

## A Clinico-Epidemiological Study of Cutaneous Leishmaniasis in a Non-Endemic Region of South Rajasthan

### Abstract

**Introduction:** Cutaneous leishmaniasis (CL) is a vector-borne protozoal infection of the skin with variable clinical manifestations. In Rajasthan, western Thar desert is endemic for this disease. **Aim:** The present study was aimed to describe clinico-epidemiological features of cutaneous leishmaniasis cases from a non-endemic area of South Rajasthan. **Materials and Methods:** A hospital-based prospective study was carried out during a period of 3 years (2017-2019). Data regarding clinical profile and treatment outcome were recorded in a predesigned proforma for analysis. Diagnosis of CL was made clinically and confirmed by demonstration of amastigotes in microscopic examination of Giemsa stained tissue smear of lesions. **Results:** Out of 24 patients, 16 (67%) were females and 8 (33%) were males. The age ranged from 3 months to 68 years (median-25). Face (67%) and extremities (29%) were the common sites affected. The most common morphological form was crusted plaques (54%) followed by nodular lesions (38%). Slit skin smear for *Leishmania donovani* bodies was positive in all patients (100%). **Conclusion:** This study highlights a focus of CL in non-endemic areas of South Rajasthan. Of late leishmaniasis is breaking out of its classical boundaries and is increasingly being reported from new geographic locations with a possibility of a novel parasite variant. Therefore, a high clinical suspicion of CL should be kept in non-endemic area.

**Keywords:** *Azole antifungals, cutaneous leishmaniasis, nonendemic area, slit skin smear*

### Introduction

Cutaneous leishmaniasis (CL), a protozoal infection caused by *Leishmania* spp. and transmitted by sand fly, is endemic in 88 countries worldwide, including Central and South America, Africa, Asia, and Southern Europe.<sup>[1]</sup> Globally around 350 million people are at a risk of infection and disease, and there are an estimated 1.5–2 million new cases, with 70000 deaths each year.<sup>[2]</sup> In India, the disease is endemic in Thar deserts of Rajasthan and certain parts of Gangetic plains including the states of Punjab, Himachal Pradesh, National Capital Region, and parts of Uttar Pradesh; however, new endemic zones are being reported within and outside these regions as well.<sup>[3-5]</sup>

Few cases of cutaneous leishmaniasis have previously been reported from non-endemic area of Rajasthan.<sup>[5-8]</sup> Herein, we report the clinical and epidemiological features of cases of CL from a tertiary care health centre in South Rajasthan.

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### Materials and Methods

This prospective study was conducted in the skin department at a tertiary care teaching hospital of South Rajasthan during a period of 3-years (2017-2019). All the clinically suspected patients with CL were included in this study. Informed consent was taken from all the patients. Patient's demographic, epidemiological and clinical data were collected using a predesigned proforma. All the cases were interrogated in detail regarding the visit to areas where CL is known to be endemic.

The clinical diagnosis was made by using criteria proposed by Bari and Rahman<sup>[9]</sup> and this was further confirmed by the demonstration of *LeishmanDonovan* bodies in *Leishman* stained slit skin smears and hematoxylin and eosin-stained skin biopsy sections (if slit skin smear is negative). The edge of the lesion was squeezed between the thumb and forefinger to make the area bloodless. A small deep incision

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was made in pinched skin with a small-bladed scalpel. It was turned at 90 degrees and scraped several times in the same direction thus collecting tissue fluid and pulp on one side of the blade. This was gently smeared on at least two glass slides, immediately fixed in 95% ethanol and stained with Giemsa stain. At least 100 different well-stained and preserved fields, mainly in and around the vicinity of mononuclear cells, were examined using light microscopy, first under high power and then with the oil immersion lens to identify Leishman-Donovan bodies, both intracellular within macrophages and lying extracellularly. All the patients were treated with azole antifungals (Itraconazole and fluconazole) except for one who was given intra-lesional sodium stibogluconate. Children  $\geq 5$  years were treated with fluconazole 6mg/kg/day. Children aged 6-12 years were given itraconazole in a dose of 100 mg daily and  $>12$  year aged patients with itraconazole 100 mg twice daily dose. Treatment was continued till complete resolution of lesions. Patients were followed up every 15 days for a reduction in the size of lesions and any side effects of drugs. Liver function tests were assessed at baseline, after 1 month, 3 months, and 6 months.

