

Determination factors of affecting the risks of non-recovery in cutaneous leishmaniasis patients using binary logistic regression

Mustafa Aksoy¹, Abdullah Yesilova², Yavuz Yesilova³, Isa An⁴

¹Harran University, Faculty of Medicine Department of Dermatology, Sanliurfa, Turkey

²Yüzüncü Yıl University, Faculty of Agriculture Biometry and Genetics Unit Van, Turkey

³Department of Dermatology, Special Locator Physician Hospital, Van, Turkey.

⁴Akcakale State Hospital Clinic of Dermatology, Sanliurfa, Turkey

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Abstract

Aim: This article aimed to make an assessment by applying the binary logistic regression from the studies reported for cutaneous leishmaniasis patients in the province of Şanlıurfa.

Material and Methods: The age and sex, the type, localization, diameter and number of lesions as well as treatments of 8000 cutaneous leishmaniasis patients were retrospectively recorded in this study. The risk of non-recovery for intralesional (IL) and intramuscular (IM) groups according to independent variables were assessed using a binary logistic regression.

Results: While there was no difference in non-recuperation risk of IL group between genders, males were 39.4% more likely to recuperate than females among the patients belonging to IM groups. All age groups, non-recuperation risk of children were decreased according to the reference level in IL group. As for the IM treatment, non-recovery risk was considered statistically insignificant. During the disease of the patients receiving both IL and IM treatments, non-recuperation risk of the patients of all-week groups was high according to the reference level. When the head and neck region was taken as reference level, the regions with the highest non-recuperation risk of the lesion for IL and IM was identified as generalized and trunk, respectively.

Conclusions: The treatment success rate is inversely proportional with the lesion duration in both IL and IM treatments. There was decreasing in the success rates of both treatments as a result of an increased in lesion size. Increased lesion diameter results in decreased success rates with both treatments.

Keywords: Cutaneous Leishmaniasis; logistic Regression; Parasitic Disease.

INTRODUCTION

Leishmania with flagellate cells is a parasitic disease arising out of a parasite, which has inflicted 350 million people in approximately 98 countries (1,2,3). Every year, nearly 0.7 to 1.3 million new cases have been reported. The leishmaniasis disease develops in different clinical forms depending on the person's immunological status, parasite biology and geographical characteristics of the place of living. This disease progresses with skin involvement (cutaneous), mucosal involvement (mucocutaneous), and also internal organ involvement (visceral). Generally speaking, the clinical picture of leishmaniasis is most often constituted by its cutaneous form (4,5).

Cutaneous leishmaniasis (CL) is divided into two as the

old world leishmaniasis and the new world leishmaniasis depending on the regions where it is seen. The new world leishmaniasis is seen in the Central and Southern America (5). The old world leishmaniasis is observed in the regions of Middle East, Africa, India, Southern and Eastern Mediterranean regions [6]. In Turkey, the old world type leishmaniasis is seen. The agent in the CL disease seen in this country is generally *Leishmania Tropica*. More than 50% of the patients in Turkey are located in the city of Şanlıurfa (7,8,9). Here, the clinical forms of cutaneous and mucocutaneous leishmaniasis are frequently seen (9).

With CL, the lesions are generally seen in the skin areas of the body not covered by clothes such as the hands and face. It frequently develops in the form of a single lesion

Received: 03.07.2018 Accepted: 23.07.2018 Available online: 26.07.2018

Corresponding Author: Mustafa Aksoy, Harran University, Faculty of Medicine Department of Dermatology, Sanliurfa, Turkey

E-mail: derma63@gmail.com

or multiple lesions; sometimes, it may also progress with several skin lesions. The skin signs initially start as pain-free papilla and turn into soft nodules over time. The nodule is generally ulcerated in the middle in the form of a volcano and it improves with cicatrices in 1-1.5 years even if it is not treated (7).

