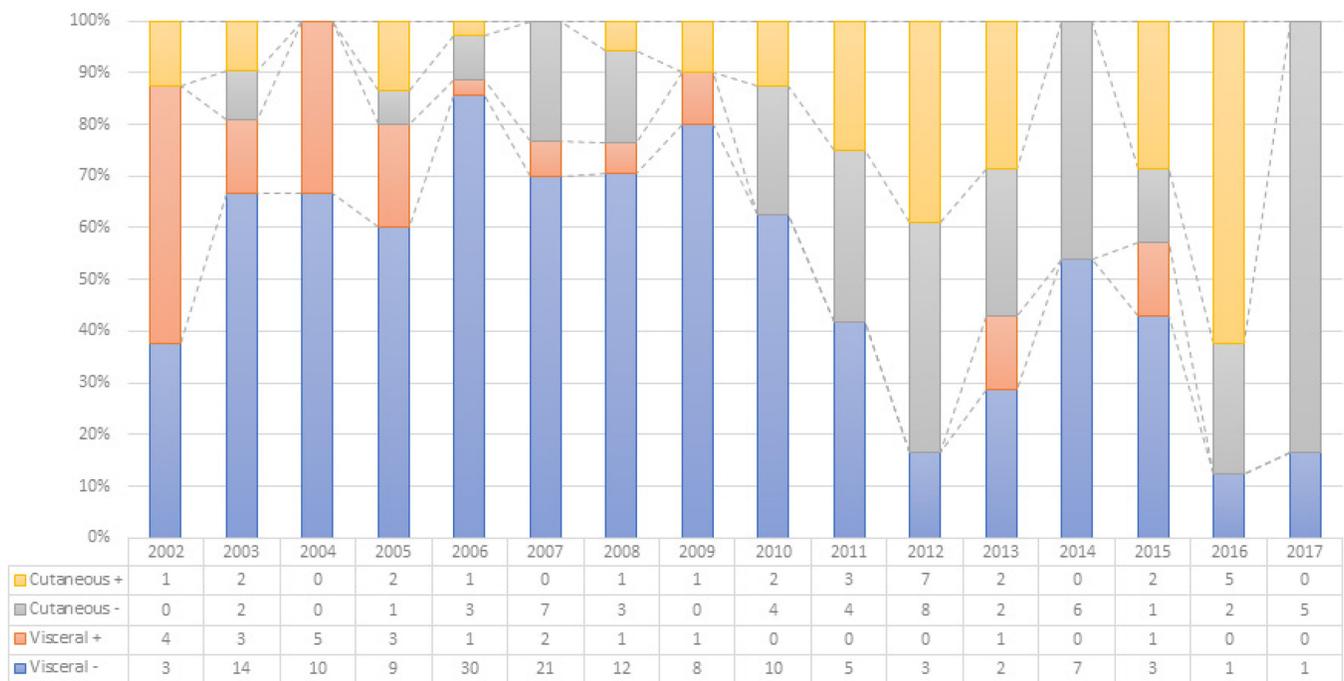
*Statistical analysis*

The frequencies, percentages, average and median values were calculated for the descriptive statistics. CL positive patients were statically compared using the chi-square method for single or two area lesions. The statistical analysis was conducted using IBM’s SPSS (version 21.0) software program (IBM Corp., Armonk, NY, USA). The significance value was considered as  $p < 0.05$ .

**Results**

In 21 of the 160 bone marrow specimens (13.1%) that were evaluated with suspected VL in this study, the presence of amastigotes was detected during direct

