Research Article

Mathematical Model Analysis and Simulation of Visceral Leishmaniasis, Kashgar, Xinjiang, 2004–2016

Yateng Song,¹ Tailei Zhang,² Hui Li³, Kai Wang⁴, and Xiaobo Lu⁵

¹College of Public Health, Xinjiang Medical University, Urumqi 830011, China

²School of Science, Chang'an University, Xi'an 710064, China

³Central Laboratory, Xinjiang Medical University, Urumqi 830011, China

⁴College of Medical Engineering and Technology, Xinjiang Medical University, Urumqi 830011, China

⁵Department of Infectious Diseases, The First Affiliated Hospital of Xinjiang Medical University, Urumqi 830054, China

Correspondence should be addressed to Kai Wang; wangkaimath@sina.com and Xiaobo Lu; xjykdluxiaobo@126.com

Received 12 September 2019; Revised 3 January 2020; Accepted 11 February 2020; Published 24 April 2020

Guest Editor: George V. Popescu

Copyright © 2020 Yateng Song et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Visceral leishmaniasis (VL), known as kala-azar, is a serious parasitic disease. After malaria, VL is the second largest parasitic killer. This paper focuses on the VL transmission around sandflies, dogs, and people. Kashgar is located on the southwestern edge of Xinjiang, where kala-azar parasite infection occurs every year. According to the cases reported in the Kashgar Prefecture from 2004 to 2016, we proposed a dynamic model based on these three populations. The SEIR model was established for human population, the SI model was established for sandfly population, and the SI model was established for dog population. We fitted the model to cumulative cases from 2004 to 2016 for the epidemic in Kashgar and predicted that the cumulative incidence of kala-azar in Kashgar would continue to increase, but its growth rate would gradually slow down, which means that the number of cases would gradually decrease every year. We also estimated the basic reproduction number $R_0 = 1.76$ (95% CI: 1.49–1.93). The sensitivity analysis shows that the mutual infection between sandfly and dog contributes the most to the basic reproduction number, while the transmission proportion of sandfly to the susceptible person and the mutual infection between sandfly and dog contribute the most to the number of leishmaniasis human cases. Therefore, according to the sensitivity analysis results, reducing the contact between sandflies and dogs is an effective way to reduce kala-azar.

1. Introduction

Visceral leishmaniasis (VL) is also called kala-azar, which is a chronic infectious disease caused by *Leishmania infantum*. VL has ranked as the second largest parasitic killer after malaria and draws worldwide attention because of its severity; about 12 million people are affected by it around the world [1]. The pathogen causing visceral leishmaniasis are *L. donovani*, *L. infantum*, and *L. chagasi*. The incubation period for VL is generally 3–6 months, at least 10 days, while the longest is 9 years [1]. Humans and dogs are the main infection sources while sandflies are the main carriers.

The World Health Organization (WHO) lists leishmaniasis as the most easily neglected disease. It is reported that approximately 30% of new clinical cases and 58,000 deaths of leishmaniasis occur worldwide each year [2]. According to the

characteristics of the source of infection, VL is mainly divided into three types: human-borne, canine-borne, and wildlife-borne in China [3]. In the early days of the People's Republic of China, human-borne kala-azar was the main disease in 16 provinces, such as Shandong and Henan. After prevention and treatment, it was basically eliminated. In recent years, VL has been prevalent in six provinces including Xinjiang, Inner Mongolia, Gansu, Sichuan, Shaanxi, and Shanxi [3]. Among six provinces, the typical VL in Xinjiang is wildlife-borne, and some areas have human-borne VL, while canine-borne is the main transmission way in Gansu.

Xinjiang is the largest provincial administrative region in China and is also a high-risk area for VL, especially in the Kashgar Prefecture in southern Xinjiang. The Kashgar Prefecture is located in the southwestern margin of the Xinjiang Uygur Autonomous Region. Due to its unique geographical

environment, there are two types of visceral leishmaniasis, human and desert [4]. Since the 1990s, the incidence of VL in Kashgar has been increasing year by year. From 2005 to 2015, Xinjiang's VL has experienced significant fluctuation. In 2007–2012, the incidence of VL in Kashgar accounted for more than 90% of the total population [5].

We utilized the data of human leishmaniasis cases from 2004 to 2016 reported by the Center for Disease Control and Prevention in Xinjiang, and then we plot bar diagrams about total, sex, and age which are presented in Figures 1(a)–1(c). From Figure 1(a), we could find that the reported cases of VL in Kashgar Prefecture of Xinjiang fluctuate considerably, with outbreaks occurring in October and November of 2008, 2009, and 2015, respectively. From Figure 1(b), it shows that there are more reported cases of VL in males than in females. Figure 1(c) shows that there are more reported cases of VL in the younger age group.

In recent years, a lot of mathematical models have been established around humans, dogs, and sandflies to understand the transmission dynamics of VL (see for instance [6–14]). For example, Muhammad and Ali [6] considered the uniform mixing of the population, established the SEIHR model for the population and the SEIR model for the dog, which used sandfly as the medium, modeled and backwarded the branching of zoonotic visceral leishmaniasis, and calculated the basic reproduction number R_0 for optimal control. Elmojtaba et al. [7] developed a mathematical model to study the dynamics of visceral leishmaniasis in Sudan, considering three different groups, analyzing the balance point and its stability and providing a basis for controlling and eliminating diseases. Zamir et al. [8] established SIR mathematical models for humans, hosts, and media, using the Routh–Hurwitz standard and next-generation methods to obtain threshold conditions and give numerical simulation results. There are three main control strategies in the controls of VL model: parameter control strategy, optimal control strategy, and control strategy selection using simulation. However, the most generalized control strategy is the parameter control strategy. When the parameters are adjusted, people can apply it to a real-world control strategy, and there is also a lot of research on optimal control strategy and control strategy selection using simulation. Simulation comparison is the most common method of VL mathematic control modeling in simulation. It can compare the human infected population with control and without control. Meanwhile, it also proves the effectiveness of the combined control strategies [9]. With reference to these established mathematical models, we have established a mathematical model based on logistic process.

The purpose of this paper is to know the transmission state about VL among humans, dogs, and sandflies in the Kashgar Prefecture of Xinjiang. Firstly, we proposed a model to simulate the cumulative data of the Kashgar Prefecture and estimate the basic reproduction number and the dynamic behavior of the model. Then, sensitivity analysis was performed on the number of leishmaniasis human/dog/sandfly cases and the basic reproduction number R_0 based on some key parameters. Finally, we explored some effective strategies for the prevention and control of VL in Kashgar.

The article is organized as follows. In Section 2, this paper introduces the model of VL and gives the expression of the basic reproduction number and the parameter value. The dynamical behaviors of the model are analyzed to better understand the transmission trends of the disease. Some mathematical analyses are given in Section 3. The numerical simulations, prediction of the epidemic trends for the next decades, estimation of the basic reproduction number, and sensitivity analysis of the basic reproduction number and the number of infected humans/sandflies/dogs are presented in Section 4. In Section 5, some brief summaries and discussion are given.

