



Review Article

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The status of Visceral *Leishmaniasis* in India

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ABSTRACT

According to the recent reports of World Health Organization (WHO), 20 000 to 30 000 deaths occur annually due to Leishmaniasis and 200 000 to 400 000 new cases occur worldwide each year. India stands with maximum number of visceral leishmanial cases (2010- 2013) and Bihar state alone reports more than 70% of the total reported cases in India. Efforts are being made by the Government of India in elimination of visceral leishmaniasis. The data is supporting the success of its elimination rate.

Keywords: Leishmania, World Health Organization, HAART

INTRODUCTION

Leishmaniasis is a group of disease caused by the protozoan *Leishmania* parasites which are transmitted by the bite of infected female phlebotomine sandflies (Figure 1). There are mainly three forms of the disease namely visceral leishmaniasis (VL, also known as kala azar and most fatal if left untreated), cutaneous [CL, the most common], muco-cutaneous [MCL]. Sandflies become infected by sucking blood from an infected animal or person. At this stage promastigote forms of the leishmanial parasite enter the human host via the proboscis. In the human host, the parasites survive and multiply within phagolysosomes of macrophages as intracellular amastigotes. (Figure 2) [1].



Figure 1: Female phlebotomine sandflies responsible for *Leishmaniasis*, source: WHO

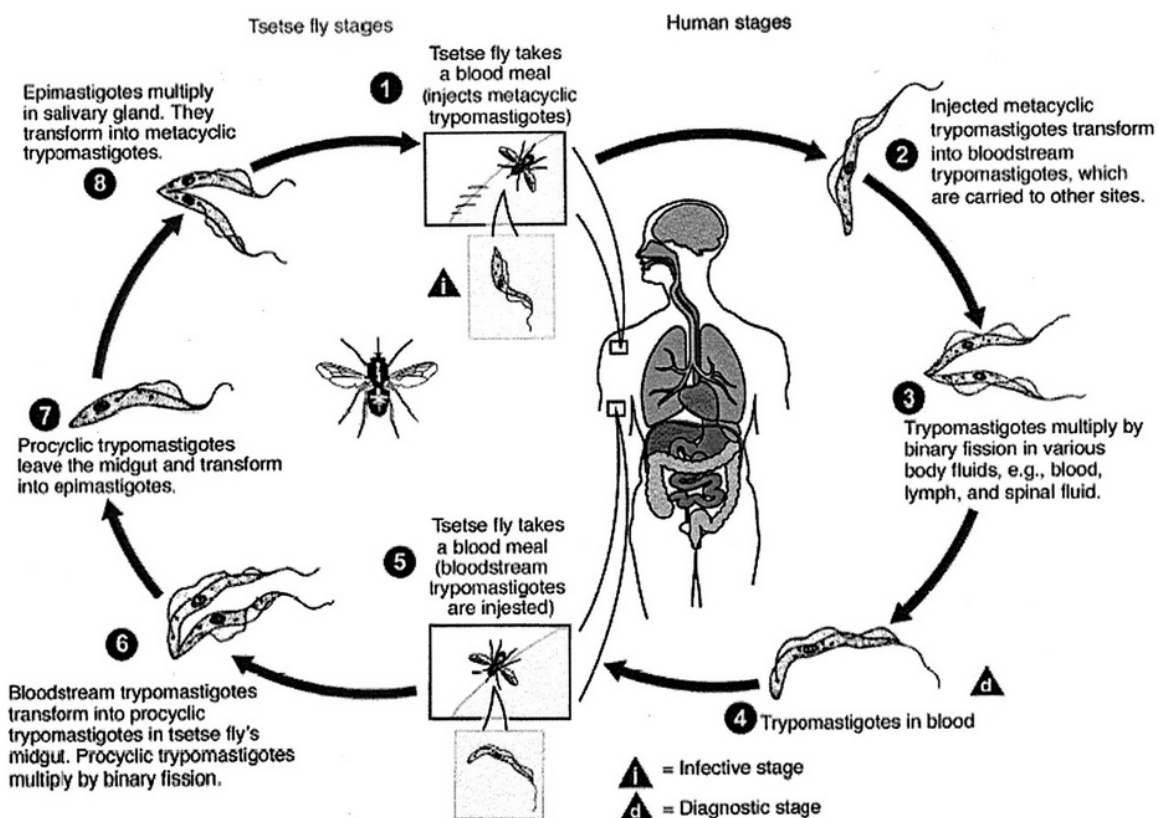


Figure 2: *Leishmaniasis* life cycle, source: Centers for Disease Control and Prevention

