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A Comparison of Demographic and Clinical Characteristics of Syrian and Turkish Patients with Cutaneous Leishmaniasis

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Abstract. Cutaneous leishmaniasis (CL) is a significant public health problem with increasing incidence, especially in extreme circumstances. In this study, we compared the sociodemographic and clinical characteristics of 685 Syrian CL patients afflicted by the Syrian conflict and 685 Turkish CL patients in 2012. Patient age, gender, duration of disease, lesion size, type, and localization were evaluated. The duration of CL disease in Syrian CL patients (4.5 ± 4.3 weeks) was shorter than that of Turkish CL patients (11.9 ± 9.7 weeks). The number of lesions was greater in Syrian patients (2.46 ± 2.43) than in Turkish patients (1.93 ± 1.47). Lesion sizes were comparable between both groups (Syrian, 11.2 ± 8.7 mm; Turkish, 10.7 ± 7.7 mm). In Syrian CL patients, nodular type lesions were the most common (325 patients, 49.1%), whereas, in Turkish CL patients, ulcer type lesions were the most common (352 patients, 51.5%). Our results indicate variations in the clinicoepidemiological features of CL between Turkish and Syrian patients within Sanliurfa province. This highlights the impact of social unrest and environmental conditions on the epidemiology of CL within this region. Approaches to prevention, control, and treatment of CL in these areas should take into consideration the emerging changes in clinicoepidemiological parameters of the disease.

INTRODUCTION

Cutaneous leishmaniasis (CL), caused by parasites of the genus *Leishmania* and transmitted by the sandfly vector (*Phlebotomus papatasi*), is a skin infection affecting people in different regions of the world.[1] About 350 million people in 98 countries are at risk of CL, making it a significant public health problem.[2] Based on the causative species and geographical distribution of the disease, CL is divided into Old World CL (southern Europe, the Middle East, Asia, and Africa) and New World CL (Latin America).[2] Old World CL is found in the regions of the Middle East, the littoral Mediterranean, the Arabian Peninsula, Africa, near Asia, and the Indian subcontinent. In the Old World, CL is caused by *Leishmania major* (zoonotic CL), *L. tropica* (anthroponotic CL), *L. aethiopica*, and some zymodemes of *L. infantum*.[3] Recently, the incidence of CL due caused by *L. major* has been reported in Turkey, likely due to migratory patterns.

In 2003 and 2004, about 25,000 cases were reported annually in Syria, which is to the south of Turkey, and of these, more than 10,000 cases were reported in the Syrian city of Aleppo alone.[4] Because of the internal conflict in Syria over the past 3 years, Syrian citizens have fled to neighboring countries, primarily Turkey. Refugees coming into Turkey from Syria have been housed in camps close to the Turkish border. CL patients who have had to migrate to Sanliurfa province Turkey, which borders Syria, live in camps and physicians who work in these camps administer an initial intralesional antimonial treatment. Patients who do not respond to initial treatment usually receive other antileishmanial treatment, primarily systemic antimonials at the Dermatology Clinic of Harran University Medical Faculty.

Syrian and Turkish residents within the Sanliurfa province are affected by major epidemiological factors that could significantly alter the incidence of CL. One major factor is the Southeastern Anatolia Project, an ongoing large-scale irrigation project, which has caused several environmental changes that could increase the activity of sandflies,[5] worsen the progression of the disease, and cause an explosion in the incidence.[6–8] Further, the incidence of CL can show seasonal changes, with the most suitable conditions for the spread of disease being a long, hot season following a wet season.[7,9]

Although a number of studies have described the epidemiology of leishmaniasis in Syria and Turkey, studies comparing epidemiologic burden and lesion characteristics between Turkish and Syrian patients have not been explored. This knowledge is of huge importance for control interventions and treatment selection of the disease. This is especially critical during extreme circumstances such as conflicts and natural disasters, which usually results in a significant increase in the number of cases. To address this issue, our study, which was conducted in 2012, was aimed at comparing the sociodemographic and clinical characteristics of 685 Syrian CL patients afflicted by the Syrian civil war with 685 Turkish CL patients.

