# Is Detecting Visceral Leishmaniasis (Kala-azar) Cases through Existing Control Program Cost-Effective and Early in Nepal?

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## Abstract

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| **Objective** | To assess cost-effectiveness of early case detection for kala-azar by evaluating existing health-facility-based program against alternative outreach program from providers' and patients' viewpoint. |
| **Methods** | Research design included cost-effectiveness analysis (CEA) in which inputs and outcomes were measured and compared. An interview of 50 kala-azar cases generated patients' cost data while Siraha District Hospital and Kala-azar Project were assessed for provider's cost. Outcome measure was number of cases detected which, with some assumptions, was converted to number of deaths averted. |
| **Findings** | The costs per case detected in outreach and health-facility-based programmes were USD 124 and 191 respectively (1999 prices). Aversion of one death cost these programmes USD 131 and 200 respectively. Median costs to patients were USD 25 in outreach programme while it was six times higher in health-facility-based programme (USD 146), of which indirect costs due to absence from work accounted for more than half in both cases. |
| **Conclusion** | It is worthwhile to invest in outreach program for early VL case detection rather than relying only on the existing passive nature of the control program. However, it is desirable that countries endemic for kala-azar like Nepal should have a mixed strategy with both the programs, as evidences show that it would help reduce patients' burden of disease substantially and the health care delivery would also become more efficient and equitable. |



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| **Keywords** | Visceral Leishmaniasis, Kala-azar, Cost-effectiveness, Early case detection, Nepal |


## Introduction

Visceral leishmaniasis (VL), also known as Kala-azar, is a disease, which, if untreated, has a potential to claim life in almost hundred per cent cases with developed signs and symptoms, and has therefore been a major public health concern for a long time. Approximately 500,000 new cases of VL are evidenced per year throughout the world, of which 90 per cent cases live in five countries: Bangladesh, Brazil, India, Nepal and Sudan[1]. In Nepal, approximately 5.5 million people are at risk of infection from VL, covering 12 districts in the eastern Terai region, which borders with the Indian State of Bihar that housed 430,000 VL cases over the past 11 years and is again the centre of an epidemic VL[2,3]. The disease has long been believed to be an extension from Bihar, owing to free mobility of population living in these two regions due to the open border[4]. A total of 13,251 cases with 320 deaths have been reported during the period 1980-98 in the country[2]. The rate of internal migration to VL affected Terai region over the last 20 years has been very high.

VL control in Nepal continues to rely heavily on the passive case detection at the district hospitals using aldehyde test or more invasive diagnostic test like bone-marrow aspiration. There has been occasional spraying during the epidemic of the disease. A VL case is treated with first line drug, sodium antimony

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gluconate (SAG), and if a case is resistant to this, second line drug amphotericin B is given under medical supervision due to its toxic nature. Outreach case detection is limited to occasional research activities, in which usually very high number of VL cases are detected[2].

