Preplanned Studies

Epidemiological Features and Spatial-Temporal Clustering of Visceral Leishmaniasis — China, 2011–2022

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Summary

What is already known about this topic?

Visceral leishmaniasis (VL), transmitted by sandflies, is a zoonotic disease of public health importance in central and western China.

What is added by this report?

A number of VL hotspots were identified in the border areas of Shanxi-Hebei, Shanxi-Shaanxi, Gansu-Sichuan, as well as the southern Xinjiang provincial-level administrative division (PLAD). Mountain zoonotic visceral leishmaniasis (MT-ZVL) expanded rapidly in the mountainous regions of Shaanxi, Shanxi, Henan, Hebei, Beijing, and Gansu PLADs from 2011 to 2022. A notable resurgence of MT-ZVL has occurred, with 671 cases in 66 historically endemic counties.

What are the implications for public health practice?

Actions are recommended to restrain the rapid expansion of MT-ZVL: Firstly, implement One Health approaches, such as timely diagnosis and treatment of patients, promoting insecticide-impregnated dog collars, and restraining the number of dogs in endemic areas. Secondly, surveillance-response systems for sandflies and infective dogs in potential risk areas should be strengthened.

Visceral leishmaniasis (VL) is the second deadliest parasitic disease globally, caused by *Leishmania* spp. and transmitted through the bite of female sandflies (*1*). The World Health Organization (WHO) classifies VL as a neglected tropical disease and prioritizes its elimination in the Roadmap for the Prevention and Control of Neglected Tropical Diseases 2021–2030 (*2*). China reports three VL types: anthroponotic visceral leishmaniasis (AVL), mountain-type zoonotic visceral leishmaniasis (MT-ZVL), and desert-type zoonotic visceral leishmaniasis (DT-ZVL), each exhibiting distinct epidemiological characteristics (*3*). Once hyperendemic across 16 provincial-level administrative divisions (PLADs) north of the Yangtze River in the 1950s, VL was largely eliminated in most endemic areas of China by the 1980s, with few cases reported in Xinjiang, Gansu, Sichuan, Shaanxi, and Shanxi PLADs (*3*). However, recent environmental changes have led to a resurgence in VL incidence. Understanding the epidemiological features and spatial-temporal clustering of this disease is crucial. This study analyzed VL case data from the National Notifiable Disease Reporting System (NNDRS) between 2011 and 2022. Joinpoint regression and spatial-temporal clustering analysis identified epidemiological features and VL hotspots. Findings indicate a large-scale MT-ZVL resurgence and new incidence hotspots within the Loess Plateau and its extensions. These findings underscore the need for proactive measures, particularly addressing the disease burden in children. This study provides policymakers with valuable insights for formulating appropriate strategies.

Data on VL cases in China from 2011 to 2022 were collected from the NNDRS. Indigenous and imported cases were defined according to epidemiological investigations of individual cases. Joinpoint regression (version 4.3.1; National Cancer Institute, Bethesda, USA) was used to identify turning points and divide the disease incidence trend into statistically significant sections. A *t*-test was used to determine significant differences in VL incidence trends within specific periods. The long-term trend of each linear segment is depicted according to the best-fit result, and the annual percentage change (APC) was calculated. Getis-Ord Gi* statistical data in ArcGIS (version 10.1; ESRI, California, USA) were used for hotspot analysis. The Getis-Ord Gi* statistic is a spatial autocorrelation index based on a weighted distance matrix. It determines the spatial clustering of locations using high (hotspot) or low (coldspot) values, with statistical significance determined by Z scores and *P*-values. Spatial-temporal cluster analysis was conducted using retrospective space-time permutation scan statistics.

Spatial clustering of VL incidence was detected based on a Poisson model using a flexible spatial scan statistic in SaTScan software (version 10.1.2; Information Management Services, Maryland, USA). All incidence data were processed separately for the 3 years for which data were available, and potential spatial clusters were detected using the restricted log-likelihood ratio (RLLR). A Monte Carlo simulation was used for permutation testing, with statistical significance determined by *P*-value. A *P*<0.05 indicated a statistically significant cluster.