This article aims to make an assessment by applying the binary logistic regression from the studies reported for CL patients in the province of Şanlıurfa.

MATERIALS AND METHODS

In this study, the age and sex, the type, localization, diameter and number of lesions as well as treatments of 8000 CL patients were retrospectively recorded. Patients diagnosed as cutaneous leishmaniasis that had been admitted to Harran University Medical Faculty, Skin and Venereal Diseases outpatient clinic and to the diagnostic center of leishmanial disease affiliated to Şanlıurfa Provincial Health Directorate between 1998 and 2014 were included in this study. Since the study was retrospective, all patients with all registered parameters of age, sex, type of lesion, localization and treatment were included in the study. The patients whose information was missing were not taken to study. To make a detailed statistical assessment of each and every parameter, the patients were divided into sections as follows: Sex: male and female; age: 0-5 years, 5-10 years and 10-15 years; number of lesions: 1-5 lesions, 6-10 lesions, 11-15 lesions and >15 lesions; lesion size: 1-10 mm, 11-20 mm, 21-30 mm and >30 mm; lesion duration: 1-10 weeks, 11-20 weeks, 21-30 weeks and >30 weeks; location of the lesion: head-neck, body, upper extremity, lower extremity, mucosal and generalized; treatment: IL (intralesional) and IM (intramuscular). After that, the patient age, sex, lesion type, localization, diameter and type and the variables influencing the IL and IM meglumine antimoniate (glucantim™) treatments administered to the patients were assessed using binary logistic regression. Ethical approval was obtained from the ethical committee of the Harran University (Number:06.10.2016/08/15).

Statistical Analysis

The required statistical analyzes were performed by Proc GENMOD and Proc LOGISTIC using SAS 9.4 statistical software program [10]. The IL and IM were considered as dependent variable in the model, respectively. On the other hand gender, numbers of lesion, localization, type of lesion, lesion duration and diameter were included in the model as independent variables. While numbers of lesion, year, lesion duration and diameter were considered as continuous dependent variables, gender, localization, and type of lesion were considered as categorical dependent variables. Finally, binary logistic regression was applied to data set.

RESULTS

Table 1 showed that the effects of localization ($p < 0.01$), number of lesions ($p < 0.01$), lesion types ($p < 0.01$), age ($p < 0.01$) and size ($p < 0.01$) on the non-recovery for IL were

found statistically significant while the effects of gender ($p > 0.05$) and duration ($p > 0.05$) were found insignificant.

Table1. Parameter estimates using binary logistic regression for IL

		Binary logistic regression for IL	
		OR (%95 CI)	p-value
Gender	Female 910 (%19.89)	Reference category	0.1832 (overall)
	Male 869 (%22.31)	1.092 (0.974-1.223)	
Age	0 ≤ age ≤ 5 990 (%33.50)	Reference category	<.0001** (overall)
	6 ≤ age ≤ 10 730 (%21.47)	0.563 (0.500-0.633)	
	11 ≤ age ≤ 15 59 (%2.79)	0.056 (0.038-0.067)	
Week	0 ≤ week ≤ 10 1589 (%20.47)	Reference category	0.2350 (overall)
	11 ≤ week ≤ 20 3 (%23.08)	1.621 (0.372-7.055)	
	21 ≤ week ≤ 30 81 (%28.93)	1.268 (0.947-1.697)	
	week ≥ 31 106 (%25.67)	1.024 (0.783-1.340)	
Diameter of lesions (mm)	0 ≤ diameter ≤ 10 1100 (%18.79)	Reference category	0.0023** (overall)
	11 ≤ diameter ≤ 20 265 (%21.12)	1.132 (0.957-1.339)	
	21 ≤ diameter ≤ 30 277 (%27.87)	1.569 (1.314-1.875)	
	diameter ≥ 31 137 (%37.43)	2.542 (1.973-3.275)	
Lesion numbers	0 ≤ lesion numbers ≤ 5 1653 (%20.07)	Reference category	<.0001** (overall)
	6 ≤ lesion numbers ≤ 10 123 (%53.95)	4.667 (3.399-6.409)	
	lesion numbers ≥ 11 3 (%75)	49.230 (4.096-591.641)	
Area of involvement	Head-neck 894 (%22.03)	Reference category	0.0043** (overall)
	Trunk 476 (%18.32)	0.759 (0.663-0.869)	
	Upper extremity 91 (%13.47)	0.577 (0.449-0.742)	
	Lower extremity 5 (%13.89)	0.487 (0.174-1.364)	
	Mucosal 74 (%23.87)	0.977 (0.732-1.303)	
	Generalized 239 (%28.49)	1.549 (1.263-1.899)	
	Lesion type		
	Papul 30 (%9.04)	Reference category	
	Nodul 539 (%17.33)	1.621 (1.083-2.425)	
	Rezidivans 59 (%33.15)	2.772 (1.612-4.767)	
Ulcer 1151 (%23.74)	2.403 (1.605-3.596)		
Intercept	-	0.208 (0.140-0.311)	<.0001