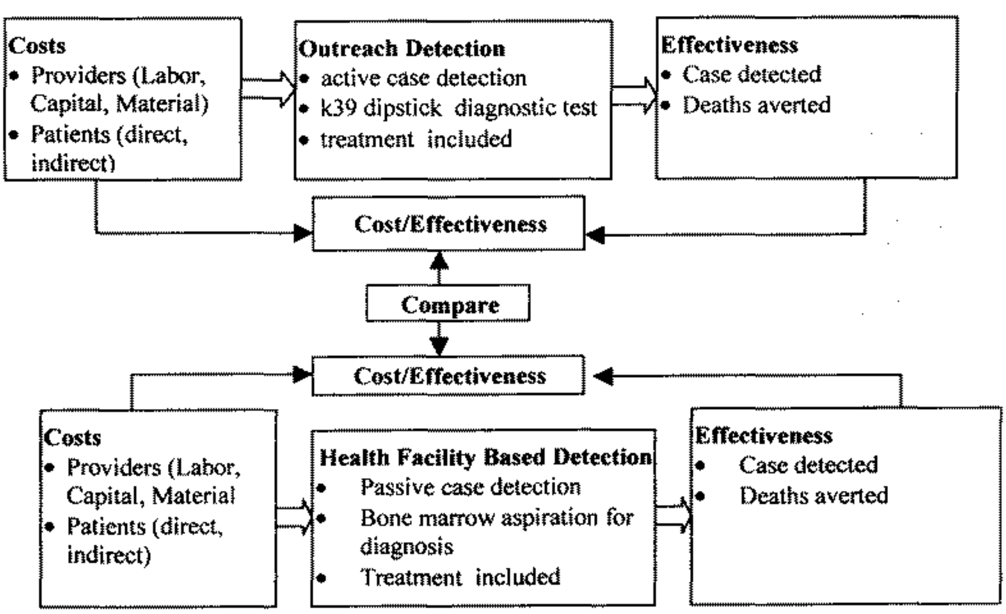
It is often suspected that delayed reporting of the cases to the health facility is the major cause of deaths due to the disease[5]. Moreover, since the current case detection method is passive and people living in the disease endemic areas have poor knowledge about VL, there may be a strong possibility of several positive cases going undetected in the community[2,6]. This observation might have implications to several economic issues such as under-utilisation of available resources and high opportunity costs associated with them. On the other hand, delayed reporting or under detection of VL cases is likely to increase the overall social costs, as VL infected individuals are important reservoir who might rapidly spread the disease in the community. Moreover, the case fatality rate associated with undetected positive cases is very high (a hundred percent among those with developed signs and symptoms). Early case detection is, therefore, needed to abolish the human reservoir and control the disease. In an attempt to reduce the long time-lag between disease onset and usual time of diagnosis, early case detection through outreach services might stand as an attractive alternative to the existing system of case management. However, any decision on policy change should be evaluated for its both costs and consequences in order to determine an efficient allocation of limited resources because in health sector market is often not readily available[7]. Although several studies have established the effectiveness of diagnostic tests such as direct agglutination test (DAT) or k39 dipstick in rapid VL case detection[8,9,10], interventions to improve early case detection have not been adequately assessed from the economic viewpoint. We report in this paper the cost-effectiveness of two interventions that help to improve earlier case detection for visceral leishmaniasis in Nepal.

## Materials and Methods

### Research Design and Viewpoint for Evaluation

A cost-effectiveness analysis (CEA) model was used to assess the efficiency of these two programs, owing to three primary considerations. First, the consequence of both interventions being considered could be expressed in the same natural unit such as 'cases detected' or 'deaths averted'. Second, the viewpoint from which the evaluation was to be carried out was narrower (providers and patients), and thirdly, the research question's main concern was 'technical efficiency' of the interventions. Figure 1 summarizes the conceptual framework of the study.

**Fig 1: Conceptual framework for the study**




The research design is Cost-Effectiveness Analysis (CEA), where similar outcomes are assessed using a ratio expressed in terms of cost per effectiveness. The outcomes are measured in natural health units such as 'cases detected' and 'deaths averted'.

**Intervention Strategies**

Outreach case detection: A program in which health workers went to the community and locate individuals who were currently ill with clinical syndrome consistent with VL and perform simple diagnostic test (k39 dipstick). If tested positive, further confirmatory test carried out and a treatment was given. The program was outreach/mobile in nature.

Health-facility-based case detection: A health facility (hospital) based program in which individuals presented to health facility on their own with some illness. If clinically found positive for VL, diagnostic tests (bone-marrow aspiration) were carried out. A treatment was given upon positive test results.

VL cases were treated in the hospitals by first-line drug (Inj. sodium antimony gluconate; 20 mg/kg body weight, not more than 850 mg/day for 30 days, and if required for another 10 days more). Cases not responding well to the above drug were treated with second line drug (Amphotericin B; 0.5 mg/kg body weight per day intravenous for 14 days) under medical supervision (hospitalization).

**Study Area, Population and Research Instruments**

The study was conducted in Siraha district of Nepal where the disease has long been endemic with annual incidence rate of 46.60 per 100,000 population at risk and case fatality rate as high as 3.88 per cent in 1997. The total area of the district is 1,188 square kilometers, covering 109 village development committees and a population of 532,587 (male female ratio 1.05), of which 130,751 males and 41,712 females are economically active. Majority of the active population is involved in farming (rice, maize and wheat) and fishing works. The houses mainly have thatched roofs and mud walls, and well (open or tube) is the main source of water supply. Government health facilities include Siraha District Hospital, Lahan Hospital, 5 primary health centres, 9 health posts and 92 sub-health posts; in addition there are several private clinics in the urban localities. The district has annual population growth rate of 2.05 and 32 percent population of age six years and above is literate. VL remains a leading cause of morbidity in the district where a population of 497,816 is at risk[2].

