

## Epidemiological profile of Kala-azar in a tertiary care center of Mid Western Nepal

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### Introduction

Visceral Leishmaniasis (Kala-azar) is one of the neglected tropical diseases caused by different species of the protozoan parasite *Leishmania*, which are obligate intracellular protozoan parasites that are transmitted by the bites of infected female sandflies.<sup>1</sup> In Nepal, Visceral Leishmaniasis (VL) is caused by *Leishmania donovani* and is transmitted by *Phlebotomus argentipes*.<sup>2</sup> Kala-azar is a serious public health problem on the Indian subcontinent, causing high morbidity and mortality.<sup>3</sup> It is an infection of the reticulo-endothelial system characterized clinically by a chronic febrile course, and associated with loss of weight and hepato-splenomegaly.<sup>4</sup>

Kala-azar is endemic in 78 countries but mainly affects economically disadvantaged populations.<sup>5</sup> Worldwide, over 12 million people are infected with *Leishmania* spp., and an additional 350 million are at risk of infection.<sup>6</sup> It occurs most commonly in South Asia (India, Bangladesh, Nepal), East Africa (Sudan, Ethiopia, Kenya), and Brazil.<sup>7</sup> The first case of Kala-azar was reported in Nepal as early as 1960s.<sup>8</sup> Twelve districts in the eastern and central Terai regions bordering the northern state of Bihar, India, are endemic for Kala-azar.<sup>2,9</sup> Six other districts were included in the list in 2016 because sporadic cases were consistently being reported by these 6 districts. Currently 18 districts are considered endemic. Over 8.5 million people living in these endemic districts are at risk of Kala-azar.<sup>8</sup>

### Abstract

**Background:** Kala-azar has been endemic in the central and eastern Terai region of Nepal neighbouring North Bihar, India. Data of Kala-azar in Mid and Far Western Nepal is scarce. We conducted this study to highlight the burden of Kala-azar in this region.

**Methods:** This study was a cross sectional study conducted from July 2019 to May 2023 in the Department of Internal Medicine of Bheri Hospital. A total of 112 patients diagnosed with Kala-azar were enrolled in study. Data about socio-demographic profile and outcome were entered in MS EXCEL and analyzed by SPSS 20.

**Results:** A total of 112 patients were enrolled in study with female predominance 86 (76.79%). Majority of the patients 37(33.03%) were of less than 15 years of age. Kala-azar cases were distributed not only to Terai districts but also in hilly and mountainous districts of Karnali and Sudur paschim provinces. 95(84.82%) cases were new and 17 cases were relapsed cases. 98(87.50%) cases improved with treatment, 5(4.46%) cases expired while one case was referred.

**Conclusions:** Kala-azar is a neglected tropical disease in Nepal. Once confined to the tropical Terai region, it has now been moving towards hills and mountains of Mid and Far Western Nepal. Public awareness campaign and strengthening the Kala-azar treatment centers would help to attain the goal of Kala-azar elimination program of Nepal.

The incidence of kala-azar at national level has been less than 1/10,000 population since fiscal year 2073/74. Bheri Hospital is the referral and treatment center of Kala-azar with Government supply of injection Amphotericin B. Moreover, we have very little data of Kala-azar in this region. Thus, we decided to determine the epidemiological profile and outcome of such patients treated at Bheri Hospital.

### Methods

This was a cross sectional single center based study conducted in the Department of Internal Medicine, Bheri hospital, Nepalgunj from July 2019 to May 2023. The ethical clearance for the study was taken from the Nepal Health Research Council ( Reg. no.20 ) before starting the study. A written permission was taken from hospital administration for the study. All case sheets of the Kala-azar patient from July 2019 to May 2023 were obtained from the record section. The epidemiological data like age, sex, address and outcomes were

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entered in the Microsoft Excel sheets. Appropriate descriptive statistics like frequency, percentage of different variables were calculated by SPSS 20. The results were expressed in tables and figure.

**Results**

A total of 112 patients were enrolled in the study during the study period. There were 26 males (23.21%) and 86 females (76.78%) with male to female ratio of 0.3. Most of the patients (37%) were of pediatric age group (less than 15). The epidemiological profile of the Kala-azar patients based on age, sex, ethnic group, geographical distribution and outcome of the patients are given in the following table.

