A Mini Review on the Current Status of Leishmaniasis and the Need to Prioritize Research on Establishing Reservoir Hosts in Sri Lanka

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Abstract: Since the first report of leishmaniasis from Sri Lanka in 1992, the number of notified cutaneous leishmaniais (CL) cases increases considerably from all 25 districts of the country. It was established that the parasite responsible for CL is *Leishmania donovani* zymodem MON-37; the species which causes the fatal Visceral Leishmaniasis (VL) around the world and the vector for this species is *Phlematous argentipes* (Diptera: Psychodidae: Phlebotominae). In addition, reports suggest the emergence of fatal VL in the country. The impact of the disease burden hampers human resources and leads to economic loss in the country. After declaring leishmaniasis as a notifiable disease in 2008, the health authorities started to implement preventive strategies to control the disease in the Island. However, achieving the goal posts challenges in terms of diagnosis, treatment, vector control and preventing vector human contact. With this background, this mini review focuses on the importance of establishing the reservoir hosts in different localities in Sri Lanka. Hence, this knowledge can be utilized as one of the major components in the existing control strategy for controlling the disease in the country.

Keywords: Leishmaniasis, Cutaneous Leishmaniasis, Reservoir Hosts

1. BACKGROUND

Leishmaniasis is a vector-borne disease caused by a flagellated protozoan from the genus Leishmania (Kinctoplastida: Trypanosomatidae: Euleishmania). Around 0.7 to 1 million new leishmaniasis cases are encountered annually around the world (WHO, 2023). The disease is widespread in the tropical and subtropical areas and found in 98 countries including Sri Lanka (Steverding, 2017). The disease is considered as one of the eight major neglected tropical parasitic diseases in the world (cited as in Siriwardana, 2012).

People who are at poor socioeconomic conditions i.e lack of financial resources, malnutrition, poor housing, population displacement and a weaker immune system are at risk to contract this disease condition (WHO, 2023). *Leishmania* parasite is transmitted by the bite of infected vector female sandfly genera *Phlebotomus* (old world sandfly) and *Lutzomyia* (new world sand fly) (Maroli, 2013). Around 70 animal species, including humans, can be the source of Leishmania parasites (WHO, 2023).

Figure 1 shows the life cycle of leishmaniasis with probable involvement of the dog or rodents as the reservoir hosts (Salwa *et al.*, 2020).

Major forms of this disease conditions are visceral leishmaniasis (VL), cutaneous leishmaniasis (CL) and mucocutaneous leishmaniasis (MCL) (WHO, 2023). Clinical manifestation of VL is irregular spikes of fever, weight loss, hepatosplenomegaly, and anaemia and 95% of the cases are fatal if untreated (WHO, 2023). Ulcers of the exposed body part of the skin is the main characteristic of the CL (WHO, 2023). Characteristic lesions of MCL are partial or total destruction of mucous membranes of the nose, mouth and throat (WHO, 2023).

2. LEISHMANIASIS IN SRI LANKA

2.1 *Cutaneous Leishmaniasis*

Though the first report of leishmaniasis was documented in 1992 in Si Lanka by Athukorale *et al* in 1992 (Athukorale *et al*, 1992), the use of term "cutaneous leishmaniasis" goes back to 1928 in Sri Lanka (cited as in Nuwangi *et al*,