2. Mathematical Model

In order to study the transmission of VL in Kashgar, we developed a mathematical model based on humans, dogs, and sandflies, where the human population is divided into four groups: the susceptible, the exposed, the infected, and the recovered denoted by S_h , E_h , I_h , and R_h , respectively. The dog population is divided into two groups: the susceptible and the infected, denoted by S_r and I_r , respectively. We divide the sandfly population into two subclasses: the susceptible and the infected, denoted by S_v and I_v , respectively. And the total population for humans, dogs, and sandflies is $N_h = S_h + E_h + I_h + R_h$; $N_v = S_v + I_v$; $N_r = S_r + I_r$. The flowchart of VL transmission is illustrated in Figure 2.

The transmission process of VL is described by the following eight differential equations:

$$\begin{cases} \frac{dS_h}{dt} = r_1 S_h \left(1 - \frac{S_h + E_h + I_h + R_h}{K_1} \right) - \beta_1 S_h I_v, \\ \frac{dE_h}{dt} = \beta_1 S_h I_v - \mu_h E_h - \omega E_h, \\ \frac{dI_h}{dt} = \omega E_h - (\mu_h + \delta_1) I_h - \gamma I_h, \\ \frac{dR_h}{dt} = \gamma I_h - \mu_h R_h, \\ \frac{dS_v}{dt} = r_2 S_v \left(1 - \frac{S_v + I_v}{K_2} \right) - (\beta_2 I_h + \beta_3 I_r) S_v, \\ \frac{dI_v}{dt} = (\beta_2 I_h + \beta_3 I_r) S_v - \mu_v I_v, \\ \frac{dS_r}{dt} = r_3 S_r \left(1 - \frac{S_r + I_r}{K_3} \right) - \beta_4 I_v S_r, \\ \frac{dI_r}{dt} = \beta_4 I_v S_r - (\mu_r + \delta_2) I_r. \end{cases} \quad (1)$$

We assume that the susceptible individuals S_h and dogs S_r are bitten by infected sandflies with β_1 and β_4 infection

FIGURE 1: The data of human leishmaniasis cases from 2004 to 2016. (a) The reported data are described at different years. (b) The reported data are described at different genders and (c) different ages from 2004 to 2016.

rates, respectively. And the transmission probability from an infected dog or an infected individual to a susceptible sandfly is β_3 and β_2 , respectively. $1/\omega$ and $1/\gamma$ indicate the latency and recovery rate of VL, respectively. The natural mortality rates of humans, vectors, and reserves are μ_h , μ_v , and μ_r , respectively. The death rate of humans and reserves caused by VL are δ_1 and δ_2 , respectively. The susceptible human population is governed by the logistic growth with carrying capacity K_1 as well as intrinsic growth rate r_1 . In the absence of disease, the vector population density grows according to a logistic curve

carrying capacity K_2 , with an intrinsic growth rate r_2 . In the absence of disease, the dog population density grows according to a logistic curve carrying capacity K_3 , with an intrinsic growth rate r_3 .

3. Mathematical Analysis

3.1. Basic Reproduction Number. The basic reproduction number R_0 refers to the number of people infected by a patient during the average period of illness when all people are susceptible. R_0 was calculated using the next-generation

FIGURE 2: Flow diagram of the VL transmission model.

matrix [15, 16]. The infected compartments are E_h , I_h , I_v , and I_r , giving $m = 4$, so we have

$$\mathcal{F} = \begin{bmatrix} \beta_1 S_h I_v \\ 0 \\ (\beta_2 I_h + \beta_3 I_r) S_v \\ \beta_4 I_v S_r \end{bmatrix},$$

$$\mathcal{V} = \begin{bmatrix} (\mu_h + \omega) E_h \\ (\mu_h + \delta_1 + \gamma) I_h - \omega E_h \\ \mu_r I_r \\ (\mu_r + \delta_2) I_r \end{bmatrix}.$$

Then,

$$F = \begin{bmatrix} 0 & 0 & \beta_1 K_1 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & \beta_2 K_2 & 0 & \beta_3 K_3 \\ 0 & 0 & \beta_4 K_3 & 0 \end{bmatrix},$$

$$V = \begin{bmatrix} \mu_h + \omega & 0 & 0 & 0 \\ -\omega & \mu_h + \delta_1 + \gamma & 0 & 0 \\ 0 & 0 & \mu_r & 0 \\ 0 & 0 & 0 & \mu_r + \delta_2 \end{bmatrix}. \quad (3)$$

Thus,

$$FV^{-1} = \begin{bmatrix} 0 & 0 & \frac{\beta_1 K_1}{\mu_v} & 0 \\ 0 & 0 & 0 & 0 \\ \frac{\omega \beta_2 K_2}{(\mu_h + \omega)(\mu_h + \delta_1 + \gamma)} & \frac{\beta_2 K_2}{\mu_h + \delta_1 + \gamma} & 0 & \frac{\beta_3 K_3}{\mu_r + \delta_2} \\ 0 & 0 & \frac{\beta_4 K_3}{\mu_v} & 0 \end{bmatrix}. \quad (4)$$

The reproduction number is given by $R_0 = \rho(FV^{-1})$, and

$$R_0 = \sqrt{\frac{K_2 (K_3 \beta_3 \beta_4 (\mu_h^2 + \delta_1 \mu_h + \gamma \mu_h + \delta_1 \omega + \gamma \omega + \mu_h \omega) + \omega K_1 \beta_1 \beta_2 (\delta_2 + \mu_r))}{\mu_v (\delta_2 + \mu_r) (\mu_h + \omega) (\delta_1 + \gamma + \mu_h)}}. \quad (5)$$

R_0 can be used as a basic indicator in the study of VL propagation dynamics model. Usually, when $R_0 = 1$, it can be used as a threshold for the demise of the disease. When $R_0 > 1$, the disease will not die and eventually turn into endemic disease; when $R_0 < 1$, the disease will die out naturally.

