Review Article

An Overview of Kala-azar Elimination Program in Nepal

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Leishmaniasis is a neglected tropical disease (NTD) caused by multiple species of *Leishmania* parasites and transmitted by the bite of female sand flies. It is endemic in 98 countries, and is mostly concentrated in low-and middle-income countries in South Asia, East Africa, Latin America and in the Middle East.[1]

The disease presents in different forms depending on the species and geographical location. Visceral leishmaniasis (VL; also known as kala-azar) presents with fever, weight loss, hepatosplenomegaly and may have neurological manifestations.[2] If untreated, it has a fatality rate of over 95%.[3] Kala-azar is a vector-borne, neglected tropical disease, endemic to certain parts of Indian subcontinent (Bangladesh, India and Nepal). Kala-azar mainly affects the economically deprived classes, ultra poor and its classical clinical features include fever, splenomegaly and hepatomegaly. Disease is associated with anemia, weight loss and weakness.[4]

With an estimated 50 000–90 000 new cases occurring annually worldwide, more than 95% of cases in 2017 occurred in just ten countries, including Bangladesh, India, and Nepal- all three belonging to the Indian subcontinent.[5] In this region, *Leishmania donovani* is the only species causing Kala-azar, the female sand fly, *Phlebotomus argentipes*, is the only vector and humans are the only known reservoir. Along with these unique characteristics, availability of effective and novel formulations for treatment, indoor residual spray and availability of rapid diagnostic test (rk39) makes Kala-azar a candidate for elimination.[6] The number of kala-azar cases in Indian Sub-continent countries has declined steadily from over 77 000 reported cases in 1992 to fewer than 10000 cases in 2014 (fig. 1).

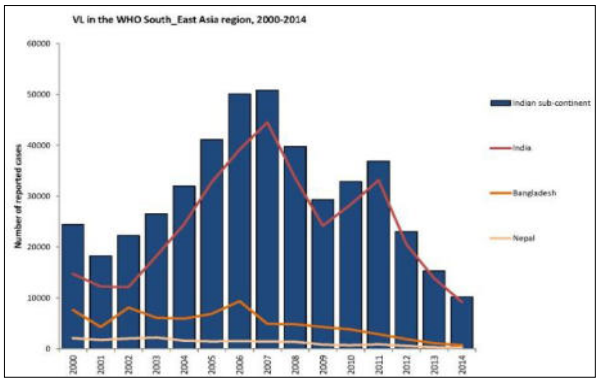

Figure 1: Number of Kala-azar cases reported in South-East Asia, 2014 (Source: WHO SEARO)

Kala-azar Elimination Program in Nepal

In 2005, the governments of Bangladesh, India, and Nepal launched an initiative to eliminate visceral Leishmaniasis as a public health problem from the region (the kala-azar elimination initiative), aiming to reduce the disease incidence to less than one visceral leishmaniasis case per 10, 000 population at the district level by the end of the year 2015. This target was achieved in 2013 and has been sustained since then. Further, in 2014, extension of this memorandum of understanding included Bhutan and Thailand, as new signatories and the target date has been further revised to 2017. That deadline has now been extended to 2020.[7] The elimination strategy in the region is mainly based on improved case

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management, effective disease surveillance, and integrated vector control, with country specific emphasis on different aspects of these activities.[7]

This program was divided into four phases. The initial step was the preparatory phase that started in 2005 and was continued for 2 years. It consisted of spraying operation, diagnosis and treatment facilities establishment in endemic countries, planning and monitoring. This was followed by the attack phase of 5 years, which included the indoor residual spraying in endemic areas, integrated vector management, early diagnosis and treatment, case detection, vector surveillance, community mobilization, external country evaluation and building research capacity. The current is the consolidation phase; total coverage spraying is modified to limit indoor residual spraying in endemic areas. Following this would be the maintenance phase for 2-3 years, in which surveillance against reintroduction of VL until VL is no longer a public health problem is planned.[8] After reaching district level elimination in 2013 and sustaining it since then, Government of Nepal, Epidemiology and Disease Control Division conducted an independent assessment of Kala-azar elimination program in the year 2017 to review and assess the progress made towards elimination. Nepal was the first country to reach the targeted threshold in each of its endemic districts in 2013. However, this threshold was surpassed in one (supposedly non-endemic) district in 2017, and the disease is now observed in an increasing number of districts hitherto considered to be non-endemic. WHO has, therefore, not yet been able to validate the achievement of visceral leishmaniasis elimination as a public health problem in Nepal.[9] The strategy for VL control broadly included three main activities: interruption of transmission by reducing vector population through indoor residual insecticides; early diagnosis and complete treatment of VL cases and health education program for community awareness. These strategies are in line with the WHO strategies for elimination of VL.[10]

Kala-azar elimination: Current status & Future perspective

Kala-azar remains a public health concern in Nepal. The first case of Kala-azar was reported in Nepal as early as 1960s. The programme initially identified 12 districts of central and south-eastern *Terai* region as KA endemic. However, six new districts were added to that list in 2016, including hilly districts, because sporadic cases have been consistently reported from other parts of the country including hilly region and Kathmandu valley and disease transmission was verified by epidemiological and entomological studies. Cases have been reported from other 27 districts but disease transmission in these districts is under verification. Irrespective of the endemicity status, new KA cases have been reported from 50 (out of 77) districts in the country (fig. 2).

