

## Leishmaniasis in the North Central Province, Sri Lanka - epidemiology and therapeutic response

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### Abstract

We analyzed 404 (401 cutaneous, 2 mucocutaneous, and 1 visceral) leishmania patients for epidemiology, geographical distribution, periodicity and treatment response over 2.5 years from June 2007 to December 2009. Three (0.8%) patients, developed leishmaniasis recidivans, and 4 (0.4%) recurred within 13 months.

### Introduction

Cutaneous leishmaniasis (CL) is a growing public health problem in several parts of the world, including Sri Lanka<sup>1,3</sup>. The causative organism was identified as *Leishmania donovani* zymodeme MON-37<sup>4</sup>. DNA sequencing and microsatellite analyses showed that these parasites are closely related to those causing visceral leishmaniasis in the Indian subcontinent<sup>5</sup>. The first case of locally acquired leishmaniasis was documented in 1992<sup>6</sup>. The first cases of mucocutaneous<sup>7,8</sup> and visceral<sup>9</sup> leishmaniasis were reported from Anuradhapura district in 2005 and 2007 respectively. Today more than 500 patients are reported annually from Anuradhapura, Polonnaruwa, Matara, Thangalle and Hambanthota districts.

WHO recommended intralesionally administered pentavalent antimony compounds; sodium stibogluconate<sup>10-13</sup> and liquid nitrogen cryotherapy<sup>14-17</sup> are the widely used therapy in Sri Lanka. Ranawaka RR et al (2009)<sup>18</sup> proved that intralesionally administered 7% hypertonic sodium chloride was effective against *L. donovani* CL which agreed with published data by Sharquie KE et al (1995, 1997)<sup>19,20</sup>.

This study analyzed the epidemiology and the treatment response of patients with leishmaniasis for over 2.5 years (June 2007 to December 2009) in North Central Province, Sri Lanka.

### Material and methods

Majority of patients in this study were from Anuradhapura district, which is the largest district

in the country with low population density of 112 persons per sq km. The majority was rural population (92.7%) engaged in farming, while 7.1% urban and 0.1% estate according to the Department of Census and Statistics, 2001 ([www.statistics.gov.lk/PopHouSat/PDF/Population/p9p8%20Ethnicity.pdf](http://www.statistics.gov.lk/PopHouSat/PDF/Population/p9p8%20Ethnicity.pdf)).

Slit-skin-smear test (SSS) was performed as a routine. In negative SSS, if clinically indicative, skin biopsy was performed. Polymerase chain reaction (PCR) and culture were not done routinely. Patients were treated with either sodium stibogluconate (SSG), intralesional hypertonic saline (HS) or liquid nitrogen cryotherapy (LN).

### Results

There were 404; 401 cutaneous leishmaniasis with 607 skin lesions, 2 mucocutaneous and 1 visceral leishmaniasis patients.

267 men and 134 women with M: F ratio of 1.9:1 were studied (Table). Average age of our population was 32 years (ranged 13 months to 80 years). Except one Sri Lankan Moor all the patients were Sinhalese. Except one man who had acquired the disease while he was in Dubai, all others were autochthonous.

48% were from Thalawa (10 km) and Padaviya (90 km to our centre) Medical Officer of Health (MOH) areas (Figure 1). 79.4% were civilians who had acquired the disease from the locality. 20.5% were military personnel who had acquired the disease while they were working in Northern and Eastern provinces; Welioya (Padaviya MOH) (55), Mulathiw (4), Tricomalee (3), Jaffna (3), Vavniya (3), Kilinochchiya (2), Toppigala (2), Mannar (2) and Ampara (1).

Average delay in presentation was 9 months (ranged 4 weeks to 5 years) (Figure 2). The mean number of patients' presentation for a given month during the period of study was 6, 10.3 and 18.8 in 2007, 2008, and 2009 respectively (Figure 3).

