Retrospective Assessment of Visceral Leishmaniasis in Saptari District, Nepal

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Abstract

Visceral leishmaniasis (VL) is still posing a major public health threat in Terai belt of Nepal, mainly bordering Bihar State of India. In order to assess the epidemiological, diagnostic and treatment trends of visceral Leishmaniasis in Saptari district, a retrospective study was carried out assessing the available data of last five years (2007-2012). Epidemiologically, VL cases seem to be in declining trend during last five years in Saptari district. The highest prevalence was recorded in the year 2007 (31.5%) VL cases, which was reduced by 3.5% in 2012. Similarly, Diagnosis practice adopted in different treatment centres of Saptari district showed rK-39 as mostly practiced method compared to bone marrow aspiration technique, both in laboratory as well as in field condition. Therapeutic trend administered in VL cases showed that majority of the patients were treated with Miltefosine with different drug dosage compared to SAG and Amphotericin B. Eventually the cure rate was found to maximum with Miltefosine as it was also used in patients with antimony resistant cases.

***Key words*:** Bone marrow aspiration, *Leishmania donovani*, Miltefosine, rK-39, SAG

Introduction

Kala-azar or visceral Leishmaniasis is the disease caused by haemoflagellate, kinetoplastid parasite *Leishmania donovani*. This disease is transmitted to man by the bite of sandfly *Phelebotomous argentipes*. More than 21 species of *Leishmania* parasite have been associated with human infection (Albrecht 1998). There are three clinical forms of Leishmaniasis i.e. cutaneous Leishmaniasis caused by *Leishmania tropica*, Muco-cutaneous Leishmaniasis caused by *Leishmania brazilliensis* and visceral leishmaniasis caused by *L. donovani*. Visceral Leishmaniasis or Kala-azar is a severe chronic life threatening vector borne parasitic infection often caused by various strains of *L. donovani*, that occur in all the age groups including infants below the age of one year. While minority of infected individuals develop a full-blown visceral Leishmaniasis characterized by fever, hepatosplenomegaly, anemia, neutropenia, and hypergammaglobulinema (Karamian et al. 2007).

Leishmaniasis is distributed worldwide, but mainly it is distributed in tropics and subtropics with a prevalence of 12 million cases and an estimated incidence of 0.5 million cases of VL and 1.5 million case of CL (Sundar et al. 2001). The disease is now endemic in 88 countries in five continents Africa, Asia, Europe, North America and South America with 350 million people are at risk (Desjeux 1992). About 90% of the global cases are reported from six countries Bangladesh, Ethiopia, Brazil, India, Nepal and Sudan (Bora 1999). In context of Nepal, the disease is endemic in 12 districts in the Eastern and Central Terai regions (WHO 2010).

The techniques, which are used for demonstration of *Leishmania* parasite, are invasive and results into severe pain in the leishmaniasis patients. However, the demonstration of these parasites were performed by bone marrow aspiration, spleen aspiration lymph node biopsy etc. The current diagnostic method used in the demonstration of Leishmanial parasite where parasitological method,

serological method, detection of anti-k39 by immunochromatographic test, ELISA and DNA detection method.

Drugs used in the treatment of VL cases are Pentavalent antimonial, Amphotericin B, Paramomycin and Miltefosine, alkyl phospholipids has the excellent anti-leishmanial activity and is the first effective oral treatment for visceral Leishmaniasis, as well as for antimony resistant infection. The recommended dosage is of 2.5 mg/kg-1 daily for 28 days. It is teratogenic and therefore drug cannot be used in pregnancy and females with 3 children bearing potential must observed contraception for the duration of treatment and an additional 3 months (Singh et al. 2006).

Materials and Methods

Detailed information recorded for each and every VL suspected patients in District Public Health Office, Rajbiraj were collected from 2007/2008 to 2011/2012. Epidemiological status of the data was analyzed on the basis of the VL suspected cases to that of diagnostically confirmed cases. History of the tools used for the confirmation of VL and antileishmanial treatment used were analyzed. Antileishmanial drug treatment failure and alternative treatment strategy applied up to the outcome were assessed. Obtained data were analyzed using SPSS (statistical package for the social sciences) version 16.0 of windows.

Results

Prevalence of visceral leishmaniasis in Saptari district during last five years showed the declining trend of VL cases from the year 2007 to 2012. Highest prevalence was recorded in the year 2007 with prevalence of 31.5% VL cases in Saptari district, which is reduced by 3.5% in 2012 (Table 1).