Table 2 displayed that the effect of localization ($p < 0.05$), number of lesions ($p < 0.05$), lesion types ($p < 0.01$), duration ($p < 0.05$), gender ($p < 0.05$) and size ($p < 0.05$) on non-recovery for IM were found statistically significant while the effect of age groups ($p > 0.05$) was found insignificant.

All of the independent variables found to have a statistically significant effect on the non-recovery IL (Table 1) and IM (Table 2) are categorical. Regression methods such as the logistic regression that are based on generalized linear models make parameter estimations by taking one of the independent variable categories as reference [10,11]. For that reason, the reference parameters taken were as follows: female for gender, 0-10 years for age, 0-10 weeks for duration, 0-10 mm for size, 0-5 for the number of lesions, head-neck level for localization and p level for lesion. The way in which the levels of these categorical independent variables of IL and IM were given in Table 1 and Table 2.

Table 2. Parameter estimates using binary logistic regression for IM		
Independent variables	Binary logistic regression for IM OR (%95 CI)	p-value
Gender		0.0127*(overall)
Female 57 (%14.4)	Reference category	
Male 90 (%21.74)	0.606 (0.412-0.893)	0.0113*
		0.3292(overall)
Age		
0 ≤ age ≤ 5 116 (%19.24)	Reference category	
6 ≤ age 1020 (%15.50)	0.769 (0.440-1.344)	0.3560
11 ≤ age ≤ 15 111 (%12.94)	0.655(0.324-1.326)	0.2399
		0.2178(overall)
Week		
0 ≤ week 10131 (%18.56)	Reference category	
11 ≤ week 201 (%33.33)	3.333 (0.261-42.602)	0.3543
21 ≤ week 309 (%24.32)	1.452 (0.636-3.313)	0.3756
week ≤ 316 (%8.45)	0.463 (0.175-1.225)	0.1209
		0.0381*(overall)
Diameter of lesion (mm)		
0 ≤ diameter ≤ 10 92 (%18.81)	Reference category	
11 ≤ diameter ≤ 20 20 (%19.05)	0.966 (0.547-1.707)	0.9062
21 ≤ diameter ≤ 30 25 (%17.61)	0.810 (0.474-1.385)	0.4409
diameter ≥ 31 10 (%12.35)	0.516 (0.242-0.991)	0.0231*
		0.0261*(overall)
Lesion numbers		
0 ≤ lesion numbers ≤ 5 141 (%19.50)	Reference category	
6 ≤ lesion numbers ≤ 10 5 (%5.56)	0.242 (0.092-0.638)	.0041**
lesion numbers ≥ 11 1 (%25)	1.610 (0.134-19.373)	0.7075
		0.0360*(overall)
Area of involvement		
Head-neck 76 (%16.49)	Reference category	
Trunk 44 (%33.33)	2.602 (1.636-4.140)	<.0001**
Upper extremity 6 (%27.27)	1.839 (0.672-5.036)	0.2360
Lower extremity 1 (%20)	1.347 (0.138-13.175)	0.7981
Mucosal 7 (%17.67)	0.853 (0.354-2.058)	0.7241
Generalized 13 (%8.39)	0.620 (0.320-1.179)	0.1427
		0.7112*(overall)
Lesion type		
Papul 1 (%10)	Reference category	
Nodul 44 (%17.25)	1.362 (0.162-11.456)	0.7763
Rezidivans 6 (%10.91)	1.431 (0.140-14.650)	0.7630
Ulcer 96 (%19.32)	1.797 (0.214-15.074)	0.5890
		0.1384
Intercept	-	0.199 (0.024-1.640)