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**Table. Characteristics of the sample by age and sex distribution, occupational distribution, clinical presentation, site and number of cutaneous leishmaniasis lesions\***

|                                                                        | Number |        | Percentage |
|------------------------------------------------------------------------|--------|--------|------------|
|                                                                        | Male   | Female |            |
| <b>Age and sex distribution</b>                                        |        |        |            |
| 0-15                                                                   | 23     | 35     | 14.3       |
| 16-30                                                                  | 112    | 35     | 36.3       |
| 31-45                                                                  | 78     | 16     | 23.2       |
| 46-59                                                                  | 43     | 34     | 19         |
| >60 years                                                              | 11     | 9      | 5          |
| <b>Occupational distribution</b>                                       |        |        |            |
| Farmers                                                                | 102    |        | 25         |
| Military personnel                                                     | 83     |        | 20.5       |
| School children                                                        | 78     |        | 19.3       |
| House wives                                                            | 32     |        | -          |
| Home guards                                                            | 24     |        | -          |
| Teachers                                                               | 10     |        | -          |
| Others                                                                 | 75     |        | -          |
| <b>Clinical presentation</b>                                           |        |        |            |
| 1. papules ( $\leq 1$ cm diameter)                                     | 181    |        | 33         |
| 2. nodules ( $> 1$ cm diameter)                                        | 56     |        | 10.2       |
| 3. plaques                                                             | 31     |        | 5.6        |
| 4. nodulo-ulcerative lesion                                            | 271    |        | 49.4       |
| 5. chronic non healing ulcers with undermined edges without induration | 9      |        | 1.6        |
| <b>Site of the lesion</b>                                              |        |        |            |
| Ear                                                                    | 5      |        | -          |
| Nose                                                                   | 3      |        | -          |
| Lip                                                                    | 8      |        | -          |
| Face                                                                   | 82     |        | 15         |
| arm                                                                    | 71     |        | 13         |
| Forearm                                                                | 164    |        | 30         |
| Hand                                                                   | 9      |        | -          |
| Fingers                                                                | 8      |        | -          |
| Thigh                                                                  | 3      |        | -          |
| Knee                                                                   | 3      |        | -          |
| Leg below knee                                                         | 107    |        | 19.5       |
| Feet                                                                   | 3      |        | -          |
| Trunk                                                                  | 54     |        | 10         |
| buttock                                                                | 1      |        | -          |
| <b>Number of lesions</b>                                               |        |        |            |
| 1                                                                      | 268    |        | 66.3       |
| 2                                                                      | 77     |        | 19         |
| 3                                                                      | 21     |        | 5          |
| 4                                                                      | 7      |        | 2          |
| >4 (5- 11 lesions)                                                     | 11     |        | 2.7        |

\* Totals may vary due to missing data.

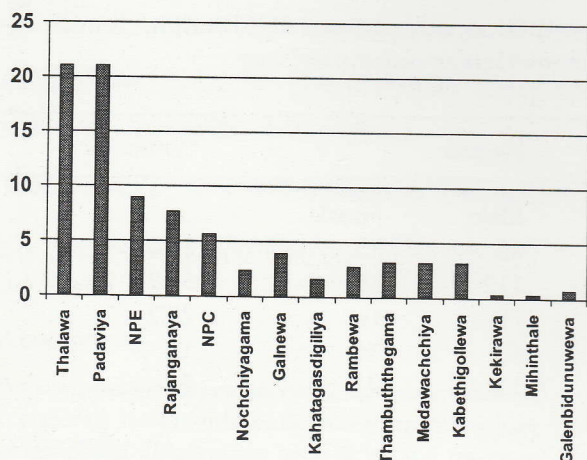


Figure 1. Proportion of subject distribution according to Medical Officer of Health (MOH) areas in Anuradhapura district, Sri Lanka, from July 2007 to June 2009.