## Results

Out of a total of 24 patients, 16 (67%) were females and 8 (33%) were males. Table 1 summarizes the demographic and clinical details of the patients. The age of patients ranged from 1 year to 68 years (median-25 year). The majority (19; 79%) of patients belonged to Udaipur district and adjacent villages. Five patients belonged to other districts. Duration of disease ranged from 15 days to 1 year (Median-11.25 months). The total number of lesions was 27; 21 (87.5%) patients had a single lesion while 3 patients (12.5%) had two lesions. Face was the most commonly involved site (16; 67%), followed by extremities (7; 29%), upper trunk, and neck (2 each). The most common clinical variant was crusted plaques [Figures 1a, b and 2a, b] seen in 13 (54%), followed by nodular [Figure 3a and b] seen in 9 (38%), and nodulo-ulcerative 2 (8%). The size of lesions varied from 1cm to 6 cm. Mucosal involvement in the form of lower lip lesion was seen in one patient. A definite history of insect bite was present in one patient. There was no history of sleeping outdoors and living in mud houses in any of the patients. Family history was present in one patient. Only two patients admitted to a definite history of visit to a known endemic region.

**Table 1: Clinical and demographic profile of patients with cutaneous Leishmaniasis**

Age (years)	Sex	No. of lesion(s)	Site	Type of lesion(s)	Duration	Treatment	Treatment duration (Days/months)	Scarring
45	M	1	Right upper chest	Nodulo-ulcerative	8 months	Itra 100mg BD	4 months	Yes
53	F	2	Left arm, Left wrist	Nodular	4 months	Itra 100mg BD	3 months	Yes
9	F	1	Nose	Nodular	6 months	Itra 100mg OD	4 months	Yes
35	F	1	Right hand	Crusted plaque	3 months	Itra 100mg BD	1 month	Yes
1	F	1	Nearright eye	Crusted plaque	15 days	Flu 200mg twice a week	15 days	No
55	F	1	Left side neck	Nodulo-ulcerative	15 days	Itra 100mg BD	1 month	Yes
13	M	1	Left cheek	Crusted plaque	1 month	Itra 100mg BD	1 month	Yes
20	F	2	Nose, right angle of mouth	Crusted plaque	6 months	Itra 100mg BD	4 months	Yes
45	F	1	Nose	Nodular	15 days	Itra 100mg BD	2 months	No
68	F	1	Right eyelid	Nodular	3 months	Itra 100mg BD	1 month	No
35	F	1	Right cheek	Nodular	1 year	Itra 100mg BD	3 months	Yes
2	F	1	Nose	Nodular	6 months	Flu 200mg three times a week	1 month	No
11	F	1	Nose	Crusted plaque	5 months	Itra 100mg OD	2 months	No
24	F	1	Right cheek	Nodular	5 months	Itra 100mg BD	3 months	Yes
26	M	1	Right hand	crusted plaque	3 months	SSG (100mg/ml)	2 months	No
7	M	1	Nose	Nodular	6 months	Itra 100mg OD	2 months	No
26	M	1	Below left eye	Crusted Plaque	3 months	Itra 100mg BD	1 month	Yes
6	F	1	Nose	Plaque	1 year	Itra 100mg OD	1 month	Yes
8	F	1	Right cheek	Crusted plaque	6 months	Itra 100mg OD	3 months	Yes
11	M	2	Right cheek, Left hand	Crusted plaque	3 months	Itra 100mg BD	2 months	Yes
12	F	1	Left cheek	Crusted plaque	4 months	Itra 100mg BD	2 months	Yes
47	M	1	Left forearm	Nodular	5 months	Itra 100mg BD	1 month	Yes
27	M	1	Left arm	Crusted plaque	1 year	Itra 100mg BD	1 month	Yes
62	F	1	Left hand	Crusted plaque	2 months	Itra 100mg BD	2 months	No

Flu: Fluconazole, Itra: Itraconazole, SSG: Sodium stibogluconate, OD: Once daily, BD: Twice daily





Figure 1: (a) Erythematous crusted plaques over bridge of nose and right angle of mouth; (b) Post-inflammatory hyperpigmentation and scar over bridge of nose 4 months post-treatment

