Afghanistan Journal of Infectious Diseases
AJID
https://ajid.ghalib.edu.af/index.php/ajid

January 2026, Vol. 4, No.1, pp:24-30

Trends the Future Burden of Visceral Leishmaniasis in Afghanistan, Iran, and Pakistan: A Regional Epidemiological Modeling Study

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ARTICLE INFO

Type: Original Article
Received: 17/10/2025
Accepted: 30/12/2025

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To cite this article:
Olfatifar M, Badri M. Trends the Future Burden of Visceral Leishmaniasis in Afghanistan, Iran, and Pakistan: A Regional Epidemiological Modeling Study. Afghan J Infect Dis. 2026; 4(1): pp:24-30.

DOI:
https://doi.org/10.60141/ajid.143

ABSTRACT

Background: Visceral leishmaniasis (VL) remains one of the world's most severe neglected tropical diseases, causing substantial morbidity and mortality in low-resource settings. Despite regional control efforts, the disease persists as a major health challenge in the Middle East and South Asia. We aimed to estimate and forecast the sex-specific and national burden of VL in three neighboring countries of Afghanistan, Iran, and Pakistan through 2040.
Methods: To estimate the future prevalence of VL we applied an illness–death model using sex-specific data from the Global Burden of Disease 2021. Historical data from 1990–2021 were used to calibrate the model and forecast national trajectories of VL prevalence to 2040.
Results: In 2023, Afghanistan had the highest age-standardized VL prevalence (0.0176), followed by Iran (0.0159) and Pakistan (0.0093). Projections indicate strikingly divergent trends by 2040: prevalence is expected to rise to 0.045 (95% CI: 0.03–0.08) in Afghanistan and 0.211 (95% CI 0.10–0.45) in Pakistan representing increases of 156% and over 2,100%, respectively while Iran is projected to experience a sustained decline to 0.002 (95% CI: 0–0), an 87% reduction compared with 2021. These patterns are consistent across both sexes, though male prevalence remains roughly twice that of females.
Conclusion: Afghanistan's decline likely reflects under-detection due to health system fragility, while Pakistan's surge may result from both improved surveillance and genuine spread. Iran's continued reduction demonstrates the impact of sustained public health investment. Strengthening surveillance and incorporating health system indicators into predictive models are crucial for accurate projections and effective regional control.

Keywords: Leishmaniasis, Neglected tropical disease, Disease burden, Epidemiology

Introduction

Leishmaniasis is a poverty associated, vector-borne neglected tropical disease (NTD) and a major global public health concern, with an estimated 0.7 to 1 million new cases annually reported from nearly 100 endemic countries (1,2). Visceral leishmaniasis (VL), also known as kala-azar, remains one of the world's most prevalent NTDs, disproportionately affecting populations in low- and middle-income countries with limited health infrastructure (3). It is caused by protozoan parasites of the *Leishmania donovani* complex and transmitted through the bite of *Phlebotomus* sandflies (4). Over 90% of global VL cases are reported from specific endemic regions, including East Africa, Southeast Asia, and South America (2,5,6).

Determining which parasites infect specific species and their roles in transmitting the infection to animal reservoirs and humans is challenging because of the diversity of *Phlebotomus* species, *Leishmania* species, and their focus-specific distribution. For instance, *L. donovani* is primarily anthroponotic, while *L. infantum* is mainly zoonotic, although the two are morphologically indistinguishable. In contrast, the geographical variation of VL vectors and parasites is relatively well characterized (5). Despite decades of targeted control efforts, the disease continues to present a substantial public health challenge due to its complex variation of reservoirs, environmental determinants, and socioeconomic vulnerability of affected populations.

Similar to many other NTDs, leishmaniasis exhibits a focal distribution and primarily occurs in remote or hard-to-reach regions, which complicates the extrapolation of data from official reporting sources (7). The evidence base for NTDs is widely recognized as being particularly limited and challenging (8,9). Regarding VL, it is the most severe form of the disease, is fatal if left untreated. Moreover, a large proportion of leishmaniasis-related deaths go unrecorded, and even when treatment is available, VL can still result in considerable fatality rates (6).

In Afghanistan, VL remains endemic, with persistent transmission in multiple provinces, particularly in areas with fragile health systems and conflict-related disruptions (10). However, the true epidemiological burden of VL in Afghanistan is uncertain due to severe underreporting, diagnostic limitations, and the absence of a systematic national surveillance system (11). Visceral leishmaniasis occurs irregularly across most parts of Iran. The disease is endemic in the southern and northwestern areas of the country, with approximately 100 new symptomatic cases reported each year (12). In Pakistan, the disease was reported in the northern mountainous areas and parts of Azad Jammu and Kashmir (13). It is primarily attributed to *L. infantum*, occurs sporadically in northern regions. Mountainous and agricultural communities, as well as the presence of dogs, have been identified as the most common risk factors for VL in these areas (14).