3.2. Dynamic Behaviors for the Model. The dynamical behavior of model (1) is analyzed to better understand the transmission trends of the disease. We begin with elementary properties of solutions to the model (1). From biological considerations, we study model (1) in the set

$$\Gamma = \left\{ (S_h, E_h, I_h, R_h, S_v, I_v, S_r, I_r) \in \mathbb{R}_+^8 : 0 < S_h \leq K_1, 0 < S_v \leq K_2, 0 < S_r \leq K_3, N_h \leq \frac{(\mu_h + r_1)^2 K_1}{4\mu_h r_1}, N_v \leq \frac{(\mu_v + r_2)^2 K_2}{4\mu_v r_2}, N_r \leq \frac{(\mu_r + r_3)^2 K_3}{4\mu_r r_3} \right\}. \quad (6)$$

In fact, by using

$$\begin{aligned} \frac{dS_h}{dt} &\leq r_1 S_h \left(1 - \frac{S_h}{K_1} \right), \\ \frac{dS_v}{dt} &\leq r_2 S_v \left(1 - \frac{S_v}{K_2} \right), \\ \frac{dS_r}{dt} &\leq r_3 S_r \left(1 - \frac{S_r}{K_3} \right), \end{aligned} \quad (7)$$

we can deduce that $S_h(t) \leq K_1$, $S_v(t) \leq K_2$, and $S_r(t) \leq K_3$ whenever $S_h(0) \leq K_1$, $S_v(0) \leq K_2$, and $S_r(0) \leq K_3$. Adding the first four equations of (1) yields

$$\begin{aligned} \frac{dN_h}{dt} &= r_1 S_h \left(1 - \frac{N_h}{K_1} \right) - \mu_h N_h - \delta_1 I_h + \mu_h S_h \\ &\leq (r_1 + \mu_h) S_h - \frac{r_1 S_h^2}{K_1} - \mu_h N_h \\ &\leq \frac{(r_1 + \mu_h)^2 K_1}{4r_1} - \mu_h N_h. \end{aligned} \quad (8)$$

In view of system (8), it is easy to check that $N'_h(t) \leq 0$ wherever $N_h \geq ((r_1 + \mu_h)^2 K_1 / 4\mu_h r_1)$. The same conclusion can be drawn for N_v and N_r . According to the above analysis, Γ is a maximum positive invariant set of (1). There always exists a disease-free equilibrium $P_0 (K_1, 0, 0, 0, K_2, 0, K_3, 0)$. In the following, we will show the stability for the disease-free equilibrium.

Theorem 1. *The disease-free equilibrium P_0 is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.*

Proof. The Jacobian matrix of model (1) at P_0 is given by

$$J(P_0) = \begin{bmatrix} -r_1 & -r_1 & -r_1 & -r_1 & 0 & -\beta_1 K_1 & 0 & 0 \\ 0 & -(\mu_h + \omega) & 0 & 0 & 0 & \beta_1 K_1 & 0 & 0 \\ 0 & \omega & -(\mu_h + \delta_1 + \gamma) & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \gamma & -\mu_h & 0 & 0 & 0 & 0 \\ 0 & 0 & -\beta_2 K_2 & 0 & -r_2 & -r_2 & 0 & -\beta_3 K_2 \\ 0 & 0 & \beta_2 K_2 & 0 & 0 & -\mu_v & 0 & \beta_3 K_2 \\ 0 & 0 & 0 & 0 & 0 & -\beta_4 K_3 & -r_3 & -r_3 \\ 0 & 0 & 0 & 0 & 0 & \beta_4 K_3 & 0 & -(\mu_r + \delta_2) \end{bmatrix}. \quad (9)$$

It is easy to see that there are four negative eigenvalues of $J(P_0)$: $-r_1, -r_2, -r_3, -\mu_h$. The other eigenvalues are determined by the following fourth-order equation:

$$\lambda^4 + a_1 \lambda^3 + a_2 \lambda^2 + a_3 \lambda + a_4 = 0, \quad (10)$$

where

$$\begin{aligned}
a_1 &= m_1 + m_2 + n + \mu_v, \\
a_2 &= m_1 m_2 + \mu_v n - \beta_3 \beta_4 K_2 K_3 + (m_1 + m_2)(\mu_v + n), \\
a_3 &= m_1 m_2 (\mu_v + n) + (m_1 + m_2)(\mu_v n - \beta_3 \beta_4 K_2 K_3) \\
&\quad - \omega \beta_1 \beta_2 K_1 K_2, \\
a_4 &= m_1 m_2 (\mu_v n - \beta_3 \beta_4 K_2 K_3) - n \omega \beta_1 \beta_2 K_1 K_2,
\end{aligned} \tag{11}$$

$$\begin{aligned}
m_1 &= \mu_h + \omega, \\
m_2 &= \mu_h + \delta_1 + \gamma, \\
n &= \mu_r + \delta_2.
\end{aligned} \tag{12}$$

The inequality $R_0 < 1$ implies that

$$\begin{aligned}
\beta_3 \beta_4 K_2 K_3 &< \mu_v n, \\
\omega \beta_1 \beta_2 K_1 K_2 &< m_1 m_2 \mu_v, \\
m_1 m_2 \beta_3 \beta_4 K_2 K_3 + n \omega \beta_1 \beta_2 K_1 K_2 &< m_1 m_2 \mu_v n.
\end{aligned} \tag{13}$$

From (13), we have $a_i > 0$ for $i = 1, 2, 3, 4$. On account of the above inequalities, we have

$$\begin{aligned}
a_1 a_2 - a_3 &= (m_1 + m_2 + n + \mu_v)[m_1 m_2 + \mu_v n - \beta_3 \beta_4 K_2 K_3] + (m_1 + m_2)(\mu_v + n) - m_1 m_2 (\mu_v + n) - (m_1 + m_2)(\mu_v n - \beta_3 \beta_4 K_2 K_3) \\
&\quad + \omega \beta_1 \beta_2 K_1 K_2 \\
&= m_1 m_2 (m_1 + m_2) + (\mu_v + n)(\mu_v n - \beta_3 \beta_4 K_2 K_3) + (m_1 + m_2 + n + \mu_v)(m_1 + m_2)(\mu_v + n) + \omega \beta_1 \beta_2 K_1 K_2 > 0.
\end{aligned} \tag{14}$$

Furthermore,

$$\begin{aligned}
a_3(a_1 a_2 - a_3) - a_1^2 a_4 &= [m_1 m_2 (\mu_v + n) + (m_1 + m_2)(\mu_v n - \beta_3 \beta_4 K_2 K_3) - \omega \beta_1 \beta_2 K_1 K_2] \\
&\quad [m_1 m_2 (m_1 + m_2) + (\mu_v + n)(\mu_v n - \beta_3 \beta_4 K_2 K_3) + (m_1 + m_2 + n + \mu_v)(m_1 + m_2)(\mu_v + n) + \omega \beta_1 \beta_2 K_1 K_2] \\
&\quad - m_1 m_2 (\mu_v n - \beta_3 \beta_4 K_2 K_3)(m_1 + m_2 + n + \mu_v)^2 + n \omega \beta_1 \beta_2 K_1 K_2 (m_1 + m_2 + n + \mu_v)^2 \\
&> (m_1 + m_2)(\mu_v n - \beta_3 \beta_4 K_2 K_3)[m_1 m_2 (m_1 + m_2) + (m_1 + m_2 + n + \mu_v)(m_1 + m_2)(\mu_v + n) + \omega \beta_1 \beta_2 K_1 K_2] \\
&\quad - m_1 m_2 (\mu_v n - \beta_3 \beta_4 K_2 K_3)(m_1 + m_2 + n + \mu_v)^2 \\
&= (m_1^2 + m_2^2)(\mu_v n - \beta_3 \beta_4 K_2 K_3)(m_1 + m_2)(\mu_v + n) + (m_1^2 + m_2^2 + m_1 m_2)(\mu_v n - \beta_3 \beta_4 K_2 K_3)(\mu_v + n)^2 > 0.
\end{aligned} \tag{15}$$

Therefore, each eigenvalue of equation (10) admits negative real part. When $R_0 < 1$, the disease-free equilibrium P_0 is locally asymptotically stable. When $R_0 > 1$, we conclude from $a_4 > 0$ that equation (10) has at least one positive real root; hence, the disease-free equilibrium P_0 is unstable.