Table 1: Prevalence of Visceral leishmaniasis in Saptari district during last five years

Year wise cases	Frequency	Percentage
2007/08	90	31.5%
2008/09	82	28.7%
2009/10	74	25.9%
2010/11	30	10.5%
2011/12	10	3.5%

Diagnosis practice adopted in Saptari district for the diagnosis of VL was observed high (83%) with rk-39, during the year 2007 to 2012. However, Bone marrow was found to be only (4%) for identification of VL cases. This result indicated that rK-39 was the mostly applied diagnostic test to confirm the VL cases in Saptari district (Table 2).

Table 2: Trend of diagnostic test used for VL confirmation in Saptari district

Year	Diagnostic test used					Total
	Bone Marrow (BM) (+ve)	**rK-39 (+ve)**	**BM (-ve) rK-39 (+ve)**	**BM (+ve) rK-39 (-ve)**	**Others**	
2007/08	2 (2.2%)	71 (78%)	10 (11%)	7 (7%)	0 (0%)	90 (32%)
2008/09	8 (9.7%)	68 (82%)	4 (4%)	2 (2%)	0 (0%)	82 (29%)
2009/10	1 (1.35%)	57 (77%)	1 (1.35%)	0 (0%)	15 (20%)	14 (26%)
2010/11	0 (0%)	30 (100%)	0 (0%)	0 (0%)	0 (0%)	30 (11%)
2011/12	0 (0%)	10 (100%)	0 (0%)	0 (0%)	0 (0%)	10 (4%)
Total	11 (4%)	236 (83%)	15 (5%)	9 (3%)	15 (5%)	286 (100%)

The trend of different drug used from the year 2007 to 2012 for the treatment of VL cases has been presented below. Out of 286 patients recovered, the highest number of drug used was Miltefosine 225

(79%) which was followed by Amphotericin B 60 (21%), in 2009/10 (82%), in 2010/11 (93%) and 100% percent in 2011/12. Similarly there is a decreasing trend of use of Amphotericin B, from the year 2007 25(28%), 2008 21(24%), 2009 12(16%) and in 2010 2(7%) while nil in the year 2070. Similarly SAG was only used in 1 patient during the year 2009. The data clearly indicated high efficacy of miltefosine in treatment of VL (Graph 1).