From 2011 to 2022, 3,041 VL cases were reported from 400 counties in 24 PLADs. Of these, 2,572 (84.6%) were indigenous cases that occurred in 124 endemic counties. These cases comprised 173 AVL, 788 DT-ZVL, and 1,611 MT-ZVL cases. The remaining 469 (15.4%) cases were imported to 276 non-endemic counties (Table 1).

Figure 1 presents the results of the joinpoint regression, showing the long-term trends of crude incidence of three types of VL between 2011 and 2022. The incidence of MT-ZVL declined during 2011–2015 (APC=–17.98, *P*<0.05) but increased significantly during 2015–2022 (APC=14.06, *P*<0.05). Conversely, the incidence of DT-ZVL increased rapidly during 2011–2015 (APC=163.20, *P*<0.05) and decreased during 2015–2022 (APC=–57.75, *P*<0.05). Overall, the incidence of AVL showed a slight decline between 2011 and 2022.

As shown in Table 1, approximately three-quarters of VL cases were distributed across three provinces: Xinjiang (*n*=947, 31.1%), Gansu (*n*=829, 27.3%), and Shanxi (*n*=481, 15.8%) PLADs. A total of 118 endemic counties were identified in eight PLADs, including Xinjiang (28 counties), Shanxi (29 counties), Gansu (19 counties), Shaanxi (14 counties), Henan (13 counties), Sichuan (7 counties), Hebei (5 counties), and Beijing (2 counties) PLADs. In

TABLE 1. Distribution and endemic types of visceral leishmaniasis cases in CLADs in China (2011–2022).

Types	PLADs (No. of cases)	CLADs (No. of cases)
AVL	Xinjiang (171)	Kashgar City (73), Shache County (20), Kuqa County (14), Atush City (13), Shule County (11), Yingjisha County (11), Shufu County (9), Akto County (7), Shaya County (7), Wushi County (4), Aksu City (2)
	Xinjiang Production and Construction Corps (2)	45th regiment farm (2)
DT-ZVL	Xinjiang (761)	Jiashi County (637), Bachu County (48), Minfeng County (19), Yuepuhu County (13), Korla City (8), Zepu County (7), Yuli County (6), Gaochang District (5), Luntai County (3), Qiemo County (3), Yizhou District (3), Luopu County (2), Moyu County (2), Toksun County (2), Awati County (1), Cele County (1), Ruoqiang County (1)
	Xinjiang Production and Construction Corps (21)	Tumshuk City (13), Jiashi farm (4), 2nd regiment farm (1), 42nd regiment farm (1), 46th regiment farm (1), 50th regiment farm (1)
	Gansu (6)	Dunhuang City (2), Guazhou County (1), Yumen County (3)
MT-ZVL	Gansu (769)	Wudu District (283), Zhouqu County (210), Dangchang County (117), Wenxian County (61), Diebu County (46), Xihe County (17), Lixian County (8), Qingshui County (6), Maiji District (5), Huanxian County (3), Qinzhou District (3), Qingcheng County (3), Zhenyuan County (3), Tongwei County (2), Gangu County (1), Qin'an County (1)
	Shanxi (462)	Pingding County (115), Suburb of Yangquan City (100), Mining of Yangquan City (46), Urban of Yangquan City (37), Wuxiang County (20), Xiangfen County (20), Quwo County (19), Xiangning County (16), Xiangyuan County (16), Yuxian County (16)Hejin City (10), Luzhou County (8), Daning County (6), Fushan County (5), Lucheng District (4), Xiyang County (4), Yaodu District (4), Qin County (3), Gaoping City (2), Jiangxian County (2), Heshun County (1), Houma City (1), Lingchuan County (1), Qinshui County (1), Tunliu District (1), Wenshui County (1), Yicheng County (1), Yushe County (1), Yuanqu County (1)
	Shaanxi (153)	Hancheng City (63), Huazhou District (26), Linwei District (21), Baota District (9), Yichuan County (8), Ningqiang County (5), Qingjian County (5), Suide County (4), Yanchuan County (3), Yanchang County (3), Zhenba County (3), High-tech District (1), Weicheng District (1), Zizhou County (1)
	Sichuan (136)	Jiuzhaigou County (39), Heishui County (37), Wenchuan County (23), Maoxian County (19), Lixian County (9), Beichuan County (7), Pingwu County (2)
	Henan (58)	Linzhou City (24), Gongyi City (12), Dengfeng City (5), Xin'an County (4), Xingyang City (3), Long'an District (2), Xinmi City (2), Jianxi District (1), Lingbao City (1), Mengjin County (1), Qibin District (1), Shangjie District (1), Yanshi District (1)
	Hebei (28)	Jingxing County (21), Gaobeidian City (3), Xindu District (3), Lincheng county (1), Jingxing mining District (1)
	Beijing (4)	Changping District (2), Mentougou District (2)