Theorem 2. As $R_0 < 1$, the disease-free equilibrium is globally asymptotically stable in Γ .

Proof. Let us consider the following Lyapunov function:

$$\begin{aligned}
V(t) &= \omega n \beta_2 K_2 E_h(t) + m_1 n \beta_2 K_2 I_h(t) + m_1 m_2 n I_v(t) \\
&\quad + m_1 m_2 \beta_3 K_2 I_r(t),
\end{aligned} \tag{16}$$

where

$$\begin{aligned}
m_1 &= \mu_h + \omega, \\
m_2 &= \mu_h + \delta_1 + \gamma, \\
n &= \mu_r + \delta_2.
\end{aligned} \tag{17}$$

The derivative of $V(t)$ along solutions of (1) is

$$\begin{aligned}
\dot{V}(t) &= \omega n \beta_1 \beta_2 K_2 S_h I_v - m_1 m_2 n \beta_2 K_2 I_h + m_1 m_2 n S_v (\beta_2 I_h + \beta_3 I_r) \\
&\quad - m_1 m_2 \mu_v n I_v + m_1 m_2 \beta_3 \beta_4 K_2 S_r I_v - m_1 m_2 n \beta_3 K_2 I_r \\
&\leq [m_1 m_2 \beta_3 \beta_4 K_2 K_3 + n \omega \beta_1 \beta_2 K_1 K_2 - m_1 m_2 \mu_v n] I_v \\
&= m_1 m_2 \mu_v n (R_0^2 - 1) I_v \\
&\leq 0.
\end{aligned} \tag{18}$$

By LaSalle's invariance principle, the omega limit set of each solution starting from Γ lies in an invariant set contained in

$$\Omega = \{(S_h, E_h, I_h, R_h, S_v, I_v, S_r, I_r) \in \Gamma: I_v = 0\}. \quad (19)$$

It can be verified that the only invariant set contained in Ω is the singleton $\{P_0\}$. Then, the disease-free equilibrium P_0 is globally asymptotically stable. This completes the proof. In the following, we will consider the dynamical behavior of model (1) when $R_0 > 1$.

Theorem 3. *For any solution $(S_h(t), E_h(t), I_h(t), R_h(t), S_v(t), I_v(t), S_r(t), I_r(t))$ of (1) with initial values $S_h(0) > 0, E_h(0) \geq 0, I_h(0) \geq 0, R_h(0) \geq 0, S_v(0) > 0, I_v(0) \geq 0, S_r(0) > 0, I_r(0) \geq 0$, and $I_h(0) + I_v(0) + I_r(0) > 0$, there exists $\nu > 0$ such that*

$$\begin{aligned} \liminf_{t \rightarrow \infty} I_h(t) &> \nu, \\ \liminf_{t \rightarrow \infty} I_v(t) &> \nu, \\ \liminf_{t \rightarrow \infty} I_r(t) &> \nu, \end{aligned} \quad (20)$$

as $R_0 > 1$.

$$M_{\partial} = \{(S_h(0), E_h(0), I_h(0), R_h(0), S_v(0), I_v(0), S_r(0), I_r(0)) : (S_h(t), E_h(t), I_h(t), R_h(t), S_v(t), I_v(t), S_r(t), I_r(t)) \in \partial X_0, t \geq 0\}. \quad (22)$$

We first claim that

$$M_{\partial} = \{(S_h, 0, 0, R_h, S_v, 0, S_r, 0) : S_h, R_h, S_v, S_r \geq 0\}. \quad (23)$$

Suppose that $(S_h(0), E_h(0), I_h(0), R_h(0), S_v(0), I_v(0), S_r(0), I_r(0)) \in M_{\partial}$. It suffices to show $E_h(t) = 0$ for all $t \geq 0$. If it is not true, then there exists $t_0 > 0$ such that $E_h(t_0) > 0$. Then, $E_h'(t) \geq (\mu_h + \omega)E_h(t)$ implies $E_h(t) > 0$ for all $t \geq t_0$. From the third equation of (1), it may be concluded that

$$\begin{aligned} I_h(t) &= e^{-(\mu_h + \delta_1 + \gamma)(t-t_0)} I_h(t_0) + \int_{t_0}^t e^{-(\mu_h + \delta_1 + \gamma)(t-\theta)} \omega E_h(\theta) d\theta \\ &\geq \int_{t_0}^t e^{-(\mu_h + \delta_1 + \gamma)(t-\theta)} \omega E_h(\theta) d\theta > 0, \end{aligned} \quad (24)$$

for all $t > t_0$. This is a contradiction with

$$(S_h(0), E_h(0), I_h(0), R_h(0), S_v(0), I_v(0), S_r(0), I_r(0)) \in M_{\partial}. \quad (25)$$

Thus, (23) is valid.

Denote

$$\begin{aligned} \Omega &= \bigcup \{ \omega(S_h(0), E_h(0), I_h(0), R_h(0), S_v(0), I_v(0), S_r(0), I_r(0)) : \\ &\quad (S_h(0), E_h(0), I_h(0), R_h(0), S_v(0), I_v(0), S_r(0), I_r(0)) \in M_{\partial} \}, \end{aligned} \quad (26)$$

where $\omega(S_h(0), E_h(0), I_h(0), R_h(0), S_v(0), I_v(0), S_r(0), I_r(0))$ is the omega limit set of the solution to (1) through $(S_h(0), E_h(0), I_h(0), R_h(0), S_v(0), I_v(0), S_r(0), I_r(0))$. Restricting (1) on M_{∂} yields

Proof. Let

$$X = \{(S_h, E_h, I_h, R_h, S_v, I_v, S_r, I_r) \in \mathbb{R}_+^8 : S_h > 0, S_v > 0, S_r > 0\},$$

$$X_0 = \{(S_h, E_h, I_h, R_h, S_v, I_v, S_r, I_r) \in X : I_h + I_v + I_r > 0\},$$

$$\partial X_0 = X \setminus X_0.$$

(21)