MATERIALS AND METHODS

Data collection. The study composed of 685 Syrian and 685 Turkish CL patients who were registered with the Dermatology Clinic of Harran University Medical Faculty and the Oriental Boil Center of the Sanliurfa Public Health Directorate between January 1, 2012 and January 1, 2013. Approval for the study was granted by the Local Ethics Committee. The patients were divided into two groups: Syrian CL (Group 1) and Turkish CL (Group 2). A retrospective evaluation was made of the data previously recorded for

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TABLE 1
Age and gender distribution of Syrian and Turkish CL patients (mean ± SD)

	Syrian patients (Group 1)	Turkish patients (Group 2)	*P* value
Age (years) (*N* = 685)	16.83 ± 15.60	17.54 ± 16.70	> 0.05
Sex (*N* = 685)			
Female	341 (49.8%)	401 (58.5%)	< 0.01
Male	344 (50.2%)	284 (41.5%)	< 0.01

CL = cutaneous leishmaniasis; SD = standard deviation.

TABLE 3
Evaluation of lesion forms in Syrian and Turkish CL patients

	Syrian patients (Group 1)	Turkish patients (Group 2)	*P* value
Type (Group 1 = 661 patients, Group 2 = 683 patients)			
Ulcer	319 (48.3%)	352 (51.5%)	< 0.01
Papule	17 (2.6%)	37 (5. 4%)	< 0.01
Nodule	325 (49.1%)	294 (43. 1%)	< 0.01
Recidivans	0	0	–

CL = cutaneous leishmaniasis.

all the patients: age, gender, family anamnesis, duration of disease (weeks), lesion diameter (mm), lesion type (ulcer, papule, nodule, and recidivans), and lesion localization (head-neck, upper and lower extremities, trunk, mucosal, or generalized).

The diagnosis of CL was confirmed by positive demonstration of *Leishmania* parasites (amastigotes) in skin smears or histopathological paraffin sections in all patients. Skin smears were obtained by slit-skin scrapings from the active edge of the sore, which were air dried and fixed in methanol and then stained with Giemsa stain for microscopic examination.

Statistical analysis. The SAS 9.12 statistical software program (Cary, NC) was used in the statistical evaluation of the data. Two proportions tests were used to reveal the difference between the group rates of characteristics such as age, number, duration of disease, and diameter. Proportion tests were used to reveal the difference between the group rates of characteristics such as gender, lesion type, and lesion localization. Results are expressed as mean ± standard deviation (SD).

RESULTS

General characteristics of the groups. Syrian CL (Group 1) composed of 685 CL patients (341 females, 344 males) with a mean age of 16.83 ± 15.60 years. Turkish CL (Group 2) composed of 685 CL patients (401 females, 284 males) with a mean age of 17.54 ± 16.70 years (Table 1). Majority of CL patients in both Syrian and Turkish groups were children (0–15 years). The gender-based incidence of CL was found to be disproportionate between Syrian and Turkish patients, and this difference was statistically significant ($P < 0.01$). Unlike Syrian patients that had similar incidences of CL in males and females, Turkish patients showed more females (58.5%) than males (41.5%) with the disease (Table 1).

Relationship between duration of disease, lesion size, and number in the groups. As seen in Table 2, the duration of CL disease in Group 1 (4.5 ± 4.3 weeks) was shorter than that of Group 2 (11.9 ± 9.7 weeks) and this difference was determined to be statistically significant ($P < 0.01$). The number of lesions was greater in the Group 1 patients (2.46 ± 2.43) than in the Group 2 patients (1.93 ± 1.47). This difference was statistically significant ($P < 0.01$). The difference between the two groups with respect to lesion size (Group 1, 11.2 ± 8.7 mm; Group 2, 10.7 ± 7.7 mm) was not found to be statistically significant ($P > 0.05$) (Table 2).

Evaluation of the lesion forms. In Syrian CL patients, nodular type lesions were the most common (325 patients, 49.1%). Ulcer type lesions were determined in 319 patients (48.3%) and papular type in 17 patients (Table 3). In Turkish CL patients, ulcer type lesions were determined in 352 patients, nodular type in 294, and papular type in 37 patients (Table 3). The nodular type lesions were determined as higher in Syrian CL patients, whereas ulcer and papular type lesions were higher in Turkish CL patients ($P < 0.01$ for each lesion type) (Table 3). No recidivans type lesions were determined in any patient in either group of CL patients. Lesion forms observed in CL patients in our study are depicted in Figure 1.