For programme evaluation, Siraha District Hospital was chosen to represent health-facility-based case detection while a part of Kala-azar Project[11] was selected to represent outreach case detection. For estimation of patients' costs, all known cases of VL diagnosed at the hospital in 1998-99 formed the sampling frame for the health-facility-based detection. This sampling frame was prepared using information available through medical records of the hospital, whereas that for outreach programme was prepared using Kala-azar project's database. A sample of 50 VL cases (22 from health-facility-based detection and 28 from outreach detection) were traced in the community where they lived, and an interview was conducted to assess the patients' costs. Table 1 summarises data requirement, their source and study instruments. Standard costing methods, as suggested in[7], were used in the estimates. A data entry program was developed on Epi Info version 6.04 (Year 2000 compatible). The data thus entered was later exported to Microsoft Excel 97 for analysis.

**Table 1: Summary of data requirement and their source**

| Data requirement | Study instruments | Source |
|---|---|---|
| **1. Costs to providers** | Accounts record | Secondary |
| **2. Clinical data** | Program's database | Secondary |
| No. of cases, patient history, tests performed, results of tests, diagnosis, treatment, clinical outcome of treatment, etc. | | |
| **3. Other patient specific data** | Structured interview | Primary |
| Patient characteristics, information related to direct and indirect costs, time taken to recover, etc | | |
| **4. Probability** | Past epidemiological information / estimates | Secondary |

**Measurement of Effectiveness**

Effectiveness was defined at two levels: cases detected and deaths averted. The primary effectiveness, the *cases detected*, was measured by counting the number of individuals who fell on the following criteria: "not having a past history of VL but presents with fever for more than two weeks, may or may not have spleen/liver/limphnode enlarged on clinical examination, and reported positive for VL on serological test". The next level of effectiveness, *deaths averted*, was measured using a formula based on five key assumptions, as outlined below:

No. of deaths averted = $N_{dt} \times (1-p_0)$
Where, $N_{dt}$ = Number of cases detected and subsequently treated
$p_0$ = Probability that a case dies due to VL even after treatment (case fatality rate)

*Underlying assumptions of this formula:*

1. Not all cases that were detected as having VL and subsequently given treatment for the disease would survive. If $p_0$ is the probability that a VL case would die even after treatment, $1-p_0$ would give the survival rate of patients undergoing treatment for VL.
2. The number of deaths and disability among these detected cases by a cause other than VL was assumed to be zero.
3. Detection of a VL cases and subsequent treatment to them was assumed to provide these cases with a chance to survive, given that the supply of other interventions (which might also contribute to aversion of deaths among these cases) did not remain limited.
4. The formula incorporated only quantitative aspect (number of deaths averted), not health related quality of life years among averted deaths, assuming that the period in which detected and treated VL cases lived with disability was considerably small (less than a year).
5. The formula gave equal weights to all population.

**Cost Measurements**

Table 2 identifies the resource use, ways of measurement and valuation. The overhead costs were apportioned to the respective programs using standard allocation criteria. Economic (opportunity) costing approach as suggested in[7] was used in the estimation. A discount rate of 10 per cent was used to find the present value of the capital items, which was later annualised based on the discount rate and useful life years. The annual costs so obtained were then apportioned to VL activities by using defined allocation bases. Material costs were calculated based on two headings. "Direct to activity costs" included costs of investigations, drugs and meals. "Indirect to activity costs" were the overhead costs. As no data could be obtained as to how much supplies were received by the laboratory, an indirect approach was used to estimate unit costs of the investigations using market price of each unit of input required to have one investigation. Similar approach was adopted to estimate drug costs. The costs of false positives and false negatives were not considered, assuming that the probability of the diagnostic test giving false results is negligible, and also owing to the study's narrower perspective.