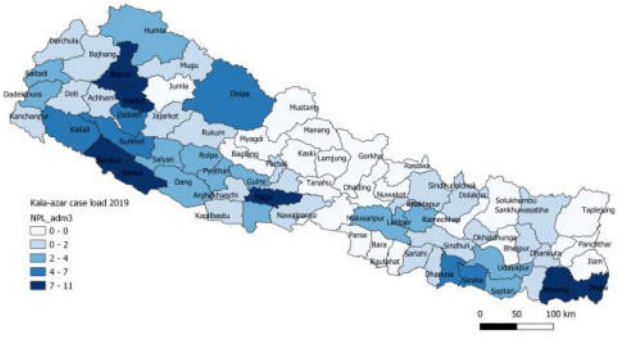

Figure 2: Spatial distribution of KA cases in Nepal, 2017 *(Source: National Guideline on KA Elimination Program, 2019)*

Despite this geographical expansion of the disease, the programme has seen a steady

decline in incident cases and mortality since 2003. Over 8.6 million people living in these 18 endemic districts are at risk of Kala-azar. The highest number of KA cases was reported in 2003 and since then the cases are in decreasing trend. In 2017, 271 new cases were reported and 202 cases in 2019 (fig 3).[11]

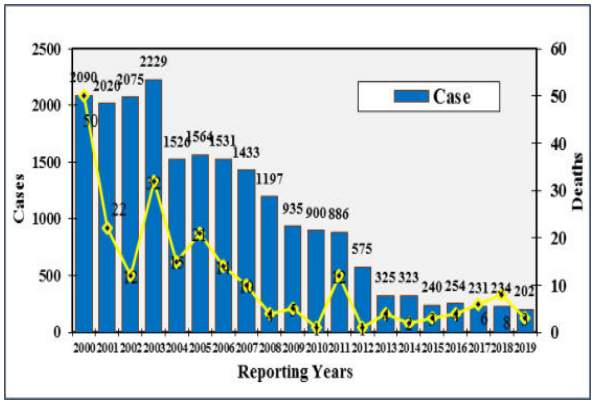

Figure 3: Trend of Kala-azar cases and death in Nepal; 2000 – 2017

Since 2000, Kala-azar cases have been reported in increasing numbers from the areas/districts hitherto considered as non-endemic districts of Nepal. Kala-azar cases are now being reported also from hills, Kathmandu valley and some mountainous districts. In 2018, 54.3% (127 out of 234 cases) of all reported cases were from 32 non-endemic districts, some of which are in immediate geographical proximity to endemic districts. This shift in occurrence of cases in non-program districts has prompted to verify the existence of vector and other evidences.

Diagnosis, Treatment and Vector control

Effective disease surveillance is important in disease control. Early detection and treatment of cases help reduce transmission and help monitor the spread and burden of disease. For the diagnosis of VL in Nepal, rK39 rapid test have been used in peripheral health services. rK39 immunochromatography is considered to be simple, sensitive, specific, non-invasive and economic. Over the past few years, many new formulations of alternative treatments of VL are available in all government hospitals free of cost. Based on WHO recommendations, the kala-azar elimination programme replaced miltefosine with a single dose infusion of liposomal amphotericin B (AmBisome) as first line treatment in 2016 in Nepal. Miltefosine, the first effective oral treatment against VL, has low toxicity; however, teratogenicity[12] and treatment relapse have been reported in a couple of studies in the Indian subcontinent[13]. Measures to control vectors have primarily been indoor residual spraying of insecticides in endemic villages reporting kala-azar cases. Synthetic pyrethroid has been used for vector control using indoor residual spraying in Nepal.

In conclusion, the goal of elimination of VL in Nepal can be achieved if current strategies and monitoring programs are improved and strengthened, active case detection and treatment programs are initiated, newer combination drugs and vaccines are developed, and uninterrupted drug supplies and healthcare coverage are ensured. Along with this, policies that drive health education and behavioral changes have to be strongly advocated. Partnership and collaboration with various stakeholders and other vector-borne disease control programs is critical at all levels. Decentralization or public–private partnership in combating the disease can be an important step in the elimination as there can be a wider coverage for diagnosis and treatment. Strong and sustained political commitment and policies are also crucial for elimination along with providing adequate resources.

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