

*Editorial*

Cutaneous leishmaniasis in India

Devinder Mohan Thappa¹ , Nidhi Ramesh¹, Avani Sai Gajula¹¹Department of Dermatology, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India.***Corresponding author:**

Nidhi Ramesh,
Department of Dermatology,
Jawaharlal Institute of
Postgraduate Medical
Education and Research,
Puducherry, India.

nidhiramesh3021@gmail.com

Received: 05 January 2024

Accepted: 06 January 2024

Published: 29 January 2024

DOI

10.25259/CSDM_7_2024

Quick Response Code:

Leishmaniasis comprises protozoal infections caused by different *Leishmania* species transmitted by sandflies. Over 20 *Leishmania* species are implicated and are classified as Old and New World groups. Old World species (including *Leishmania major*, *Leishmania infantum*, *Leishmania aethiopica*, and *Leishmania tropica*) are transmitted by female sandflies of the *Phlebotomus* genus. In contrast, New World species (such as *Leishmania amazonensis*, *Leishmania mexicana*, *Leishmania panamensis*, *Leishmania braziliensis*, and *Leishmania guyanensis*) are transmitted by sandflies of the genera *Lutzomyia* and *Psychodopygus*.

The disease can manifest as cutaneous leishmaniasis (CL), mucocutaneous leishmaniasis, and visceral leishmaniasis (VL) (and its sequela, post-kala-azar dermal leishmaniasis [PKDL]). The manifestation depends on parasite species, host genetics, immune system, nutrition, and possible coinfections.

Leishmaniasis is recognized by the World Health Organization as a neglected tropical disease. According to the 2019 Global Burden of Disease study, there were an estimated 4.6 million prevalent cases of CL mainly concentrated in Central and South America, Southern Europe, Central Africa, and parts of Southern and Central Asia. By 2022, 90 countries across five continents had reported endemic CL.

Annually, from 2019 to 2022, around 212,000 new cases were reported worldwide with roughly 85% of CL cases originating from eight countries: Afghanistan, Algeria, Brazil, Colombia, the Islamic Republic of Iran, Iraq, Peru, and the Syrian Arab Republic.

The disease often enters non-endemic countries through immigrants and returning travelers, and a rising trend has been seen over the past two decades. Recent concern has emerged due to coinfections of *Leishmania* with human immunodeficiency virus (HIV), as HIV-infected individuals exhibit more extended periods of parasitemia potentially serving as reservoirs for the parasite. This factor may contribute to the increased disease incidence in specific areas.

The CL in India has historically been confined to specific regions within the Thar Desert of Rajasthan State and parts of the Gangetic plains. However, emerging endemic foci are being identified in Kerala, Punjab, Assam, Haryana, Delhi, Jammu, and Kashmir, primarily caused by *L. tropica*. Atypical forms of leishmaniasis have surfaced in Kerala and Himachal Pradesh attributed to *Leishmania donovani*.

The most commonly reported cutaneous variant in India is the noduloulcerative or Oriental sore followed by ulcerated plaques. Rarer variations such as lupoid, psoriasiform, verrucous, rhinophymatous, and impetigo-like lesions have also been documented. These lesions typically appear singularly on exposed skin.

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The spread of CL within India hints at potential local transmission facilitated by local vectors and reservoirs. While some studies suggest purely human-to-human transmission without intermediate hosts, others indicate the likelihood of animal reservoirs. Identified vector species transmitting the infection in the Indian subcontinent include *Phlebotomus papatasi* and *Phlebotomus sergenti*.

Most patients affected are young adults residing in rural areas near forests living in houses made of mud walls and earthen floors with livestock nearby and actively engaged in agricultural activities.

The overall decrease in reported cases in earlier affected areas in India is credited to changes in vector habitats, government-initiated insecticide sprays, and improvements in sanitation practices. With urbanization reducing outdoor sleeping and animal husbandry practices, there is decrease in sandfly exposure. However, recent surges in new endemic areas appear to be linked to natural disasters, deforestation, construction projects, conflict, and immunosuppression.

The CL was historically present in Rajasthan's Thar Desert, notably centered around Bikaner due to its hot semi-arid climate, ideal for sandfly reproduction. During the 1960s, concurrent with the successful malaria eradication efforts, malaria and CL saw a decline in this region. However, after the cessation of these programs, CL has recently resurfaced. In 1994, 142 smear-positive cases were reported in a study while a recent survey conducted over 10 years (2001–2011) reported 1379 smear-positive cases. In addition, there are emerging reports of cases from southern Rajasthan.

