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Can visceral leishmaniasis be eliminated from Asia?

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Abstract

Data on the burden of visceral leishmaniasis (VL) in Indian sub-continent are vital for elimination programme planners for estimating resource requirements, effective implementation and monitoring of elimination programme. In Indian sub-continent, about 200 million population is at risk of VL. Nearly 25,000–40,000 cases and 200–300 deaths are reported every year, but these are grossly under-estimates. Recent well-designed multicentric studies identified VL burden of 21 cases/10,000 among sampled population in Indian sub-continent (Bangladesh, India and Nepal). This estimates 4,20,000 cases per 200 million risk population clearly indicating that the disease is highly under-reported. Chemical and environmental vector control studies show that the indoor residual spraying (IRS) and long-lasting insecticidal nets (LLINs) are effective and significantly reduce sandfly densities. The findings documented from different sources revealed that some gaps and weakness in existing policies for introducing VL vector control interventions. Our studies emphasize the need of integrated vector management with both IRS and LLIN vector control interventions. Active case detection with rK39 strip test as diagnostic tool is the key element for detection of VL cases. The use of oral drug miltefosine for the treatment after assessing feasibility at community level is important. Kala-azar elimination in Indian sub-continent is possible if elimination programmes ensure access to health care and prevention of kala-azar for people at risk with particular attention to the poorest and marginalized groups. The evidence-based policy should be designed that motivates to implement the programmes, which will be cost-effective. Maintaining the acceptable level of incidence requires public awareness, vector control, appropriate diagnosis and treatment. The five pillars of VL elimination strategies identified are: early diagnosis and complete treatment; integrated vector management and vector surveillance; effective disease surveillance through passive and active case detection; social mobilization and building partnerships; and clinical and operational research which need to be re-enforced to effective implementation.

Key words Asia – elimination programme – vector control – visceral leishmaniasis

Introduction

Visceral leishmaniasis (VL) or kala-azar is a re-emerging serious public health problem in the Indian sub-continent targeting the poor. VL predominantly affects the rural economy characterized by low human development and poverty; VL has become a priority for the health and economic sectors in order to achieve sustained economic growth through health labour force and reduction of expenditure for disease. In view of the increasing political commitment to VL elimination and better funding opportunities, here presented reviews are based on the recently conducted TDR/WHO collaborative studies and available visceral leishmaniasis information from member countries. The attempts have been made to estimate

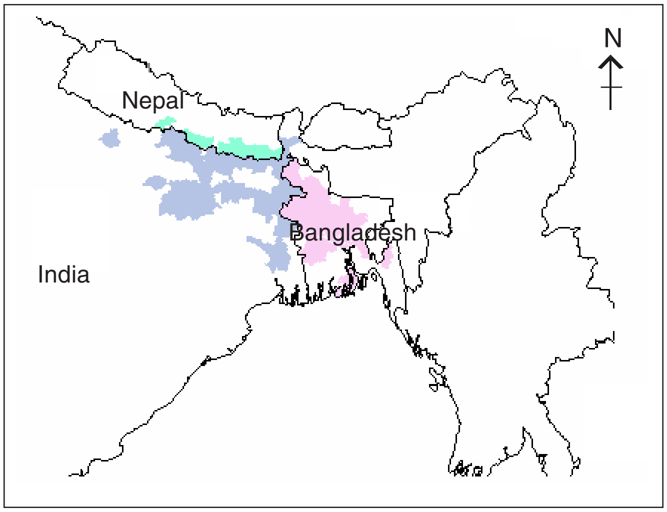

Fig. 1: VL endemic areas in Bangladesh, India and Nepal (1995–2000)

the annual incidence of the disease; describe the social and economic aspects of the disease; and vector control strategies and effectiveness of different intervention programmes.

VL has developed epidemic cycles taking place almost regularly every 15–20 years[1]. About 200 million population is at risk of VL. Nearly 25,000–40,000 cases and 200–300 deaths are reported every year, but these are possibly gross under estimates and there is a need to determine the true burden of the disease[2]. These official figures are likely to under estimate grossly the real prevalence[3]. The disease has been reported from 109 districts (45 in Bangladesh, 52 in India and 12 in Nepal) of three countries (Fig. 1 & Table 1). There is an increasing trend of VL cases in India and fluctuating trends were found in Nepal and Bangladesh (Fig. 2). The Bihar state only has captured almost 50% cases out of total cases in Indian sub-continent (Fig. 3). Due to this situation and being a border or near to border area of neighbour countries, Bihar seems as a source of VL. There might be at least two reasons: (i) possibility of weak data record system; and (ii) intervention activities determined by past cases[4]. There is also a report about the occurrence of the disease in Bhutan (S. Bhattacharya, Personal communication).

