How Far Are We from Visceral Leishmaniasis Elimination in Bangladesh? An Assessment of Epidemiological Surveillance Data

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Introduction

On the Indian subcontinent, Visceral Leishmaniasis (VL), or kala-azar, is caused by Leishmania donovani, which is transmitted from man to man by the sand fly Phlebotomus argentipes, the only known vector [1]. Of the 200,000 to 400,000 new cases of VL worldwide, more than 90% are reported from India, Bangladesh, Sudan, South Sudan, Ethiopia, and Brazil [2]. VL affects the poorest communities in these countries and is almost always fatal if not treated. The first report of VL ever came from Jessore, currently located in southwestern Bangladesh, where an epidemic outbreak killed an estimated 75,000 people between 1824 and 1827 [3]. Over the next decades, kala-azar became endemic in the region and spread slowly through Bengal, where it devastated the population of Burdwan and other areas. Subsequently, the disease spread eastward into Assam. Between 1892 and 1898, one-third of the population of the Nowgong district in Assam, India died [4]. Another epidemic of VL in conjunction with the Spanish Influenza epidemic claimed a further 200,000 lives in Assam and in the Brahmaputra valley between 1918 and 1923 [5]. Up to 1940, more than 1,000,000 VL cases were reported in former Bengal where the first mass treatment measures were undertaken [6,7]. The incidence finally declined because of the dichlorodiphenyltrichloroethane (DDT) spraying by the Malaria Eradication Programs in the 1950s, and VL was thought to be eliminated by 1970. Between 1968 and 1980, only 59 cases were reported in Bangladesh [8]. But since the 1980s, after the interruption of DDT spraying, there has been a dramatic resurgence of VL, with 73,467 cases reported from Bangladesh between 1994 and 2004, and many more reported in India [3].

In 2005, Bangladesh, India, and Nepal joined efforts to eliminate kala-azar. Elimination was thought feasible in this region because (i) human beings are considered the only reservoir host of L. donovani, (ii) Phlebotomus argentipes is the only vector, (iii) the disease is confined to a limited number of districts, (iv) a rapid diagnostic test allows easy diagnosis, and (v) effective oral treatment was available [9]. The respective Health Ministers of the three countries signed a Memorandum of Understanding (MOU) with the aim to reduce the annual incidence rate of VL to less than one per 10,000 inhabitants in the endemic communities by 2015, an elimination goal endorsed by the World Health Organization (WHO) [9]. The five strategies adopted in the VL elimination initiative were (i) early diagnosis and treatment, (ii) strengthened epidemiological surveillance, (iii) integrated vector management, (iv) social mobilization, and (v) operational research [9].

For any disease control program, proper epidemiological surveillance is a key issue. It allows for the establishment of the past and present disease burden, and will guide the program to take timely and appropriate action on case detection, patient
management, vector control, and community awareness. In an elimination initiative, routine surveillance data are essential to keep track of the elimination target, though additional measures are required to ascertain the elimination status of given areas. As the set VL elimination target of 2015 is fast approaching, we have analyzed the available epidemiological information in Bangladesh to advise the national and regional disease control policy.

Methods

Context
Bangladesh is administratively divided into six divisions, namely: Chittagong, Barishal, Dhaka, Khulna, Rajshahi, and Sylhet. All of the divisions except Sylhet are reporting VL cases, but not to the same extent. Each division is further subdivided into districts (a total number of 64), sub-districts, called upazilas or thanas (a total of 482), Union Parishads (UPs), and wards. The governmental health care system is structured along the same administrative divisions, with a national, divisional, district, upazila (sub-district), union, and ward level. Three levels in this system deliver VL treatment: (i) the Upazila Health Complex (UHC) (the lowest level, offering indoor facilities with 31 to 50 beds) (ii) the District Sadar Hospital (DSH) (a 200- to 500-bed hospital), and (iii) Medical Colleges. A UHC caters to a population of 200,000 to 300,000, while a DSH covers approximately 2 to 5 million inhabitants.