EXPERIMENTAL SECTION

Worldwide view of *Leishmaniasis*

According to the recent reports of World Health Organization (WHO), 900 000–1.3 million new cases of *Leishmaniasis* and 20 000 to 30 000 deaths occur annually. An estimated 200 000 to 400 000 new cases of VL occur worldwide each year [2]. The report provides worldwide VL cases of 81 countries for the period 2005- 2013. According to the data, among all, India stands with maximum number of VL cases (2010- 2013) while nine countries: Cyprus, Egypt, Guatemala, Jordan, Kazakhstan, Malta, Nicaragua, Nigeria, Turkmenistan are in the list where no cases were reported in 2013 (Table 1).

Table 1: Number of VL cases reported worldwide (2010-2013), source: WHO

Country	2013	2012	2011	2010
Afghanistan	16	24	21	11
Albania	ND	ND	ND	22
Algeria	54	70	81	87
Angola	ND	ND	ND	ND
Argentina	7	24	15	21
Armenia	7	ND	ND	9
Azerbaijan	14	22	15	35
Bangladesh	1103	1902	2874	3800
Bhutan	4	2	4	6
Bolivia (Plurinational State of)	ND	ND	ND	1
Bosnia and Herzegovina	1	0	0	1
Brazil	3253	3118	3840	3716
Bulgaria	ND	2	3	4
Cote d'Ivoire	ND	ND	ND	ND
Cameroon	ND	ND	ND	ND
Central African Republic	ND	ND	ND	ND
Chad	ND	ND	ND	ND
China	120	218	293	402
Colombia	13	9	11	34
Croatia	2	0	0	ND
Cyprus	0	0	1	1
Democratic Republic of the Congo	ND	ND	ND	ND

Djibouti	ND	ND	ND	ND
Egypt	0	0	0	ND
El Salvador	1	0	1	0
Eritrea	ND	ND	ND	ND
Ethiopia	2100	2500	2032	1936
France	ND	10	17	5
Gambia	ND	ND	ND	ND
Georgia	ND	ND	ND	143
Greece	76	47	41	28
Guatemala	0	0	0	2
Honduras	3	0	7	7
India	13869	20571	33155	28382
Iran (Islamic Republic of)	81	94	90	91
Iraq	575	1045	1167	1843
Israel	ND	ND	ND	ND
Italy	62	81	62	71
Jordan	0	0	0	ND
Kazakhstan	0	0	2	ND
Kenya	181	457	406	ND
Kyrgyzstan	ND	ND	ND	ND
Lebanon	2	ND	ND	ND
Libya	ND	ND	ND	ND
Malta	0	3	2	ND
Mauritania	ND	ND	ND	ND
Mexico	4	4	0	9
Monaco	ND	ND	ND	ND
Montenegro	ND	ND	ND	1
Morocco	111	113	107	139
Nepal	325	575	886	708
Nicaragua	0	0	0	1
Niger	ND	ND	ND	ND
Nigeria	0	57	0	0
Oman	ND	1	0	1
Pakistan	7	14	10	ND
Paraguay	107	76	114	144
Portugal	8	5	13	17
Romania	ND	ND	ND	ND
Saudi Arabia	5	8	7	8
Senegal	ND	ND	ND	ND
Serbia	2	1	2	ND
Slovenia	ND	ND	ND	ND
Somalia	673	394	290	ND
South Sudan	2364	5012 4353	11862 10468	9166
Spain	ND	213	235	153
Sri Lanka	ND	ND	ND	ND
Sudan	2389	5153	7418	6957
Syrian Arab Republic	30	17	18	19
Tajikistan	63	46	25	40
Thailand	3	5	1	2
The former Yugoslav republic of Macedonia	ND	ND	ND	ND
Tunisia	38	37	55	36
Turkey	33	13	30	36
Uganda	ND	87	690	81
Ukraine	ND	ND	ND	3
Uzbekistan	35	40	24	23
Venezuela (Bolivarian Republic of)	ND	ND	15	15
Yemen	ND	ND	0	ND
Zambia	ND	ND	ND	ND

ND = No Data

A View on Visceral Leishmaniasis

Over 90% of new cases occur in 6 countries: Bangladesh, Brazil, Ethiopia, India, South Sudan and Sudan. The trends of reported VL cases in 2013 are shown in Figure 3.

