



## Clinico-epidemiological Trends of Cutaneous Leishmaniasis along the Satluj Valley of Himachal Pradesh-A new focus with emerging infection

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### Abstract

**Background:** Cutaneous leishmaniasis (CL) is an endemic disease in well defined regions across the globe. Bihar, Uttar Pradesh (UP) and deserts of Rajasthan are well known foci for CL in India. But recently, subalpine valley along the Satluj River has been identified as a new emerging focus for CL in Himachal Pradesh.

**Methods:** All newly diagnosed cases of CL were registered and detailed clinico-epidemiological parameters were recorded. Imprint smears for LD bodies and biopsy for histopathology were done in atypical cases to confirm clinical diagnosis. Children less than 18 years, unconfirmed cases and those patients who lost on follow up examination were excluded out from this study.

**Results:** Out of total 337 registered cases, 222 adults including 121 females and 101 males were enrolled for this study. Most of the cases were affected in the age group of 20-40 years. Face and neck were commonly affected sites in 64.41%. Psoriasiform plaques and nodules were most frequently observed clinical types in 41.44% and 40.09% cases respectively. Most (72%) of the cases had single lesion and duration of lesion ranged between 1-6 months in 81.98% cases. All cases were treated effectively with intralesional injection of sodium stibogluconate (I/L SSG). Most cases recovered completely after 2<sup>nd</sup> cycle of I/L SSG, only 2(0.9%) patients took 5 months for complete recovery. Immediate side effects like pain, swelling and bleeding were observed almost in every patient while post inflammatory hyper pigmentation, scarring and millia formation were observed as long term side effects.

**Conclusion:** CL is still emerging and spreading along Satluj valley of Himachal Pradesh (HP). We recommend skillful diagnosis, availability of diagnostic tests, annual record keeping and reporting in this institute. So that exact disease burden can be identified to promote the effective treatment and preventive measures in coming future.

**Keywords:** Leishmaniasis, Epidemiology, Emerging, Himachal Pradesh (HP).

## INTRODUCTION

Leishmaniasis is a protozoal disease caused by various species of leishmania parasite. It is transmitted by the bite of infected female sandfly of *Phlebotomus* and *Lutzomyia* species. Disease is endemic in approximately 98 countries across the world. <sup>[1]</sup> According to WHO, 1 to 1.5 million new cases of CL and 400,000 to 600,000 new cases of VL are detected every year. <sup>[2]</sup> The global prevalence of the disease is estimated as 12 million cases, further 350 million people are considered at risk of contracting the infection. <sup>[3]</sup>

Leishmaniasis is amongst the top 5 diseases targeted by WHO under special research programme for tropical diseases. <sup>[4]</sup>

Clinical types are cutaneous leishmaniasis (CL), mucocutaneous leishmaniasis (MCL), diffuse cutaneous leishmaniasis (DCL) and most lethal type is known as Kala-Azar or visceral leishmaniasis (VL). CL is caused by leishmania tropica complex in old world and by *L. braziliensis* complex in the new world. <sup>[5]</sup> More than 90% cases of CL occur in developing countries like Afghanistan, Algeria, Brazil, Iran, Iraq, Peru, Saudi Arabia and Syria. <sup>[6]</sup> In India, disease is prevalent in specific areas of Bihar, West Bengal, Uttar Pradesh, Assam, deserts of Rajasthan and the foothills of Sikkim. <sup>[7]</sup> Sharma et al firstly reported 38 new cases of CL during 1988 to 2001 from the Satluj valley of HP. <sup>[8]</sup> Between 2001-2003 *L.tropica* and *L.donovani* were identified as causative protozoan and *phlebotomus longiductus* as the transmitting vector for CL in this area. <sup>[9]</sup> The recent emergence of CL along this region of HP appears to be due to extensive deforestation and construction activities (disturbing the sylvatic cycle) due to establishment of major hydroelectric projects along Satluj River. Labor employment from Bihar, Jharkhand, Uttar Pradesh and Nepal (endemic areas for leishmaniasis) is supposed to introduce the causative parasite. Further, cattle rearing, farming and horticulture activities by rural inhabitants are known to attract both anthropophilic and zoophilic vectors. <sup>[7]</sup>