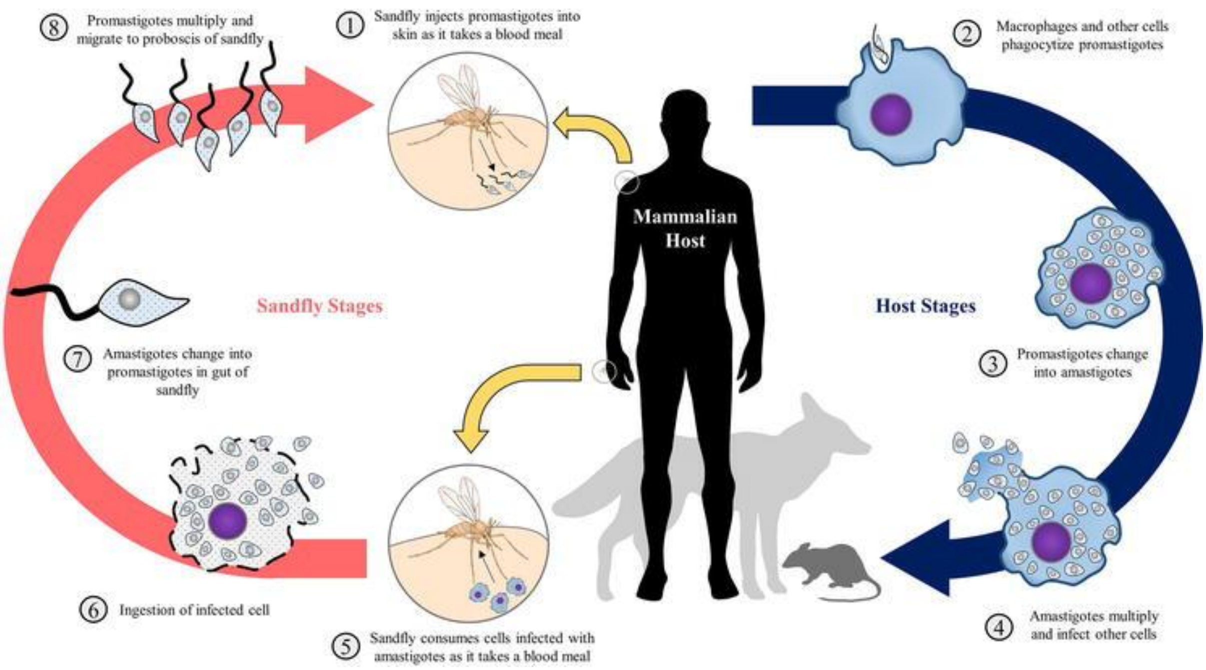

Figure 1: Life cycle of leishmaniasis (Salwa et al, 2020)

2022) and even further up to 1904 (Castellani, 1904). Thereafter, a few cases of leishmaniasis were reported by Naotunne *et al* (Naotunne *et al*, 1999), where all were young men had cutaneous lesions in exposed parts of the body and with activities linked to the scrub jungle.

In this context, majority of the cases reported in Sri Lanka from various places were CL (Nuwangi *et al*, 2022; Siriwardana *et al*, 2019 a,b; Siriwardana *et al*, 2019; Galgamuwa *et al*, 2018; De Silva *et al*, 2017; Kariyawasam *et al*, 2017; Sandanayaka *et al*, 2014; Khalil *et al*, 2014; Semage *et al*, 2014; Alvar *et al*., 2012; Siriwardana *et al*, 2012; Karunaweera, 2009; Nawaratna *et al*, 2007; Siriwardana *et al*, 2007; Karunaweera *et al*, 2003). Subsequently, more cases of CL were reported particularly among the military personnel who were working in the north and eastern parts of the country (Wijesundera, 2001).

In this context, table 1 shows the recent notification of leishmaniasis from 25 districts after the disease has been made notifiable disease in 2008 (Annual Health Bulletin, 2020). Hence, Sri Lanka is considered as an endemic country for leishmaniasis (Siriwardana *et al*, 2012) and the health authorities are fighting against to eliminate the disease from the country. Table 1 shows an increasing trend in notification of leishmaniasis and the major districts affected are Hambantota, Kurunegala, Matara, Polonnaruwa, Matale and Anuradhapura (Annual Health Bulletin, 2020).