Abbreviation: CLADs=county-level administrative divisions; PLADs=provincial-level administrative divisions; AVL=anthroponotic visceral leishmaniasis; MT-ZVL=mountain-type zoonotic visceral leishmaniasis; DT-ZVL=desert-type zoonotic visceral leishmaniasis.

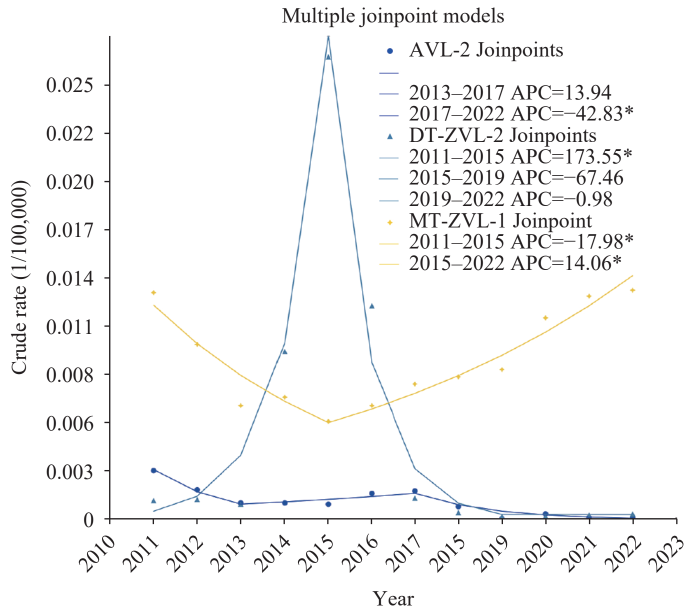

FIGURE 1. The joinpoint regression analysis for the trend of visceral leishmaniasis incidence.
Abbreviation: AVL=anthroponotic visceral leishmaniasis; APC=annual percentage change.
*indicate statistically significant in the the Annual Percentage Change(APC).

addition, 7 regimental farms from the Xinjiang Production and Construction Corps (XPCC) were also considered endemic counties. Among these counties, three were responsible for 43.9% (1,130/2,572) of indigenous cases: Jiashi County (637 cases) in Xinjiang, Wudu District (283 cases), and Zhouqu County (210 cases) in Gansu Province. Jiashi County recorded the highest annual incidence (1.4/10,000), followed by Zhouqu County (1.3/10,000); other counties reported less than 1.0/10,000. Sixty-eight counties in seven PLADs were identified as re-emerging areas between 2011 and 2022, including 27 counties in Shanxi, 13 in Henan, 11 in Shaanxi, 9 in Gansu, 5 in Hebei, 2 in Beijing, and 1 in Sichuan. A total of 675 indigenous cases were reported in these re-emerging counties, most of which (671/675) were the MT-ZVL type. The remaining four cases, reported from two counties in Gansu Province, were the DT-ZVL type.