Estimation of visceral leishmaniasis (VL) burden

Multicentric studies were conducted in Bangladesh, India and Nepal on the determination of the burden of disease, health care seeking behaviour, behaviour and knowledge of care providers in the formal and informal sector and policy applications both in public and private sectors[5]. The VL cases estimation was made for Bangladesh, India and Nepal and it shows that annual total number of VL cases occurred from Bangladesh, India and Nepal are 136,500, 270,900 and 12,600 respectively. The allocated budget per head per year for risk population by national programme was calculated and it was around US$ 0.2, 0.4 and 0.3 for Bangladesh, India and Nepal respectively (Table 2).

Major findings were that the current burden of disease (21 cases/10,000 population) is 20 times higher than the elimination target in 2010/2015, treatment delay is high (symptoms to diagnosis > 3 weeks 20%; diagnosis to treatment > 3 weeks 31%), community

Table 1. Risk population, burden of disease and visceral leishmaniasis budget allocation

Countries	Population at risk in million	Annual VL cases	Estimated cases based on WHO/TDR study 21/10,000 population	Annual budget allocated in million US$	Budget allocated per head for risk population (US$ per person/year)
Bangladesh	65	5,067	136,500	14	0.2
India	129	33,613	270,900	50	0.4
Nepal	6	1,341	12,600	2	0.3

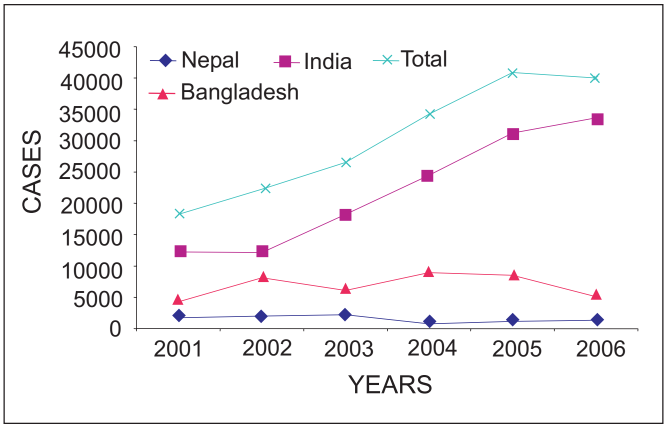

Fig. 2: Burden of kala-azar in Indian sub-continent

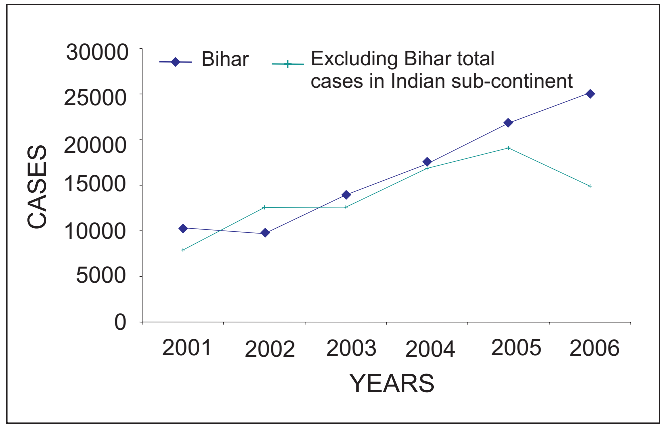

Fig. 3: VL cases in Bihar and other endemic areas

knowledge about VL and precaution is acceptable in India and Nepal, but less so in Bangladesh. The rK39 test is used by 45–58% of care providers in India and Nepal, but not yet in Bangladesh; knowledge among care providers on drugs other than antimony, miltefosine in particular, is good in India and Nepal, but unsatisfactory in Bangladesh. Policies, compared in Bihar and West Bengal, were found to be deficient and not available for the private sector. A blueprint plan for a focussed intervention in VL "hot spots" identified by GIS mapping was presented. Based on the current identified burden of the disease 21 cases/ 10,000 among sampled population in Indian sub-continent (Bangladesh, India and Nepal), about 420,000 cases per 200 million risk population could be estimated. This clearly indicates that the disease is highly under-reported.

Economic impacts

The occurrence of the VL disease pushes the people further into poverty from which they are not able to come out of. VL leads to a loss of about 400,000 DALYs (Disability adjusted life years) every year in this region[6]. This amounts to a loss of approximately US$ 140 million annually (calculated at a loss of about US$ 350 per DALY lost which is average yearly income in the endemic countries of the region).