Next, we will show that system (1) is uniformly persistent with respect to $(X_0, \partial X_0)$. Obviously, X is positively invariant with respect to (1). Set $a = \max\{\mu_h + \delta_1 + \gamma, \mu_v, \mu_r + \delta_2\}$. The inequality $(I_h(t) + I_v(t) + I_r(t))' \geq -a(I_h(t) + I_v(t) + I_r(t))$ and $I_h(0) + I_v(0) + I_r(0) > 0$ imply $I_h(t) + I_v(t) + I_r(t) > 0$ for all $t \geq 0$ as $I_h(0) + I_v(0) + I_r(0) > 0$. Therefore, X_0 is also a positive invariant set for system (1). Furthermore, by Theorem 3, there exists a compact set $\mathcal{C}$ in which all solutions of (1) initiated in X will enter and remain forever after. The compactness condition ($C_{4.2}$) in Thieme [17] is easily verified for this set $\mathcal{C}$. Denote

$$\begin{cases} \frac{dS_h}{dt} = r_1 S_h \left(1 - \frac{S_h + R_h}{K_1} \right), \\ \frac{dR_h}{dt} = -\mu_h R_h, \\ \frac{dS_v}{dt} = r_2 S_v \left(1 - \frac{S_v}{K_2} \right), \\ \frac{dS_r}{dt} = r_3 S_r \left(1 - \frac{S_r}{K_3} \right). \end{cases} \quad (27)$$

A trivial verification shows that system (27) has a unique equilibrium $(K_1, 0, K_2, K_3)$. Thus, $P_0(K_1, 0, 0, 0, K_2, 0, K_3, 0)$ is the unique equilibrium of (1) in M_{∂} . It is easily seen that $(K_1, 0, K_2, K_3)$ is globally asymptotically stable. Therefore, we have $\Omega = \{P_0\}$. And P_0 is a covering of Ω , which is isolated and is acyclic (since there exists no solution in M_{∂} which links P_0 to itself). Finally, the proof will be done if P_0 is a weak repeller for X_0 , i.e.,

$$\limsup_{t \rightarrow \infty} \text{dist}(\Psi(t), P_0) > 0, \quad (28)$$

where $\Psi(t) = (S_h(t), E_h(t), I_h(t), R_h(t), S_v(t), I_v(t), S_r(t), I_r(t))$ is an arbitrary solution with initial value in X_0 . By Leenheer and Smith (Proof of Lemma 3.5, [18]), we only need to prove that $W^s(P_0) \cap X_0 = \emptyset$ where $W^s(P_0)$ is the stable manifold of E_0 . Suppose it is not true, then there exists a solution $(S_h(t), E_h(t), I_h(t), R_h(t), S_v(t), I_v(t), S_r(t), I_r(t))$ in X_0 , such that as $t \rightarrow \infty$,

$$\begin{aligned} S_h(t) &\longrightarrow K_1, E_h(t) \longrightarrow 0, I_h(t) \longrightarrow 0, R_h(t) \longrightarrow 0, \\ S_v(t) &\longrightarrow K_2, I_v(t) \longrightarrow 0, S_r(t) \longrightarrow K_3, I_r(t) \longrightarrow 0. \end{aligned} \quad (29)$$

When $R_0 > 1$,

$$\begin{aligned} &\omega\beta_2 K_2 (\mu_r + \delta_2) \beta_1 K_1 + \beta_3 K_2 (\mu_h + \omega) (\mu_h + \delta_1 + \gamma) \beta_4 K_3 \\ &> (\mu_h + \omega) (\mu_h + \delta_1 + \gamma) (\mu_r + \delta_2) \mu_v. \end{aligned} \quad (30)$$

On account of (30), we may choose $\rho > 0, \sigma > 0, \eta > 0$, and $\epsilon > 0$ such that

$$\begin{cases} 0, & < \omega\beta_2 (K_2 - \epsilon) (\mu_r + \delta_2) - \rho \ll 1, \\ 0, & < \beta_3 (K_2 - \epsilon) (\mu_r + \omega) (\mu_h + \delta_1 + \gamma) - \sigma \ll 1, \\ 0, & < \eta - (\mu_h + \omega) (\mu_h + \delta_1 + \gamma) (\mu_r + \delta_2) \ll 1. \end{cases} \quad (31)$$

$$\rho\beta_1 (K_1 - \epsilon) + \sigma\beta_4 (K_3 - \epsilon) - \eta\mu_v > 0. \quad (32)$$

From (31), we see that $((\mu_h + \omega)/\omega)\rho < (\mu_h + \omega)(\mu_r + \delta_2)\beta_2(K_2 - \epsilon) < (\beta_2(K_2 - \epsilon))/(\mu_h + \delta_1 + \gamma)\eta$, $\eta\beta_3(K_2 - \epsilon) > \sigma(\mu_r + \delta_2)$. Therefore, there exists ξ such that

$$\frac{\mu_h + \omega}{\omega} \rho < \xi < \frac{\beta_2(K_2 - \epsilon)}{\mu_h + \delta_1 + \gamma} \eta. \quad (33)$$

For $\epsilon > 0$, by (29), there exists $T > 0$ such that

$$\begin{aligned} K_1 - \epsilon &< S_h(t) < K_1 + \epsilon, \\ K_2 - \epsilon &< S_v(t) < K_2 + \epsilon, \\ K_3 - \epsilon &< S_r(t) < K_3 + \epsilon, \end{aligned} \quad (34)$$

for all $t \geq T$. Let

$$L(t) = \rho E_h(t) + \xi I_h(t) + \eta I_v(t) + \sigma I_r(t). \quad (35)$$

The derivative of L along the solution $(S_h(t), E_h(t), I_h(t), R_h(t), S_v(t), I_v(t), S_r(t), I_r(t))$ is given by

$$\begin{aligned} L'(t) &= [\xi\omega - \rho(\mu_h + \omega)]E_h + [\eta\beta_2 S_v - \xi(\mu_h + \delta_1 + \gamma)]I_h + [\rho\beta_1 S_h + \sigma\beta_4 S_r - \eta\mu_v]I_v + [\eta\beta_3 S_v - \sigma(\mu_r + \delta_2)]I_r \\ &\geq [\xi\omega - \rho(\mu_h + \omega)]E_h + [\eta\beta_2 (K_2 - \epsilon) - \xi(\mu_h + \delta_1 + \gamma)]I_h + [\rho\beta_1 (K_1 - \epsilon) + \sigma\beta_4 (K_3 - \epsilon) - \eta\mu_v]I_v \\ &\quad + [\eta\beta_3 (K_2 - \epsilon) - \sigma(\mu_r + \delta_2)]I_r \\ &\geq \varrho L(t), \end{aligned} \quad (36)$$

for all $t \geq T$, where

$$\varrho = \min \left\{ \frac{\xi\omega - \rho(\mu_h + \omega)}{\rho}, \frac{\eta\beta_2 (K_2 - \epsilon) - \xi(\mu_h + \delta_1 + \gamma)}{\xi}, \frac{\rho\beta_1 (K_1 - \epsilon) + \sigma\beta_4 (K_3 - \epsilon) - \eta\mu_v}{\eta}, \frac{\eta\beta_3 (K_2 - \epsilon) - \sigma(\mu_r + \delta_2)}{\sigma} \right\} > 0. \quad (37)$$

Hence, $L(t) \longrightarrow \infty$ as $t \longrightarrow \infty$, which contradicts to the boundedness of $L(t)$. This completes the proof.