Hotspot analysis and spatiotemporal cluster analysis showed consistent results. Major high-incidence regions were observed in southern Gansu Province and northern Sichuan Province from 2011 to 2019, in southern Xinjiang Uygur Autonomous Region from 2014 to 2016, and in the border areas of Shanxi-Hebei provinces and Shanxi-Shaanxi provinces from 2019 to 2022.

VL cases occurred mainly in preschool children, particularly those aged 0–2 years, who accounted for 42.3% (n=1,285) of all cases (Table 2). VL type exhibited different age distributions. Notably, DT-ZVL most commonly affected young age groups, while AVL and MT-ZVL tended to occur in individuals ≥15 years. Approximately 87.8% of imported cases occurred in individuals ≥15 years. In terms of occupation, farmers were the most affected population, excluding preschool children. Farmers accounted for 26.4% and 56.7% of total cases in endemic and non-endemic areas, respectively.

The peak incidence of DT-ZVL occurred from April to May, while that of MT-ZVL occurred from October to November. No significant peak incidence of AVL was observed, likely due to the small number of cases.

DISCUSSION

The present study showed a low prevalence of VL in China between 2011 and 2022, with an average of 253 cases reported annually. However, a rapidly increasing trend was observed in MT-ZVL. Notably, this type re-emerged in 66 counties with 671 indigenous cases, mostly distributed across the Loess Plateau and its extension zone. MT-ZVL is estimated to expand further as urbanization causes young adults in mountainous areas of China to relocate from rural areas, leaving abandoned fields and vacant houses that provide reservoir hosts and sandflies with a favorable

TABLE 2. Demographics of visceral leishmaniasis cases in China (2011–2022).

Characters	Endemic area				Imported cases in non-endemic area (*n*, %)	Total (*n*, %)
	AVL (*n*, %)	DT-ZVL (*n*, %)	MT-ZVL (*n*, %)	Subtotal (*n*, %)		
Age group (year)						
0–2	54 (31.2)	737 (93.5)	462 (28.7)	1,253 (48.7)	32 (6.8)	1,285 (42.3)
3–6	25 (14.5)	19 (2.4)	168 (10.4)	212 (8.2)	19 (4.1)	231 (7.6)
7–14	17 (9.8)	4 (0.5)	113 (7.0)	134 (5.2)	6 (1.3)	140 (4.6)
≥15	77 (44.5)	28 (3.6)	868 (53.9)	973 (37.8)	412 (87.8)	1,385 (45.5)
Gender						
Male	100 (57.8)	441 (56.0)	1,025 (63.6)	1,566 (60.9)	354 (75.5)	1,920 (63.1)
Female	73 (42.2)	347 (44.0)	586 (36.4)	1,006 (39.1)	115 (24.5)	1,121 (36.9)
Occupation						
Pre-school children	80 (46.2)	756 (95.9)	612 (38.0)	1,448 (56.3)	48 (10.2)	1,496 (49.2)
Students	20 (11.6)	4 (0.5)	164 (10.2)	188 (7.3)	14 (3.0)	202 (6.6)
Farmers	47 (27.2)	23 (2.9)	608 (37.7)	678 (26.4)	266 (56.7)	944 (31.0)
Workers	2 (1.2)	0 (0.0)	41 (2.5)	43 (1.7)	31 (6.6)	74 (2.4)
Officials	5 (2.9)	0 (0.0)	31 (1.9)	36 (1.4)	8 (1.7)	44 (1.4)
Housewives	14 (8.1)	1 (0.1)	69 (4.3)	84 (3.3)	35 (7.5)	119 (3.9)
Retiree	1 (0.6)	1 (0.1)	39 (2.4)	41 (1.6)	12 (2.6)	53 (1.7)
Others	4 (2.3)	3 (0.4)	47 (2.9)	54 (2.1)	55 (11.7)	109 (3.6)
Total (*n*)	173	788	1,611	2,572	469	3,041

Abbreviation: AVL=anthroponotic visceral leishmaniasis; MT-ZVL=mountain-type zoonotic visceral leishmaniasis; DT-ZVL=desert-type zoonotic visceral leishmaniasis.

ecological environment.