**Table 1.** Gender wise distribution of Kala-azar patients

Gender	Frequency (n)	Percentage (%)
Male	26	23.21
Female	86	76.78

**Table 2.** Age wise distribution of Kala-azar patients

Age group	Frequency (n)	Percentage (%)
0-15	37	33.03
15-30	32	28.57
30-45	21	18.75
45-60	13	11.60
60-75	5	4.46
75 above	4	3.57

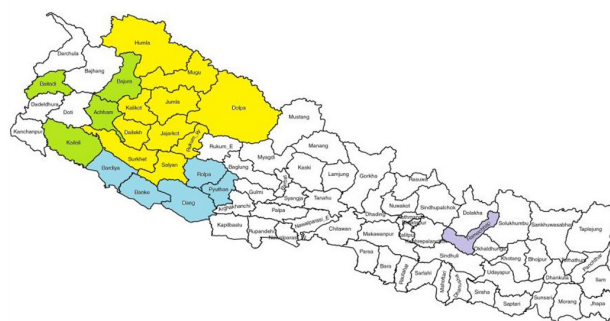
Kala-azar cases were distributed throughout the districts of Lumbini, Karnali and Sudur Paschim districts. Bardiya 15.17%, followed by Kalikot 11.60% and Banke 10.71% districts had the most numerous cases (Table 3).

**Table 3.** Geographical distribution of Kala-azar patients

District	Frequency (n)	Percentage (%)
Bardiya	17	15.17
Kalikot	13	11.60
Banke	12	10.71
Bajura	11	9.83
Surkhet	9	8.03
Mugu	7	6.25
Dang	7	6.25
Salyan	7	6.25
Dailekh	5	4.46
Humla	4	3.57
Dolpa	3	2.67
Pyuthan	3	2.67
Kailali	3	2.67
Jajarkot	3	2.67
Rukum West	2	1.78
Achham	2	1.78
Rolpa	1	0.89
Jumla	1	0.89
Baitadi	1	0.89
Ramechhap	1	0.89

Rolpa, Pyuthan, Dang, Banke and Bardiya were districts from Lumbini Province. Kailali, Achham, Baitadi and Bajura were districts from Sudur paschim province. However all districts from Karnali Province reported Kala-azar cases. Ramechhap was the only district from Bagmati province to report Kala-azar case at Bheri Hospital, Nepalgunj.(Figure 1)

**Figure 1.** Map of Nepal with provinces and districts with Kala-azar cases reported at Bheri Hospital, Nepalgunj



In the map, shaded districts represent Kala-azar cases. Districts shaded with blue belong to Lumbini Province, green represents Sudur Paschim Province and Yellow denoted districts of Karnali Provinces and violet represents Ramechhap district of Bagmati Province.

Most of the patients belong to the caste and ethnic groups from the hilly region. Tharu community from terai was also found to be infected with kala-azar.(Table 4)

**Table 4.** Caste and Ethnic group distribution of Kala-azar patients

Caste and Ethnic group wise	Frequency (n)	Percentage (%)
Brahman/ Chhetri (Hill)	64	57.14
Brahman/ Chhetri (Terai)	0	0
Terai middle caste	1	0.89
Dalit (Hill)	14	12.50
Dalit (Terai)	1	0.89
Newar	2	1.78
Janjati (Hill)	17	15.17
Janjati Terai (Tharu)	13	11.60
Muslims	0	0
Others	0	0

During the study period out of 112 cases , 95 were newly diagnosed, 17 relapses after initial treatment. Seven relapse cases were treated at Bheri Hospital before. The patients were treated with liposomal Amphotericin B according to the national guidelines of Kala-azar treatment. Relapse cases were diagnosed on the basis of clinical manifestations and demonstration of LD bodies on Bone Marrow Aspiration cytology. (Table 5.)

**Table 5.** Case Distribution of Kala-azar patients

Case Type	Frequency (n)	Percentage (%)
New Case	95	84.82
Relapse	17	15.17
Relapse case treated previously at Bheri Hospital	7	6.25
Visceral Leishmaniasis	111	99.10
Post Kalazaar Dermal Leishmaniasis	1	0.89

Kala-azar can be fatal if remained undiagnosed and untreated. During the course of treatment of patients according to the National guidelines of Kala-azar, the majority 87.50% patients were successfully discharged from hospital. There were 5(4.46%) mortality. However 8(7.14%) patients left the hospital against medical advice and one of them was referred to higher center for further management.(Table 6)

**Table 6.** Outcome of Kala-azar patients

Outcome	Frequency (n)	Percentage (%)
Discharge	98	87.50
Leave against Medical Advice (LAMA)	8	7.14
Death	5	4.46
Refer	1	0.89

## Discussion

There were a total of 112 patients treated for Kala-azar in the Department of Internal medicine in Bheri Hospital during July 2019 to May 2023. There was female predominance with 76.78% while male were 23.32%. This was in contrast to the study by S Rijal et al. where male and female prevalence were 47.3% and 52.6 % respectively.<sup>10</sup> Kala-azar infection was found in all age categories, however majority of the cases were in 0 to 15 years age group comprising 33%. This was consistent with a study conducted among the Ugandan and Kenyan Pokot community where the most affected age group were between 5 and 14 years.<sup>11</sup>