In 2003, Karunaweera *et al* reported that *Leishmania donovani* zymodeme MON-37 is responsible for causing CL in Sri Lanka (Karunaweera *et al*, 2003). *Leishmania donovani* which causes the fatal VL in South-East Asia, Latin America and Eastern Africa is identified as the causative agent for CL in Sri Lanka (Nuwangi *et al*, 2022; Siriwardana *et al*, 2019; Kariyawasam *et al*, 2017; Khalil *et al*, 2014: Karunaweera, 2009; Nawaratna *et al*, 2007: Siriwardana *et al*, 2007; Karunaweera *et al*, 2003).

2.2 *Visceral leishmaniasis*

The first report on VL was in 2007 from North Central Province of the country (Abeygunasekara *et al*, 2007). Thereafter, a few cases of VL were reported as well (Ranasinghe

Table 1: Annual notification of leishmaniasis[1].

Districts	Number of Leishmania cases reported				
	2018	**2019**	**2020**	**2021**	**2022**
Colombo	5	6	3	1	5
Gampaha	68	174	60	13	46
Kalutara	9	3	0	0	4
Kandy	41	60	79	35	55
Matale	211	283	348	287	351
Nuwara Eliya	0	1	1	1	1
Galle	5	5	6	2	0
Hambantota	749	810	760	523	573
Matara	508	621	403	344	252
Jaffna	3	0	3	2	2
Kilinochchi	9	15	13	1	2
Mannar	4	1	1	1	0
Vavuniya	13	4	1	2	4
Mullaitivu	2	8	7	0	4
Baticaloa	0	0	1	0	2
Ampara	3	5	8	15	15
Trincomale	20	7	1	1	8
Kurunegala	533	839	496	410	520
Puttalam	6	11	10	11	9
Anuradhapura	515	554	344	340	521
Polannaruwa	263	321	378	516	540
Badulla	12	19	31	25	33
Monaragala	51	22	0	52	172
Ratnapura	223	191	156	123	236
Kegalle	17	68	52	32	34
Kalmune	1	0	0	2	0
Total	**3271**	**4028**	**3162**	**2739**	**3389**

et al, 2012; Ranasinghe, *et al*, 2011; Ranawaka *et al*, 2010). Interestingly, the same zymodeme; MON-37 of *L. donovani* causing CL was isolated from the patients identified with VL (Ranasinghe *et al*, 2012). Though number of VL cases reported from the country is low, an outbreak in the future cannot be denied (Siriwardana *et al*, 2007), as there are reports on subclinical forms of VL (Sundar *et al*, 2006). Further, a patient affected by mucocutaneous leishmaniasis was also report in Sri Lanka in 2005 (Rajapaksa *et al*, 2005).

2.3 Vector for leishmaniasis in Sri Lanka

The primary vector transmitting VL in India is the sandfly *Phlebotomus argentipes* (Kishore *et al*, 2006) and the same species was reported as the vector for CL in Sri Lanka (Siriwardana *et al*, 2012) which is widely distributed all over the country (Surendran *et al*, 2007; Lane *et al*, 1990). Though there were reports on two sibling species A and B of *Phlebotomus argentipes* in Sri Lanka (Surendran *et al*, 2005), sibling species A was identified as the potential vector (Gajapathy *et al*, 2013). However,

[1] https://www.epid.gov.lk/weekly-epidemiological-report

Premachandra *et al* reported that the sandfly species *Sergentomia zeylanica* may also play a possible role in transmitting CL in the Southern part of the country (Premachandra *et al*, 2012) which must be further studied in other parts as well.

2.4 Challenges in controlling Cutaneous Leishmaniasis in Sri Lanka

In controlling leishmaniasis in Sri Lanka, factors related to parasite and the clinical features of the disease condition are given more priority than epidemiology and vectors (Karunaweera, 2009). Further, an insufficient organized effort in control activity is also observed (Karunaweera, 2009).