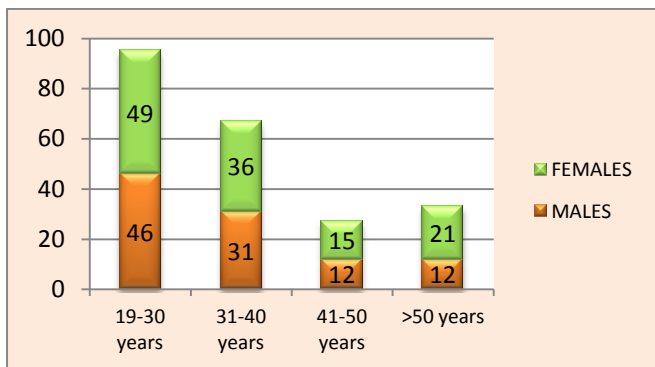
Moreover, survival and adaptation of vector, as well as the parasite in bizarre habitats is well described by various studies also. <sup>[10, 11]</sup> We conducted this study at MGMSC, Khaneri-Rampur, a hospital, draining the patients from all prevalent foci lying nearby to Satluj River. The alarming increase of new cases in the routine skin OPD and unavailability of data after 2003 on such a prevalent disease, prompted us to evaluate the disease burden in this region.

## MATERIAL AND METHODS

All newly diagnosed cases of CL were registered from August 2016 to September 2017. Demographic profile including age, sex, occupation, locality, family history and history of high risk activities (keeping domestic animals, farming/horticultural activities) were recorded. Clinical details about number, size, site, duration and type of lesion were also noted down. The diagnosis of CL was mainly based on the clinical criteria proposed by Kubba and AI- Gindan. <sup>[12]</sup> In typical cases treatment was initiated after clinical diagnosis while in atypical/ doubtful cases, imprint smears for Leishman Donovan (LD) bodies and tissue smears for histopathology were taken. As facilities for Novy-MacNeal-Nicolle (NNN) culture medium and PCR were not available in this institute so unproven cases were referred to higher centre for further workup. Thus old cases, children (<18 years) and unconfirmed cases were excluded out from this study. All cases of CL were started on I/L SSG on three alternate days per month. Monthly follow up visits were conducted to note down the treatment response along with minor side effects.

## RESULTS

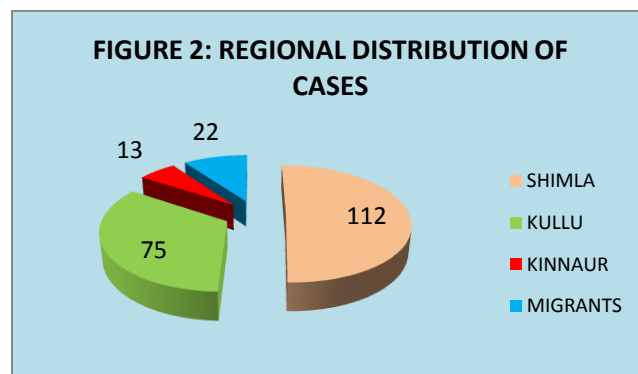
Out of total 337 registered cases of CL, 222 adults including 121 females and 101 males (M: F=1:1.20) were studied. Almost all age groups were affected but 19-30 years age group was most commonly affected. (Figure 1)



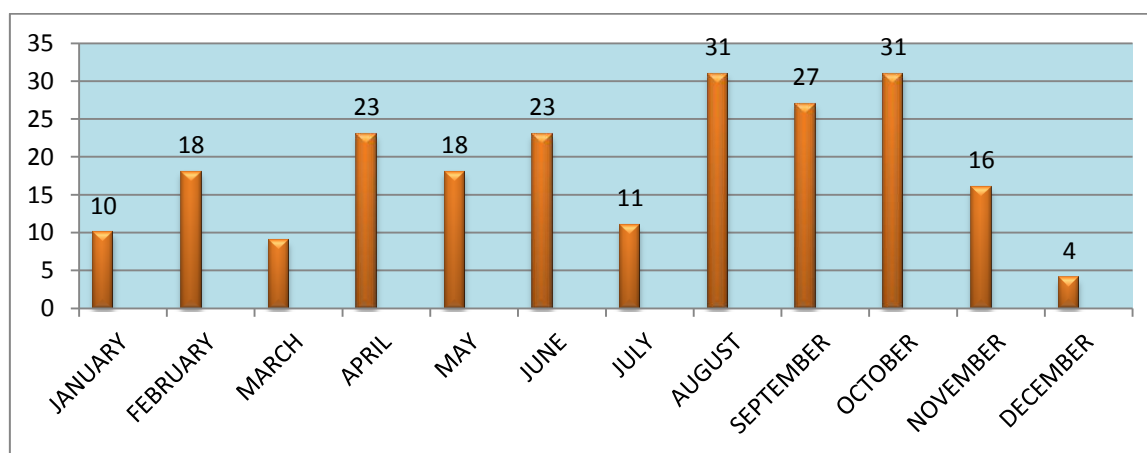
**Figure 1:** Age and sex wise distribution of cases