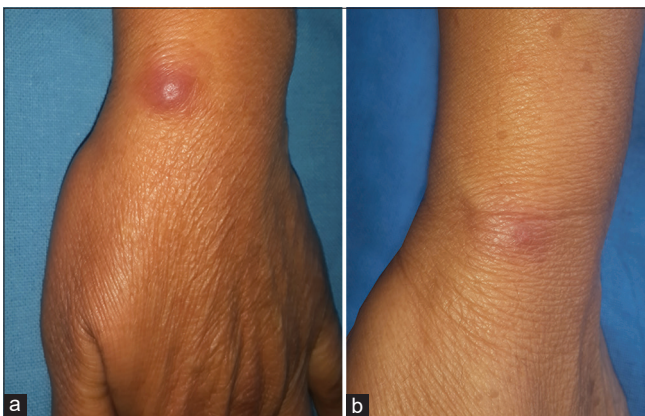


Figure 3: (a) Erythematous nodule over left wrist; (b) Regression of the nodule over left wrist (3 months post-treatment)

Slit skin smear for *Leishmania donovani* bodies [Figure 4] was positive in all patients. All except one patient were treated with azole antifungals. A total of 21 patients were given itraconazole (16- twice daily, 5- once daily). One patient was treated with intra-lesional sodium stibogluconate at a dose of 0.5 ml/cm<sup>2</sup> (100 mg/ml solution) of lesion once a week for 8 weeks. Patients showed regression of lesions [Figures 1b, 2b and 3b] over a period of 15 days to 4 months (median-2months). Scarring was seen in 16 patients (67%). No side effects were noted in any patient. None of our patients reported relapse of disease activity during a 6 months follow-up.

### Discussion

Cutaneous leishmaniasis is a widely distributed vector-borne disease caused by several species of *Leishmania* including *L. major*, *L. Tropica*, and *L. aethiopica* (together known as *L. tropica* complex) in

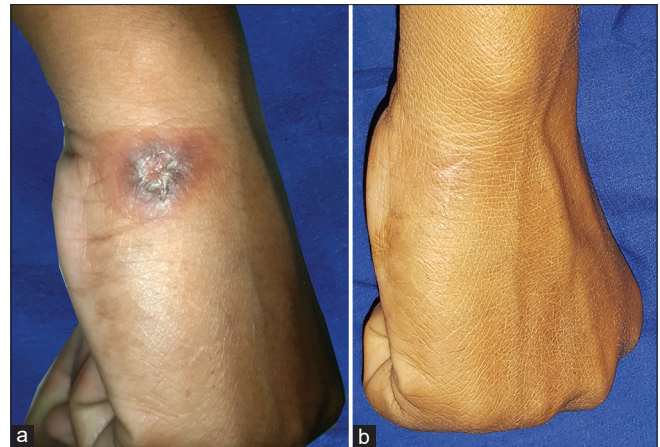


Figure 2: (a) Erythematous to hyperpigmented plaque over right hand; (b) Post-treatment scarring over right hand after 1 month

