



Assessment of treatment outcomes of visceral leishmaniasis (VL) treated cases and impact of COVID-19 on VL management and control services in Bangladesh

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ABSTRACT

Background: COVID-19 has largely impacted the management of Visceral leishmaniasis (VL), like several other Neglected Tropical Diseases. The impact was particularly evident in Lower and Middle-Income countries where the already inadequate healthcare resources were diverted to managing the COVID-19 pandemic. Bangladesh achieved the elimination target for VL in 2016. To sustain this success, early diagnosis and treatment, effective vector control, and periodic surveillance are paramount. However, the specific control measures for VL in Bangladesh that were hampered during COVID-19 and their extent are unknown. **Methods:** This study aimed at identifying the gaps and challenges in the follow-up of treated VL patients by interviewing both the treated VL cases and their health service providers. We followed VL cases treated between 2019 and 2020 in five VL endemic subdistricts (upazilas) both retrospectively and prospectively to monitor clinical improvement, relapse, or other consequences. Moreover, interviews were conducted with the health service providers to assess the impact of COVID-19 on VL case detection, treatment, reporting, vector control operations, and logistic supply chain management.

Results: There was no added delay for VL diagnosis; however, VL treatment initiation and reporting time increased almost two-fold due to COVID-19. Indoor Residual Spraying activity was significantly hampered due to a shortage of insecticides. Out of 44 enrolled and treated VL patients, two relapsed (4.5 %), two developed Para Kala-Azar Dermal Leishmaniasis (4.5 %), and three (6.8 %) Post Kala-Azar Dermal Leishmaniasis (PKDL). The health service providers highlighted patients' unwillingness to visit the hospital, financial constraints, and distance from the hospitals as the main reasons for missed follow-up visits (20.5 %). Building good communication in the community, awareness schemes, and incentive-based approaches were suggested as possible solutions to mitigate these problems.

Conclusion: Long-term follow-up is required for the early detection and management of VL relapse and PKDL cases. Effective vector control measures, capacity development, and identification of new VL hotspots are pivotal in the VL endemic regions to sustain the elimination goal.

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Introduction

COVID-19 has inflicted a massive crisis on low- and middle-income countries (LMIC), including Bangladesh. Bangladesh imposed its first lockdown in the form of a public holiday on 26th March 2020, which eventually extended in multiple steps [1] interrupting various disease control programmes and healthcare service deliveries. In April 2020, the World Health Organisation (WHO) postponed all mass drug administrations (MDAs), active case-searching activities, and community-based surveys for Neglected Tropical Diseases (NTDs) [2,3]. Visceral leishmaniasis (VL), commonly recognized as kala-azar, has been a major public health problem in the Indian sub-continent, especially in Bangladesh, India, and Nepal, for a long time until recently [4]. Following a Memorandum of Understanding (MoU) signed in 2005, these countries constrained the transmission of VL and are on the verge of eliminating the disease. The VL elimination target was to reduce VL incidence below 1 per 10,000 population at the upazila, block, and district levels for three consecutive years in Bangladesh, India, and Nepal, respectively, by 2015, which later was extended to 2020 [5,6]. However, the recent WHO/NTD Roadmap 2030 has targeted validating 32 countries for VL elimination as a public health problem by 2023, 56 countries by 2025, and 64 countries by 2030, defined by < 1 % case fatality rate due to primary VL [7].

The fragile health system and limited resources have posed severe challenges in coping with the COVID-19 pandemic and mitigating its consequences. Different strategies and measures have been employed for COVID-19 control in Bangladesh [8]; however, there is no evidence of how much COVID-19 control measures (including lockdown and travel restrictions) have impacted VL healthcare services. According to modelling exercises presented by the NTD Modelling Consortium, VL is one of the diseases in which the impact of disrupting the current programmes is greatest in high-endemic regions with a high risk of disease resurgence [9,10]. The impact of COVID-19 on VL case detection, treatment, reporting, vector control operation, and logistic supply chain management has not been assessed to date. Anecdotal evidence suggests that the uncertainty of COVID-19 has reduced access to care and negatively affected care-seeking behaviour. The fear of the disease and lockdowns imposed by governments are reported to have resulted in interruptions (and even cessation) of public health programs both from the provider side and the public.