Jammu and Kashmir, particularly near the Chenab river near Himachal Pradesh to the North, has recently experienced a rise in disease occurrence. A 10-year prospective study (2009–2019) reported 1300 cases. Cases are predominantly seen in the Poonch and Rajouri districts in the Jammu division and Kupwara and Baramulla districts in the Kashmir division, which border areas in Pakistan such as Muzaffarabad, Punjab, and Pakistan Occupied Kashmir, where CL is widespread. This region has relatively warmer temperatures, experiencing hot and arid summers and cold, dry winters with sub-zero temperatures creating favorable conditions for *Leishmania* and *Phlebotomus*.

The CL was not known in Himachal Pradesh until the late 1980s. A recent study identified 161 localized CL cases over two years (2001–2003). The disease mainly affects regions along the Satluj River with subtropical and temperate climates. Interestingly, this area experiences both cutaneous and visceral forms of the disease with the latter being more frequent. The visceral disease, caused by *L. donovani*, is predominant in the southeastern region along the Sutluj and Ravi river belts. Atypical CL by *L. donovani* has been reported in Kinnaur, Shimla, and Kullu along the Satluj river.

Molecular analysis revealed novel variants of *L. donovani* as the primary cause of CL in Himachal Pradesh with fewer cases linked to *L. tropica* and *L. major*.

Since 2009, Kerala has emerged as a notable area affected by CL, particularly within the Kanikkaran tribe and tribal villages in the Agasthyamala Biosphere Reserve forest along the Western Ghats with 27 cases reported here. The manifestation of the disease is unusual, characterized by clinical isolates identified as *L. donovani* variants, with *Phlebotomus argentipes* identified as the prevailing vector species in this region. The genetic lineage of the parasite closely aligns with isolates from neighboring Sri Lanka forming a unified biogeographical unit alongside the Western Ghats. In addition, a few instances of indigenous VL cases have also been documented in this area.

The PKDL is considered an immunological manifestation of VL, which is more commonly observed after the apparent cure of VL in India, around Two to three years after treatment for VL, though it can occur concurrently. Most PKDL cases are concentrated in six countries, notably India, contributing to 75% of these cases followed by Sudan (9%), South Sudan (8%), and Bangladesh (7%). Within India, Bihar (94%) reports the highest prevalence followed by West Bengal (1.4%), Jharkhand (0.7%), and Uttar Pradesh (3.5%). A peak of 1982 cases was reported in 2017, and a decline in prevalence has been observed since with only 617 PKDL cases reported in 2020. Mixed/polymorphic lesions are the most common form followed by hypopigmented macular and papulonodular lesions. Unusual clinical lesions include erythrodermic, fibroid type, plaque, and ulcerated skin lesions.

The transition from VL to PKDL or their simultaneous appearance is suspected to involve inadequate treatment, ultraviolet-B radiation exposure, and host genetic factors. While PKDL is not a life-threatening disease, it carries significant socioeconomic implications. More importantly, in the Indian subcontinent, as the transmission of VL is anthroponotic, unattended cases of active PKDL serve as reservoirs of *L. donovani* in VL endemic areas, especially during the inter-epidemic period, posing a substantial threat to the VL elimination program. Consequently, prioritizing PKDL eradication within the ongoing VL elimination efforts is essential to achieve the targeted goal of <1 case/10,000 individuals at the district or subdistrict levels in VL endemic areas. We are approaching the elimination of VL; yet, cases of CL might slip under the radar in regions where the disease is not traditionally prevalent. Thus, it is crucial to maintain a high level of clinical suspicion in these areas.

The CL is intruding into newer regions along with findings of atypical leishmaniasis in the known and more unexplored disease territories. New endemic foci with atypical leishmaniasis should be identified since atypical

VL and CL disease often exhibit peculiar variations in disease severity and duration and can serve as reservoirs of the disease. While the newer geographical niches endemic to the disease warrant more comprehensive implementation of the control programs, continuous monitoring of the disease type and the associated parasite species and their variants should be implemented as part of the ongoing leishmaniasis elimination and maintenance programs. Achieving the goal of

VL elimination should encompass a comprehensive approach that also addresses the elimination of CL. In addition, the role of PKDL patients as a reservoir for leishmaniasis transmission should be considered since even a single PKDL case can trigger a new outbreak of VL.

How to cite this article: Thappa DM, Ramesh N, Gajula AS. Cutaneous leishmaniasis in India. *CosmoDerma*. 2024;4:8. doi: 10.25259/CSDM_7_2024