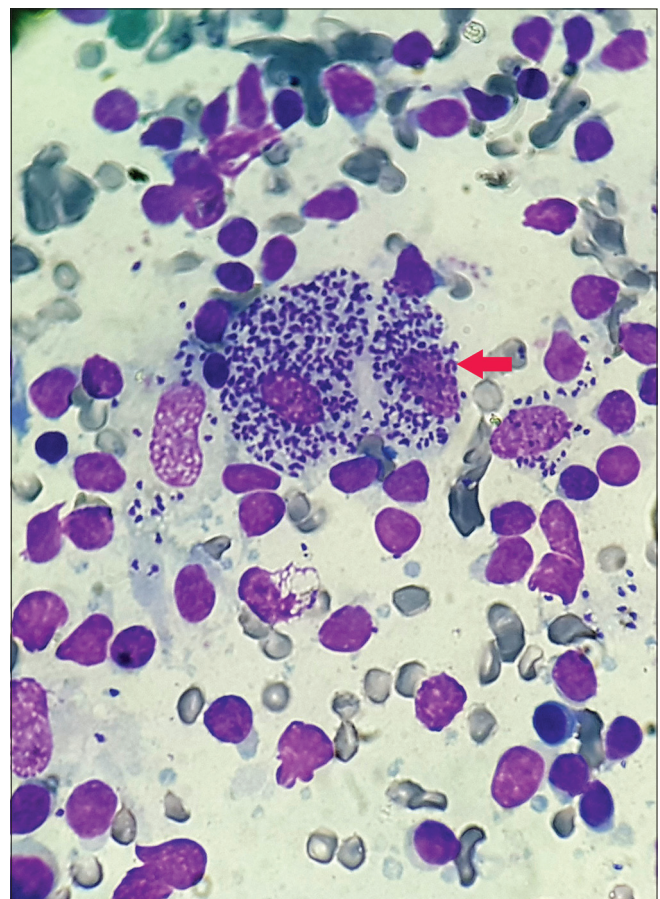


Figure 4: Multiple intracellular and extracellular *Leishmania donovani* bodies (red arrow) in slit skin smear (Giemsa stain, x100)

the old world and *L. braziliensis* and *L. mexicana* in the new world.<sup>[10]</sup> CL is an endemic disease of tropics but now spreading to areas that were previously known to be non-endemic. New endemic foci of infection are being observed in India too.<sup>[11]</sup> In India cases of CL have been reported from Thar deserts of Rajasthan, Punjab, and Kerala where it is mainly caused by *Leishmania tropica* and now recently from Himachal Pradesh due to

*Leishmania donovani* and *L. tropica*.<sup>[12,13]</sup> CL has been rarely reported from South Rajasthan.

In our study, a female preponderance was found. In total 16 out of 24 patients (67%) were females. This may be due to greater cosmetic concern in women. This finding is consistent with some earlier studies.<sup>[3,13]</sup> Face and extremities were the sites commonly involved in our study. Kaul *et al.*<sup>[3]</sup> and Sharma *et al.*<sup>[14]</sup> also noted lesions on the face to be the most common. Most patients (21; 87.5%) had single lesion, a finding comparable with other studies.<sup>[2,13,14]</sup>

The usual clinical picture of cutaneous leishmaniasis varies from erythematous papules to nodulo-ulcerative forms, and, lesions are mostly seen on the exposed parts of the body.<sup>[15]</sup> In our patients crusted plaque was the most common.

The clinical diagnosis of CL in endemic areas is easy. The diagnosis can be rapidly confirmed by demonstration of amastigotes in skin smears. Skin biopsy and cultures can be done in some patients. Modern methods for the diagnosis, including immunofluorescence, use of monoclonal antibodies, DNA probes, polymerase chain reaction, and electron microscopy have limited value as these are expensive and time-consuming and are not routinely employed.

Skin smears demonstrated amastigotes (*Leishman-Donovan* bodies) in all of our cases [Figure 4]. The rate of high skin smear positivity is in accordance with a few other studies.<sup>[6,16]</sup> Demonstration of parasite in direct smears remains the easiest and the most specific method of diagnosis. The smear is positive in 5070% of the cases, depending on the duration of lesions; newer lesions being more likely to yield the parasite. At times when the smear is negative, possibility of lupus vulgaris and deep mycosis should be kept in mind. Organisms are scarce and difficult to identify in histological examination stained with H and E stain.

Azoles have been reported to be an effective treatment in CL<sup>[7,17-19]</sup> and several studies have demonstrated the *in vitro* and *in vivo* efficacy.<sup>[20-22]</sup> Oral fluconazole has been successfully used in the treatment of CL, especially in children.<sup>[23]</sup> Most of our patients were treated by azole antifungals and were found to be efficacious, without any side effects. Intralesional sodium stibogluconate was used in one patient as the patient had impaired liver function tests. Although sodium stibogluconate was advocated as the first-line therapy in past, its use now has become limited due to its non-availability, the emergence of resistance, and pain during injection.<sup>[1,24]</sup>

### Limitation of study

The study population was small and we could not succeed in the identification of the species of *Leishmania* and search for any animal reservoir. Also culture, histology and

serology were not performed. Furthermore, only suspected cases were enrolled in the study and we could have missed non-suspected Leishmaniasis patients.

### Conclusion

Cases of CL may be missed in non-endemic regions. Therefore, a high index of clinical suspicion should be kept in mind in such areas. The emergence of CL in non-endemic area is of great epidemiological importance. This may be considered as indirect evidence of a new indigenous focus of CL.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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