Effective treatment and follow-up plans are vital to improving patient outcomes and reducing disease transmission. The single-dose AmBisome regimen has proven to be an excellent choice for VL treatment in the Indian sub-continent. However, to ascertain the outcome of the treatment, patients need to go through follow-up visits on the 1st and 6th months after treatment. Assessment at the 1st-month visit determines the initial cure, whereas 6th months visit determines the final cure of VL. If there is no improvement of the initial condition within one month or recurrence of symptoms and signs for VL within six months, the patient is considered a treatment failure case. Recurrence of symptoms and signs of VL after the final cure is regarded as a relapse case [11]. Prior studies demonstrated that there was a VL relapse of up to 7 % among treated cases in Bangladesh and India. Both new and relapse VL and PKDL cases can transmit *Leishmania donovani* if untreated [12,13]. Moreover, there is a significant relationship between the treatment regimens for VL and the development of Post Kala-azar Dermal Leishmaniasis (PKDL) and relapse [14]. Hence, the success of the National Kala-azar Elimination Programme (NKEP) in Bangladesh in sustaining the elimination target for VL depends largely on patient follow-up to identify progression of treated VL cases towards VL relapse and PKDL. Besides treatment and follow-up, effective control measures such as Indoor Residual Spraying (IRS) and Active Case

Detection (ACD) will also play a pivotal role in sustaining VL elimination in the Indian Sub-continent.

Therefore, in this study, we followed VL-treated cases and assessed the treatment outcome. Furthermore, we tried to explore the impact of the COVID-19 pandemic on VL control activities, including VL case management, patient follow-up, and sandfly control measures based on the issues faced by both parties.

Methodology

Study design

This implementation research was conducted to identify the gaps and challenges in the follow-up activity of treated VL patients as per National strategy, strengthen the efficiency of the National Kala-azar Elimination Programme (NKEP) for better follow-up of treated VL cases, and to assess the impact of COVID-19 pandemic on the follow-up of treated Visceral Leishmaniasis (VL) patients. VL cases in five VL endemic subdistricts (upazilas), namely Gafargaon, Trishal, Fulbaria, Nagarpur, and Madhupur, treated within 2019–2020 were recruited in the study. We conducted interview of the patients during enrolment using a semi-structured questionnaire to understand their perspective regarding the gaps and challenges in the VL follow-up activities during the COVID-19 period. We also followed them up twice, 6 months apart to monitor clinical improvement, relapse, or other consequences. Treated VL cases were followed up both retrospectively and prospectively. Research assistants were trained to follow up on the cases and document the clinical conditions of the study participants.

Furthermore, a cross-sectional study was conducted among the health service providers to assess the impact of COVID-19 on VL case detection, treatment, reporting, vector control operation, and logistic supply chain management.

Study sites and population

Situation analysis and follow-up of treated VL cases as per strategy were conducted in five VL high-endemic upazilas. VL-treating clinicians, focal persons of VL in the upazila health complex, and patients treated for VL were included in the study. Eligible participants were:

Previously treated VL patients who had completed treatment within 2019–2020 were residents in one of the five high-burden upazila identified for the study, were available for interview, further follow-up, and were willing to participate in the study. VL focal persons in the study upazillas (Medical Officer, Disease Control) or at the national level (Medical Officer (Kala-azar) and In-charge, Surya Kanta Kala-azar Research Center (SKKRC)) who were willing to provide interviews.

Interview of VL patients and focal person in the upazila on the impact of COVID-19

The VL focal person of the upazila was interviewed using a semi-structured questionnaire to collect data on how well VL cases were detected during the ongoing COVID-19 pandemic (active and passive). VL reporting frequency to the centre was assessed compared to previous records. The frequency, timing, and IRS coverage, including other vector control operations, were also assessed. Program experience with supply chain management was explored in the interview. The focus was on drugs and diagnostics available for VL, stock out, and challenges of access faced by patients during the COVID-19 pandemic due to disruptions in supply chain management.