The epidemiological characteristics of the three VL types in this study were mostly consistent with previously reported results (*4*–*5*). The findings indicated that most (93.5%) DT-ZVL cases were aged 0–2 years. In contrast, the proportion of MT-ZVL cases among children younger than 5 years declined from 86.5% in the 1950s (*3*) to 39.1% in this study. This decline may be related to population structure changes due to urbanization and family planning policies in China (*5*).

Four main hyperendemic regions were identified through spatiotemporal cluster analysis during the study period. Two high-incidence regions were located in the traditionally predominant VL-endemic areas of southern Gansu and northern Sichuan and southern Xinjiang Uygur Autonomous Region. A declining trend of VL was noted in recent years. However, this area warrants continued attention because incidence might increase in the near future according to the cyclical incidence pattern, with approximate 8-year intervals in southern Xinjiang and 16-year intervals in southern Gansu and northern Sichuan (*3*).

Two other high-incidence regions, representing re-emerging areas, were found along the borders of Shanxi-Hebei and Shanxi-Shaanxi provinces between 2017 and 2022. Consistent with previous reports (*4*–*5*), this study found that preschool children were the highest-risk population. Our findings support prioritizing the protection of preschool children in endemic areas.

This study indicated that MT-ZVL re-emerged in numerous historically endemic counties in the mountainous areas of central and western China, particularly along provincial borders. In these areas, MT-ZVL has spread to city outskirts and high-latitude regions, such as the Mentougou and Changping districts of Beijing (*6*–*7*). Similar expansions have been reported in Europe and South America (*8*–*10*). The resurgence of MT-ZVL in the mountainous areas of central and western China may be related to ecological changes. These areas harbor natural foci of MT-ZVL. In recent years, urbanization has prompted many young adults to relocate from rural areas, leaving behind abandoned fields and vacant dwellings. These areas provide suitable environments for the propagation of sandflies and reservoir hosts. As a substantial number of dogs kept as guard dogs, sheepdogs, and pets in rural mountainous areas contracted canine visceral leishmaniasis, MT-ZVL transmission to humans began. The resurgence of MT-ZVL presents a considerable challenge to counties that previously achieved elimination decades ago, as they face shortages of professionals, control technologies, and funding for prevention and control. Therefore, surveillance should be strengthened in potential risk areas, and control measures should be implemented early in the resurgence.

In MT-ZVL endemic areas, proactive measures such as timely diagnosis and treatment of patients, control of roaming dog populations, and promotion of insecticide-impregnated dog collars should be implemented to reduce VL incidence in dogs. The effectiveness of insecticide-impregnated dog collars depends directly on their coverage and the persistence of the active ingredient. Dogs were the most important VL reservoirs in re-emerging areas due to their wide range of activity and high *Leishmania* spp. infection rate (*4*). Therefore, roaming dog management should be a crucial part of VL control programs. Since 2022, several counties with more severe MT-ZVL epidemics have been selected as pilots supported by the central government transfer payment public health program. These pilots, such as Hancheng in Shaanxi Province and Jingxing County in Hebei Province, promote the use of insecticide-impregnated dog collars in towns that reported local cases within the past 3 years. The number of local cases declined rapidly in the following years; however, sporadic cases were still reported in towns within the pilot areas where insecticide-impregnated dog collars were not used.

The present study was subject to at least two limitations. Since VL has often been neglected, this study may be subject to the underestimation of VL cases due to a small number of misdiagnosed and mistreated cases. In addition, this study did not analyze the information on the infection location of imported cases in non endemic areas for lacking of relevant data.

We conducted the first analysis of the epidemiological features and spatiotemporal clustering of VL in China from 2011 to 2022 and highlighted new VL hotspots and a notable resurgence of MT-ZVL in mountainous regions of central China. Interventions such as insecticide-impregnated dog collars should be promoted in MT-ZVL endemic areas to control the rapid rebound of MT-ZVL. Concurrently, surveillance-response systems for sandflies and infective dogs should be strengthened in potential risk areas.

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