NPC: Nuwaragampalatha Central  
NPE: Nuwaragampalatha East

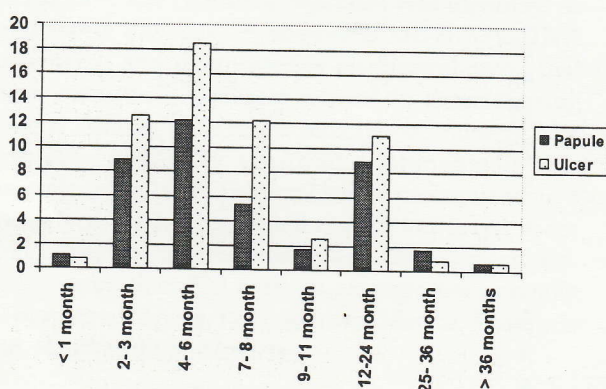


Figure 2. Proportion of subjects' presentation to the skin clinic from the time of first appearance of cutaneous leishmaniasis lesions.

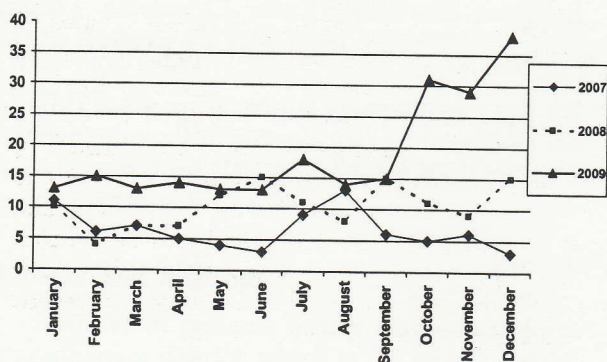


Figure 3. Distribution of the cutaneous leishmaniasis cases according to the month of presentation from January 2007 to November 2009 in Anuradhapura district, Sri Lanka.

91% of lesions were located on exposed areas of the body. 11 (4.5%) had at least one other family member affected. 14.3% had associated photo-dermatitis which disappeared when CL healed. 43.7% of cutaneous lesions had hypopigmented halo around.

### Mucocutaneous leishmaniasis

41-year old male farmer from Eppawala (Thalawa MOH) with a non-healing ulcer on the lower lip was extensively investigated for a granulomatous mid line lesion since 2001<sup>8</sup>. His SSS done in 2006 and 2007 were negative, and repeated in October 2008 was positive, and confirmed with positive PCR and culture. Due to delayed diagnosis he was left with total destruction of nasal septum, phintrum and lower lip.

The second patient, 55-year old postmaster from Rambewa MOH (15 km) presented with a non-healing ulcer on left buccal mucosa for 6 months duration. He was diagnosed with tissue biopsy showing numerous amastigotes.

### Visceral leishmaniasis

45-year old male farmer who is a heavy alcoholic from Thabuththegama MOH (15 km) was extensively investigated for pancytopenia, hepatosplenomegaly with massive spleen in medical unit since 2007. He defaulted follow up in 2008 when he was informed liver biopsy, and readmitted in 2009 with worsening of symptoms. He died following liver biopsy and visceral leishmaniasis was diagnosed seeing Kupffer cells filled with amastigotes. In post mortem specimens spleen and liver were infiltrated with numerous amastigotes.

### Treatment response

87 (136 lesions) and 67 (93 lesions) patients were treated with SSG and HS respectively in a study conducted by Ranawaka RR et al.<sup>18</sup> SSG showed 100% cure within 1-6 injections (mean 3.24); while HS, 92.2% cure within 1-10 injections (mean 5.27). Except for post inflammatory hyperpigmentation which faded-out over 6-8 months there were no systemic or local side effects with either SSG or HS. Two (0.8%) patients, whom were treated with SSG, and one treated with hypertonic saline developed leishmaniasis recidivans. One (0.4%) patient who was initially treated with SSG recurred after 13 months.

65 patients (121 lesions) were treated with LN; showed 91.7% cure rate within 1-7 cryosessions (mean 3.57). Pain which last 15-30 minutes, ulceration (33%),

post inflammatory hypopigmentation (46.9%), and visible scar (43%), were the drawbacks in LN; three (4.6%) patients recurred within 6 months of cure<sup>16</sup>.

## Discussion

Young men of 16-45 age groups were the mostly infected. Majority (79.4%) were civilians, in contrast to the observation in 2003<sup>4</sup> where most of them were military personnel.