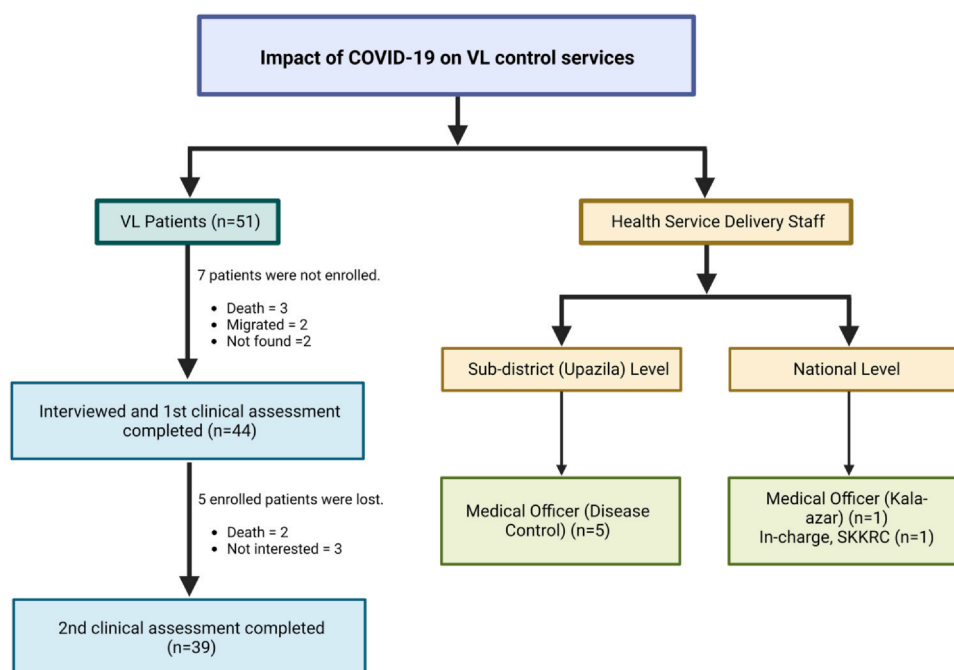


Fig. 1. Schematic view of study participant enrolment.

Enrolled participants were interviewed to collect data on any delay in VL follow-up services, general health status and health seeking behavior during COVID-19 period.

Interview of VL patients and health service providers on post-treatment VL outcome

VL-treating clinicians from the hospitals and focal persons of VL in the upazila health complex (UHC) from the selected five upazilas were interviewed to collect data on the status of follow-up of the treated VL cases. From Surya Kanta Kala-azar Research Center (SKKRC), we interviewed the hospital in charge and the medical officer (Kala-azar); from the UHCs, we interviewed Medical Officer (Disease Control). We conducted a total of 7 interviews for this purpose. Information was collected on gaps and challenges in following up on treated VL patients.

Treated VL patients were invited for follow-up and were interviewed to collect data on barriers to follow-up from the patients' perspectives. During the study period, 51 VL patients from five endemic upazilas were treated. We enrolled 44 VL-treated patients for this study. Among the seven missed patients, three had died before the study initiation, three could not be traced using their contact details, and the rest had migrated to another country. Information was collected regarding the compliance to follow-up and the reasons in case of less compliance.

Statistical analysis

A well-checked data entry program was developed using Microsoft Access 2019. All the data were double-checked before entering into this program. Data quality was maintained as per data management guidelines. Data were analyzed using STATA version 13. Descriptive statistics were generated to see the nature of the data. Differences between the means were compared through parametric and non-parametric methods depending on the distribution of the variables. Differences between proportions, such as proportions of relapse according to the treatment regimen, symptoms of VL and PKDL at follow-up, and other characteristics, were compared with the Chi-square test. A p-value < 0.05 was regarded as statistically significant.