Remark 1. Theorems 1~3 state that the basic reproduction number R_0 is a sharp threshold value for model (1). As $R_0 < 1$, the disease-free equilibrium P_0 is globally stable, i.e., the disease will go to extinction. As $R_0 > 1$, the disease is uniformly persistent, i.e., the disease will become an endemic in the meaning of persistence.

4. Results

We applied model (1) to study the infection status of VL in Kashgar, Xinjiang. Most of the parameters were obtained from the literature, and some of them were assumed or simulated to have more realistic results. These parameter values are listed in Table 1. The interpretation of the parameters values are as follows:

- (1) According to the population statistics in Kashgar Prefecture in Xinjiang Statistical Yearbook 2004–2016 [20], we have estimated the carrying capacity of population $K_1 = 5000000$.
- (2) According to the terrain and climate factors of Kashgar and the survival habits of the sandflies [21–24], the carrying capacity of sandflies $K_2 = 7000000$ has been estimated in Kashgar. In 2015, the number of dogs in Kashgar Prefecture of Xinjiang was close to 80,000 [25], so we have assumed the carrying capacity of dogs in Xinjiang $K_3 = 100000$.
- (3) The values of the parameter r_1 are obtained by numerical differentiation according to the population data in Kashgar, and the value of r_2 is calculated according to the life cycle of the sandflies (see [19]); the value of r_3 is assumed because there is no the specific data about dog.

TABLE 1: Parameter values (and their sources).

Parameters	Value	Interpretation*	Source
r_1	0.019	Intrinsic growth rate of human	Calculated
r_2	0.026	Intrinsic growth rate of vector	[19]
r_3	0.296	Intrinsic growth rate of reserve	Assumption
K_1	5000000	Human carrying capacity	Assumption
K_2	7000000	Vector carrying capacity	Assumption
K_3	100000	Reserve carrying capacity	Assumption
β_1	$1.35e-08$	Transmission probability from an infected sandfly to a susceptible human	Fitting
β_2	$3.565e-17$	Transmission probability from an infected human to a susceptible sand fly	Fitting
β_3	$3.515e-05$	Transmission probability from an infected reserve to a susceptible sandfly	Fitting
β_4	$1.23e-05$	Transmission probability from an infected sandfly to a susceptible reserve	Fitting
μ_h	0.0125	Natural mortality rate of human	[10]
μ_v	25.55	Natural mortality rate of vector	[11]
μ_r	0.1	Natural mortality rate of reserve	[12]
$1/\omega$	0.33	Human incubation period	[13]
δ_1	4.015	VL-induced death rate of humans	[8]
δ_2	3.65	VL-induced death rate of reserve	[13]
$1/\gamma$	2.5	Recovery period of VL	[14]

We model cumulative cases as a Poisson-distributed random variable because the Poisson distribution describes the number of observed events in an interval of time. We calibrate the model by sampling from the posterior distribution of parameter vector $\theta | \mathbf{y} = \{\beta_1, \beta_2, \beta_3, \beta_4\} | \mathbf{y}$, where vector $\mathbf{y}$ is derived from $(d/dt)Y(t) = \omega E_h$ and $Y(t)$ denotes the reported cumulative cases. We conduct sampling via MCMC (Markov Chain Monte Carlo) using the Metropolis–Hastings acceptance rule. The posterior density is

$$f_{\Theta|\mathbf{y}}(\theta | \mathbf{y}) = \prod_T \mathcal{L}(Y(t) | \theta) f_{\Theta}(\theta). \quad (38)$$

The prior density $f_{\Theta}(\theta)$ is the joint probability of four univariate priors. We consider that $\beta_1, \beta_2, \beta_3$, and β_4 are distributed according to $u(0, 1)$. The program was implemented in R version 3.6.0. We sampled from 30,000 MCMC iterations and discarded the first 10,000 samples as a burn-in period. On the basis of these 20,000 samples, the point estimates and 95% confidence intervals for the transmission coefficients were calculated. The results are shown in Table 2.

The MCMC method was used to fit the cumulative incidence data of VL in Kashgar from 2004 to 2016, and the 95% confidence interval of the fitted curve was obtained (see Figure 3). It can be seen from the figure that the fitted values of the model matches are in accordance with the accumulated data values in the Kashgar Prefecture. Only some data fluctuate, but in any case, the cumulative data of VL in Kashgar are increasing year by year. This model is used to predict the prevalence of VL in the Kashgar Prefecture over the next decade (see Figure 4).

The basic reproduction number $R_0 = 1.76$ (95% CI: 1.49–1.93). The result shows that $R_0 > 1$; according to the threshold theory, the disease will not disappear in the Kashgar Prefecture in a short period of time, and an endemic disease will be formed.

It is well known that the basic reproduction number R_0 is a very important parameter in the infectious disease model. In our model, R_0 is determined by the parameters of $\omega, \delta_1, \delta_2, \gamma, \mu_h, \mu_r, \mu_v, \beta_1, \beta_2, \beta_3$, and β_4 . We use the Latin hypercube

TABLE 2: Parameter values for point estimation and 95% interval estimation.

Parameters	Point estimation	95% confidence interval
β_1	$1.35e-08$	$[1.06e-08, 1.94e-08]$
β_2	$3.565e-17$	$[2.87e-19, 2.44e-15]$
β_3	$3.515e-05$	$[2.067e-05, 1.002e-04]$
β_4	$1.23e-05$	$[3.18e-06, 2.36e-05]$

FIGURE 3: Cumulative incidence simulation of VL in Kashgar from 2004 to 2016.

FIGURE 4: Prediction of cumulative incidence in 10 years from 2016 to 2026.

TABLE 3: Partial rank correlation coefficients (PRCCs) for R_0 on each input parameter variable.

Parameters	Distribution	2000 samples		3000 samples	
		PRCC	p value	PRCC	p value
ω	$N(3.03, 0.15^2)$	$9.295e-04$	0.504	$4.379e-04$	0.499
δ_1	$N(4.015, 0.2^2)$	$-1.995e-04$	0.493	$-1.619e-04$	0.496
δ_2	$N(3.65, 0.2^2)$	-0.247	<0.001	-0.2474	<0.001
γ	$N(0.4, 0.02^2)$	$-1.281e-03$	0.493	$3.011e-04$	0.502
μ_h	$N(0.0125, 0.0006^2)$	$8.376e-04$	0.511	$-1.041e-03$	0.505
μ_r	$N(0.1, 0.005^2)$	$-6.862e-03$	0.481	$-6.146e-03$	0.495
μ_v	$N(25.55, 3.28^2)$	-0.2327	<0.001	-0.2334	<0.001
β_1	$N(1.35e-08, 1e-08)$	$3.792e-04$	0.506	$-5.341e-05$	0.502
β_2	$N(3.565e-08, 2e-17^2)$	$-3.859e-04$	0.493	$-3.456e-04$	0.509
β_3	$N(3.515e-08, 1.5e-05^2)$	0.914	<0.001	0.914	<0.001
β_4	$N(1.23e-08, 5e-06^2)$	0.906	<0.001	0.906	<0.001

sampling (LHS) and partial rank correlation coefficients (PRCCs) to examine parameters which have a significant influence on the transmission of VL [26]. Using model (1), 2000 and 3000 samples are randomly generated by assuming a uniform distribution for each parameter based on values from Table 1.