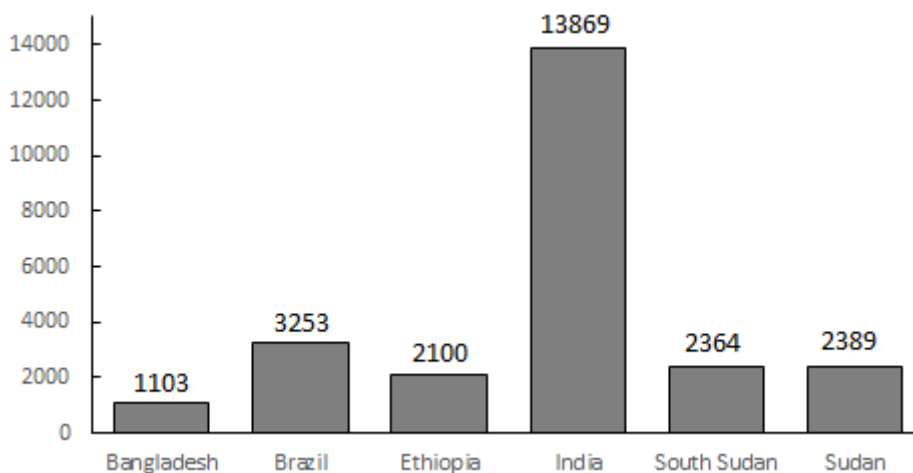


Figure 3: Reported VL cases of six countries in 2013

The VL elimination programs in South-East Asia are making consistent progress towards elimination, and cases are declining in the three major endemic countries: Bangladesh, India and Nepal (Figure 4a-c).

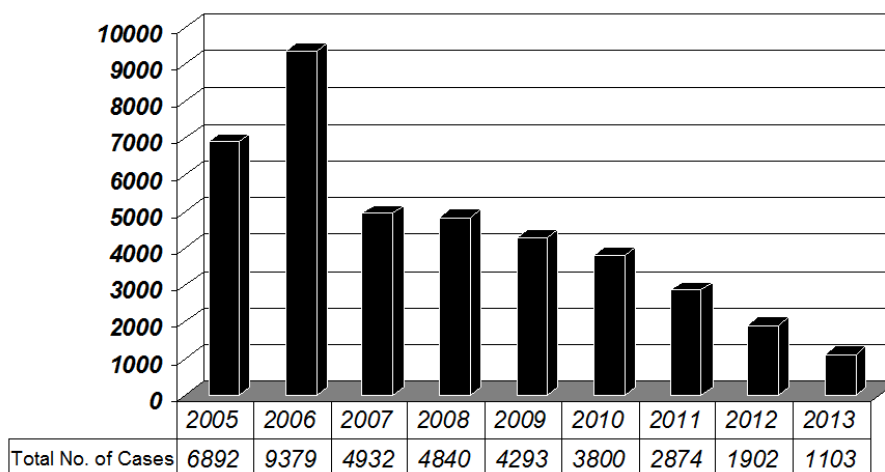


Figure 4a: Reported VL cases of Bangladesh (2005-2013)

