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Visceral Leishmaniasis in Afghanistan: Analysis of Cases from 2018 to 2022

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ABSTRACT

Background: Visceral leishmaniasis (VL) is a neglected but typically fatal vector-borne protozoan disease. It leads to substantial health problems and/or death for up to 400,000 people per year. Afghanistan is an endemic country for VL. We aimed to analyze VL cases from 2018 to 2022 and enlighten the epidemiological profile of the disease in the country.

Methods: A descriptive analysis of VL cases from 2018 to 2022 was conducted during July to September 2022. Secondary data of the VL surveillance were retrieved from Malaria and other Vector Borne Disease Control Program (MVDP) of Ministry of Public Health, Kabul, Afghanistan. while the outcome of registered cases were confirmed through phone calls. Data were managed and analyzed using MS Excel, Epi Info V.7.2.1, and GIS.

Results: Overall, 77 cases were registered and reported from 2018 to 2022. Most of the cases 48 (62%) were male, and 68 (88.3%) were aged 0-5 yr with a mean of 3.6 ± 2.1. Geographically, 28 cases (36%) were reported from Faryab Province followed by Baghlan 9 (12%) and Ghazni 1 (1.2%) provinces. Only Four (5%) and 7 (9%) cases reported family members with Cutaneous Leishmaniasis and VL respectively. Common clinical manifestations among patients were fever (96%), weight loss (96%), and splenomegaly (91%). Upon follow up, 35 (45.5%) of the cases were lost, 31 (40.2%) were cured, and 11 (14.3%) deceased. The outcome of treatment was significantly associated with treatment type, Glucantime.

Conclusion: We found higher proportion of VL among under-five males. Most of the cases were reported from the northern region and the family history of VL was reported by patients. Fever and weight loss were the frequent clinical manifestations. Early diagnosis and Glucantime had good outcome compared to late diagnosis and SSG. Awareness activities, access to diagnosis, health education and interventions are recommended in high-risk provinces. In addition, further studies are encouraged to determine the prevalence of the disease among the general population.

Keywords: Visceral leishmaniasis, Leishmaniasis, Treatment outcome, Afghanistan

Introduction

Leishmaniasis is a parasitic disease resulting from infection with protozoa of the genus *Leishmania*, transmitted to both animals and humans via the bite of blood-feeding female sand flies (1). Despite constituting one of the Neglected Tropical Diseases (NTDs), this parasitic infection ranks ninth in terms of global disease burden among infectious diseases (2). There are three types of leishmaniasis, with Visceral Leishmaniasis (VL) ranked as the second deadliest parasitic disease globally (3,4). The World Health Organization (WHO) prioritized its elimination in the Roadmap for the Prevention and Control of Neglected Tropical Diseases 2021–2030 (5). The majority (approximately 90%) of visceral leishmaniasis cases worldwide are concentrated in only seven countries. Four of these are in Eastern Africa (Sudan, South Sudan, Ethiopia, and Kenya), two are in Southeast Asia (India and Bangladesh), and Brazil accounts for nearly all cases in South America (6).

Important drivers for the emergence and spread of leishmaniasis include environmental factors such as alterations in temperature and water storage, irrigation habits, deforestation, climate changes, development of drug resistance, increase traveling to endemic regions and dog importation. War, poor socio-economic status and low-level household are also major contributors to the spread of this disease (7). The findings of determinants studies shows that age, sex, residence, season, travel history to endemic areas, and mean monthly precipitation were found to be statistically significant for VL (8). In Ethiopia, the seroprevalence significantly associated with outdoor sleeping, the presence of damp floors, and sleeping outdoor near animals (9). Comparing the efficacy of Insecticidal Wall Painting (IWP) with routine Indoor Residual Spraying (IRS) program in Bangladesh, IWP showed excellent performance in reducing sand fly density and increasing its mortality. The effect of IWP for controlling sand flies was statistically significant for up to at least 24 months (10).

In 2020 over 85% of new CL cases occurred in 10 countries: Afghanistan, Algeria, Brazil, Colombia, Iraq, Libya, Pakistan, Peru, the Syrian Arab Republic and Tunisia (11). To date, no published literature comprehensively describes the epidemiological landscape of VL in Afghanistan. Despite the substantial annual incidence of VL in neighboring countries of Afghanistan, namely Iran, Pakistan, Turkmenistan, and Uzbekistan, with reports numbering in the hundreds, scientific literature documents only 23 confirmed VL cases within Afghanistan since 1980 (12).

