

# Factors Associated with Early Referral for Pediatric Cutaneous Leishmaniasis

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**ABSTRACT** Determinants of early referral to healthcare providers, which may be useful for health policy, have not been investigated in pediatric cutaneous leishmaniasis with multivariate analyses. We aimed to explore determinants of early healthcare seeking in children with cutaneous leishmaniasis. Records of 1115 children with cutaneous leishmaniasis admitted to our hospital in Adana, Turkey were reviewed. Effects of age, sex, residential distance, lesion number, and facio-cervical onset on early referral were evaluated with multivariate logistic regression analyses. The mean duration of the disease was 12.7 months. Early referral was significantly more likely in patients aged 1-5 and 6-10 years (odds ratio 2.32 and 1.32, respectively) than patients aged 11-18 years. A borderline-significant association was present for faciocervical onset. Early referral in younger children might be due to the fact that the younger the child, the greater the parental concerns about their child's health problems. The rate of late referral in older children may be decreased by some school-based health interventions.

**KEY WORDS:** leishmaniasis, epidemiology, prevention, healthcare utilization, public health

## INTRODUCTION

For the development of a health policy to address an infection, it is useful to know the knowledge, attitude, and practice of the population regarding this infection. Early or late referral to healthcare is among such practices. If early or late referral influences results of treatment in a disease, determination of the factors affecting early or late referral is necessary for efforts to inform and to guide the public.

If left untreated, cutaneous leishmaniasis may heal spontaneously. However, it may leave disfiguring scars. Early treatment reduces such scars. To prevent lifelong scars especially in children, it is necessary to ensure their early referral to healthcare providers. Therefore, first of all, the factors affecting early or late referral must be determined. Although many large

series of pediatric patients with cutaneous leishmaniasis have been reported since 2004 (1-9), the factors affecting early or late referral have not been investigated with multivariate analyses. In this study, we aimed to perform such an evaluation in our pediatric patients with cutaneous leishmaniasis.

## PATIENTS AND METHODS

The demographic and clinical features of our patients with cutaneous leishmaniasis, who were admitted to our tertiary hospital in Adana, Turkey, from 1987 to 2002, have been reported previously (10,11). Although it is a tertiary health center, our hospital (more precisely, our department) has been a well-known healthcare center for patients with cutaneous

leishmaniasis in Adana and its nearest neighboring provinces since the 1990's. Thus, we were the first healthcare providers for almost all of these patients until 2011. In 2011, the Turkish Ministry of Health prepared an action plan for leishmaniasis and put it into practice (12). Thereafter, such patients could not be referred to us directly.

In the present study, we reviewed our records for the years 2003 to 2010. We found a total of 1115 pediatric patients with cutaneous leishmaniasis, whose ages ranged from 1 to 18 years. In all of these patients, the diagnosis of cutaneous leishmaniasis had been established by observation of amastigotes on Giemsa-stained smears taken from clinically suggestive lesions.

In the review of these 1115 patients' records, data concerning their age, sex, and place of residence along with number, site, and duration of their lesions was extracted. When the duration of a lesion was less than 12 months, this referral was classified as early; while in the opposite case referral was classified as late. Similarly, some other categories were also created: age groups (1-5 years, 6-10 years, and 11-18 years), residential distance to our hospital (less and more than one hour by land route; i.e. near and far), number of lesions (solitary and multiple), and location of the first lesion (faciocervical and other).

Statistical analyses were done with IBM SPSS Statistics for Windows, Version 20.0 (13). Pearson's chi-square tests were used for bivariate analyses. In multivariate logistic regression analyses, the dependent variable was referral status (early and late), while independent variables were ones with a *P*-value of less than 0.10 in bivariate analyses. Multivariate analyses were done not only in the whole group of the patients but also were repeated separately in different

age groups. The same independent variables were included in models in these separate analyses, but age in years was used instead of the age group. This study was approved by the Clinical Researches Ethics Committee of the Medical Faculty of Çukurova University (Date: 04.05.2018, Number: 77/22).

## RESULTS

The mean and peak ages of the 1115 patients were 10.0 years (SD=4.5) and 11 years, respectively. Of them, 222 (19.9%) were 1-5 years old; 348 (31.2%) were 6-10 years old; and 545 (48.9%) were 11-18 years old. Women and men were almost equal in number: 566 (50.8%) and 549 (49.2%), respectively. Residences of 732 patients (65.7%) were near our hospital, and those of 383 patients (34.3%) were far from the hospital.

The vast majority of the patients, namely 1090 patients (97.8%), had only a single lesion. Two lesions were present in 21 patients; three lesions in 2 patients; five lesions in 1 patient; and six lesions in 1 patient. In other words, multiple lesions were found only in 25 patients (2.2%). Because of these multiple lesions, there were a total of 1149 lesions in the 1115 patients.