Results

Socio-demographic background of the treated VL cases

A total number of 44 VL patients was interviewed at baseline, which dropped to 39 at the end of the study. Among the 5 participants lost to follow-up, two had died during the study period due to ageing, and the other three had declined to come as they felt healthy. The mean age of the enrolled participants was 35.2 (16.3) years. Many participants were female (54.5 %) and housewives (40.9 %). Almost two third of the patients (68.1 %) were illiterate, and about half of them lived in tin-shed houses (52.2 %) with a median income of 12000 BDT (approx. 140 USD) (Range: 8000–15000) per month. The average number of bed nets in the house was 2.48 (1.25), and almost every household (38) used bed nets on a regular basis.) (Table 1).

Treatment history

At the time of enrolment, all patients completed their treatment, and records revealed that most of them (81.8 %) were treated with a single dose of Liposomal Amphotericin B (SDLAmB) monotherapy. Four patients reported that they had either VL relapse or PKDL after the end of treatment up to the time of enrolment in this study. Among these four patients, two had VL relapse, one had PKDL, and one had the simultaneous presence of VL relapse and PKDL, often regarded as Para kala-azar Dermal Leishmaniasis (Para-KDL) (Table 1).

Impact of COVID-19 on VL care

Regarding the impact of COVID-19 on these VL patients, we found that 35 out of 44 had their after-treatment follow-up visits as per schedule. Nine VL patients did not go to the hospital for a follow-up visit, mostly because of their positive perception of their health status. Out of 35 patients, 25 had a thorough check-up (from history taking and asking for overall health conditions to proper physical examination) at the follow-up. The ten patients reporting not having a thorough follow-up either missed one or more of the following

Table 1
Household screening information of the study area.

Indicators	% (n)
Total no. of participants (N)	44
Age in years, Mean (SD)	35.23 (± 16.33)
Sex of the patients	
Male	45.45 (20)
Female	54.55 (24)
Demographic Information	
Educational status	
Illiterate	31.82 (14)
Literate	68.18 (30)
Occupation	
Farmer	25.00 (11)
Housewife	40.91 (18)
Business	4.55 (2)
Student	15.91 (7)
Labour	4.55 (2)
Unemployed	2.27 (1)
Service	6.82 (3)
Monthly household expenditure	
Median (IQR)	12000 (8000–15000)
Type of house	
Kuccha	25.00 (11)
Pucca	22.73 (10)
Tin-shed house	52.27 (23)
Cattle shed	
Yes	50.00 (22)
No	50.00 (22)
Bed nets in the house	
Mean (SD)	2.48 (± 1.25)
Use of bed net	
All times	86.36 (38)
Sometimes	13.64 (6)
Treatment Specific Information	
VL treatment regimen for the latest episode	
Multi-Dose Liposomal Amphotericin B (MDLAmB) monotherapy	18.18 (8)
Single Dose Liposomal Amphotericin B (SDLAmB) monotherapy	81.82 (36)
Treatment status	
Completed	100.00 (44)
Withdrawn	0.00 (0)
History of VL relapse or PKDL or both (Para-KDL) after treatment	
VL relapse	4.55 (2)
PKDL	2.27 (1)
Both	2.27 (1)
Impact of COVID-19	
Follow-up visit on time	
Yes	79.55 (35)
No	20.45 (9)
A thorough check-up at the follow-up visit	
Yes	71.43 (25)
No	28.57 (10)
Cancelled or deferred appointment with a doctor due to COVID-19	
Yes	36.36 (16)
No	63.64 (28)

follow-up assessments - a) Enquiry on symptoms for VL, b) Measuring the spleen size, c) Measuring the weight, d) Measuring the haemoglobin, e) Observing for any skin lesions. Interviewing these participants revealed that two enrolled patients experienced a shortage of diagnostics and drugs for VL treatment due to the pandemic. Moreover, 1/3 (36.3 %) had faced a cancellation or postponement of an appointment with a doctor or healthcare professional due to COVID-19 (Table 1). Further investigation discovered that hospitals treating only COVID-19 patients were the key reason behind these cancellations or delays.