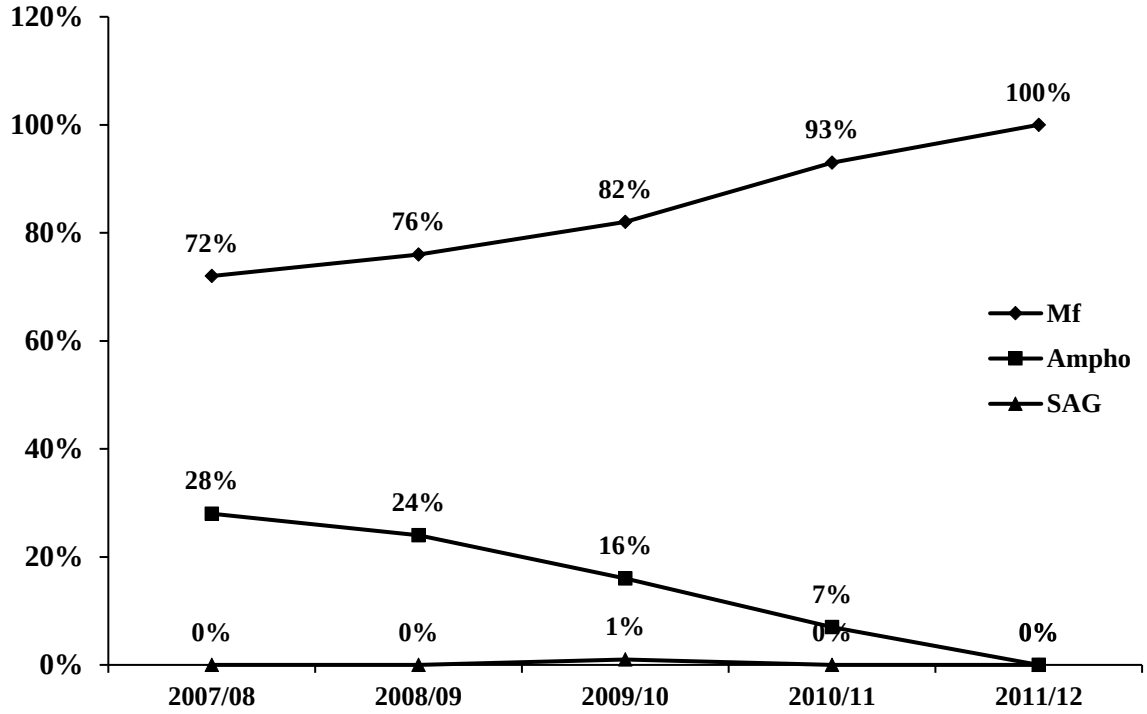

Figure 1: Trend of antileishmanial drugs used in treatment of VL in Saptari district

Drug administered in the VL patients and their cure rate during the year 2007 to 2012 indicated that the highest number of cases were recovered with miltefosine 190(66%), initial cure 34(12%) and death 1(0.03%). Similarly with fungizone recovered 45(16%), initial cure 9(3%) and death 0(0%) while relapse and defaulter is 6(2%) and SAG which has only been used in one patient of the year but the result is death. So the data revealed higher efficacy of miltefosine towards leishmaniasis (Table 3).

Table 3. Cure rate of VL according to treatment regime during the year 2007 – 2012

Antileishmanial drugs	Recovered (%)	Initial cure (%)	Death (%)	Others (%)
Miltefosine	190 (66%)	34 (12%)	1 (0.03%)	0 (0%)
Amphoterifin B	45 (16%)	9 (3%)	0 (0%)	6 (2%)
SAG	0 (0%)	0 (0%)	1 (0.03%)	0 (0%)
Total	235 (82.1%)	43 (15%)	2 (0.69%)	6 (2.1%)

Discussion and Conclusion

The analysis of prevalence of visceral leishmaniasis in Saptari district during last five year showed the declining trend of VL cases (31.5%) in the year 2007 to (3.5%) in the year 2012. This declining trend was observed in the number of cases in 2006, when the kala-azar elimination programme started, (targeting less than 1/10000 population by 2015), but between 2007 to 2010, there is an increasing

number of cases had been reported (BPKIHS 2010). It was supported by the national incidence of 0.95 per 10,000 risk populations of Eastern and central Terai regions with incidence rate more than 1 is only 3 districts, Morang, Saptari and Siraha (EDCD 2012). It has been reported that leishmaniasis is endemic in 88 countries, Particularly in Africa, Latin America, South and central Asia, the Mediterranean Basin and Middle East with over 200 million people at risk (WHO 2012). In American region, 3668 VL cases/year was reported (Rey et al. 2005), with the highest prevalence in Brazil (Latin America) with estimated 4200 to 6300 cases annually during 2002 to 2007 (Maia-elkhoury et al. 2007). In African region, 8569 cases/year was reported (Zijlstra et al. 1994, Seaman et al. 1996), which suggested that East African regions, seems to be more affected with VL cases compared to American region.

Globally, the recent data shows that, estimated annual VL incidence in South Asia is about 162,100 to 313,600 with high burden in countries like India, Bangladesh and Nepal (Singh et al. 2006, Bern et al. 2005). India accounts far estimated 34,918 VL cases/year (Bora, 1999) and Bangladesh was estimated of 6224 VL cases per year (Singh et al. 2010) and Nepal, 1477 VL cases/year was reported (Pandey et al. 2011), which suggested that VL cases reported from Nepal were very low in comparison to that of India and Bangladesh respectively (WHO 2012).

The trend of different drug, used for treatment of Kala-azar during year 2007 to 2012, indicated that highest number of drug used is miltefosine (79%) and is confirmed by the administration of Miltefosine to Kala-azar patients as an effective oral drug (Croft et al. 2003, Sunder et al. 2001). In addition to it, it is the only oral drug for therapeutic effect in KA cases when compared to other drugs like SAG and Amphotericin-B, which were given parentally and thus are very painful and inconvenient to the patients. In Asia and Indian subcontinent including Nepal, Miltefosine is the first line drug used in the treatment of VL cases (EDCD 2012).

The VL cases had been sharply declined in 2012 compare to 2007 in Saptari district of Nepal. Diagnosis trend indicated that maximum number of cases was detected through rK-39 and it was assumed to be the confirmatory test for VL in laboratory as well as field condition. Therapeutic trend showed that Miltefosine is the standard first line treatment for VL cases compare to SAG and amphotericin B.

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