Epidemiological surveillance system
Disease surveillance is organized as follows. At the end of each month, the UHC and DSH send their morbidity and mortality reports to the Civil Surgeon Office at the district headquarters. The District Civil Surgeon transmits these reports to the Director of Disease Control at the Directorate General of Health Services (DGHS), who will notify country data to the World Health Organization. As is commonly the case in routine surveillance, these figures are an underestimation of the true number of VL cases. Medical colleges do not report although some VL patients get reported when they are referred back to the UHC or DSH after some days of treatment. This happens quite often, as VL drugs are provided for free in the public health services but are not always available in the medical colleges. Another important factor to consider when analyzing trends in the surveillance data is the recent change in drug policy. While the injectable Sodium Stibogluconate (SSG) was the only drug of choice for many years, since the middle of 2009, the oral drug Miltefosin was introduced as first-line drug (except for women of childbearing age and pregnant women). As this drug is not available in the local market, patients are now more motivated to attend a UHC to get this oral medication. The recent introduction of single-dose AmBisome therapy also attracts VL patients to the UHC, as does the recent involvement of one international Non-governmental organization (NGO), Médecins Sans Frontières (MSF), in VL care.
Data collection and analysis
We have collected all data on VL available at the central level (DGHS) for the years 1994 to 2013. We also collected district-level data for the Mymensingh district from the Civil Surgeon’s Office in Mymensingh for the same period. As the VL elimination target is set at the upazila level “to reduce VL incidence rate below one per 10,000 population per year at upazila level,” [9] we calculated the Incidence Rates (IR) for each upazila. We used the total population of the upazila in the corresponding year in the denominator. The data were analyzed by using SPSS, Minitab, and Microsoft Excel.

Results
From 1994 to 2013, the DGHS of Bangladesh reported 109,266 cases of VL and 329 VL-related deaths from 37 endemic districts. During this 20-year period, there were three years (1997, 2002, and 2006) with more than 8,000 reported cases. The highest number of cases was reported in 2006, and the annual number of cases diminished after that peak year (Figure 1). Altogether, 37 districts reported VL cases at some point during this period. The number of districts reporting VL cases increased from 21 districts in 1994 to 29 districts in 1998 and 2008. Sixteen districts reported VL cases consistently from 1994 to 2013 (Figure 2). The highest number of VL cases was reported from the Mymensingh district, accounting for 49.04% (53,582) of the total number of cases (Figure 2). The Mymensingh district reported 110 deaths due to VL, or 33.85% of the country’s total. The second highest number of cases occurred in the Pabna district (12,067 or 11.04%) (Figure 2) with 11 deaths, followed by the Tangail and Jamalpur districts where 10,170 (9.31%) and 6,965 (6.37%) cases, respectively, were reported (Figure 2), including 45 (13.85%) and eight (2.46%) deaths. Twelve districts reported more than 1,000 cases in the study period, six between 500 and 999, and 19 reported between one and 499 cases. Figure 3 compares the VL case load in the country for the period of eight years before (1998–2005) and after (2006–2013) the signing of the MoU, and shows that except the Mymensingh district, all other endemic districts experienced a remarkable decline of cases. Figure 4 shows 16 upazilas located in nine districts where the average IR ranged between 1.06 to 18.25 per 10,000 population from 2008 to 2013.