Initially twelve districts in the eastern and central Terai regions bordering the northern state of Bihar, India, were endemic for Kala-azar.<sup>2,9</sup> After addition of six other districts in 2016, currently 18 districts are endemic to kala-azar.<sup>8</sup> Over 8.5 million people living in these endemic districts are at risk of Kala-azar.<sup>8</sup> For the first time in Nepal the epidemiology of Leishmania donovani infection has been described in an extensive community-based study in Morang, Sunsari and Saptari districts. The overall Leishmania infection rate was 9% but there was wide variation among endemic clusters.<sup>10</sup>

The first case of Kala-azar from non endemic hilly region of Doti was reported in 2009 and was treated at Sukraraj Tropical and Infectious Disease Hospital (STIDH), Kathmandu.<sup>12</sup> Kala-azar, once confined to the tropical Terai regions of Nepal, is moving towards the hills and the mountains of the country including the Palpa and Surkhet districts.<sup>13</sup> The people of Palpa and Surkhet districts were screened for the febrile diseases for Kala-azar and skin lesions for post-kala-azar dermal leishmaniasis (PKDL). After screening a population of 2,202 at the baseline, 2,345 individuals were followed during 12 months with only one VL case detected.<sup>13</sup>

The annual number of VL cases in Nepal was 218 in 2018, which was 10 times lower than in 2006.<sup>14</sup> The incidence of kala-azar at national level has been less than 1/10,000 population since FY 2073/74(2013). However, the trend of Kala-azar cases has been

increasing in a few years. In 2077/78, there has been slight increase in reported cases (212 Kala-azar cases) compared to previous year (203).<sup>15</sup> In FY 2078/79(2021-2022), two districts, Okhaldhunga and Kalikot, crossed the elimination threshold with 1.62 per 10,000 in Okhaldhunga and 4.14 per 10,000 in Kalikot.<sup>16</sup>

Many people from Mid and Far western districts of Nepal are found to migrate to the Uttarakhand Himalayas of India as labourers. Sporadic cases of Kala-azar have been reported from the natives of Himalayan region such as Kumaon (350–900 m above mean sea level) and Garhwal (1500–2500 m above mean sea level) region.<sup>17</sup> This phenomenon of migrations of the disease from India towards the hilly regions of Nepal points towards the new endemicity of disease in these regions.

Kala-azar can be fatal if remained undiagnosed. Since it is a neglected tropical disease, a high suspicion should be given to the cases of fever along with hepato- splenomegaly, weight loss and anaemia. WHO states 95% mortality if not treated.<sup>18</sup> In our study there were 4.46% of mortality. The case fatality rate (CFR) varied from 0.23% to 13.2% in Nepal.<sup>19</sup> The mortality rate of VL was 3.7% in Eastern Uganda and 4.8% in Ethiopia. The finding of another two pocket studies conducted in Tigray, Ethiopia, reported 12.4% and 18.5% proportion of death among VL patients.<sup>20</sup> In USA 3,800 cases of visceral leishmaniasis are recorded each year, with an average case fatality rate of 7%.<sup>21</sup> A total of 34564 cases and 584 deaths of Kala-azar were reported during 1980-2019 in Nepal.<sup>22</sup>

Owing to presence of only human reservoir and high cure rates of kala-azar in the Indian sub-continent (Bangladesh, India and Nepal), kala-azar has been targeted for elimination as a public health problem.<sup>23</sup> Kala-azar has been Slated for elimination as a public health problem (achieving annual incidence of < 1 case/10,000 population at the district level. The Government of Nepal is committed to the WHO regional strategy to eliminate kala-azar. Nepal is also signatory to the MOU on strengthening collaboration in the regional elimination efforts along with Bangladesh and India during WHA 2005 which was renewed in 2014 with inclusion of Bhutan and Thailand.<sup>8</sup>

Kala-azar elimination can not be achieved only by focusing on treatment of cases. The vector control measures should be applied. More over personal protective measures preventing sand flies bites should be taken. A study highlighted these issues. In the study conducted by S Koirala et al. it was found that fewer than 5% of respondents slept outdoors in farm outhouses, and of those respondents sleeping indoors a small proportion did so in the kitchen. These groups sleeping outdoors or the kitchen did not use any bed nets or any personal vector control measures such as mosquito coils, repellents, etc. This, therefore, constitutes an important group of hosts susceptible to sandfly bites and hence at risk of acquiring kala-azar. There is a need, therefore, for health workers to make such people aware that sleeping outside without taking appropriate personal vector control measures exposes them to infection from the bites of sandflies.<sup>24</sup>

## Conclusion

Kala-azar is a neglected tropical disease in Nepal. There are eighteen endemic districts reported till now. The disease once confined to Tropical Terai is moving towards hills and mountains of Mid and Far Western Nepal. Extensive community based study should be done in these regions to find the local pockets of vectors (sand flies). The Kala-azar elimination program should focus on public awareness campaigns regarding personal protective measures and treatment centers should be strengthened and expanded.

**Conflict of Interest:** None.

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