While the risk of non-recovery in men for IL is 1.092 higher as compared to women in Table 1 (OR=1.092: 95% CI: 0.974 to 1.223), it was found statistically insignificant (p>0.05). As seem in Table 2, the risk of non-recovery in men for IL is 39.4% (0.394) lower as compared to women (OR=0.606: 95% CI: 0.412 to 0.893) and this difference was found statistically significant (p<0.05).

In Table 1, the age group of 0-5 years for children was taken as reference; the risk of non-recovery for children in the age group of 6-10 years was found to be 43.7% (OR=0.563: %95 CI: 0.500 to 0.633) lower as compared to the reference level and the risk for non-recovery for children in the age group of 11-15 years was found to be 94.4% (OR=0.056: %95 CI: 0.038 to 0.067) less as compared to the reference level (Figure 1). In Table 2, the age group of 0-5 years for children was taken as reference; the risk of non-recovery for children in the age group of 6-10 years was 23.1% (OR=0.769: %95 CI: 0.440 to 1.344) lower as compared to the reference level and the risk of

non-recovery for children in the group age group of 11-15 years was found 35.5% (OR=0.655: %95 CI: 0.324 to 1.326) lower as compared to the reference level (Figure 1).

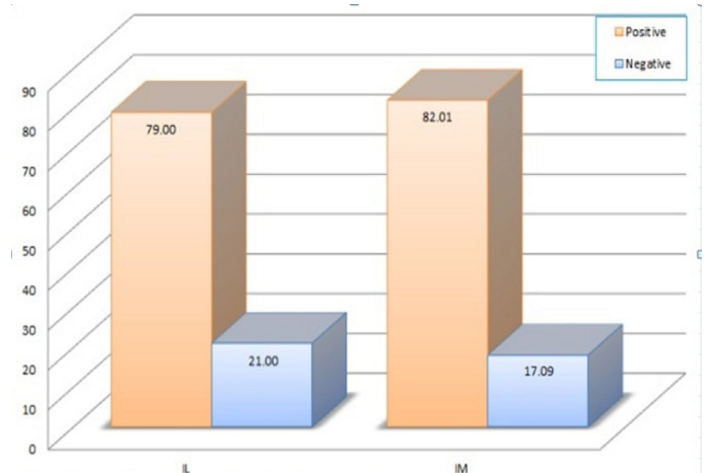


Figure 1. Percentage of positive and negative for IL and IM

In Table 1, for the IL group, the duration of 0-10 days was taken as reference; the risk of non-recovery for children in the group 11-20 days was 1.621 (OR=1.621: %95 CI: 0.372 to 7.055) times higher as compared to the reference level, and the risk of non-recovery for children in the group 21-30 days was found to be 1.268 (OR=1.268: %95 CI: 0.947 to 1.697) times higher as compared to the reference level and the risk of non-recovery for children in the group 31 days and above was found to be 1.024 (OR=1.024: %95 CI: 0.783 to 1.340) times higher as compared to the reference level; however, all of them were found statistically insignificant. In Table 2, for the IM group, the duration of 0-10 days was taken as reference; the risk of non-recovery for children in the group 11-20 days was 3.333 (OR=3.333: %95 CI: 0.261 to 42.602) times higher as compared to the reference level, and the risk of non-recovery for children in the group 21-30 days was found to be 1.452 (OR=1.452: %95 CI: 0.636 to 3.313) times higher as compared to the reference level and the risk of non-recovery for children in the group 31 days and above was found to be 53.7% (OR=0.463: %95 CI: 0.175 to 1.225) lower as compared to the reference level; however, all of them were found statistically insignificant.