The most affected upazilas are situated in the Dhaka division, reporting the highest number of cases of all the divisions (78,079, including 25 deaths from 1994 to 2013). Table 1 shows that cases were reported from 101, 81, 84, 75, 76, and 62 upazilas out of 130, 134, and 140 upazilas at risk, respectively, from 2008 to 2013. The most affected division, Dhaka, reported 4,226, 3,679, 2,115, 3,273, 1,464, and 1,094 cases from 2008 to 2013, respectively, followed by the Rajshahi division, with 573, 530, 604, 584, 359, and 272 cases. From 2008 to 2013, the Khulna division reported 37, 82, 157, 82, 46, and 49 cases, respectively. The Barishal division reported 84 cases from 2008 to 2013, and the Chittagong division reported a very low number of cases (Table 1).
Table 2 shows that Mymensingh is the most affected district. The Incidence Rate (IR) per 10,000 people per year varies from 0.1 to 16.5 in the seven affected upazilas (Table 3). As Table 3 shows, almost all cases are concentrated in five of the seven upazilas. The Tangail district has three endemic upazilas, there are two affected upazilas in the Pabna district, and the other six districts have six endemic upazilas (one in each) (Table 2). Among the five most endemic upazilas in the Mymensingh district, the Fulbaria upazila diagnosed 4,085 cases from 2008 to 2013. The second highest case number diagnosed is in the Trishal upazila, where 4,020 cases were diagnosed, followed by Bhaluka (1,501), Muktagacha (1,310), Gafargaon (1,053), Haluaghat (120 cases), and Nandail (21 cases). Other upazilas diagnosed few cases from 2008 to 2013 (Table 3). The IR in the five highly endemic upazilas in the Mymensingh district, the Fulbaria upazila diagnosed 4,085 cases from 2008 to 2013. The second highest case number diagnosed is in the Trishal upazila, where 4,020 cases were diagnosed, followed by Bhaluka (1,501), Muktagacha (1,310), Gafargaon (1,053), Haluaghat (120 cases), and Nandail (21 cases). Other upazilas diagnosed few cases from 2008 to 2013 (Table 3).

From 2008 to 2013, there were 16 upazilas in nine districts with an average IR exceeding the elimination target, ranging between 1.06 to 18.25 per 10,000 inhabitants (Table 2).

From 2011 to 2013 there were 409, 325, and 240 post kala-azar dermal leishmaniasis (PKDL) cases reported from the Mymensingh district. No country-wide PKDL data are available up to 2012, and 325 cases were reported country-wide in 2013.

**Discussion**

The VL elimination program was launched in 2005, and its target was set to reduce the number of cases at upazila level below one case per 10,000 people by 2015 [9]. However, as the initial situation in 2005 and the current epidemiological situation are not well captured, it is extremely difficult to say in 2014 how far we are from the elimination target. Surveillance data from the Disease Control Department of DGHS show that cases were reported from 37 districts from 1994 to 2013, whereas previously, 45 districts were considered endemic [10]. Unfortunately, upazila-level data on VL are not available at DGHS before 2007, making it difficult to properly assess the trends at this level. Moreover, the level of underestimation of VL cases has probably reduced significantly during recent years, as was observed also in India, for at least two reasons: (1) the introduction of a rapid diagnostic test, which has improved access to diagnosis, and (2) the recent policy making free VL treatment available in the public services with drugs that are not available in the private market. This changing, under-reporting ratio does not facilitate the interpretation of trends.

About half of the total numbers of VL cases were reported from a single district (Mymensingh), where five upazilas are highly endemic. Therefore, the national program should intensify its efforts in these areas with high priority. Due to VL, there is a huge
Figure 4. VL-endemic upazilas above target, where incidence rate is above one per 10,000 people from 2008 to 2013, with their respective districts.
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Table 1. Cases and deaths reported from 37 endemic districts under five divisions showing the number of VL-endemic upazilas as well as the number reporting cases that year.

| Division | District | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | Deaths (2008–2013) |
|----------|----------|------|------|------|------|------|------|-------------------|
|          |          | Cases | Cases | Cases | Cases | Cases | Cases | Upazila Reporting |
|          |          | Upazila | Upazila | Upazila | Upazila | Upazila | Upazila | Endemic |
|          |          | Endemic | Reporting | Endemic | Reporting | Endemic | Reporting | Endemic | Reporting | Endemic | Reporting | Endemic | Reporting | Endemic | Reporting | Endemic | Reporting | Endemic | Reporting | Endemic | Reporting | Endemic | Reporting |
| Rajshahi |          | 13    | 57    | 573   | 39    | 530   | 43    | 604     | 76     | 38    | 548     | 76     | 36    | 359     | 76     | 32    | 272     | 6      |
| Khulna   |          | 5     | 4     | 37    | 8     | 5     | 82    | 8       | 157    | 8     | 4       | 82     | 8     | 46      | 8      | 3     | 49      | 2      |
| Barishal |          | 3     | 1     | 2     | 3     | 2     | 2     | 3       | 2      | 3     | 2       | 31     | 3     | 22      | 3      | 2     | 13      | 0      |
| Dhaka    |          | 14    | 47    | 4,226 | 35    | 3,679 | 33    | 2,115   | 51     | 31    | 3,273   | 51     | 34    | 1,464   | 51     | 27    | 1,094   | 27     |
| Chittagong |        | 2     | 1     | 2     | 0     | 0     | 0     | 2       | 0      | 0     | 2       | 0      | 0     | 2       | 0      | 0     | 0       | 0      |
| Total    |          | 37    | 130   | 101   | 4,840 | 134   | 81    | 4,293   | 140    | 84    | 2,879   | 140    | 75    | 3,934   | 140    | 62    | 1,428   | 35     |