Farmers (41.89%), laborers (31.53%), house wives (10.6%), employees (9.46%) and students (6.30%) were predominantly affected professions. Family history was positive in 14(6.30%) cases while history of keeping domestic animals was found in 48(21.62%) cases. Rampur is a rural town situated on the bank of Satluj River and inhabited by mixed local population. Further, the establishment of multiple hydroelectric projects in this area has resulted in migration of mass population from Nepal, UP, Bihar and

Uttarakhand. The dwellings are located close to the river and surrounded by abundant vegetation. So we observed that all patients were exposed to vector in the domiciliary and peridomiciliary area. Most of the patients were inhabitants of district Shimla (Rampur division); Kullu (Nirmand block) and Kinnaur (Tapri division) while 9.91% were migrants from other states. (Figure2)



Although patients visited the hospital throughout the year but their number was comparatively higher in the months of August, September and October as shown in figure 3.



**Figure 3:** Month wise distribution of cases (n)

A total of 309 lesions were observed in 222 patients. Time between the onset of skin lesion and clinical diagnosis ranged from 2 weeks to 2 years. Most (81.98%) cases presented between 1-6 months of lesion onset, while 18(8.11%) cases presented between 6-9 months, 14(6.31%) cases after 9 months while 8(3.60%) cases within 1 month of lesion onset. Most (72.07%) cases presented with one lesion, 37(16.67%) with two lesions, 13(5.86%) with three lesions, 5(2.25%) with four lesions and only 7(3.15%) patients had

more than five lesions. As per morphology; plaques and nodules were observed more frequently in 92 (41.44%) and 89(40.09%) cases respectively. Other types of lesions have been described in figure 4. Lesions were present predominantly on exposed body sites. In 90.54% cases face and neck were primarily affected sites. Lesions were also present over upper limb, trunk and lower limb as shown in figure 5. In 26 (11.71%) patients with multiple lesions, more than one body sites were affected.

FIGURE 4: MORPHOLOGICAL DETAILS

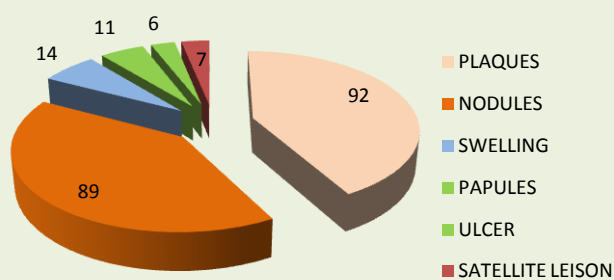
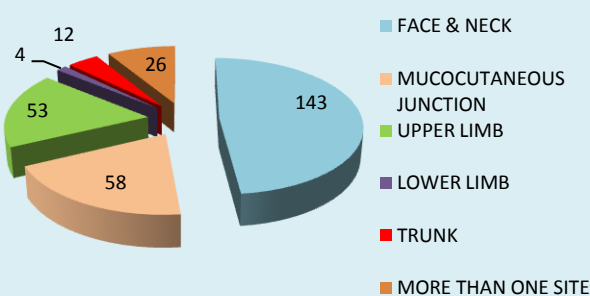


FIGURE 5: LESIONAL DISTRIBUTION



In 46 cases biopsies were performed for HPE and imprint smears. Histopathology reports revealed chronic granulomatous inflammation comprised of parasitized macrophages, lymphocytes, epithelioid and plasma cells in 84.8% (39/46) cases with intracellular LD bodies only in two (4.35%) cases. While imprint smears were detected positive for LD bodies in 52.16% (24/46) cases. All cases were treated with 0.5–5 ml (100 mg/ml) of SSG per lesion on three alternate days per month (one cycle). In most (78%) cases complete healing was observed by the end of 2<sup>nd</sup> month. Further, 34(15.31%) cases recovered after 3<sup>rd</sup> months and 11(4.95%) cases took 4 months for complete recovery. Only 2(1.35%) resistant cases with diffuse involvement of face by multiple lesions took 5 months for complete healing. As per side effects; severe pain and swelling were noticed almost in every case during I/L SSG infiltration. Bleeding, ulceration and secondary infection were early side effects observed in 46.84%, 32.9% and 9% cases respectively. Post treatment hyperpigmentation, scarring (hypertrophic and atrophic) and millia formation were observed in 33.3%, 20.7% and 2.25% cases respectively.

4(1.8%) cases treated for lesions over chin region, presented later with enlargement of submandibular lymph node. USG and FNAC revealed it as reactive lymphadenitis with no evidence of leishmaniasis in the lymph node.