In Table 1, for the IL group, the size of '0-10 mm in diameter' was taken as reference; the risk of non-recovery for children in the group '11 mm-20 mm in diameter' was 1.132 (OR=1.132: %95 CI: 0.957 to 1.339) times higher as compared to the reference level (p>0.05), the risk of non-recovery for children in the group 21 mm-30 mm in diameter was found to be 1.569 (OR=1.569: %95 CI: 1.314 to 1.875) times higher as compared to the reference level (p<0.01) and the risk of non-recovery for children in the group '31 mm and above in diameter' was found to be 2.542 (OR=2.542: %95 CI: 1.973 to 3.275) times higher (p<0.01) as compared to the reference level. In Table 2, for the IM group, the size of 0 to 10 mm was taken as reference; the risk of non-recovery for children in the group '11 mm - 20 mm in diameter' was 3.4% (OR=0.966: %95 CI: 0.547 to 1.707) lower as compared to the reference level (p>0.05),

the risk of non-recovery for children in the group '21 mm - 30 mm in diameter' was found to be 19% (OR=0.810: %95 CI: 0.474 to 1.385) lower as compared to the reference level ($p>0.05$) and the risk of non-recovery for children in the group '31 mm and above in diameter' was found to be 49.4% (OR=0.516: %95 CI: 0.242 to 0.991) lower ($p<0.01$) as compared to the reference level.

In Table 1, for the IL group, the group with 0-5 lesions was taken as reference; the risk of non-recovery for children in the group '6-10 lesions' was 4.667 (OR=4.667: %95 CI: 3.399 to 6.409) times higher as compared to the reference level ($p<0.01$) and the risk of non-recovery for children in the group '11 and more lesions' was found to be 49.230 (OR=49.230: %95 CI: 4.096 to 591.641) times higher ($p<0.01$) as compared to the reference level. In Table 2, for the IM group, the group with 0-5 lesions was taken as reference; the risk of non-recovery for children in the group '6-10 lesions' was 75.8% (OR=0.242: %95 CI: 0.092 to 0.638) lower as compared to the reference level ($p<0.01$) and the risk of non-recovery for children in the group '11 and more lesions' was found to be 1.610 (OR=1.610: %95 CI: 0.134 to 19.373) times higher ($p>0.05$) as compared to the reference level.

In Table 1, for the IL group, the head-neck area was taken as reference; the risk of non-recovery for the lesion in the torso area was 24.1% lower as compared to the reference level (OR=0.759: %95 CI: 0.663 to 0.869: p -value <0.01), the risk of non-recovery for the lesion in the upper extremity area was 42.7% lower as compared to the reference level (OR=0.577: %95 CI: 0.449 to 0.742: p -value <0.01), the risk of non-recovery for the lesion in the lower extremity area was 51.3% lower as compared to the reference level (OR=0.487: %95 CI: 0.174 to 1.364: p -value=0.1710), the risk of non-recovery for the lesion in the mucosa area was 2.3% lower as compared to the reference level (OR=0.977: %95 CI: 0.732 to 1.303: p -value=0.8759) and the risk of non-recovery for the lesion in the generalized area was 1.549 (OR=1.549: %95 CI: 1.263 to 1.899: p -value <0.001) times higher as compared to the reference level. In Table 2, for the IM group, the head-neck area was taken as reference; the risk of non-recovery for the lesion in the torso area was 2.602 times higher as compared to the reference level (OR=2.602: %95 CI: 1.636 to 4.140: p -value <0.01), the risk of non-recovery for the lesion in the upper extremity area was 1.839 times higher as compared to the reference level (OR=1.839: %95 CI: 0.672 to 5.036: p -value=0.2360), the risk of non-recovery for the lesion in the lower extremity area was 1.347 times higher as compared to the reference level (OR=1.347: %95 CI: 0.138 to 13.175: p -value=0.7981), the risk of non-recovery for the lesion in the mucosa area was 14.7% lower as compared to the reference level (OR=0.853: %95 CI: 0.354 to 2.058: p -value=0.7241) and the risk of non-recovery for the lesion in the generalized area was 38% (OR=0.620: %95 CI: 0.320 to 1.179: p =0.1427) lower as compared to the reference level.