Follow-up

We also evaluated the symptoms of VL and PKDL as well as the changes in weight and haemoglobin level of the participants at the

Table 2
Medical conditions of VL-treated cases at the time of follow up.

Indicators	Enrollment % (n)	Follow up % (n)	P-value
Total no. of participants (N)	44	39	
Information on Suspected VL			
Referral of VL patients			
Yes	0.00 (0)	2.56 (1)	0.285
No	0.00 (0)	0.00 (0)	
Not applicable	100.00 (44)	97.44 (38)	
Fever > 2 weeks			
Yes	0.00 (0)	2.56 (1)	0.285
No	100.00 (44)	97.44 (38)	
Loss of appetite			
Yes	20.45 (9)	28.21 (11)	0.410
No	79.55 (35)	71.79 (28)	
Loss of weight			
Yes	4.55 (2)	17.95 (7)	0.050
No	95.45 (42)	82.05 (32)	
Abdominal enlargement/Splenomegaly			
Yes	2.27 (1)	0.00 (0)	0.344
No	97.73 (43)	100.00 (39)	
Information on Suspected PKDL			
Referral of PKDL patients			
Yes	2.56 (1)	2.56 (1)	0.312
No	0.00 (0)	5.13 (2)	
Not applicable	97.73 (43)	92.31 (36)	
Lesion on the face, neck, upper and lower limbs			
Yes	0.00 (0)	0.00 (0)	–
No	100.00 (44)	100.00 (39)	
Papules/nodules of skin on the face, neck, upper and lower limbs			
Yes	2.27 (1)	7.69 (3)	0.250
No	97.73 (43)	92.31 (36)	
Prevalence of VL relapse or PKDL or both			
Yes		15.91 (7)	
No		84.09 (37)	
Types of Cases			
VL relapse		4.55 (2)	
PKDL		6.82 (3)	
Both		4.55 (2)	

time of enrolment and after the 6th months follow-up period. Among the symptoms of VL, several participants (two at baseline and seven at the end) complained of experiencing weight loss. However, after measuring the weight, we found that 2/3rd of all participants (26) had gained weight at the end compared to the baseline. In addition, an elevation of the haemoglobin level was observed among 24 participants (61.5 %), while 3 participants (7.69 %) had an unchanged haemoglobin level. The patients were asked about compliance with follow-up visits. A majority had no opinion regarding this matter but expressed a positive attitude regarding the current setup. However, some participants suggested arranging follow-up visits at nearby healthcare centres.

At baseline, we found only one PKDL suspect but no suspected VL relapses. During the 6th-month follow-up, we found one suspected Para-KDL case (both VL symptoms and PKDL-like lesions) and two suspected PKDL cases. The Para-KDL case was referred to the nearest healthcare facility, where the diagnosis was confirmed. The other two suspected PKDL cases already had a confirmatory diagnosis for PKDL and started receiving treatment between the baseline and end-line period, so they were not referred. Overall, from 2019 to the end of the study (August 2022), we have found 7 (15.9 %) cases who had either VL relapse or PKDL or Para-KDL. Among them, two had VL relapse (4.5 %), two had Para-KDL (4.5 %), and three (6.8 %) had PKDL (Table 2).

KA diagnosis, treatment, and reporting during the COVID-19 pandemic

If we look at the changes in detecting the total number of VL and PKDL patients before and after COVID-19, different results have been observed in different upazilas during the pandemic. For instance, the

service provider of Trishal Upazila Health Complex reported a higher detection rate of VL & PKDL patients during COVID-19 compared to the pre-pandemic period. In this regard, he said that 19 patients (VL - 12 & PKDL - 7) were diagnosed during the COVID-19 period (2020–2021), while the number of patients was only three (VL - 1, PKDL - 2) prior to COVID-19 in the same UHC (2019–2020). A similar fluctuation was also observed in two more UHCs (Fulbaria and Gafargaon), where the patients' detection rate jumped during the pandemic, while one (Nagorpur) observed a decrease in case detection and the other had (Modhupur) no changes in detected cases.