Prior to 2018, a standardized surveillance system for VL was not established which may account for the underreporting of VL in the country. Currently there is a functional surveillance system to investigate the VL cases. This study aims to fill this critical knowledge gap by delineating the epidemiological characteristics of VL cases across Afghanistan. The findings of this research are expected to provide valuable insights for policymakers, facilitating the improvement and strengthening of access to diagnosis and treatment services for VL patients within the country.

Methods and Materials

Study design and data source

A descriptive retrospective study with an analytical component was used, utilizing secondary data of VL surveillance from 2018 to 2022. The current VL surveillance established in 2018 operates under the Malaria and other Vector Borne Disease

Control Program (MVDP) of Ministry of Public Health (MoPH). This system collects data on cases of VL through paper-based forms in central and provincial level. The follow-up on treatment outcomes was made through phone calls using the contact information provided in the forms on case-wise basis during 2022 for the purpose of this study. For the sake of this study, data were extracted from annual cases of VL registered in the MVDP along with the treatment outcome follow-up reports case-wise.

Study population and setting

The study included all VL cases registered in Afghanistan during the study period. The majority of VL cases were reported from the Indira Gandhi Children's Hospital (IGCH) in Kabul, which serves as the primary referral center for complicated cases of VL. Patients were diagnosed through bone marrow aspiration at IGCH and rapid diagnostic tests (RDT) at the provincial level. The data collection and analysis were completed over a two-month period (July-August 2022).

Data collection and management

The data was entered, cleaned, and analyzed using Epi-Info version 7.2, GIS, and Microsoft Excel. The reporting forms captured patient details including name, father's name, age, sex, and weight, as well as place of residence, clinical presentation (signs and symptoms), and family history of Cutaneous Leishmaniasis (CL) or VL. It also recorded diagnostic details such as the type of diagnosis and place of diagnosis, treatment information including the type of antimonials prescribed, and patient contact information. The reporting forms were coded prior to data entry. Data entry was performed in Epi-Info, data cleaning was conducted in Excel, analysis was carried out using Epi-Info V 7.2, while GIS was used for geographical plotting of the cases.

Data analysis

Variables analyzed included the frequency of cases by age and gender, annual and provincial distribution of cases, clinical features such as signs and symptoms, and timing of diagnosis, particularly focusing on late diagnosis. Additionally, the type of diagnostic method (Bone Marrow Aspiration, RDT, or Aldehyde test) was assessed, along with treatment outcome categories (cured, died, non-responsive) via phone. The types of antimonial prescribed, including Sodium Stibogluconate and Glucantime, and their association with treatment outcomes were evaluated. The duration of clinical symptoms manifestation and diagnosis as well as age and sex of the cases and its effect on treatment outcomes were also analyzed.

Ethical considerations

Data were retrieved from VL surveillance of MVDP of Ministry of Public Health under official permission. The data repository was not subject to any modification except the exclusion of personal identifiers (e.g., name, phone number) to ensure the confidentiality of study subjects. Data repository is only accessible for the permitted individuals while the risk of re-identification of cases has been mitigated by the exclusion of personal identifiers and restricted access to data.

Results

During the study period, 77 patients were enrolled, and diagnosed with VL throughout the country and included in the analysis. Most of the cases, 68 (88.3%) were in the age category of under-five years old with an average age distribution of 3.6 ± 2.1 (Table 1). Almost two-third of the cases were males 48 (62.3%). Among the cases, only 7 (9%) reported the history of VL among their family members. Furthermore, more than one-quarter of the cases 21 (27.3%) were diagnosed 7-24 months after clinical manifestation of the VL. Bone Marrow Aspiration was the prominent diagnostic approach 64 (83.1%).

Fever 97.4%, splenomegaly 92.2%, Fever 96% and splenomegaly 91% were reported among the cases and four-fifth of the cases 62 (80.5%) received Sodium Stibogluconate. Slightly less than half of the cases 35 (45.5%) did not respond to the phone for collecting of the treatment outcome 11 (14.3%) deaths were reported due to VL during the study period..