In Anuradhapura district 90.7% was Sinhalese, followed by 8.3% SL Moors and 0.7% SL Tamils. In this study group except one SL Moor all the infected patients were Sinhalese. The difference in clothing, cultural and social behaviour may partly explain our observation.

Although majority of our patients lived in moderately built brick houses with 5-6 members in one family, only 11 (7 families) had multiple family members infected. These patients, who had intra-familial infection, did not show higher incidence of multiple lesions or severe disease<sup>21</sup>. Why some individuals are more prone to get infection than other members of the family, to be further studied.

In the North Central Province 48% of the patients were from Thalawa and Padaviya MOH. From Welioya (Padaviya MOH) high number of military personnel still present as reported in 2003<sup>4</sup>.

Belli A et al<sup>22</sup> described hypopigmented halo around the lesion in atypical CL due to *L. chagasi*, which was also noted on 13.9-44% Sri Lankan patients<sup>23</sup>. This was an important differentiating feature, noted in 43.7% of CL lesions in this study group, which was marked on dark skinned individuals. These lesions have misdiagnosed clinically and histopathologically as tuberculoid leprosy, since both diseases show granulomatous pathology.

Seasonal pattern with monsoonal rainy periods (November-January) was not noted in the North Central Province (Figure 3). But in 2008 and 2009 there was marked increase in patient presentation to the clinic following awareness programmes. But still there is an average of 9 months delay.

The first visceral leishmaniasis in Sri Lanka was diagnosed by liver biopsy showing amastigotes within Kupffer cells<sup>9</sup>. If not vigilant there is a possibility to under diagnose visceral leishmaniasis, and end up in fatality as in our patient. Patients with high suspicious of visceral and mucocutaneous leishmaniasis should undergo PCR and culture.

The natural healing time reported on *L. major* CL was 9 months or more and *L. tropica* was 1 year or more<sup>23</sup>. Natural healing time for *L. donovani* CL is not studied yet. But from this study we observed that 23.6% of lesions lasted for more than 11 months. Therefore natural healing time in *L. donovani* CL can probably take 12 months or more.

In Sri Lanka only method of disease control is the early identification of patients and early treatment. We used three modes of treatments where none of them showed systemic side effects. Most effective therapy was SSG. Disadvantage in SSG was its high cost, possible systemic side effects, and interrupted supply.

HS was effective although average number of injections required per lesion was higher<sup>18</sup>. HS was cheap (US\$ <1 per 500 ml) compared to SSG (US\$ 150 per 100 ml), no systemic side effects and could easily made locally at all centers. There was no significant association between the rapidity of clinical response and the size, the duration and the location of the lesions<sup>18</sup>.

Many centers in Sri Lanka use LN as the first line of treatment in spite of local side effects. Authors recommend to avoid LN on face, areas of cosmetically concerned and the lesions >2 cm. We recommend giving cryotherapy fortnightly (not weekly); and to use cryoguns (instead of cotton swabs attached to eakles); which may minimize ulceration, and therefore scarring<sup>16</sup>.

Disadvantage in all 3 therapies were that these were painful procedures, needed several hospital visits and professionally trained medical staff. Ideal therapy to control an infectious disease should be cheap, less toxic, orally or topically administered drug which can be issued by field medical staff such as public health inspectors and public health midwives.

Most number of patients was reported from Padaviya and Padavi Sripura, which are situated 90 km and 120 km respectively from Teaching Hospital Anuradhapura, the nearest tertiary care centre. Due to long distance and traveling difficulty infected patients are reluctant to seek treatment. We must train medical officers and more importantly Medical Lab Technicians in these endemic areas to diagnose and treat patients. A trained Medical Lab Technician should confine to leishmania investigations at least in high endemic areas to avoid false negative results in pauci parasitic specimens.

Vector, reservoir host and disease transmission in Sri Lanka had not been understood yet<sup>24,25</sup> and need further studies to be conducted by responsible

authorities and implement vector control programme as early as possible. From this analysis it is evident that the disease is confined to a few MOH areas in the North Central Province. Therefore if started early, disease control by controlling the vector would be easy and will be successful. Unless these actions are implemented urgently spread of this fatal disease is unavoidable in the near future.

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