Evaluation of lesion localization. As seen in Table 4, the most common location of the lesions in the CL patients in both groups was the head and neck region: Syrian CL group with 223 (32.55%) patients and Turkish CL group with 302 (44.15%) patients ($P < 0.01$). In Syrian CL group, this was followed by generalized location (187 patients, 27.30%). In Turkish CL group, generalized locations were seen in 116 patients (16.96%). A statistical difference was found in these regions of lesion localization between Syrian and Turkish groups ($P < 0.01$). Lesion localizations in the lower extremities were observed in 184 patients (26.86%) in the Syrian group and 200 patients (29.24%) in the Turkish group ($P > 0.05$). In the upper extremities, localizations were seen in 72 (10.51%) Syrian and 47 (6.87%) Turkish CL patients ($P < 0.01$). There were mucosal involvements in 16 (2.34%) Syrian and 17 (2.49%) Turkish CL patients ($P > 0.05$). In both groups, the region with the least involvement was the trunk: three patients (0.44%) in the Syrian group and two patients (0.29%) in the Turkish CL group ($P > 0.05$) (Table 4).

DISCUSSION

Old World CL has been endemic in Turkey since 1950. The vast majority of cases of CL in Turkey are located in the region of southeast Anatolia, primarily in the province of Sanliurfa.[9] Its geographical location, which is adjacent to Syria and Iraq where Old World CL is also endemic, favors spread of the disease, especially with the increased migration

TABLE 2
Distribution of Syrian and Turkish CL patients according to disease duration, lesion size and number of lesions (mean ± SD)

	Syrian patients (Group 1)	Turkish patients (Group 2)	*P* value
Duration (weeks) (Group 1 = 685, Group 2 = 685)	4.5 ± 4.3	11.9 ± 9.7	< 0.01
Size (mm) (Group 1 = 685, Group 2 = 685)	11.2 ± 8.7	10.7 ± 7.7	> 0.05
Number (Group 1 = 685, Group 2 = 685)	2.46 ± 2.43	1.93 ± 1.47	< 0.05

CL = cutaneous leishmaniasis; SD = standard deviation.

FIGURE 1. Clinical manifestations of cutaneous leishmaniasis (CL) lesions on patients in Sanliurfa, Turkey. Erythematous papular lesions on the dorsum of right hand (**A**), erythematous papular lesions on the forearm (**B**), erythematous papules and nodules on the right cheek (**C**), and erythematous plaque with surface ulceration on the lower leg (**D**).

of refugees due to the Syrian conflict.[10] CL can affect all age groups but infection affects mostly children (5–9 years old). Incidence in the elderly is extremely rare, which is probably due to acquired immunity. Most elderly people will have been infected in early childhood, which will have most probably resulted in long-term immunity.[9] The increased outdoor activity characteristic of children will also increase exposure to the vector in this age group. In this study, the vast majority of both Syrian and Turkish patients were children. This age-based incidence of CL is similar to previous studies on this subject in both Syria and Turkey.[7,9,11–15] Interestingly, in contrast to Syrian patients, a higher female (58.5%) to male (41.5%) ratio was observed in Turkish patients. Similar reports of higher female incidence were observed in a recent study in Nizip, southern Turkey (61% female, 39% male), which is geographically close to Sanliurfa and is also endemic for CL.[10]

TABLE 4
Localization of lesions in Syrian and Turkish CL patients

	Syrian patients (Group 1)	Turkish patients (Group 2)	*P* value
Location (Group 1 = 685 patients, Group 2 = 684 patients)			
Head-neck	223 (32.55%)	302 (44.15%)	< 0.01
Upper extremity	72 (10.51%)	47 (6.87%)	< 0.01
Lower extremity	184 (26.86%)	200 (29.24%)	> 0.05
Trunk	3 (0.44%)	2 (0.29%)	> 0.05
Mucosal	16 (2.34%)	17 (2.49%)	> 0.05
Generalized	187 (27.30%)	116 (16.96%)	< 0.01

CL = cutaneous leishmaniasis.