Regarding patient diagnosis, we observed no impact on diagnosing patients during the COVID-19 pandemic. It usually took one day to diagnose a patient at the primary level. In this study, all the service providers (6) reported the same time to detect VL from the suspected patients in that UHC. Furthermore, almost all service providers (5/6) reported delays in initiating treatment following diagnosis due to the COVID-19 pandemic. During the pandemic, it took at least two days longer to start the management of diagnosed patients, while it just began immediately after the diagnosis in non-Covid times. By looking at the context, we observed a significant delay in notifying reports to the national program during the COVID-19 pandemic. Moreover, reporting to the federal program took around 10–14 days during the COVID-19 pandemic, while the average notification duration was only six days. All providers indicated that they were available during the pre-covid and covid periods in providing care to the VL patients.

Kala-azar response activity during COVID-19

Upon further interview, we found that only 1/3rd of the service providers participated in any early response activities during the COVID-19 pandemic, where the average duration of response after notification from the national program was seven days, ranging from 5 to 10 days. Besides, all the service providers reported completing active case detection during their visit to the target area, except SKKRC, which was converted into a dedicated COVID-19 hospital. All the service providers reported vector surveillance measures were active during COVID-19, except at Nagorpur and SKKRC. Though vector surveillance was active during COVID-19, IRS activities could not reach their full potential due to the lack of insecticides unavailable during the COVID-19 pandemic.

Supply chain management

The effective tools for managing Kala-azar are the rK39 rapid diagnostic test, drugs, and insecticides. All interviewees were satisfied with the Kala-azar management activities and supply equipment availability, except for insecticides which seriously impacted the national Kala-azar management plan during the COVID-19 pandemic.

Follow-up for treated VL cases

All the UHC medical officers were involved in the treatment and follow-up of kala-azar patients. However, the interval of completing the follow-up for these patients was changed. Some service providers reported giving follow-ups after one month, while some reported giving follow-ups every six months. None of the service providers reported any complaints while providing treatment to the VL patients during the pandemic. The stated barriers that were responsible for hindering giving optimum patient care were:-

- The unwillingness of patients to participate in the follow-up because they felt healthy
- Reluctance to receive treatment

- Patient's geographical location is far away from the treatment centre
- Distance of hospital from their home
- Financial constraints

Service providers shared some suggestions for making the follow-up fair and on time.

- Enhancing communication with health workers at the field level
- Reminding patients about their follow-up dates
- Free routine investigations or incentives during follow-up
- Training of the service providers

Discussion

Among the five patients we lost in this study, three expressed their unwillingness to come for follow-up, which was identified as one of the hindrances to optimum patient care by the service providers. At the end of the study in August 2022 in this study, we found 7 cases who developed either VL relapse or PKDL or Para-KDL after successful completion of treatment. A long-term follow-up of VL patients might be helpful to identify such cases at an early stage, as the median time to develop PKDL after VL treatment is 36 months [15,16]. Despite the high acceptance of VL treatment and post-treatment follow-up until cure among the patients, many fail to show up for further follow-up visits. The service providers suggest that enhanced communication with the patients through health workers might play a crucial role in such instances.

From this study, we have got evidence that COVID-19 impacted the healthcare delivery services for the VL-affected and the general population. As the tertiary care centre for VL treatment, SKKRC was taken up as a dedicated COVID-19 hospital; few patients faced difficulty receiving the treatment and getting healthcare. Since then, COVID-19-related morbidity and mortality controlled through extensive vaccine coverage, social awareness campaigns, and dedicated COVID-19 hospitals have now taken up their regular operations. However, this is not the case for SKKRC, which is yet to restart VL case management. This situation has created a gap in the health system in diagnosing relapse and treatment failure cases, as parasitological confirmation through qPCR is only available at SKKRC outside the capital city of Dhaka. Therefore, patients suffering from VL must travel far only to get a confirmatory diagnosis and receive treatment. The NTD modelling consortium predicted that settings in the Indian subcontinent that achieved the VL elimination goal (< 1 new case per 10,000 population annually) could face a setback of up to 5 years with interrupted control measures. This setback can push the incidence above the elimination target in the high-endemic regions with possible sporadic outbreaks [17]. Moreover, this short-term upsurge in VL cases could lead to an increasing number of Post Kala-azar Dermal Leishmaniasis (PKDL) cases in the future [18]. Therefore, the National Programme must take the necessary steps to revitalize the tertiary centre for VL - SKKRC to ensure the early diagnosis and treatment of the disease and sustenance of the elimination goal.