Understanding the future disease burden is vital for developing sustainable control strategies and optimizing health resource allocation, given the compounded challenges of population displacement, poverty, and deteriorating public health infrastructure.

Recent advances in epidemiological modeling, as well as comprehensive datasets such as the Global Burden of Disease (GBD) study, create an unprecedented opportunity for long-term disease projections. One class of compartmental frameworks, so-called illness-death models (IDMs), simulates transitions between health states susceptible, diseased, and dead, considering sex and time-specific parameters (15).

Using GBD 2021 data, we applied an illness-death model to estimate and project the burden of VL in Afghanistan up to 2040. By comparing trends with neighboring endemic countries Iran and Pakistan, the research provides a contextualized forecast of both epidemiological patterns and health disparities. The projections aimed to guide policy planning, resource allocation, and tailored surveillance and control strategies for Afghanistan's specific needs.

Methods

Data Sources

To project the future burden of VL, epidemiological data were obtained from GBD 2021 via the Global Health Data Exchange (GHDx) repository (https://vizhub.healthdata.org/gbd-results/). The dataset included sex-disaggregated and age-standardized measures of VL prevalence, incidence and mortality rates in Afghanistan, Iran, and Pakistan from 1990 to 2021. Additional demographic information required for population-based projections was sourced from the GHDx population forecasting platform (https://vizhub.healthdata.org/population-forecast/).

Modeling approach

The illness-death model to simulate the natural history of VL. The model's structure is defined by a system of discrete-time differential equations (16). This framework tracks transitions between three core health states: susceptible, active disease, and death. Specifically, it simulates the movement from susceptibility to active VL infection via an incidence rate, as well as transitions to death from any cause via a general mortality rate. Individuals with active disease can further transition back to a healthy state through remission or to death via VL-specific mortality. The model explicitly accounts for sex-specific epidemiological differences. We calibrated the model using historical GBD data from 1990 to 2021. By fitting the model to the observed data from this period and minimizing the sum of least squares. This calibrated model was then used to produce annual projections of VL prevalence for Afghanistan, Iran, and Pakistan up to the year 2040.

Results

Projected national trajectories of visceral leishmaniasis to 2040

Our analysis predicted markedly different national trajectories for VL in the three endemic countries between 2023 and 2040. In 2023, Afghanistan had the highest baseline prevalence for both sexes combined (0.0176), followed by Iran (0.0159) and Pakistan (0.0093). A consistent sex disparity was evident in all countries, with male prevalence roughly double that of females (e.g., Afghanistan: 0.0243 in males vs. 0.0106 in females) (Figure 1).

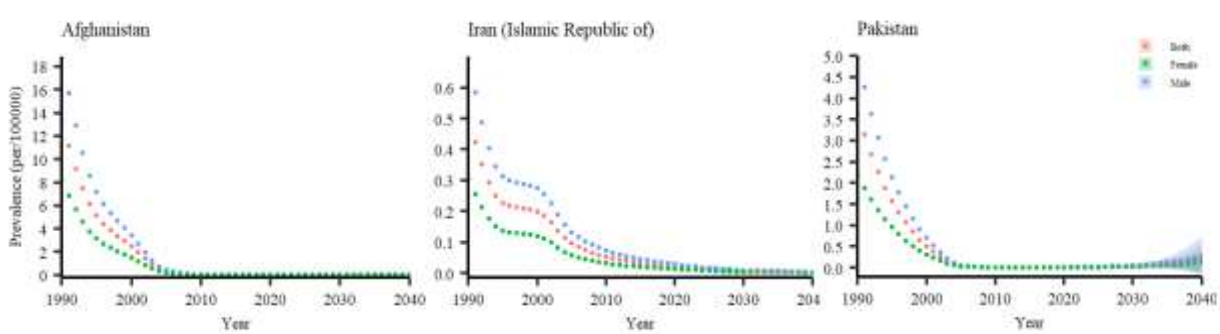

Figure 1: Observed and projected age-standardized prevalence rate (ASPR) of visceral leishmaniasis in Afghanistan, Iran, and Pakistan 1990-2040

Projections through 2040 indicate a striking epidemiological divergence. Afghanistan is expected to experience a steady increase, with combined-sex prevalence rising from 0.0176 in 2023 to 0.045 (95% CI: 0.03–0.08) by 2040, representing a 155.7% increase relative to 2021 (Table 1). Pakistan is projected to undergo the most rapid and exponential growth, with prevalence climbing from 0.0093 in 2023 to 0.211 (95% CI: 0.1–0.45) by 2040 an increase of over 2,167% compared to 2021 levels (Table 1). Conversely, Iran is expected to follow a continuous downward trend, with prevalence decreasing from 0.0159 in 2023 to 0.002 (95% CI: 0–0) by 2040, reflecting an 87.4% reduction since 2021 (Table 1).