Differences in the duration of CL were noted between Turkish and Syrian patients in this study. The mean duration of disease of Syrian CL patients at 4.5 ± 4.3 weeks was shorter than that of the Turkish CL patients at 11.9 ± 9.7 weeks. This shorter duration of disease observed in Syrian patients could be due to a number of reasons. First, it is likely that the species and strains of *Leishmania* infecting patients are different in Turkey and in Syria, resulting in a greater duration of the disease in Turkish patients. Causative agents of CL in Turkey are primarily *L. tropica* and *L. infantum*[16,17] which have been shown to have a duration of up to a year or longer. In Syria, the major cause of CL is *L. major*[18] which generally has a shorter duration of 2–8 months. Although unconfirmed, it seems likely that these diverse *Leishmania* species account for the diversity in the duration of disease between the two groups of patients. Unfortunately, the limitations of clinical diagnosis of patients in these countries are often unable to distinguish between species and strains of disease-causing *Leishmania*. A second reason for the observed

differences in disease duration relates to the immune status of patients from Syria and Turkey. Interestingly, recent reports have shown that the increased migration of Syrian refugees into southern Turkey has resulted in the higher incidence of CL due to *L. major* in Turkey.[17,18] As such, acquired immunity against *L. major* in Turkish patients is expected to be far less than in Syrian patients, which could potentially result in increased duration of lesions in Turkish patients. In a previous study of 160 CL patients in Tunisia, the mean duration of the disease was reported to be 12.7 months (range 1–96 months).[19] In another study of CL patients in Turkey by Uzun and others, the mean disease duration was determined as 11–12 months.[7]

An evaluation of the characteristics of CL lesions caused by *Leishmania* species is vital to our understanding of its epidemiology and determining the appropriate treatment approaches for the disease. In this study, the mean diameter of the lesions of Syrian CL patients (11.2 ± 8.7 mm) was similar to that of the Turkish patients (10.7 ± 7.7 mm) and these findings were consistent with previous reports. In a study of 3,074 Turkish CL patients, the mean lesion diameter was reported as 13.3 ± 11.3 mm[7] and in another study in Iraqi patients, lesion diameter was reported to average about 10 mm.[20] Other studies indicate sizes of CL lesions to range between 5 and 200 mm.[11] However, our analysis of lesion numbers between Syrian and Turkish patients in this study revealed significantly greater numbers of CL lesions in Syrian patients. The number of lesions in Turkish CL patients was determined as 1.93 ± 1.47, whereas in the Syrian patient group, the mean number was determined as 2.46 ± 2.43. Previous studies on CL have often reported the number of lesions to be 1–2,[13,19,21] which is consistent with the number reported on Turkish patients in this study. The higher number of lesions in Syrian patients is likely because of multiple insect bites by the sandfly vector which is probably due to the unprotected living conditions peculiar to refugee camps. Another contributing factor could be a delay in access to treatment by Syrian patients who live in the camps. These results highlight the effect of war on the epidemiology of CL, which should affect treatment and control interventions.

The head and neck region was determined in this study to be the area with the most CL lesions in both Syrian and Turkish CL patients. There was least involvement of the trunk in both Syrian and Turkish CL patients. Previous reports have shown that CL lesions are generally seen on uncovered parts of the body and less often on covered areas.[1,14,20–24] This is not surprising since these are the areas that are readily accessible by the sandfly. A study in Turkey by Gurel and others[9] reported the location of CL lesions as 57.5% in the head and neck region, 32.2% in the upper extremities, 10.2% in the lower extremities, 0.8% in oral mucosa, 0.2% on the trunk, and no mucosal involvement. Abdellatif and others[11] reported on lesion locations in Syrian CL patients as 45.8% in the head and neck region, 26.5% in the upper extremities, 24.1% in the lower extremities, and 3.6% on the trunk. With respect to lesion types, results from this study also agree with previous findings. The most frequent type of CL lesion was ulcer in both the Syrian (49.86%) and Turkish (51.68%) CL patients. In both groups, there was no recidivans type of lesion. Yemisen and others[15] reported ulcerated lesions in 58.2% of CL patients, nodular lesions in 30.5%, recidive papules in 5.1% and papular lesions in 4.2%. Another study showed lesion types in CL patients, which were about 35.7% papulo-ulcerated, 59.3% nodulo-ulcerative, and 5% plaque type.[11]

In conclusion, we demonstrated variations in the clinicoepidemiological features of CL between Turkish and Syrian patients within the Sanliurfa province. Specifically, we showed that the disease duration is significantly higher for Turkish patients, whereas the number of lesions is greater in the Syrian patient group. Our results highlight the impact of social unrest and environmental conditions on the epidemiology of CL within this region. Recent reports in a nearby area in southern Turkey, Nizip, revealed a higher threat for the spread of CL following the hosting of refugees due to favorable climactic conditions and increased vector potential.[10] Approaches to prevention, control, and treatment of CL in these areas should take into consideration the emerging changes in clinicoepidemiological parameters of the disease.

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