**Figure 1.** The distribution of visceral and cutaneous leishmaniasis cases by year.

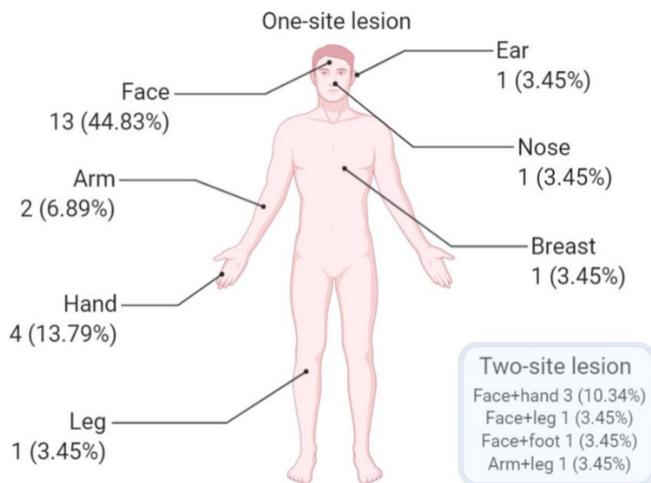


examination with Giemsa staining. In 15 specimens (9.4%), the presence of promastigotes was observed in the resulting culture. In both the methods, positive results were obtained in 14 cases and 138 were found to be negative. When the positive detection of at least one of the methods was considered, a total of 160 cases 22 (13.7%) were diagnosed as VL. *Leishmania* was detected in 29 of the 77 patients (37.7%) evaluated with suspected CL, and 6 of them (7.8%) positively grew in the culture (Table 1). The patients VL and CL were evaluated, and their yearly distribution is illustrated in Figure 1. Half of all patients evaluated as VL-positive were male (11) and half were female (11). Most patients were 10 years of age or younger (18 patients, representing 81.8%), and the remaining patients were between 11 and 20 years of age (4 patients, representing 18.2%). All the VL patients were Turkish nationals. A total of 14 out of 29 patients (48.3%), who were positive for CL, were male, and 15 (51.7%) were female. Most of the patients were 10 years of age or below (i.e. eight patients, representing 27.6%), and the average age was 32.4 years. A total of 23 patients (79.3%) had a single area lesion, which was significantly more than those with two lesions ( $p < 0.05$ ). The most common site where lesions were observed was on the face (44.83%). Other sites were hands (13.79%), arms (6.89%), legs (3.45%), nose (3.45%), ears (3.45%) and chest (3.45%). In 6 patients, 2 different lesion combinations were detected on 2 areas of the body, which were face–hands, face–leg and arm–leg sites (Figure 2). Of the 29 patients, 22 (75.9%) were Turkish nationals, 4 (13.8%) were Syrian nationals, 2 (6.9%) were Afghan nationals and 1 (3.4%) was a Turkmenistan national.

### Discussion

According to the World Health Organisation’s (WHO) epidemiological data for 2017, it was reported that more than 1 billion people were at risk of VL and CL. Globally, 616 million people were VL-positive and 431 million people were CL-positive [12]. Leishmaniasis is caused by over 20 known *Leishmania* species or subspecies and mainly affects poor people in Africa, Asia and Latin America. The disease is associated with malnutrition, population displacement, inadequate accommodation conditions, a poor immune system and lack of resources [13]. Istanbul, which acts as a bridge between Asia and Europe, is the most crowded city in Turkey. Leishmaniasis is not endemic to the city; however, 44% of the Turkish population is at risk of CL and 9% is at risk of VL. Considering these details, a significant increase in leishmaniasis cases is not surprising [14]. The specific conditions created by war in Turkey’s neighbouring countries might increase the risk factors for spreading the disease among the population and could transform the disease into a regional threat. In this study, 22 of the 29 patients (75.9%) who were diagnosed with CL were Turkish citizens; 4 (13.8%) were Syrian nationals, 2 (6.9%) were Afghan nationals and 1 (3.4%) was Turkmenistan national. All the patients with VL were Turkish nationals. Due to Turkey’s geographic location, increasing travel opportunities and (as of December 2011) the 4 million migrants who fled to Turkey because of the civil war in Syria, an increase has been observed in the number of leishmaniasis cases emanating from foreign countries. In 2016, there were 1713 CL cases originating from foreign countries globally. Turkey ranks first, with 1089 cases [11,13]. In global studies conducted in countries where VL is endemic, it was reported that the disease was evident in children [15-17]. In accordance with these studies, this research revealed that many patients with VL were 10 years of age or younger (18 patients, representing 81.8%) and the remaining patients were between 11 and 20 years of age (4 patients, representing 18.2%). Although CL affects all age groups from babies to the elderly, many of the patients are in the paediatric age group [18-20]. However, this study found that the most-affected age group was 0-10-year-old children (8 patients representing 27.6%). This could be explained by the fact that younger patients might access hospitals more often than older patients. Furthermore, the elderly population might acquire immunity. Typically, CL is characterised by the appearance of one or more lesions on the exposed parts of the body (face, neck, arms and legs). This study found the most common site of the

**Figure 2.** Site and number of cutaneous leishmaniasis lesions in patients.



body to be the face. Although a total of 23 patients exhibited a single lesion on different parts of the body, 6 patients had a combination of 2 lesions in two areas. A possible reason for the sites of lesions is that these sites are the most accessible for vector bite. The limitations of this study are as follows. First, the study was retrospective in design. Second, direct microscopy and culture methods are routinely used in the laboratory diagnosis of leishmaniasis. Since routine diagnosis is not possible with molecular tests, evaluation of the *Leishmania* parasite was not made at the species level.

## Conclusion

In conclusion, leishmaniasis is endemic in various regions of Turkey. Intense migration from neighbouring countries due to civil war along with a high leishmaniasis incidence affects the disease prevalence in Turkey. With this massive migration, the risk of incidence has increased in non-endemic areas. For the purpose of reducing this risk and taking precautions, more care must be given to the health controls of the refugees coming from the area with high leishmaniasis incidence and the hygiene conditions must also be carefully considered in residential areas.

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