Table 2. Test of intervention effect for the pre-post control group design

Model	Parameter	p-value		
		LLIN	IRS	EVM
Simple	Intervention effect	0.042	0	0.024
Full	Intervention effect	0.044	0.001	0.025
	Type of wall	0.881	0.260	0.925
	Type of dwelling	0.996	0.032	0.020
Type of dwelling	Intervention effect	0.042	0	0.024
	Type of dwelling	0.970	0.043	0.021
Type of wall	Intervention effect	0.044	0	0.025
	Type of wall	0.876	0.289	0.875

LLIN— Long-lasting insecticidal net; IRS——Indoor residual spray; EVM— Environmental vector management.

VL not only worsens the poverty amongst the people, it contributes to poor development of the area and stresses the overstretched health system. The major problems for producing desired outcomes were: (i) lack of VL specific control and national programmes; (ii) no collaboration or interface with the poverty focussed programmes; (iii) programmes were based on the supply side rather than the demand side; (iv) programmes were not based on public goods perspective; and (v) lack of coordination among the endemic countries to implement curative and preventive VL control programmes. Allocation of resources for controlling VL by the government from different sources is another important aspect of cost analysis. Allocation strategies are most important to gain the allocative efficiency. It is revealed that there was a very small amount in allocation of government resources for VL control among the countries. There may be at least two reasons: (i) allocated amount has captured only preventive services because it is difficult to estimate shared cost of VL in the government hospitals where other treatment and diagnosis services are also available; and (ii) the government has been paying less attention to control VL because government assumes that VL is less productive area for investment and resources have diverted to other areas.

Social impacts

VL affects the rural poor, causing significant morbidity and mortality. High cost of diagnosis and treatment causes substantial social and economic hardship for affected families. The burden of leishmaniasis is disproportionate on the poorest segments of the population. In endemic areas, increased infection risk is mediated through poor housing conditions and environmental sanitation, lack of personal protection measures and economically driven migration and employment that bring people into contact with infected sandflies. Poverty is associated with poor nutrition and other infectious diseases, which increase the risk that a person (once infected) will progress to the clinically manifested disease. Lack of health care access causes delay in appropriate diagnosis and treatment and eventually increases leishmaniasis morbidity and mortality. Leishmaniasis diagnosis and treatment are expensive and families must sell assets and take loans to pay for care, leading to further impoverishment and reinforcement of the vicious cycle of disease and poverty[1,7]. Visceral leishmaniasis has a huge social impact due to lost educational potential, reduced economic productivity, and stigma. VL results in missed days of work for adults, especially the family breadwinner. Therefore, VL not only occurs in the context of poverty, but through their adverse social impact they may also promote poverty. The stigmatizing nature of VL often causes afflicted individuals to turn away from social contact. The interruption of public health services and forced human migrations has produced resurgences in VL.

Vector control studies and strategies

The recent TDR supported multicentric study on chemical and environmental vector control as a contribution to the elimination of VL on the Indian subcontinent shows that the IRS and to a lesser extent environmental vector management (EVM) as well as LLINs significantly reduced sandfly densities for at least five to six months in study households independent of type of walls and if people shared their house with cattle or not. IRS was effective in all sites but LLINs only in Bangladesh and India. Mud plastering did not reduce sandfly densities (Bangladesh study); lime plastering in India and one Nepali site resulted in a significant reduction of sandfly densities but not in the second Nepali site.

In Varanasi, India in 2007, Regional Technical Advisory Committee (RTAC) for VL elimination together with the research teams concluded that chemical sandfly control with IRS can contribute to the regional VL elimination programme and should be continued and strengthened in India and Nepal; and operational research about performance and real life efficacy should be attached to routine control. In

Bangladesh where vector control has largely been abandoned during the last decade, the insecticide treatment of existing bednets (coverage above 90% in VL endemic districts) could bring an immediate reduction of vector populations but should also be accompanied by operational research for detecting the most cost-effective strategy. Four different models were tested, simple not controlling for any covariates, full model controlling for type of wall and type of dwelling and the two semi-controlled models (Table 2).

Management plan of the disease

In 2005, the three countries agreed to initiate a VL elimination programme with high level political commitment and the target of reducing annual VL incidence to 1/10,000 population by 2015[8,9]. Visceral leishmaniasis elimination in this region is possible because of its unique epidemiological features. Favouring factors are: human beings the only reservoir host; *Phlebotomus argentipes* the only vector in the region; VL focalized in 109 districts in three countries; the disease easy to diagnose even in field settings through recently developed rK39 dipstick test and can be treated completely with effective drugs. The five pillars of the VL elimination strategy identified so far are: (i) providing access to early diagnosis and treatment; (ii) strengthening disease and vector surveillance; (iii) integrated vector management; (iv) social mobilization and networking; and (v) operational research.