## DISCUSSION

Leishmaniasis is thought to be a disease of low altitude, with no occurrence of cases above 2000 feet (600 m)<sup>3</sup>. However, recently number of cases has been reported from subalpine valley of HP.<sup>[7]</sup> CL was not known to occur in Himachal Pradesh before 1988. During 1988–2001, thirty-eight new cases of CL were diagnosed,<sup>[8]</sup> while 161 new cases of CL were reported between 2001–2003.<sup>[9]</sup> Further, Raina et al diagnosed eighteen cases of VL over a period of five years (2003–2007).<sup>[7]</sup> All these patients were inhabitants of sub-alpine valley along the Satluj River with altitude ranges of 700 to 2,900 meters above sea level.<sup>[9]</sup> The majority (66%) were seen during the summer months. Previous data revealed 36 new cases in 2001, 40 in 2002 and 97 in 2003,<sup>[9]</sup> while we registered 337 (222 adults and 115 children) new cases of CL over one year period. This observation indicates that disease is emerging and progressing in uncontrolled manner. CL is prevalent in all age groups, but amongst adults, 20–40 years age group is affected more.<sup>[14]</sup> This observation suggests that outdoor activities increase the exposure to vector in this age group. Most studies show male preponderance for CL<sup>[2, 12]</sup> but some studies describe that females are affected more than males,<sup>[9, 15]</sup> while in few studies sex difference was not observed.<sup>[11,13]</sup> In our study, females outnumbered the males, the reason for female preponderance is that high risk activities (grass cutting, cattle rearing and field work) are handled by females as per culture of this region. Further farmers/horticulturists, laborers, house wives and students are high risk groups for CL as per literature also. 10,<sup>[8]</sup> CL is a disease of hot, dry and damp areas with a minimal rainfall.<sup>[12]</sup> The climate of this valley is mildly warm and dry during summers and temperate during winters

with minimal Rain fall throughout the year. Sharma et al <sup>[9]</sup> reported a higher incidence of CL during the summer, while Aara et al <sup>[13]</sup> found more cases of CL during winter. In our study cases were registered round the year but their number was higher during August to October. This finding could be caused by the fact that maximum exposure to high risk activities (agricultural and horticultural activities.) occur during June and July further lesions develop over next 2–3 months. <sup>[14]</sup> Our results are according to the study by Aara et al describing a period of 2 days to 38 months between the appearance of a lesion and the first diagnosis of CL. <sup>[13]</sup> In our study most (81.98%) of the patients presented within a period of 1-6 months of lesion onset in accordance with various studies. <sup>[13, 15]</sup> 6.31% cases presented after 9 months of lesion onset, while only 3.60% cases presented within 1 month of lesion onset in accordance with study by Rahi et al. <sup>[15]</sup> Most (72.07%) cases presented with a single lesion and 16.67% cases with two lesions in agreement with the study by Belal et al. <sup>[3]</sup> Lesion size varied from 0.5 to 8 cm in agreement with other studies. <sup>[3]</sup> Variable types of lesions were appreciated in our patients. Non-ulcerated nodules and psoriasiform plaques were most frequently observed morphologies in accordance with other study. <sup>[16]</sup> We observed that face and upper extremities were the most prevalent sites for CL, in line with study by Khatri et al. <sup>[17]</sup> However, Al Samarai et al reported the extremities as most commonly affected sites for CL. <sup>[18]</sup> The distribution differences of CL lesions can probably be explained by the habits of the people exposing certain parts of the body. As per literature, imprint smears are positive in 50-70% of the cases and younger lesions are more likely to yield the parasite. However histopathology shows more of granulomatous inflammation with scanty LD bodies as seen in our study. Repeated processing of biopsy specimens with dehydrating solutions is responsible for this discrepancy. <sup>[19]</sup> The results of imprint smears positivity are comparatively low in our study but these findings

are in collaboration with study by Sharma et al <sup>[9]</sup> and Aara et al. <sup>[13]</sup>

WHO has recommended intralesional infiltration of SSG as safe and effective treatment for CL and we followed the same. <sup>[20]</sup> Intolerable pain during the intralesional SSG is the major side effect but it can be overcome by anaesthetizing the lesion prior to infiltrating the drug. Minor side effects like post leishmania scarring, hyperpigmentation, keloid and millia formation are well reported in literature.

## CONCLUSION

This is the first study to report such a high number of CL from newly identified focus in Himachal Pradesh. CL is emerging into a major public health in subalpine valley along the Satluj River. We recommend skillful clinical diagnosis, availability of quality diagnostic tests, annual record keeping and reporting from this institute. So that effective treatment and preventive measures can be streamlined in coming future. Though we didn't encounter any case of VL but we emphasize that physicians must keep a very high clinical suspicion. Because 18 cases of VL have already been reported from this region in recent past.

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