Of these lesions, 822 (71.5%) were located on the face; 25 (2.2%) on the neck; 223 (19.4%) on the upper limbs; 78 (6.8%) on the lower limbs; and 1 (0.1%) on the back. Of the facial lesions, 432 involved the cheeks; 164 the forehead; 84 the chin; 52 the nose; 47 the ears; 28 were around the eyes; and 15 involved the lips. As for the first lesions, they were located on the faciocervical area in 834 patients (74.8%) and on other areas in 281 patients (25.2%).

The mean and median duration of lesions were 12.7 months (SD=12.8) and 12 months, respectively.

**Table 1.** Bivariate analyses of early referral for pediatric cutaneous leishmaniasis

Variables	<i>n</i>	The proportion of patients with early referral (%)	<i>P</i> -value
Age group			<0.001
1-5 years old	222	61.7	
6-10 years old	348	47.4	
11-18 years old	545	39.6	
Sex			0.714
Female	566	47.0	
Male	549	45.9	
Residential distance to our hospital			0.252
Near (≤1 hour by land route)	732	45.2	
Far (>1 hour by land route)	383	48.8	
Number of lesions			0.289
Solitary	1090	46.7	
Multiple	25	36.0	
Location of the first lesion			0.004
Faciocervical	834	48.9	
Other	281	39.1	

**Table 2.** Multivariate logistic regression analysis of early referral for cutaneous leishmaniasis in all children

Variable	Odds ratio	95% confidence interval	P-value
Age group			
1-5 years	2.32	1.68-3.22	<0.001
6-10 years	1.32	1.00-1.74	0.048
11-18 years (reference group)			
Location of the first lesion			
Faciocervical	1.30	0.98-1.73	0.070
Other (reference group)			

Early referral (duration of less than 12 months) was observed in 518 patients (46.5%), and late referral (duration of equal to or more than 12 months) was found in 597 patients (53.5%). The proportion of those with early referral in various subgroups of patients is presented in Table 1. Early referral was significantly more common in children aged 1-5 years than in older children (61.7% versus 47.4% and 39.6%; *P*-value <0.001) and in patients with faciocervical onset than in others (48.9% versus 39.1%; *P*-value =0.004).

In the multivariate logistic regression analysis done in the whole study population, only the age group and location of the first lesion were used as independent variables (Table 2). The age group of 1-5 years (odds ratio [OR] =2.32; 95% confidence interval [CI] =1.68-3.22; *P*-value <0.001) and the age group of 6-10 years (OR=1.32; 95% CI=1.00-1.74; *P*-value =0.048) were significantly associated with the likelihood of early referral compared with the 11-18 age group. A borderline-significant association was present between the likelihood of early referral and the faciocervical onset (OR=1.30; 95% CI=0.98-1.73; *P*-value =0.070).

In the multivariate logistic regression analysis done in patients aged 1-5 years, age showed a significant negative association with the likelihood of early referral (OR=0.73; 95% CI=0.58-0.92; *P*-value =0.008) (Table 3). In other words, increase in age by each one year decreased the odds of early referral by 27% in

this age group. However, there was no effect of age on the likelihood of early referral in other age groups.

In the multivariate logistic regression analysis done in patients aged 1-5 years, the faciocervical onset showed a borderline-significant negative association with the likelihood of early referral (OR=0.42; 95% CI=0.17-1.05; *P*-value =0.064) (Table 3). However, there was a borderline-significant positive association between the likelihood of early referral and the faciocervical onset both in patients aged 6-10 years (OR=1.61; 95% CI=0.92-2.81; *P*-value =0.097) and in patients aged 11-18 years (OR=1.43; 95% CI=0.99-2.07; *P*-value =0.056).

When each year from 2003 to 2010 was evaluated separately, the frequency of early referral was higher in children aged 1-5 years than in older children for almost all years. This frequency ranged between 44% and 80% in children aged 1-5 years, between 25% and 62% in children aged 6-10 years, and between 30% and 53% in children aged 11-18 years.