Source: Malaria and Vector-Borne Disease Control Unit, Directorate General of Health Services, Government of Bangladesh, Dhaka.
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Table 2. Number of VL cases and annual Incidence Rate (IR) per 10,000 in upazilas.

| District  | Upazila         | 2008  | 2009  | 2010  | 2011  | 2012  | 2013  | Average IR |
|-----------|-----------------|-------|-------|-------|-------|-------|-------|------------|
| Mymensingh| Trishal         | 1,492 | 1,279 | 735   | 564   | 252   | 235   | 18.25      |
|           |                 | 36.54 | 30.91 | 17.53 | 13.27 | 5.85  | 5.38  |            |
| Mymensingh| Fulbaria        | 1,315 | 781   | 456   | 1,608 | 397   | 211   |            |
|           |                 | 30.25 | 17.73 | 10.22 | 35.55 | 8.66  | 17.82 |            |
| Mymensingh| Bhaluka         | 235   | 285   | 125   | 107   | 86    | 73    |            |
|           |                 | 6.93  | 8.29  | 3.59  | 3.03  | 2.40  | 2.01  | 4.35       |
| Mymensingh| Mukttagacha     | 198   | 343   | 214   | 99    | 82    | 127   |            |
|           |                 | 4.93  | 8.42  | 5.19  | 2.37  | 1.94  | 2.96  | 4.30       |
| Mymensingh| Gafargaon       | 260   | 240   | 260   | 292   | 241   | 82    |            |
|           |                 | 4.62  | 4.21  | 4.50  | 4.98  | 4.06  | 1.36  | 3.95       |
| Jamalpur  | Madarganj       | 115   | 109   | 47    | 88    | 64    | 35    |            |
|           |                 | 4.50  | 4.21  | 1.79  | 3.31  | 2.37  | 1.28  | 2.91       |
| Khulna    | Terokhada       | 46    | 43    | 39    | 17    | 16    | 21    |            |
|           |                 | 3.81  | 3.51  | 3.15  | 1.35  | 1.26  | 1.63  | 2.45       |
| Tangail   | Shakhipur       | 70    | 58    | 103   | 73    | 25    | 32    |            |
|           |                 | 2.64  | 2.15  | 3.78  | 2.64  | 0.89  | 1.13  | 2.20       |
| Panchagar | Debiganj        | 18    | 49    | 44    | 96    | 38    | 16    |            |
|           |                 | 0.88  | 2.37  | 2.10  | 4.52  | 1.76  | 0.73  | 2.06       |
| Rajshahi  | Godagar        | 70    | 102   | 14    | 47    | 17    | 24    |            |
|           |                 | 2.29  | 3.29  | 0.45  | 1.47  | 0.53  | 0.73  | 1.46       |
| Pabna     | Faridpur       | 23    | 23    | 19    | 18    | 20    | 17    |            |
|           |                 | 1.69  | 1.67  | 1.36  | 1.27  | 1.39  | 1.17  | 1.42       |
| Sirajganj | Chauhali       | 26    | 30    | 19    | 20    | 26    | 23    |            |
|           |                 | 1.53  | 1.74  | 1.09  | 1.13  | 1.45  | 1.26  | 1.37       |
| Tangail   | Nagopur        | 39    | 47    | 25    | 39    | 38    | 37    |            |
|           |                 | 1.37  | 1.63  | 0.86  | 1.32  | 1.27  | 1.22  | 1.28       |
| Gaudpur   | Shreepur       | 55    | 53    | 42    | 58    | 15    | 49    | 1.19       |
|           |                 | 1.49  | 1.41  | 1.11  | 1.51  | 0.38  | 1.29  |            |
| Tangail   | Modhupur       | 80    | 45    | 55    | 50    | 48    | 49    | 1.14       |
|           |                 | 1.72  | 0.96  | 1.15  | 1.03  | 0.98  | 0.99  |            |
| Pabna     | Chamtihor      | 27    | 36    | 36    | 31    | 30    | 13    |            |
|           |                 | 1.02  | 1.35  | 1.33  | 1.13  | 1.08  | 0.46  | 1.06       |