**Table 2: Identification, measurement and valuation of costs**

| Resource use | How to measure | Basis of valuation |
|---|---|---|
| **Health providers' costs** | | |
| Staffing (direct) | Time (hours) | Salary/Wage rate |
| Capital (direct) | Units/amounts consumed | Market prices (conversion costs) (Annualized) |
| Consumables (direct) | Units/amounts consumed | Market prices |
| Overheads (allocated) | Units/amount consumed | Market prices |
| | Time (hours) | Wage rates/Salary |
| **Patients' costs** | | |
| Direct | Units/amounts consumed | Market prices/Actual expenses |
| Indirect (time lost from work) | Time (Hours/days/weeks/years) | Wage rate/salary or other labor costs |

*Note:* This table is adapted from Donaldson and Shackley[12]

**Cost-effectiveness Ratios and Sensitivity Analysis**

Cost-effectiveness ratios were expressed as cost in Nepalese Rupees as well as in US dollars (1999 values) per unit of outcome (expressed as "cases detected" and "deaths averted"). A one-way sensitivity analysis was performed on those parameters of costs and effectiveness, which was subject to appreciable uncertainty (discount rate in cost function and probability of survival in effectiveness formula).

## Results

The total costs incurred by the two interventions from both providers' and patients' viewpoint are summarized in Table 3. The share of capital costs in health-facility-based program was about 60 percent, of which 92 percent was due to building alone. Of total material costs, those direct to the activity accounted for about 55 percent. Drugs alone accounted for 39 percent of the total material costs in health-facility-based program.

**Table 3: Total costs (1999 value) of programs from providers' and patients' perspectives (exchange rate USD 1= Rs 68.15)**

| Viewpoint for analysis | Health-facility-based program | | | Outreach program (adjusted) | | |
|---|---|---|---|---|---|---|
| | Rs | USD | % of Total | Rs | USD | % of Total |
| **Providers (per year)** | | | | | | |
| Staffing | 209,433 | 3,073 | 9.48 | 25,200 | 369 | 18.64 |
| Material | 691,010 | 10,139 | 31.28 | 110,000 | 1,614 | 81.36 |
| Capital | 1,308,378 | 19,198 | 59.23 | - | - | - |
| Total | 2,208,821 | 32,411 | 100.00 | 135,200 | 1,983 | 100.00 |
| **Patients (per VL case)** | **Health-facility-based program (n=22)** | | | **Outreach program (n=28)** | | |
| | Rs. | USD | | Rs | USD | |
| Direct (per patient; median value) | 2,154 | 31.61 | | 112 | 1.64 | |
| Indirect (per patient; median value) | 8,540 | 125.31 | | 1,525 | 22.38 | |
| Total | 9,954 | 146.06 | | 1,670 | 24.50 | |

The actual costs incurred by the outreach program was USD 9,985 of which 40 percent was due to expenses related to staffing alone. However, a market survey revealed that the unit prices of some of the inputs that the outreach program paid were higher than the existing market rates. This prompted the investigators to adjust the costs of outreach program. The rates which were common and usually paid by non-governmental agencies for similar intervention were used in the adjusted estimates, assuming that it was the rate in a competitive labour market. The total providers' costs (adjusted) of outreach case detection program thus came down to USD 1,983 of which 19 percent was due to staffing alone (Table 3). The detection activities accounted for 72 per cent of the total costs and the rest cost was for the treatment of detected cases.

The median age of VL cases interviewed was 25.5 and 25 years respectively in outreach and facility-based program. The respective daily earnings of these groups were Rs 35 and 40 (less than a US dollar). Median values were used to explain the differences in costs of two programs, as there were substantial variation in the observation, and the mean was affected largely by extreme values. The median total cost to cases detected by health-facility-based program was about 6 times higher than that in outreach program. This is largely attributed by the total indirect costs to patients, which included opportunity costs of relatives accompanying the patient to hospitals and taking care at home in addition to costs due to his/her own absence from work. Indirect costs accounted for about 86 per cent of the total costs to patients detected by facility-based program.

In order to convert primary effectiveness (cases detected) into higher level (deaths averted), a multiplication factor of 0.95 was taken based on available epidemiological data. The cost-effectiveness ratios are given in Table 4. The difference in average costs from provider's viewpoint (USD 67 per case detected) is substantial in the context of Nepal, where per capita income is just above USD 200.