Regional strategies, challenges and issues

The regional elimination programme is trying to ensure access to health care and prevention of kala-azar for people at risk with particular attention to the poorest and marginalized groups. The strategies in implementation are focusing on: effective disease surveillance through active and passive case detection (PCD); early diagnosis by dipstick and complete treatment; effective vector control through integrated vector management with a focus on indoor residual spray, insecticide-treated nets and environmental management; social mobilization of the population at risk and partnership; and clinical and operational research to support the elimination programme[10].

As the programme improves and capacity increases, PCD should be supplemented with active case detection (ACD) that is supported by laboratory diagnosis. While ACD is recommended at least once a year in the beginning (if possible two times per year), it will become more important as the number of cases reported by PCD declines. ACD should also be supplemented by laboratory confirmation of suspected cases [Operational research is ongoing in Bangladesh, India and Nepal to assess the cost effectiveness of action (through contact tracing) and PCD]. Partnerships will be necessary at all levels, i.e. at district and state levels, at national level and with international stakeholders. Partnerships networking and collaboration will be required with other programmes like vector-borne disease programmes (malaria, dengue and filaria) and others, e.g. HIV/AIDS, TB, and leprosy. Anaemia control, improvement in nutritional status and poverty alleviation programmes should be made partners of kala-azar elimination programme. Operational research is recommended to establish monitoring of drug resistance, drug-efficacy and quality of drugs used in the programme. Research is also needed in searching for cases of post-kala-azar dermal leishmaniasis (PKDL) and for satisfactory treatment of cases of PKDL. An important operational research issue is to evaluate the public-private mix. Networking is an important strategy to optimize operational research and link it with programme implementation.

Several constraints have still to be overcome: limited sound data about VL incidence in the region; little information about peoples' access and use of diagnostic and treatment services in the public and private sectors; speculation about their non-adherence pattern to treatment-based on a suspected lack of knowledge about the disease. Even though the political commitment is high, the resource allocation until recently has been low in Bangladesh and Nepal, implementation has been inadequate, and the capacity of the health system insufficient. However, this information is of vital importance for designing appropriate and locally adapted VL elimination strategies.

Conclusion

Summary of information on the VL in Indian subcontinent is shown in Table 3. The estimated number of VL cases based on multicentric epidemiological studies and institution-based reporting data from the Indian sub-continent (Bangladesh, India and

Table 3. Summary information of visceral leishmanias (VL) in Indian sub-continent

Characteristics	Bangladesh	India	Nepal
Endemic districts	45	52 districts of four states	12
Population at risk (in million)	65	129	6
Reported cases each year (cases in 2006)	5067	33,613	1341
Annual deaths 2006	22	175	12
Drugs for treatment	Sodium antimony gluconate	Miltefosine	Sodium antimony gluconate, amphotericin B, miltefosine
Diagnosis	Direct agglutination test and rK39 test	Syndromic approach and use of rK39 for confirmation	rK39 test and parasitological test
Target year for elimination	2015	2010	2015
Vector control	Indoor residual spraying	Use of DDT spraying, entomological monitoring, sanitation and personal protection, together with indoor spraying for three consecutive years	Indoor residual spraying
Constraints	• facilities for early diagnosis and prompt treatment are generally inadequate· • during the past several years Bangladesh has not done IRS either for malaria control or visceral leishmaniasis elimination programme • standard operating procedures have been developed, but are not uniformly applied	• under reporting • increasing PKDL cases • indiscriminate use of drugs, especially by private doctors and quacks • sodium antimony gluconate resistance	• under reporting, • not enough information about PKDL cases • indiscriminate use of drugs, especially by private doctors and quacks • poor allocation of resources

Nepal) suggest to revise the earlier estimations on the VL burden. Rural-urban and male-female prevalence differentials must be kept in mind. The countries refine their estimates as much as possible when more surveillance and research data available. Recent multicentric research study on chemical and environmental vector control as a contribution of VL on the Indian sub-continent shows that the IRS and LLIN significantly reduced sandfly densities.

The evidence-based policy should be designed that motivate to implement and the programmes will be cost-effective. Policies to control VL will have to include many activities that involve public awareness and modifying personal behaviour. The cost and effectiveness of public information campaigns and various programmes should have been studied in a number of contexts in VL elimination. The five pillars of VL elimination strategies identified are: early diagnosis and complete treatment; integrated vector management and vector surveillance; effective disease surveillance through passive and active case detection; social mobilization and building partnerships; and clinical and operational research which need to be re-enforced to effective implementation.

Dynamic models of epidemiology should have been integrated with economic policy models for VL elimination. Elimination of VL is not eradication, which implies that the incidence of disease should be maintained at acceptable minimum level. Maintaining the acceptable level of incidence requires that resources be devoted to the programmes, and that the programmes should be cost-effective.

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