Approximate number of population was determined based on national growth rate of 1.34 from 2001 to 2013 and Incidence Rate (IR) was calculated per 10,000 people.

Note: in the table first value = reported cases, second value = IR.

Source: Malaria and Vector-Borne Disease Control Unit, Directorate General of Health Services, Government of Bangladesh, Dhaka.

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Table 3. Number of kala-azar cases and deaths reported by the Mymensingh district from 2008 to 2013.

| District:                        | Number Diagnosed cases | Total (%) | Number Treated cases | Total (%) | Incidence rate per 10,000 people | Deaths | Case Fatality Rate |
|----------------------------------|------------------------|-----------|----------------------|-----------|----------------------------------|--------|-------------------|
| Mymensingh district, all upazilas| 12,118                 | 100.0     | 12,089               | 100.0     | 4.0                              | 24     | 0.20              |
| Mymensingh district, 5 highest endemic upazilas | 11,969 | 98.8 | 11,943 | 98.8 | 9.3 | 23 | 0.19 |
| Upazila:                        |                        |           |                      |           |                                  |        |                   |
| Fulbaria                        | 4,085                  | 33.7      | 4,045                | 33.5      | 15.7                             | 3      | 0.07              |
| Trishal                         | 4,020                  | 33.2      | 4,284                | 35.4      | 16.5                             | 8      | 0.20              |
| Bhaluka                         | 1,501                  | 12.4      | 1,526                | 12.6      | 4.5                              | 6      | 0.40              |
| Muktakacha                      | 1,310                  | 10.8      | 1,325                | 11.0      | 5.5                              | 2      | 0.15              |
| Gafargaon                       | 1,053                  | 8.7       | 763                  | 6.3       | 5.2                              | 4      | 0.38              |
| Haluaghat                       | 120                    | 1.0       | 117                  | 1.0       | 0.7                              | 1      | 0.83              |
| Nandail                         | 21                     | 0.2       | 21                   | 0.2       | 0.1                              | 0      | 0.00              |
| Dobawra                         | 4                      | 0.0       | 4                    | 0.0       | 0.0                              | 0      | 0.00              |
| Ishwarganj                      | 2                      | 0.0       | 2                    | 0.0       | 0.0                              | 0      | 0.00              |
| Phulpur                         | 1                      | 0.0       | 1                    | 0.0       | 0.0                              | 0      | 0.00              |
| Sadar                           | 1                      | 0.0       | 1                    | 0.0       | 0.0                              | 0      | 0.00              |
| Gautipur                        | 0                      | 0.0       | 0                    | 0.0       | 0.0                              | 0      | -                 |

(Source: Office of the Civil Surgeon, Mymensingh District).
Note: Mean number of kala-azar cases reported per 10,000 per year, based on mean number of estimated district population from 2008 to 2013. doi:10.1371/journal.pntd.0003020.t003
Box 1. Importance of Proper Disease Surveillance for VL Elimination Program

- Measure the past and present disease burden.
- Guide national program to take timely and appropriate action on:
  - Patient management
  - Vector control
  - Community awareness through IEC
- Prevent unnecessary program expenditure, i.e., accurate surveillance record will provide guidance on specific areas in which to take necessary actions instead of in the whole upazila or union.
- Predict future burden.

Key Learning Points

- Human resources responsible for epidemiological surveillance, including data management, require intensive training and supervision.
- Effective surveillance is crucial to understand the real burden of disease and for taking timely action.
- It is essential to have a proper referral system for the VL patients so as to avoid the duplication of reporting.
- Community-level health staff needs training to identify the cause of death.
- The private sector clinics and practitioners should be involved in the reporting system for VL.

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