Table 1: Descriptive Statistics of Demographic and Clinical Characteristics of Visceral Leishmaniasis in Afghanistan, 2018-2022 (N=77)

Variables	***Frequency***	***Percentage***
Age (mean and SD)	3.6 ± 2.1	
Age groups (in years)		
0-5	68	88.3
6-13	9	11.7
Sex		
Male	48	62.3
Female	29	37.7
Family History of Leishmaniasis		
History of family members with cutaneous leishmaniasis	4	5
History of family members with Visceral leishmaniasis	7	9
Duration between Clinical Manifestation and Diagnosis		
0-6 Months	56	72.7
7-24 Months	21	27.3
Type of Diagnosis		
Bone Marrow Aspiration	64	83.1
Rapid Diagnostic Test	9	11.7
Formaldehyde test	4	5.2
Sign and Symptoms		
Fever	75	97.4
Weight loss	75	97.4
Splenomegaly	71	92.2
Abdominal pain	11	14.3
Body pain	11	14.3
Diarrhoea	25	32.5
Advised Treatment		
Glucantime	15	19.5
SSG	62	80.5
Treatment Outcome		
Cured	31	40.2
Died	11	14.3
Did not respond to phone	35	45.5

The time trend analysis of the cases shows that 67.5% of cases were reported during 2019 and 2021 aggregately (Figure1). The highest number of deaths, 6 (54%) was recorded in 2019. Additionally, with the establishment of the new VL surveillance in 2018, 16 cases were reported while during peaks of COVID-19 outbreaks (2020-2021), the cases didn't decline. The lower number of cases during 2022 could potentially be attributed to the study time conducted during midst of 2022.

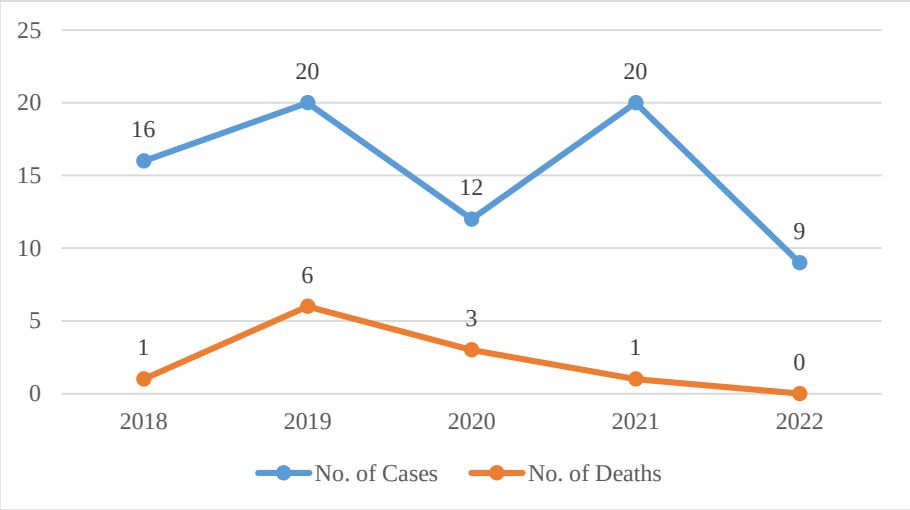

Figure 1*:* Time trend analysis of VL cases in Afghanistan, 2018-2022 (N=77).

Overall, VL cases were registered from 18 out of 34 provinces of Afghanistan with geographical distribution elucidating a chain-like spread of the cases in the northern region of Afghanistan (Figure 2). The highest number of cases was reported from Faryab Province 28 (36%) followed by Baghlan 9 (12%) while VL was not reported from Kabul, Capital Province of Afghanistan. On the other hand, VL was reported from some of the provinces in the eastern and southern region which is not in comparable level to the number of cases in northern region.