Some Upazilas reported having increased VL & PKDL cases diagnosed at the UHCs, which might be due to the conversion of SKKRC with a COVID-dedicated hospital. Also, patients who might have stayed at home with a fever in a typical scenario went to the UHCs to get tested for COVID and got diagnosed with VL incidentally, and thus the total VL case detection at the Upazila level might have increased. Similar instances were also found in Brazil for diagnosing cutaneous leishmaniasis, which rose to over 57 % during the COVID-19 pandemic compared to the previous 03 years' average cases. However, the number of diagnosed VL cases decreased at the primary and secondary healthcare facilities [19].

Interviews of the enrolled patients revealed that they also had problems seeking healthcare for general conditions as hospitals treated only COVID-19 patients. This, however, requires further evaluation as the government has declared that dedicated COVID hospitals and other public health centres are open to treat all kinds of patients. Fear of getting COVID-19 infection might be a reason behind this finding. We also found that patients' self-evaluating their health status was crucial for going or not to the follow-up visit. Many patients did not go to the hospital or attend a physician at the scheduled time as they felt healthy. This factor probably deserves further evaluation. However, we did not assess the patient delay for diagnosis and treatment of the disease as most of the patients ($n = 34$, 77.3 %) were diagnosed before COVID-19 outbreak and only 10 were diagnosed during the pandemic. Despite the chances of recall bias and very small sample size, we understand this is a limitation of the study.

When interviewing the focal person, we did not find during the Covid-19 pandemic any delay in diagnosing VL patients, treatment initiation, and VL reporting to the national program. However, IRS activity was severely hampered during the pandemic period, which could result from the same reason for the social distancing mentioned above. Previous modelling-based studies have suggested that this stagnation of IRS-related activities could result in a rise in VL case numbers [20,21].

Conclusion

A strong patient monitoring and follow-up structure should be in place to track each of the VL cases for early detection and treatment of side effects, relapses, and complications. The COVID-19 pandemic created a noticeable negative impact on VL treatment and control activities in VL endemic regions. This study pointed to some explanations from patients' and service providers' perspectives as well as to possible consequences. Effective vector control measures, availability of trained human resources and logistics, and periodic surveillance are pivotal in the VL endemic regions to sustain the elimination goal and should be maintained even under the adverse conditions of a pandemic.

Ethical approval

The activities started after the study was approved by the icddr,b Ethical Review Committee (PR-20137) and World Health Organization Ethical Review Committee (ERC.0003528).

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Declaration of Competing Interest

We have no conflict of interest to declare.

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(Gafargaon, Trishal, Fulbaria, Nagarpur, and Madhupur), and the hospital in charge and medical officer (kala-azar) of Surya Kanta Kala-azar Research Center (SKKRC).

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jiph.2023.09.003.