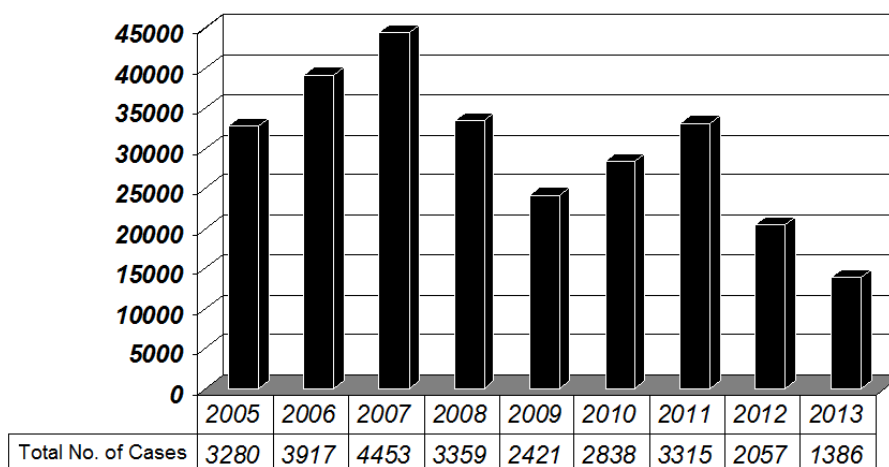


Figure 4b: Reported VL cases of India (2005-2013)

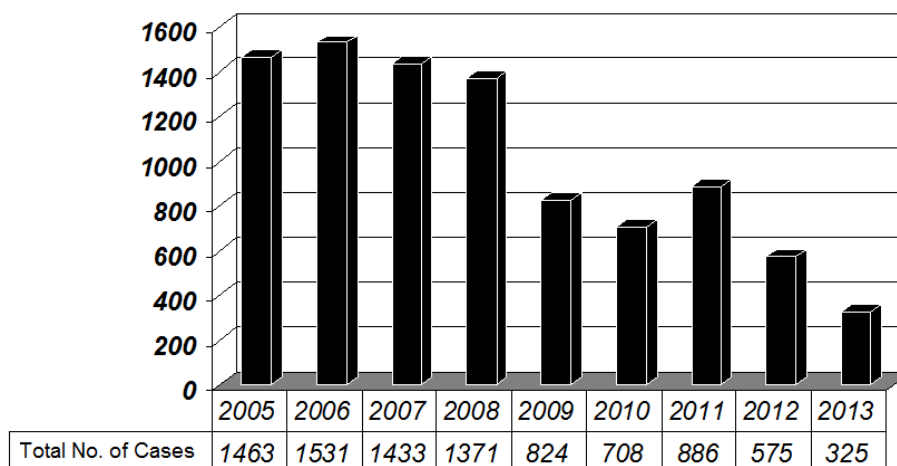


Figure 4c: Reported VL cases of Nepal (2005-2013)

RESULTS AND DISCUSSION

Leishmaniasis–HIV Co-infection

Leishmaniasis–HIV co-infection had been reported from 35 endemic countries in last 25 years. It intensifies the burden of visceral and cutaneous leishmaniasis by leading serious forms that are more challenging to manage. VL-HIV infection, as HIV-infected people are especially vulnerable to VL, while VL accelerates HIV replication and progression to AIDS, poses major challenge in areas where there is high co-infection rate. By the end of 1990, the number of new cases has declined in Europe region, mainly due to access to highly active antiretroviral therapy (HAART). In other parts of the world, however where there is constrained accessibility to such treatment method, the prevalence is still high [3].

In India, the first case of VL–HIV co-infection was reported from Uttarakhand state and large number of such cases has been reported from the VL endemic state of Bihar. HIV–*Leishmania* is not alarmingly high in India. So far, 102 cases of HIV–*Leishmania* co-infections have been reported from India. The number was high during 1997–2007 and it has been decreased due to the low prevalence of HIV in VL and CL endemic regions and because of accessibility of highly active antiretroviral therapy for HIV-infected patients. However, the number of new cases has come down after HAART therapy [4].

Status of Visceral *Leishmaniasis* in India

VL is a major issue in India especially in the eastern part of the country. The states such as Bihar, Jharkhand, parts of eastern Uttar Pradesh, West Bengal, and adjoining areas of Nepal are mostly affected by VL. According to the published data by National Vector Borne Disease Control Programme (NVBDCP, Central nodal agency of India) in 2016, the cases have declined by 32% and 10% respectively in comparison with the year 2014. The death rate due to VL has also reduced from 11 deaths in 2014 to 0 in May 2016 [5]. Currently it is endemic in 54 districts across the four states. Bihar state alone reports more than 70% of the total reported cases of VL with approximately 35 million people at risk of contracting the disease. (Table 2)

In 2014, the same agency also published the data of *Leishmaniasis* and its elimination rate across four most affected states [6]. According to the report, in Bihar 33 out of 38 districts are badly affected. Out of 33 districts, 10 are affected by VL and contribute to about 70% cases of the state. The details are given in Table 2 and the VL endemic trend of all 4 states are given in Figure 5.