2.5 Challenges in the diagnosis of CL in Sri Lanka

The direct smear method is considered as the golden standard and showing high specificity in identifying the parasites (de Vries *et al*, 2015). Sensitivity of the direct smear method varied between 60-70% and requires special professional skill, particularly to the ability to identify the morphology of amastigote form of the parasite (Amarasinghe & Wickramasinghe, 2020). Further, low positivity may be reported, due to low sensitivity of the tests, lapses in sample collection and deficiency in the laboratory techniques. This may lead to improper diagnosis (Iddawela *et al*, 2018) in turn that may affect the effort to eliminate the disease from the country.

Moreover, culturing the parasite was done with low and variable sensitivity (Khoshnood, 2021; Faber *et al*. 2003). Commercial kits available for rapid diagnosis have also not provided the promising solution for the successful diagnosis (De Silva, 2017). Though molecular diagnosis using PCR technology is highly sensitive, need of well-established laboratory and the skill and training for the laboratory technicians limits the usage of this technique in all laboratories in Sri Lanka (Amarasinghe & Wickramasinghe, 2020). Therefore, in many low resource settings, CL is diagnosed without laboratory confirmation, mainly based on the history and clinical examination which is a major limitation (de Vries *et al*, 2015) and potentially hinders the efforts to eliminate leishmaniasis from the country.

2.6 *Challenges in the treatment of CL in Sri Lanka*

Though most of the CL is self-healing, the wounds may be subjected to secondary bacterial infection and may also end up with permanent disfiguring scars (Croft *et al*, 2006). Sodium stibogluconate and liquid nitrogen cryotherapy are being used to treat the CL patients in Sri Lanka (Ranawaka *et al*, 2011; Sriwardena *et al*, 2007). Intra-lesional hypertonic sodium chloride is also being tried among CL patient in Sri Lanka, however, more studies are needed to comment on the effectiveness of this method (Ranawaka *et al*, 2011).

The availability of the drug sodium stibogluconate which is used as local infiltrate in dermatological units is limited (Karunaweera, 2009). Further, the sensitivity to *Leishmania* species for the above drug also varies (Croft, *et al*, 2006). Further, emerging drug resistance is a significant problem in the control of CL (Croft *et al*, 2006).

Though cryotherapy is mainly used to treat CL in Sri Lanka, this is not recommended to be used in the face and to the patients having the potential to develop keloids (Ranawaka *et al*, 2011). Further, delayed response to treatment of typical lesions is a crucial challenge (Sriwardena *et al*, 2007). Moreover, heat therapy is also considered as another treatment modality, however, requirement of special equipment limits its usage (Aronson *et al*, 2010; Reithinger *et al*, 2005). Also, it has been observed that some patients showed low compliance for treatment and smear positive for a longer period after the treatment (Sriwardena *et al*, 2007). It is worth to note that the access to treatment for the patients from the remote areas is a considerable challenge, as they must repeatedly travel long distance for several weeks (Sriwardena *et al*, 2007). Moreover, the local *L. donavani* variant may undergo genetic changes that may lead to unexpected outcomes when the treatment is given repeatedly (Siriwardana *et al*, 2019 a,b).

2.7 Challenges in the CL vector control in Sri Lanka

Sandfly, which is the known vector for CL is widely distributed in different parts of the country (Surendran *et al*, 2005 a,b). Further, it has been reported that the low altitude is favorable for breeding of the sand fly (Galgamuwa *et al*, 2018; Nawaratna *et al*, 2007; Rajapaksa *et al*, 2007). Notably, this lower altitude land area is larger when compare with that of the high altitude land area in the country. The sandfly control programs are generally carried out in the endemic region when an outbreak is reported. However, CL infections have been reported from almost all the districts of the country. Lack of holistic approach in controlling sandflies is less effective (Amarasinghe & Wickramasinghe, 2020). The major challenge faced by the health authorities in the country is the difficulty in identifying the breeding sources of the sandfly.