**Table 4: Cost-effectiveness of visceral leishmaniasis case detection programs**

| | Health-facility-based program | Outreach program |
|---|---|---|
| **Effectiveness** | | |
| Population at risk of VL* | 497,816 | 39,102 |
| Number of cases detected ($E_1$) | 170 | 16 |
| Case detection rate (per 100,000 population at risk) | 34.1 | 40.9 |
| Probability of survival ($1 - p_0$) | 0.95 | 0.95 |
| Number of deaths averted ($E_2$) [$= E_1 \times (1 - p_0)$] | 161.5 | 15.2 |
| **Cost-effectiveness Ratio** | | |
| ***Providers' perspective*** | | |
| Costs (in Rupees) | 2,208,821 | 135,200 |
| Costs (in USD)** | 32,411 | 1,983 |
| Cost per case detected (in USD)** | 191 | 124 |
| Cost per death averted (in USD)** | 200 | 131 |
| ***Patients' perspective*** | | |
| Cost per case detected (median value, Rupees) | 9,954 | 1,670 |
| Cost per case detected (median value, USD)** | 146 | 25 |

* Data obtained from Ministry of Health[2]. ** Exchange rate USD 1= Rs 68.15.

**Sensitivity Analysis**

Table 5 presents the results obtained by changing values for discount rate and probability of survival. The costs of health-facility-based program was sensitive to the discount rate used to annualize the capital costs. With the discount rate of 3 per cent or less the health-facility-based program became comparable with the outreach program. The cost-effectiveness was not so sensitive to the probability of survival. Even with the highest value of case fatality rate found in the country (13 percent), the cost-effectiveness ratios changed to slightly higher point than the estimated ones.

**Table 5: Sensitivity analysis of cost-effectiveness ratio and costs, according to different values of discount rate and probability of survival**

**Change in results for health facility based detection program**

| Discount rate | Capital costs (Rs.) | Total costs (Rs.) | $C/E_1$ = Costs per case detected in Rs. | $C/E_2$ = Costs per death averted in Rs. |
|---|---|---|---|---|
| 3 per cent | 635,556 | 1,535,999 | 9,035 (USD 133) | 9,511 (USD 140) |
| 5 per cent | 808,364 | 1,708,807 | 10,052 (USD 147) | 10,581 (USD 155) |
| 10 per cent | 1,308,378 | 2,208,821 | 12,993 (USD 191) | 13,677 (USD 200) |

**Change in effectiveness estimates**

| Probability of Survival = (1 – CFR)* | Programs | Total costs (Rs.) | No. of cases detected | No. of Deaths averted | Cost/death averted (Rs) | Cost/death averted (USD) |
|---|---|---|---|---|---|---|
| 1 – 0.13 | Outreach | 135200 | 16 | 13.92 | 9712 | 143 |
| | Health facility | 2208821 | 170 | 147.9 | 14934 | 219 |
| 1 – 0.05 | Outreach | 135200 | 16 | 15.2 | 8895 | 131 |
| | Health facility | 2208821 | 170 | 161.5 | 13677 | 200 |
| 1- 0.0124 | Outreach | 135200 | 16 | 15.8 | 8556 | 126 |
| | Health facility | 2208821 | 170 | 167.9 | 13155 | 193 |

CFR= Case fatality rate. Source: Ministry of Health (*2*).

## Discussion

This was the first study comparing cost-effectiveness of early case detection for VL under two separately run programs in Nepal or elsewhere (to the best of our knowledge). The results indicate that the outreach program is more cost-effective to improve early case detection than the existing health-facility-based program. Some points need further discussions in this respect. The adjusted labor costs in outreach program, for example, might raise some interesting questions. From the perspective of government provider, does it allow for the sustenance of the program, as the provider has to pull up some additional resources in order to pay at market rates? Moreover, paying at government rate itself might disregard the real wage rate prevalent in that area and workers might not be willing to work for the government provider. On the other hand, is the outreach program still be a better alternative if the labor costs were not adjusted? The figures from the analysis indicate that it is not.