We select eleven parameters as input variables and calculate the corresponding PRCC and p values for the eleven parameters. Table 3 and Figure 5 show the exact PRCC and p values of each input parameter and the effect on the basic reproduction number R_0 , respectively. We assume the significance level $\alpha = 0.05$. The larger the absolute value of PRCC, the stronger the correlation between the input parameters and R_0 . It can be seen from Table 3 that only δ_2 , μ_v , β_3 , and β_4 have significant impact on R_0 . More concretely, parameters δ_2 and μ_v have negative impact on R_0 and parameters β_3 and β_4 have positive impact.

We perform sensitivity analysis of infected humans, infected sandflies, and infected dogs through evaluating the PRCCs with the parameters of interest of model (1) over time by choosing a normal distribution with mean value and standard deviation shown in Figure 6. In Figures 6(a)–6(c), we plot the PRCCs over time with respect to the infected humans, sandflies, and infected dogs, respectively. Figure 6(a) indicates that there are three PRCC values that are significantly different from zero. The first three parameters with most impact on the outcome (the number of infected humans) are the sandfly-to-human transmission (β_1), transmission from an infected dog to a susceptible sandfly (β_3), and transmission from an infected sandfly to a susceptible dog (β_4). Figure 6(c) indicates that there are two PRCC values that are significantly different from zero. The first two parameters with most impact on the outcome (the number of infected humans) are the transmission from an infected dog to a susceptible sandfly (β_3) and transmission from an infected sandfly to a susceptible dog (β_4). Figure 6(c) indicates that there are two PRCC values that are significantly different from zero. The first two parameters with most impact on the outcome (the number of infected humans) are the transmission from an infected sandfly to a susceptible dog (β_4) and transmission from an infected dog to a susceptible sandfly (β_3).

FIGURE 5: Partial rank correlation coefficient (PRCC) results for the dependence of R_0 on each parameter.

Through sensitivity analysis, we demonstrate that the infection rate from infected dogs to susceptible sandflies β_3 and infected sandflies to susceptible dogs β_4 is the most sensitive parameter of R_0 . And β_1 , β_3 , and β_4 are the most sensitive parameters for the number of leishmaniasis human cases. Therefore, it is necessary to change the values of the parameters to observe their effects on the number of leishmaniasis human cases and R_0 (see Figure 7). From Figure 7(a), we observe that the number of leishmaniasis human cases decrease with the decrease of β_1 . We change the values of β_3 and β_4 to 4, 2, 1/2, and 1/4 times the original values. We observe the effects of different values on the number of leishmaniasis human cases, and we find that the change of parameter β_3 , β_4 can influence not only the number of leishmaniasis human cases, but also the peak time. As Figures 7(b) and 7(c) illustrate, when fixing other parameters at constant, the number of leishmaniasis human cases fall with the decrease of β_3 and β_4 , respectively. And the peak of outbreak will be postponed.

FIGURE 6: Sensitivity analysis: PRCC of the eleven parameters for (a) the number of infected humans, (b) the number of infected sandflies, and (c) the number of infected dogs.

Finally, in order to find better control strategies for VL transmission, we focus on changing the values of the parameters β_3 and β_4 to confirm the influence on the basic reproduction number R_0 (see Figure 8).

It can be seen from the figure that the parameters β_3 and β_4 have a strong influence on R_0 , and the value of the

basic reproduction number R_0 increased with the increases of β_3 and β_4 ; when β_3 is less than $6.854878e-06$ or β_4 is less than $2.39872e-06$, $R_0 < 1$, and the disease can be eliminated. This suggests that reducing the proportion rate between sandflies and dogs can effectively control the prevalence of VL.

FIGURE 7: The influence of different values of parameters on the number of diseases of VL. (a) Versus β_1 . (b) Versus β_3 . (c) Versus β_4 .

FIGURE 8: The influence of parameters on R_0 (red horizontal line is contour of $R_0 = 1$). (a) Versus β_3 . (b) Versus β_4 .

Through the above sensitivity analysis results, we find that the main cause of the outbreak of VL is the mutual contact infection between dogs and sandflies. Therefore, we can get some effective strategies to reduce the prevalence of VL: the effective way is to reduce the contact between dogs and sandflies, and thus we can give the dog a collar with impregnated insecticide, increase the control of dog and reduce its active area, spray insecticides vigorously, etc.

5. Conclusion and Discussion

VL is a serious parasitic disease. It has been endangered for several decades in Xinjiang and has become a major parasitic disease affecting the local social and economic development. Kashgar is a high-risk area for the occurrence of VL. In order to reveal the spread of VL in Kashgar and predict the prevalence of VL, this paper proposes a dynamic model of VL propagation with logistic growth. The model describes the transmission of VL among humans, dogs, and sandflies.

We use model (1) to fit the cumulative data of VL in Kashgar. As it can be seen from the simulation results in Figure 2, our model is consistent with the actual data of the cumulative cases of VL in Kashgar. The results show that there are certain reliability and rationality to study the prevalence of VL in Kashgar using logistic growth of the VL model. Using model (1), the basic reproduction number is estimated to be 1.76 (95% CI: 1.49–1.93) in the Kashgar Prefecture of Xinjiang. According to the threshold theory, it shows that VL will not disappear in the Kashgar area in a short time, and it may gradually become an endemic disease. According to the predictions for the next decade (see Figure 4), the cumulative incidence of VL in Kashgar is growing slowly, which means that the number of cases will gradually decrease over the next decade.

By selecting the sensitivity analysis of the parameters of interest for the basic reproduction number R_0 and the number of leishmaniasis human cases (see Figures 5 and 6), we can find that the most important factors affecting the basic reproduction number R_0 are β_3 and β_4 , indicating that the infection between sandfly and dog has the greatest impact on R_0 , and the most sensitive parameters affecting the number of leishmaniasis human cases are β_1 , β_3 , and β_4 , which explains that the infection among the infected person, the dog, and the sandfly has the strongest impact on the number of diseases of VL. From Figure 7, we find that reducing the values of β_1 , β_3 , and β_4 can effectively reduce the value of the basic reproduction number R_0 and the number of leishmaniasis human cases. When the values of β_3 and β_4 drop to $6.854878e-06$ and $2.39872e-06$, respectively, the value of the basic reproduction number R_0 will decrease to 1, and VL will not be epidemic but gradually disappear in Kashgar. Therefore, in order to control the spread of the disease, effective strategies should be taken to prevent and control leishmaniasis in Kashgar; we can decrease the incidence of leishmaniasis in humans by reducing the contact between sandflies and dogs. Without considering costs, we can vector controls (e.g., environmental clean-up and insecticide sprayed around buildings) and dog controls (e.g., insecticide releasing dog collars and dog vaccinations).