## DISCUSSION

On June 10, 2020, we conducted a search in PubMed with the following terms, "cutaneous leishmaniasis" and "logistic regression", and found a total of 48 results. Among them, 25 results were studies on Old World cutaneous leishmaniasis. However, none of them used duration of the disease as a dependent variable. On the other hand, searches using other

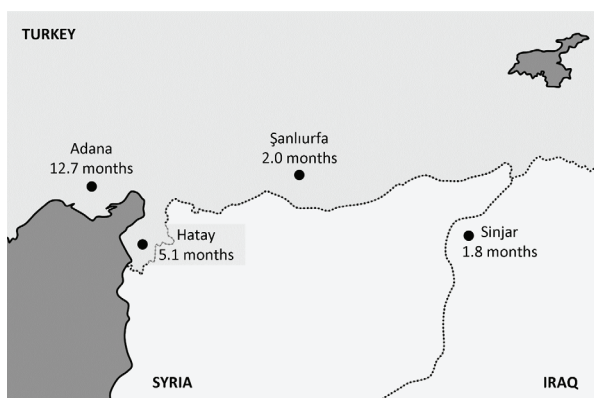
**Table 3.** Multivariate logistic regression analyses of early referral for cutaneous leishmaniasis in three age groups

Variable	Age group		
	1-5 years OR (95% CI)	6-10 years OR (95% CI)	11-18 years OR (95% CI)
Age*	0.73 (0.58-0.92) †	1.05 (0.90-1.22) §	0.95 (0.88-1.03) §
Faciocervical onset	0.42 (0.17-1.05) †	1.61 (0.92-2.81) ‡	1.43 (0.99-2.07) ‡

OR: odds ratio; CI: confidence interval.

\* Each one-year increase in age.

† *P* is equal to 0.008; ‡ *P* is between 0.05 and 0.10; § *P* is more than 0.10.



**Figure 1.** Average duration of pediatric cutaneous leishmaniasis in Adana, Turkey, and in its neighbours.

terms found some studies in which subgroups of patients were compared in terms of duration between appearance of lesions and seeking healthcare.

The average duration in pediatric and adult patients was found to be 12 and 13 months, respectively in a report from Tunisia (14) and 6.53 and 7.77 months, respectively, in a multicentric report from Lebanon, Saudi Arabia, Pakistan, and Syria (9). However, the differences were not significant. In a study from Sri Lanka, clinical features of 88 male and 32 female patients were compared (15). Of these 120 patients, 71 thought that the lesion did not require immediate action since it would resolve spontaneously. Among these 71 patients, men sought medical advice on average 4.8 months after noticing the lesion, while women sought medical advice after 7.1 months. However, the difference was not significant. The average duration in patients with and without head and neck involvement was found to be 5.8 and 6.9 months, respectively, in a report from Lebanon (16). However, the difference was not significant.

We found seven case series which were conducted in different countries of the world and comprised more than 100 pediatric patients with cutaneous leishmaniasis that reported the average duration of the disease and were published between 2004 and 2020. In studies from Tunisia (1), Iran (2), India (5), and Turkey (Hatay) (8) and a multicentric report from Lebanon, Saudi Arabia, Pakistan, and Syria (9), the average duration ranged from 4 to 12 months. Our figure of 12.7 months was slightly over this range. However, another study from Turkey (Şanlıurfa) (6) and a study from Iraq (7) reported this figure to be almost 2 months. As shown in Figure 1, by also taking into account the study from Turkey (Hatay) (8), we may say that, the average duration of disease decreases as one goes eastward from our city; in other words, patients seek healthcare earlier.

Among the five variables (age, sex, residence, lesion number, and site), we found age to have a significant association and faciocervical onset to have a borderline-significant association with early referral among pediatric patients with cutaneous leishmaniasis in Adana, Turkey. The highest frequency of early referral was in the age group of 1-5 years, and early referral was more frequent in the children with faciocervical onset. Moreover, although not strictly significant, faciocervical onset led to early referral particularly in children older than 5 years of age. These findings may be interpreted as described in the next paragraph below.

In younger children, the decision to seek healthcare is made essentially by their parents or other caregivers. On the other hand, older children have significant social relations to persons outside the household. Therefore, their peers and teachers also affect them. The younger the child, the more likely it is that the parents are very anxious about their child's health problems. Thus, they will seek healthcare earlier. Older children start to come face-to-face with more persons outside the household and to worry about their facial skin lesions with the assumption that others will dislike them. Therefore, they will be motivated to seek healthcare and will encourage their parents to seek healthcare earlier.

In contrast to our findings, another study from Turkey (Şanlıurfa) reported that the average duration of the disease to be longest in 0-5 years old children, as compared to children aged 6-10 and 11-15 years (6). As mentioned before, the overall average duration of 2 months in this study was very short, as compared with our figure of 12.7 months. Both of these differences could be explained by the fact that Şanlıurfa has been an endemic area for a longer time, as compared with our city. As long as an endemic state for a disease lasts, healthcare seeking behaviors for this disease will be modified in this endemic area.

In conclusion, healthcare seeking behaviors of pediatric patients with cutaneous leishmaniasis and their parents may vary from country to country, even from region to region. If older children are late in seeking healthcare, school screening for cutaneous leishmaniasis or informing teachers about the disease may be implemented in order to encourage early referral.

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