The difference in the share of staffing costs in facility-based program (9.5 per cent) and outreach program (18.6 per cent) reflects importance of staff involvement in outreach services. This is further attributed to zero capital investment in case of outreach services; most of them were recurrent costs going to case detection alone. Moreover, health-facility-based program might have some drug-resistant cases and defaulters, which might have increased the costs to the program. It was considered to be zero in outreach detection program, assuming that outreach program results in early case detection. Notably, cost of hospitalization as estimated in outreach program may not reflect the true economic costs, as the minimum charge taken by the hospital for a case has been used to estimate costs of hospitalization if the detected cases were to be treated by the outreach program.

The large variations found in the patients' costs may largely be attributed to the severity of the disease, accuracy of the diagnosis made, patients' compliance, drug resistance and attitude towards seeking health care. Opportunity costs of patients due to absence from work in case of health-facility-based program was more than three fold higher than that in outreach program. Interestingly, median opportunity costs to relatives due to patient's care at home was zero for cases detected by outreach program. Most cases newly detected could take care of themselves and did not require any support from their relatives, and in case of those who required, the hours per day of the support was less than that for cases detected by the facility-based program.

The results therefore show that patients of visceral leishmaniasis are bearing a substantial disease burden, mainly in terms of indirect costs due to absence from work. Especially among patients with income below the poverty line, the economic consequences of VL can be devastating. These consequences seemed more depressing in health facility-based program than outreach program, as most of the cases detected by this program who were living under absolute poverty (daily earning less than USD 1) was found to be incurring costs above USD 70 than the same group of cases detected by outreach program.

An important drawback of the effectiveness measure used in this study was its ignorance of many confounding factors other than VL that would lead the case to death in worst scenario and to early recovery in the best scenario. Nevertheless, the primary effectiveness measure (cases detected) was supposed to have certain value in itself because if a case is detected, it was assumed that the health system would treat it and stop the transmission of the disease.

It is important to note that the k39 dipstick was found to be very practical, easy to use in the field settings, and effective in detecting VL cases. Moreover, the affordability of the test (it is available at USD 1.12 per test) may also imply its greater use in future by the health system. However, it can not replace bone marrow aspirates, as it gives positive results to already treated VL cases. It may nevertheless be used to detect new VL cases, thus limiting the use of bone marrow aspirates, which is both costlier (USD 4.0 per test) and more invasive. The economic costs of having k39 dipstick in terms of manpower is also much less, as it can be done by any health worker with little training in the community.

Since the two programs being evaluated are likely to be complimentary in nature, a relevant question here could be "can we add outreach program to the existing health- facility-based program to improve early case detection?" The study results provide enough evidence of this possibility. As seen in earlier discussions, if outreach program is implemented, it would reduce the patient's burden of disease substantially. However, one should be aware of the additional costs that would be required if a decision to integrate outreach detection to the health facility is to be taken. It is, therefore important to calculate marginal rather than average costs of the programs. The programs were evaluated separately, and therefore, no data on the combined costs were available. However, assuming that there would be some shared costs if these two programs were combined, the total costs of the combined program would be less than the sum of the costs of each program. In this case, the incremental cost of integrating outreach detection to health facility will be less than the average cost of outreach program. Thus, the combined program should incur USD 124 (average cost of outreach program) or less per additional case detected. From providers' perspective, it is a better alternative as the average cost of health facility-based program (USD 191 per case detected) is more than this amount.

## Conclusion and Policy Implication

It can be concluded that, given all assumptions made to estimate costs and effectiveness in this study be realistic, outreach case detection program is more efficient than the existing health-facility-based program. In case outreach program can not entirely substitute facility-based detection for they are likely to be complementary in nature, we recommend that these two programs should go together, as this would detect more cases as well as reduce the time-lag between infection and seeking health care. This integrated approach is also more cost-effective than existing system, and would be able to address equity issues by reducing patients' cost substantially.

The health system should be aware of the fact that, although treatment of VL is given free of charge at district hospitals, patients are not reporting to health facility due to both direct and indirect costs associated with treatment, as being extremely poor, they can not afford it. Thus, it is important to reduce time-lag between infection and diagnosis, or else there might be growing incidence of the disease. Growing incidence of VL could simply mean greater risk of transmission of the disease in the community, which in turn may mean the increased costs to the society.

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