In order to reduce the bite of the sandflies, we can use insecticidal bed nets. Meanwhile, we should conduct public education on the dangers and prevention of leishmaniasis for people. In short, the model we have established now can reflect the dynamics of VL in Kashgar Prefecture.

Data Availability

The data will be available upon request.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Authors' Contributions

Yateng Song and Tailei Zhang contributed equally.

Acknowledgments

This research was supported by the National Natural Science Foundation of China (grant no. 11961071).

References

- [1] K. S. Rock, R. J. Quinnell, G. F. Medley, and O. Courtenay, "Chapter two-progress in the mathematical modelling of visceral leishmaniasis," *Advances in Parasitology*, vol. 94, pp. 49–131, 2016.
- [2] A. Mubayi, C. Castillo-Chavez, G. Chowell et al., "Transmission dynamics and underreporting of Kala-azar in the Indian state of Bihar," *Journal of Theoretical Biology*, vol. 262, no. 1, pp. 177–185, 2010.
- [3] C. J. Zheng, C. Z. Xue, W. P. Wu et al., "Analysis of epidemiological characteristics of black fever reported cases in China from 2005 to 2015," *Chinese Journal of Epidemiology*, vol. 38, no. 4, pp. 431–434, 2017.
- [4] Kaisaier, C. Z. Zhu, W. P. Wu et al., "Reflections on prevention and control of VL in Kashgar, Xinjiang," *Chinese Journal of Disease Control and Prevention*, vol. 23, no. 5, pp. 23–24, 2008.
- [5] L. Y. Wang, W. P. Wu, Y. Y. Guan et al., "Epidemiological characteristics of patients with high fever epidemic area in Kashgar, Xinjiang," *Chinese Journal of Pathogenic Biology*, vol. 8, no. 6, pp. 539–540, 2013.
- [6] Z. Muhammad and R. Ali, "Zoonotic visceral Leishmania: modeling and control," *Journal of Applied & Computational Mathematics*, vol. 4, no. 4, 2015.
- [7] I. M. Elmojtaba, J. Y. T. Mugisha, and M. H. A. Hashim, "Mathematical analysis of the dynamics of visceral leishmaniasis in the Sudan," *Applied Mathematics and Computation*, vol. 217, no. 6, pp. 2567–2578, 2010.
- [8] M. Zamir, R. Sultana, R. Ali, W. Panhwar, and S. Kumar, "Study on the threshold conditions for infection of visceral leishmaniasis," *Sindh University Research Journal (Science Series)*, vol. 47, no. 3, pp. 619–622, 2015.
- [9] K. Bi, Y. Chen, S. Zhaop, Y. Kuang, and C. H. John Wu, "Current visceral leishmaniasis research: a research review to inspire future study," *BioMed Research International*, vol. 2018, Article ID 9872095, 13 pages, 2018.
- [10] Xinjiang Daily, <http://www.xjdaily.com/>.

- [11] C. Dye, "The logic of visceral leishmaniasis control," *The American Journal of Tropical Medicine and Hygiene*, vol. 55, no. 2, pp. 125–130, 1996.
- [12] M. I. Elmojtaba, "Mathematical model for the dynamics of visceral leishmaniasis-malaria co-infection," *Mathematical Methods in the Applied Sciences*, vol. 39, no. 16, pp. 4334–4353, 2016.
- [13] S. Zhao, Y. Kuang, C. H. Wu et al., "Zoonotic visceral leishmaniasis transmission: modeling, backward bifurcation, and optimal control," *Journal of Mathematical Biology*, vol. 73, no. 6-7, pp. 1525–1560, 2016.
- [14] A. D. P. Sevá, M. Martcheva, T. Necibe et al., "Efficacies of prevention and control measures applied during an outbreak in southwest Madrid, Spain," *PLoS One*, vol. 12, no. 10, 2017.
- [15] O. Diekmann, J. A. P. Heesterbeek, and J. A. J. Metz, "On the definition and the computation of the basic reproduction ratio R_0 , in models for infectious diseases in heterogeneous populations," *Journal of Mathematical Biology*, vol. 28, no. 4, pp. 365–382, 1990.
- [16] P. van den Driessche and J. Watmough, "Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission," *Mathematical Biosciences*, vol. 180, no. 1-2, pp. 29–48, 2002.
- [17] H. R. Thieme, "Persistence under relaxed point-dissipativity (with application to an endemic model)," *SIAM Journal on Mathematical Analysis*, vol. 24, no. 2, pp. 407–435, 1993.
- [18] P. D. Leenheer and H. Smith, "Virus dynamics: a global analysis," *SIAM Journal on Applied Mathematics*, vol. 63, no. 4, pp. 1313–1327, 2003.
- [19] H. Y. Hu, "A simple method for solving the accurate value of intra-phase growth rate in population," *Anhui Agricultural Science Bulletin*, vol. 16, no. 3, pp. 173–174, 2010.
- [20] Statistics Bureau of Xinjiang Uyghur Autonomous Region, http://www.kashi.gov.cn/Category_1008/Index.aspx.
- [21] G. Wang, J. Wang, J. S. Li et al., "Further study on the ecology of sandfly in the Kashgar prefecture of Xinjiang," *Chinese Journal of Disease Control and Prevention*, vol. 7, no. 1, pp. 72–76, 1992.
- [22] L. Guan, J. J. Chai, and X. P. Zuo, "Advances in biology of Xinjiang sandfly," *Chinese Journal of Disease Control and Prevention*, vol. 14, no. 4, pp. 87–91, 1999.
- [23] Z. B. Zhou, D. G. Gu, L. R. Guan et al., "Changes in the composition ratio of main species of Kashgar prefecture in Xinjiang and its relationship with visceral leishmaniasis," *International Journal of Medical Parasitic Diseases*, vol. 42, no. 2, 2015.
- [24] A. A. Pereira Filho, M. da Conceição Abreu Bandeira, R. S. Fonteles et al., "An ecological study of sand flies (diptera: psychodidae) in the vicinity of Lençóis Maranhenses National park, Maranhão, Brazil," *Parasites & Vectors*, vol. 8, no. 1, pp. 8–442, 2015.
- [25] China News Network, http://www.sohu.com/a/122899918_123753.
- [26] S. Marino, I. B. Hogue, C. J. Ray, and D. E. Kirschner, "A methodology for performing global uncertainty and sensitivity analysis in systems biology," *Journal of Theoretical Biology*, vol. 254, no. 1, pp. 178–196, 2008.