These divergent trends rising prevalence in Afghanistan and Pakistan versus declining prevalence in Iran are consistently observed in both male and female subpopulations, with Pakistan showing the most pronounced relative increase in disease burden over the coming decades.

Table 1: Projected age-standardized prevalence rate (ASPR) of visceral leishmaniasis in Afghanistan, Iran, and Pakistan from 2024 to 2040.

Sex	*Location name*	*2024*	*2025*	*2030*	*2035*	*2040*	*1990 vs. 2021*	*2021 vs. 2040*
Both	Afghanistan	0.019(0.02-0.02)	0.02(0.02-0.02)	0.026(0.02-0.03)	0.034(0.02-0.05)	0.045(0.03-0.08)	-99.867	155.712
	Iran	0.013(0.01-0.02)	0.012(0.01-0.01)	0.007(0.01-0.01)	0.004(0-0.01)	0.002(0-0)	-96.837	-87.387
	Pakistan	0.013(0.01-0.02)	0.016(0.01-0.02)	0.038(0.03-0.06)	0.089(0.05-0.16)	0.211(0.1-0.45)	-99.744	2167.018
Female	Afghanistan	0.012(0.01-0.01)	0.012(0.01-0.01)	0.016(0.01-0.02)	0.021(0.01-0.03)	0.027(0.02-0.05)	-99.870	153.913
	Iran	0.008(0.01-0.01)	0.007(0.01-0.01)	0.004(0-0.01)	0.002(0-0)	0.001(0-0)	-96.863	-89.488
	Pakistan	0.008(0.01-0.01)	0.01(0.01-0.01)	0.023(0.02-0.03)	0.054(0.03-0.09)	0.128(0.06-0.27)	-99.745	2198.991
Male	Afghanistan	0.026(0.02-0.03)	0.028(0.02-0.03)	0.036(0.03-0.05)	0.047(0.03-0.07)	0.061(0.04-0.11)	-99.870	151.229
	Iran	0.019(0.02-0.02)	0.016(0.01-0.02)	0.009(0.01-0.01)	0.005(0-0.01)	0.003(0-0)	-96.841	-86.296
	Pakistan	0.018(0.02-0.02)	0.022(0.02-0.03)	0.052(0.04-0.08)	0.123(0.07-0.22)	0.29(0.14-0.61)	-99.741	2159.578

Discussion

This regional modeling study provides the first comparative long-term projection of VL burden in Afghanistan, Iran, and Pakistan to 2040 using an illness-death modeling framework calibrated to GBD 2021. Results point to markedly divergent national trajectories, with Pakistan showing an exponential increase in predicted prevalence, Afghanistan showing a steady rise, and Iran exhibiting a sustained decline. Such trends cannot be explained by biological transmission patterns alone; rather, they reflect the interplay between true epidemiological processes and differences in surveillance quality, diagnostic infrastructure, and health system stability.

Afghanistan's projected reduction in VL prevalence presents a paradox in light of its fragile health infrastructure and known endemicity. The country's healthcare system has been critically weakened by decades of conflict, economic collapse, and population displacement, which have severely undermined disease detection and reporting (10). The density of healthcare professionals estimated at only 4.6 per 10,000 people is among the lowest in the region, and diagnostic services for NTDs remain concentrated in urban centers with limited outreach to rural or conflict-affected areas. Consequently, case underreporting is endemic, particularly in remote provinces where sandflies exposure and zoonotic reservoirs are common (11).

The apparent decline in model-derived prevalence may therefore represent an artifact of surveillance failure rather than an actual reduction in disease transmission. The GBD framework, while robust, depends on available data; when those data deteriorate or are incomplete, modeled outputs will misleadingly suggest improvement (8). The findings here reinforce previous concerns that Afghanistan’s leishmaniasis surveillance system is on the verge of collapse, emphasizing the need for emergency investments in basic data infrastructure, training of community health workers, and decentralized diagnostic capacity. Without these interventions, projections of disease reduction risk being misinterpreted as evidence of control success, while the true epidemiological burden may be worsening unseen.

In contrast, Pakistan’s extraordinary projected increase over 2,100% by 2040 suggests both expanding transmission and rapidly improving case ascertainment. Recent study indicates a notable rise in VL positivity rates, from 27% (2016–2020) to 56% (2022–2023), suggesting intensified transmission in endemic regions such as Khyber Pakhtunkhwa and Azad Jammu and Kashmir (14). These increases are likely driven by a complex interplay of environmental, demographic, and socioeconomic factors, including deforestation, agricultural expansion, domestic dog reservoirs, and inadequate housing conditions all of which favor vector proliferation (2,6).