The sandfly bites on the exposed upper part of the body compared to the lower parts (Ranawaka & Weerakoon, 2010) and farmers mostly wear cloths to cover lower parts (Nawaratna *et al*, 2007), which is a major challenge in pragmatic prevention of vector bite, as the sandflies bite in the exposed areas of human. Further, there are reports on insecticide resistance among the sandflies in the country (Surendran *et al*, 2005) which may hamper the chemical control measures.

2.8 Necessity for revisiting the strategy of controlling leishmaniasis in Sri Lanka

It has been observed that an increasing number of CL cases are notified from all the districts i.e. almost entire country is affected (Weekly Epidemiology Report, Ministry of Health, Sri Lanka, 2019-2023), except in 2021 which may be due to less outdoor activity due to COVID-19 pandemic in the country.

This increasing trend of leishmaniasis may affect the potential human resources i.e. mostly young adults (Siriwardana *et al*, 2019) and security services (Galgamuwa *et al*, 2018; Wijesundera, 2001). Moreover, the disease hampers the economy of the country by affecting the farmers involve in cattle breeding and paddy cultivation (Chandrawansa *et al*, 2008; Rajapaksa *et al*, 2007; Siriwardena *et al*, 2003). On top of that, increasing number of reports on emerging fatal VL in the country (Ranasinghe *et al*, 2012; Ranasinghe *et al*, 2011; Ranawaka *et al*, 2010) along with a patient infected with mucocutaneous leishmaniasis (Rajapaksa *et al*, 2005) are alarming.

Though the health authorities of the country considering the importance of controlling the disease by declaring leishmaniasis as a notifiable disease in 2008 and started to implement a nationwide action plan (Nawaratna *et al*, 2007), still the health authorities face challenges in controlling the disease in terms of diagnosis, treatment and vector control.

2.9 Need for identifying the reservoir host involves in the transmission of CL in Sri Lanka

The health authorities implement various strategies to eliminate leishmaniasis from Sri Lanka in terms of notification of the disease, diagnosis, treatment and vector control (Weekly Epidemiological Report, 2019). However, achieving the goal seems difficult and the disease burden remains high (Weekly Epidemiological Report 2019- 2023). Therefore, in cooperating new knowledge to the existing strategy will be useful to make the strategy more efficient and effective.

It is useful to think out of the box and use the knowledge of reservoir host and prevent vector human contact in addition to diagnosis, treatment and vector control. As leishmaniasis is a vector borne parasitic zoonosis, animal reservoirs are important to maintain the life cycle of many *Lesihmania* species by means of domestic or sylvatic cycles (Alemayehu & Alemayehu, 2017). In this regard, rodents, mongoose, rock hyraxes, dogs, cats, jackals, foxes, wolves, bats, armadillos, primates, cattle, buffaloes, goats, sheep and other domestic animals were identified the major reservoirs for leishmaniasis from all over the world (Lemma, 2018; Akhoundi *et al*, 2016; Hailu *et al*, 2016; Rohousova *et al*, 2015; Roque & Jansen, 2014; Youssef & Uga, 2014; Quinnell & Courtenay, 2009; Dereure *et al*, 2000; Saliba & Oumeish, 1999).

Limited studies suggest that dogs could serve as the reservoir host for leishmaniasis in Sri Lanka (Rosypal *et al*, 2010; Nawaratna *et al*, 2009) and not rodents (Nawaratna *et al*, 2009). So far, the definitive reservoir host contributes to the transmission of leishmaniasis in the country has not been well established (Galgamuwa *et al*, 2017). Hence, few researchers believe that CL patients may remain as the reservoir hosts (Iddawela *et at*, 2018; Siriwardana *et al*, 2007). Therefore, identifying the reservoir host in different locality of the country is inevitable in order to incorporate into the existing strategy that may help to eliminate leishmaniasis from the country.

In conclusion, establishing the reservoir hosts in different localities and using the knowledge as one of the major components in the control strategy in addition to focusing on the existing control strategy of controlling the disease i.e., diagnosis, treatment and vector control, will help in eliminating the disease from the country.

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