In Table 1, for the IL group, the papulla lesion type was taken as the reference level; the risk of non-recovery for

children with nodule type lesions was 1.621 times higher (OR=1.621: %95 CI: 1.083 to 2.425: p -value=0.0189) as compared to the reference group and the risk of non-recovery for children with recurrent type lesions was 2.772 times higher (OR=2.772: %95 CI: 1.612 to 4.767: p -value=0.0002) as compared to the reference group and the risk of non-recovery for children with ulcer type lesions was 2.403 times higher (OR=2.403: %95 CI: 1.605 to 3.596: p -value <0.0001) times higher as compared to the reference level. In Table 2, for the IM group, the papilla lesion type was taken as the reference level; the risk of non-recovery for children with nodule type lesions was 1.362 times higher (OR=1.362: %95 CI: 0.162 to 11.456: p -value=0.7763) as compared to the reference group and the risk of non-recovery for children with recurrent type lesions was 1.431 times higher (OR=1.431: %95 CI: 0.140 to 14.650: p -value=0.7630) as compared to the reference group and the risk of non-recovery for children with ulcer type lesions was 1.797 times higher (OR=1.797: %95 CI: 0.214 to 15.074: p -value=0.5890) times higher as compared to the reference level.

DISCUSSION

Treatment with antimonials will heal lesions faster and prevent relapse, local dissemination, mucosal disease (usually), and transmission. Not all lesions require treatment. Old World disease tends to be self-healing, and systemic treatment seldom is used. New World lesions more often require systemic treatment (1,12,13). The use of pentavalent antimonial components in CL treatment is considered to be the golden standard. These have been safely used for a long time as IL or systemic (IM or Intravenous) treatment. Generally speaking, the first treatment for the CL disease is IL pentavalent antimonials thanks to the few side effects and high efficacy (sodium stibogluconate and meglumine antimoniate) (4,14). Systemic treatment is provided in case of no response to the IL treatment. This treatment should be provided at the hospital because of the high number of side effects (4,15).

While there was no difference between genders in the IL patient group with respect to the risk of non-recovery (Table 1 and Table 2), it was identified that men had %39.4 lower risk of non-recovery as compared to women (Table 2 and Figure 2). When the diagnosis for the CL disease is made, IL meglumine antimoniate treatment is often administered. It is easy for patients to access this treatment (They receive treatment at CL centers without going to the hospital). For that reason, no difference may be seen in terms of the effect of sex difference on non-recovery with IL treatment. However, the patient needs to be hospitalized for IM treatment. Since men have more convenient access to hospital amenities for this form of treatment, they receive treatment earlier. Therefore, the rates of non-recovery with IM treatment remain higher among women.

In the IL group of patients, the risk of non-recovery for children (0 age 5) was decreased as compared to the reference level of all age groups. The higher the age, the lower the risk of non-recovery became (Table 1 and Figure 1). However, the risk of non-recovery with the IM treatment was found statistically insignificant as compared to the reference level of age groups (Table 2 and Figure 1).