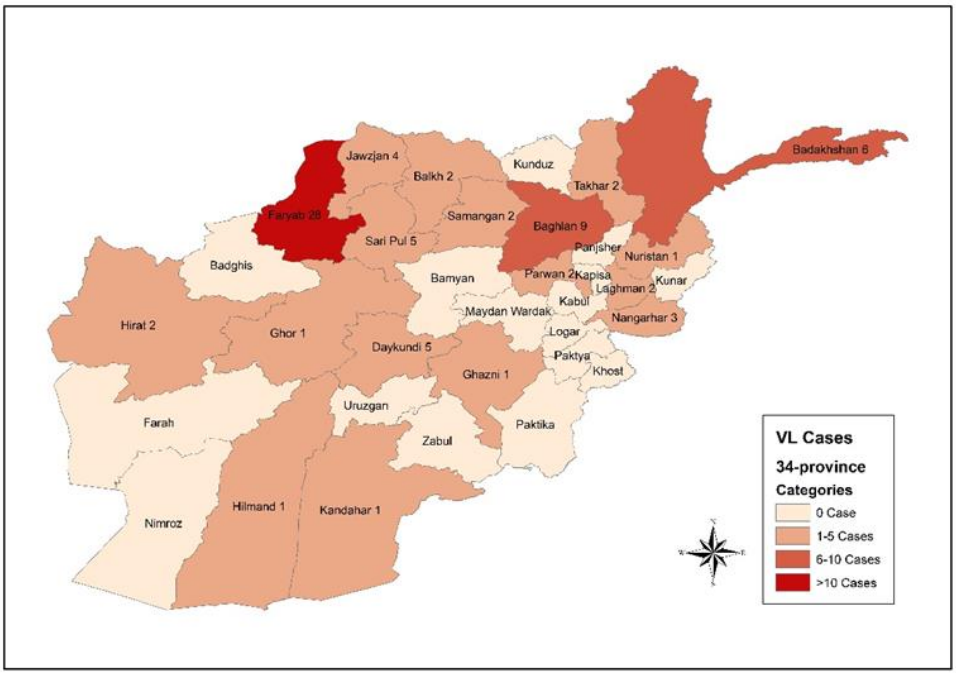

Figure 2: Geographic distribution of VL cases in Afghanistan, 2018-2022 (N=77)**.**

Association of baseline characteristics with outcome of the infection with VL was assessed among 42 patients responding to follow-up calls (Table 2). An association between type of advised treatment and outcome of the infection was found significant among the patients (X2= 4.06, *P*=0.044). Totally, all the patients receiving

Glucantime were cured while one-third of the patients receiving SSG died eventually. On the other hand, the duration between clinical manifestation and diagnosis of VL was found to be significantly associated with the outcome of infection (X2= 0.04, *P*=0.049). More than four-fifth of the patients 22 (84.6%) diagnosed during 0-6 months of clinical manifestations were cured. No significant association between age groups of the VL cases and their sex was found in this study.

Table 2: Association of baseline characteristics with treatment outcomes for visceral leishmaniasis (N=42)

Variables	***Cured N(%)***	***Died N(%)***	***Statistics and P-value***
Age groups (in years)			
0-5	28 (73.7)	10 (26.3)	X2 = 0.95, *P*=0.723
6-13	3 (75)	1 (25)	
Sex			
Male	23 (76.7)	7 (23.3)	X2= 0.50, *P*=0.382
Female	8 (66.7)	4 (33.3)	
Duration between Clinical Manifestation and Diagnosis			
0-6 Months	22 (84.6)	4 (15.4)	X2=4.12, *P*=0.042
7-24 Months	9 (56.3)	7 (43.8)	
Advised Treatment			
SSG	22 (66.7)	11 (33.3)	X2= 4.06, *P*=0.044
Glucantime	9 (100)	-	

Discussion

As an endemic neglected disease, many cases of Leishmaniasis are left undiagnosed or untreated in Afghanistan (13). The findings of this study point out the prominence of the disease among under five and males, prevalent signs and symptoms among cases, a comparatively favorable observed treatment with Glucantime in this cohort, and timely diagnosis. On average, Afghanistan reported 17 VL cases on annual basis since 2018, compared to only 23 cases in the span of 24 yr (1980-2004) (12). The observed surge since 2018 in the number of reported VL cases suggest operationalization of the surveillance system for this disease, which likely contributed to improved case detection. However, some other contextual factors, unexplored in this study, may have played a role as well. The ambiguity of specific data on VL cases is discussed in literature, although many cases of leishmaniasis were reported in 2002, there is still lack of data on specific number of VL cases (14).

Children are at a higher risk of VL, and the average incidence of the disease drops with aging and among those with a previous VL infection (15, 16). The higher incidence of and death rate among the lower age group may be explained by their increased biological susceptibility and limited immunity as described in other studies (17). From 77 cases in our study, more than 88% were among the 0-5 yr age group, which is in line with evidence emphasizing predomination of VL among under five children (18, 19). Most of the data coming from studies on children with VL are from pediatric hospitals or pediatric wards which increases the possibility that data on children aged over five or adults might be missing and point out the gap of scientific studies among them.

Many studies in Africa have shown significant association with sex and VL, evidence from Ethiopia and Kenya suggest on higher VL cases among males, the

results showed that the odds of VL infection were 68% higher among males compared to females (20-23). This may come since, socio-culturally, males are often more exposed to environments where sandflies, the vectors of the disease, are prevalent. Furthermore, the finding can be supported with males' outdoor engagement in the in the outdoor activities such as farming, herding, or sleeping outside, eventually increasing their risk of being bitten by infected sandflies which results in VL infection (24, 25). Another study conducted in Saran District of Bihar, India, from early 2009 to July of 2011 showed that males were significantly more likely to contract VL than females (26). Leishmaniasis, as well as numerous other infectious diseases, exhibits sex-related differences that cannot be explained solely in terms of environmental exposure or healthcare access (27).