Table 2: Reported VL cases in four states; source: NVBDCP

State	Population at Risk (in millions)	VL endemic districts	No. of VL affected villages (approx.)	No. of VL affected blocks	Level of elimination in blocks (%)
Bihar	34.65	Araria, East Champaran, Madhepura, Muzaffarpur, Purnia, Saharsa, Samastipur, Saran, Sitamarhi and Vaishali.	12000	426	62
Jharkhand	4.8	Dumka, Godda, Pakur and Sahibganj	1507	30	10
West Bengal	4.76	Malda, Murshidabad, Darjeeling, 24-Parganas(N), 24-Parganas(S), Nadia, Hooghly, Burdwan, Dinajpur (N), Dinajpur (S) and Birbhum	731	119	93
Uttar Pradesh	2.35	Kushinagar, Balia, Deoria, Varanasi, Gonda and Gazipur	-	6	100

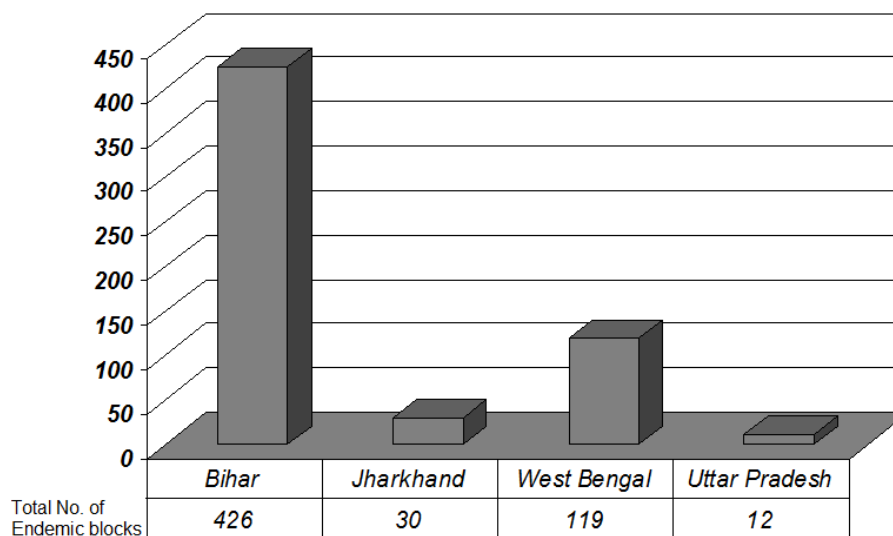


Figure 5: Trend of Reported VL cases in four states

Treatment of Visceral Leishmaniasis

Due to worst level of endemicity of *Leishmaniasis* worldwide, there is an urgent need of active medicines. Effective vaccines are not yet available and now days its treatment relies exclusively on chemotherapy. However, standard chemotherapeutics, such as pentavalent antimonials (Pentostam and Glucantime) are toxic and drug resistance is increasing dangerously in the field [7]. A liposomal amphotericin B formulation (AmBisome) less toxic than amphotericin B deoxycholate is gradually becoming the first-line therapy and considered drug of first choice for VL [8]. However, this agent is not approved for t other forms of *leishmaniasis* (CL/MCL) [9]. The first oral drug Miltefosine (Impavido) was registered against visceral leishmaniasis in the last decade. In March 2014, the CDC approved miltefosine for the treatment of VL, CL and MCL, in adults and adolescents who aged at least 12 years, weigh at least 66 lb, and are not pregnant or breastfeeding.

CONCLUSION

Standard chemotherapeutics are available to treat *leishmaniasis* completely. However, their toxicity and the appearance of drug resistance justify the search for new drug candidates to search more active drug candidates to expand the treatment options available for the disease.

In India, along with standards medicines, positive efforts are also appreciable by the Ministry of Health and Family Welfare, Government of India towards elimination of Visceral Leishmaniasis. This centrally sponsored program was started in endemic areas since 1990-91. The activities included identification of the disease, provision of medicines, insecticide spraying for vector control with DDT.

Acknowledgements

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