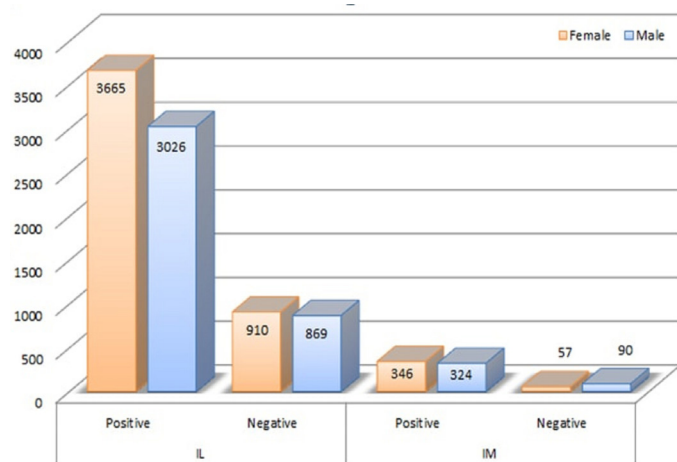


Figure 2. Distribution of gender for IL and IM

Children in the age group of 0-5 have fewer connections with the outer environment in comparison to other age groups. They are under the control of parents and it is very difficult for the parasite to contact their skin. Regarding the skin injuries to occur in this age group, the emergence of suspicion for the CL disease is delayed since they have fewer connections with the outer environment and treatment becomes difficult. The higher the age, the higher the exposure of patients' skins to the parasite is. Treatment is immediately provided upon clinical suspicion. In connection with that, the rates of non-recovery in higher age groups are lower as compared to the age group of 0-5 years. CL patients have a low possibility to receive IM treatment directly. Most often, patients that do not respond to IL treatment are referred. Since there are no obstacles in terms of the time to access treatment, there are no differences among age groups with respect to the effects on non-recovery with IM treatment.

In our study, the risk of non-recovery for patients in all week groups (the disease durations of patients that receive IL and IM treatments) was seen to be high as compared to the reference group (0 week 10), although it was found statistically insignificant (Table 1, Table 2 and Figure 3).

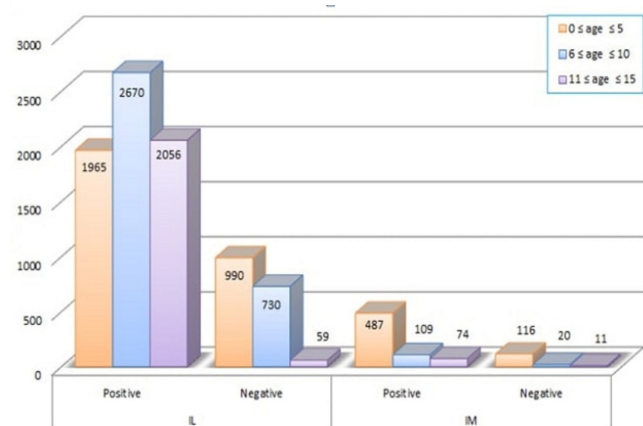


Figure 3. Percentage of week levels for IL and IM

On the other hand, the Leishmania parasite does not cause disease in everyone once it enters the human body. The development of the disease is dependent on

various factors. Factors such as the virulence of the parasite and immune system of the host are effective (add reference). The state of immune system in the initial weeks of the disease and its state in consequent weeks are different. The longer the disease duration is, the worse the adaptation of the parasite to the body is; there may be resistance at stake. For this reason, the longer the disease duration, the lower the response rate to treatment (IL and IM treatment) is.

For CL patients, it was seen that the larger the lesion diameter, the higher the risk of non-recovery from the disease for both IL and IM treatments (when the size measured as 0-10 mm in diameter is taken as reference) (Table 1, Table 2). Generally speaking, the first lesion diameter in the CL disease starts out as small and increases in size over time. In exactly the same way as in the disease duration, the smaller the lesion diameter, the higher the success rate is in parallel with the shortness of lesion duration.