VL cases are characterized by fever, weight loss, fatigue, weakness, loss of appetite, enlarged liver and spleen, anemia, and swollen lymph nodes (28, 29). The most prevalent clinical manifestation in our study was fever (96%), followed by weight loss (96%) and splenomegaly (91%). The prevalence of clinical manifestation are different in different studies. On the other hand, early and accurate diagnosis and treatment remain key components of VL control. In addition to improved diagnostic tests, accurate and simple tests are needed to identify treatment failures. Most of the VL cases in this study were diagnosed using Bone Marrow Aspiration method. In existence of other different diagnostic tests, BMS are believed to provide a safer but less sensitive method in the diagnosis of VL compared with splenic aspirates (30).

In the current study many patients experienced a significant delay in diagnosis. Delay, which frequently lasts more than six months after the onset of symptoms, is linked to higher mortality and less successful treatment outcomes. While the problem has been described in worldwide overview literature (6), Ethiopian reports have also linked delayed diagnosis to poor treatment outcomes (31). Although this study showed a statistically significant association between early diagnosis and favorable outcomes, the observational design precludes definitive causal inference. Treatment for VL is a complicated matter because of issues with cost, side effects, and efficacy of the current alternatives (32). Most of the patients in this study (81%) were treated using Sodium Stibo-Gluconate (SSG) and the rest were treated using Glucantime. SSG is shown to have efficacy and toxicity, with poor oral absorption, therefore given via intramuscular or intravenous injections (33). However, in cases of treatment failure, relapse, and severe toxicity cases L-AMB is recommended as second-line treatment (34, 35). On the other hand, upon following up the treatment outcome by phone, we noted that more than 14.3% of the patients were dead. VL has a high fatality rate, however, late follow-up and distance between the time of follow-up does not necessarily indicate that all the deaths are caused by VL. This could also have been biased by recall and low awareness on VL mortality and morbidity.

There has been limited development in control and prevention of VL, and challenges remain as instability, population movements and environmental changes test programming and political commitments (6). The pathogen's and the sandfly vector's distribution range may grow northward and higher due to climate change. Higher seasonal temperatures would result in shorter diapause periods and longer activity periods in endemic areas. As a result, there can be more sandfly generations annually. In addition to raising the danger of infection, rising temperatures hasten the leishmaniasis maturity. However, the disease may vanish from some areas if the temperature is excessively hot and dry, as this lowers the vector survival rate.

The geographical clustering of VL cases in northern provinces, such as Faryab and Baghlan, highlights distinct regional

disparities in disease burden. This pattern may reflect ecological factors conducive to sandfly proliferation, as well as socio-economic conditions that limit healthcare access. The absence of VL cases from certain regions, including the capital, Kabul, raises questions about underreporting and the possibility of undiagnosed cases outside of identified hotspots. Access to diagnostic services of VL is a problem in Afghanistan and have been limited to the capital. However, recently distribution of VL RDT to some provinces is a good initiative to be expanded to all hospitals at provincial and central levels. This study's retrospective approach, which adds recall bias and insufficient data collection, is the main limitation. Furthermore, the high rate of follow-up loss, which reflects structural flaws in patient monitoring and retention, makes it more difficult to accurately analyze treatment outcomes. Characterizing VL strains is further limited by the lack of molecular diagnostic techniques, which may have an impact on treatment plans. Moreover, small sample size of the study is another limitation of the study. The overall sample size and bivariate analysis may have been influenced by the lower statistical power due to small sample size.

Conclusion

Findings of this study elucidate the epidemiological landscape of VL in Afghanistan with higher number of cases among males in under-five age category and the northern provinces of Afghanistan. Furthermore, prominent clinical manifestations of the VL cases reported in this study were fever, weight loss and splenomegaly. The observed treatment outcomes with Glucantime were more favorable compared to SSG. Efforts should be focused on high-risk provinces with high cases, particularly on north and northeastern provinces with the majority of the reported cases and the risk factors of the disease should be investigated in the mentioned regions. Besides this, improving people awareness regarding the prevention of the VL is crucial for the affected area. In addition, further studies are encouraged to determine the prevalence of VL among all age categories in endemic areas.

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Conflict of interest

The authors declare that there is no conflict of interests.

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