However, improvements in diagnostic access and awareness also contribute to the apparent epidemic expansion. As surveillance coverage broadens into previously unmonitored rural districts, a larger fraction of existing infections is detected and reported, artificially inflating modeled prevalence. This dual phenomenon—true transmission increase compounded by improved detection is a common pattern in transitional surveillance systems (7). The results highlight the importance of distinguishing epidemiological emergence from reporting expansion when interpreting model-based forecasts.

To address these challenges, Pakistan should prioritize spatially disaggregated surveillance that differentiates between established endemic foci and newly detected regions. The adoption of a One Health framework that links veterinary surveillance with human case data could also improve understanding of zoonotic transmission pathways (3). Finally, given that VL transmission is often driven by environmental change, coupling disease monitoring with climate and land-use modeling may yield more precise and contextually valid projections.

The projected 87% reduction in VL prevalence in Iran by 2040 likely represents a genuine epidemiological improvement, reflecting decades of sustained investment in public health infrastructure and disease control. Iran has one of the most established VL surveillance systems in the Middle East, with standardized diagnostic algorithms, consistent case reporting, and integrated vector control strategies (12). Historically, the country’s main endemic foci in Fars Province and Meshkinshahr District have seen steady declines in prevalence following improved indoor residual spraying, canine reservoir management, and early case detection. These results underscore the value of continuity in health programs, even amid regional instability. Unlike Afghanistan and Pakistan, where fluctuating political and financial commitment disrupts program delivery, Iran’s stability has enabled sustained implementation of the WHO-recommended protocols for leishmaniasis management (3). The consistency of surveillance data and the reliability of diagnostic systems mean that reductions in reported prevalence are more likely to correspond to true declines in transmission rather than data artifacts. Iran's experience thus serves as a benchmark for the region, illustrating how stable governance, targeted intervention, and comprehensive data collection can transform the epidemiological landscape of a neglected tropical disease.

The striking heterogeneity observed across these contiguous countries underscores that VL epidemiology cannot be understood through biological or climatic factors alone. Socioeconomic vulnerability, conflict, and health system fragility exert a stronger influence on surveillance quality and thus on modeled outcomes. The results affirm that models like the illness–death framework (15) are only as valid as the data underpinning them; when applied to data-scarce environments, they may amplify existing biases rather than clarify true dynamics. This has profound implications for public health forecasting. Quantitative projections are invaluable for resource planning and priority setting, yet they must be interpreted with an awareness of data provenance and systemic bias. As highlighted by Conteh et al. (9), and Wamai et al. (5), neglected tropical disease data are often incomplete, outdated, or inconsistent, particularly in conflict-affected and rural settings. The model amplification effect observed in this study where uncertainty in baseline data produces exaggerated long-term differences reinforces the need for hybrid modeling approaches that integrate epidemiological data with qualitative assessments of system functionality.

Future modeling efforts should explicitly include health system indicators, such as diagnostic availability, health workforce density, and reporting completeness, as covariates in predictive frameworks. This would allow projections to take into consideration not just pathogen biology and population dynamics but the structural realities that determine whether cases are ever counted. The inclusion of such metrics would increase model validity and lead to more actionable forecasts for fragile settings.

This study has several important limitations. First, projections rely entirely on GBD 2021 data, which are themselves dependent on secondary sources with varying levels of completeness. In countries with weak surveillance systems, such as Afghanistan, underreporting and diagnostic gaps may introduce major bias, leading to unrealistic estimates of disease burden. Second, the IDM assumes continuity in reporting quality and health system capacity over time, which is unlikely in regions experiencing political instability or rapid development. Third, environmental and behavioral determinants, including climate variability, vector ecology, and migration were not explicitly modeled, limiting the ecological precision of forecasts. Finally, given the reliance on modeled rather than empirical surveillance data, uncertainty intervals may underestimate the true variability in future disease trajectories.

Conclusion

Our comparative modeling of VL burden in Afghanistan, Iran, and Pakistan highlights how surveillance system capacity fundamentally shapes epidemiological forecasts. The apparent rise in Afghanistan and Pakistan and the decline in Iran reflect not only differing epidemiological dynamics but also disparities in diagnostic capability, health infrastructure, and public health investment. These findings reinforce that disease modeling in low-resource settings must integrate both quantitative and qualitative system assessments to produce contextually valid projections. Effective VL control in the region will require sustained surveillance strengthening, regional collaboration, and the incorporation of One Health and health system resilience frameworks to ensure accurate burden estimation and informed policy action.

Acknowledgments

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethics approval

This study utilized publicly available, aggregated data from the GBD database. No individual or identifiable human or animal data were used; therefore, ethical approval and informed consent were not required.

Conflicts of interest

The authors declare no competing interests.

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