References

- [1] BetterWork COVID-19 timeline in Bangladesh (<https://betterwork.org/portfolio/covid-timeline-in-bangladesh/>) [Accessed 20.04.23].
- [2] Organization W.H. COVID-19: WHO issues interim guidance for implementation of NTD programmes. Geneva World Heal Organ 2020.
- [3] *Maladies WHO. tropicales négligées: impact de la COVID-19 et réponse de l'OMS. Relev épidémiologique Hebd* 2020;95:461–8.
- [4] Rijal S, Sundar S, Mondal D, Das P, Alvar J, Boelaert M. Eliminating visceral leishmaniasis in South Asia: the road ahead. *BMJ* 2019;364:k5224.
- [5] Organization W.H. Investing to overcome the global impact of neglected tropical diseases: third WHO report on neglected tropical diseases 2015. Vol. 3. World Health Organization; 2015. (<https://apps.who.int/iris/handle/10665/152781>) [Accessed 22.04.23].
- [6] Delhi N. Regional Technical Advisory Group on Kala-azar Elimination . 2005(December 2004). 20–3.
- [7] Abela-Ridder B, Biswas G, Mbabazi P.S., Craven M., Gerber A., Hartenstein L., et al. Ending the neglect to attain the sustainable development goals: a road map for neglected tropical diseases 2021–2030. <https://www.who.int/publications/i/item/9789240010352>. [Accessed 17.04.23].
- [8] Al Sattar A, Irin N, Belgrad JP, Haider N, Chisty NN, Mohsin MAS, et al. Measures, Gaps, and Mitigation Strategies in Bangladesh's COVID-19 Response. *Ecohealth* 2022;19:378–89.
- [9] Organization WH. Maintaining essential health services: operational guidance for the COVID-19 context 2020.
- [10] Brooker SJ, Ziumbe K, Negussu N, Crowley S, Hammami M. Neglected tropical disease control in a world with COVID-19: An opportunity and a necessity for innovation. *Trans R Soc Trop Med Hyg* 2021;115:205–7.
- [11] Ministry of Health and Family Welfare Bangladesh. National Guideline For Kala-azar Case Management 2013(Cdc):1–72.
- [12] Mondal D, Bern C, Ghosh D, Rashid M, Molina R, Chowdhury R, et al. Quantifying the infectiousness of Post-Kala-Azar Dermal Leishmaniasis toward sand flies. *Clin Infect Dis* 2019;69:251–8.
- [13] Mondal D, Kumar A, Sharma A, Ahmed MM, Hasnain MG, Alim A, et al. Relationship between treatment regimens for visceral leishmaniasis and development of post-kala-azar dermal leishmaniasis and visceral leishmaniasis relapse: a cohort study from Bangladesh. *PLoS Negl Trop Dis* 2019;13:1–16.
- [14] Mondal D, Nasrin KN, Huda MM, Kabir M, Hossain MS, Kroeger A, et al. Enhanced Case detection and improved diagnosis of PKDL in a Kala-azar-endemic area of Bangladesh. *PLoS Negl Trop Dis* 2010;4:e832.
- [15] Ghosh P, Chowdhury R, Maruf S, Picado A, Hossain F, Owen SI, et al. Gauging the skin resident Leishmania parasites through a loop mediated isothermal amplification (LAMP) assay in post-kala-azar dermal leishmaniasis. *Sci Rep* 2022;12:1–12.
- [16] Toor J, Adams ER, Aliee M, Amoah B, Anderson RM, Ayabina D, et al. Predicted impact of COVID-19 on neglected tropical disease programs and the opportunity for innovation. *Clin Infect Dis* 2021;72:1463–6.
- [17] Zijlstra EE, Alves F, Rijal S, Arana B, Alvar J. Post-kala-azar dermal leishmaniasis in the Indian subcontinent: a threat to the South-East Asia Region Kala-azar elimination programme. *PLoS Negl Trop Dis* 2017;11:e0005877.
- [18] Andrade MC, Ferreti Bonan PR, Hilan E, Marques NP, Guimarães-Carvalho SF, Martelli H. COVID-19 pandemic causes increased clinic visits with diagnosis of tegumentary leishmaniasis in Brazil in 2020. *Int J Infect Dis* 2021. 113:87–9.
- [19] Consortium NM, Consortium NM. The potential impact of programmes interruptions due to COVID-19 on 7 neglected tropical diseases: a modelling-based analysis. *Gates Open Res* 2020;4:115.
- [20] Le Rutte EA, Coffeng LE, Muñoz J, de Vlas SJ. Modelling the impact of COVID-19-related programme interruptions on visceral leishmaniasis in India. *Trans R Soc Trop Med Hyg* 2021;115:229–35.