When the group with 0-5 lesions was taken as reference, the risk of non-recovery in children in the IL group increased in parallel with the number of lesions (Table 1). In the IM group, the risk of non-recovery for children only in the group with 6-10 lesions was found to be 75.8% lower than the reference level (Table 2). With the IL treatment, lack of compliance with treatment is increased in parallel with the number of lesions when a separate administration is necessary for every lesion especially in pediatric patients. Furthermore, failure to have enough medicine penetrate every lesion also influences the treatment. These obstacles are at a minimum level at IM treatment and it is possible for every lesion to receive an equal amount of medicine.

When the head-neck area was taken as the reference level, the area with the highest risk of non-recovery was identified to be the generalized area (Table 1). When the head-neck area was taken as the reference level for the IM treatment group, the area with the highest risk of non-recovery of the lesion was identified to be the torso (Table 2). For the CL disease, treatment success rate is increased if the lesion is detected early and it is local. In that sense, a more dynamic immune system of the host and the poor adaptation of the parasite to the host play an important role. For IL treatment, the lesion being widespread (generalized) naturally increases the treatment success rate (Table 1). Our study falls short of explaining our IM treatment results. This may be entirely a coincidence.

When the papilla lesion type was taken as the reference for lesion types, the types with the highest risk of non-recovery in the IL group were recurrent and ulcer lesion types, respectively (Table 1). When the papulla lesion type was taken as the reference for lesion types, the type with the highest risk of non-recovery in the IM group was the ulcer lesion type; however, it was found statistically

insignificant (Table 2). At the junction point of the vector, papilla is seen followed by nodule and ulcer formation

is seen one-three month(s) later [9]. The picture is more complex in proportion with the advance in lesion type, i.e. when the lesion is ulcer and recurrent type. Therefore, this negatively influences both the IL and IM treatment rates.

CONCLUSION

We assessed whether the patient's age, sex, lesion diameter, duration, type and localization had an effect on treatment (IL and IM treatment) in CL patients with the binary logistic regression we applied in our study (figure 4). According to our assessment;

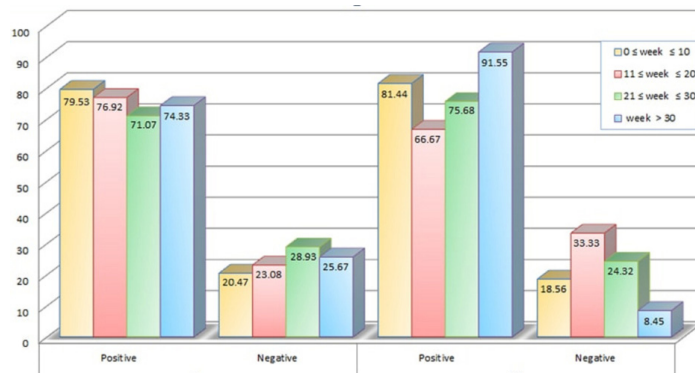


Figure 4. Percentage of positive and negative for IL and IM

1- While the difference in sex did not have any effects on treatment in IL treatment, IM treatment was less effective especially in female patients.

2- Increased age has a positive effect on treatment in IL treatment. There was no difference in IM treatment.

3- The treatment success rate is inversely proportional with the lesion duration in both IL and IM treatments.

4- Increased lesion diameter results in decreased success rates with both treatments.

5- Increased number of lesions reduces the IL treatment success rate. It doesn't have any effects on IM treatment.

6- The lesions being generalized reduce treatment success in IL treatment. The generalized nature of lesions does not seem to have an effect on IM treatment.

7- The treatment success rate is decreased in ulcer and recurrent types with both IL and IM treatments.

Competing interests: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

Financial Disclosure: There are no financial supports.

Ethical approval: Ethical approval was obtained from the ethical committee of the Harran University (Number:06.10.2016/08/15).

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