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Threshold Condition for Elimination of Zoonotic Visceral Leishmaniasis

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Abstract. In most of the communicable diseases the *Disease Free State* is obtained but after some time the new outbreaks of the infection are observed in the population. Same is the case with Visceral Leishmaniasis. We in this work focus to find threshold condition for the global stability of *Disease Free State* of Visceral strain of Leishmaniasis. For this comprehensive mathematical model of Kala Azar and Post Kala Azar strains of Leishmaniasis is formulated. The reproduction number M_0 and its biological interpretation is discussed. On the basis of the transmission sensitivity of the parameters some non-pharmaceutical interventions are made, called control strategies. With the help of these strategies *Disease Free State* is obtained. Finally threshold condition condition is obtained to maintain the state. Numerical simulations are performed to verify the findings.

AMS Subject Classification Code: 92Bxx
Key Words: Leishmaniasis, Basic reproductive number, Sensitivity Analysis, Mathematical model, Local and global stability.

1. INTRODUCTION

Leishmaniasis is an intracellular protozoan parasite which causes different strains of Leishmaniasis. Visceral leishmaniasis (VL), Cutaneous leishmaniasis (CL), Mucocutaneous leishmaniasis (MCL), and Post Kala-Azar Dermal Leishmaniasis (PKDL) are the main clinical manifestations of Leishmaniasis. Globally, leishmaniasis is highly prevalent in tropical and subtropical areas [17]. 95% of MLC instances are found in Brazil, Peru, and Bolivia, whereas 75% of CL cases are documented in nations including Algeria, Brazil, Syria, Iran, Ethiopia, Afghanistan, Costa Rica, Sudan, and Peru [4]. Furthermore, Bangladesh, India, Brazil, Sudan, and Nepal account for almost 90% of occurrences of VL [25].
An estimated 12 million individuals have contracted Leishmaniasis, with over 350 million people at risk of developing the disease [7]. Globally, the prevalence of Leishmaniasis in the human population ranges between 10 to 12 million cases, while clinical cases occur at a rate of 1.5 to 2.5 million annually, with approximately 500,000 new cases of Visceral Leishmaniasis (VL) reported each year. The disease claims the lives of 20 to 40 thousand individuals annually and leads to around 2 million cases of human's disabilities. Leishmaniasis ranks second among tropical diseases in terms of both morbidity and mortality [23, 19].
Visceral Leishmaniasis is the most severe form of the disease, affecting mammals and humans, primarily. L. Donovina is the main source of this strain. Visceral Leishmaniasis can be of Zoonotic Visceral Leishmaniasis (ZVL) and Anthroponotic Visceral Leishmaniasis (AVL), nature and affect people of all ages. The latency period of VL varies case to case. However in most of the cases it occur from 2 weeks to 48 weeks [4, 25]. Rarely, PKDL development was noted in the patient otherwise recovered from visceral leishmaniasis. The stages of development of PKDL is different in different zone of the world. In Sudan it is developed in 6 months after recovery from Vl, where in India it may take 2 to 3 years [22, 23].
Sandfly is main source of carrying the protozoa from source to sank. The incubation/exposed period of the disease in sandfly is 7 days. The birth rate of sanflies varies with temperature. The most suitable temperature for its birth is 28^o [17, 2].

Due to expensive medication, the treatment is restricted to human population. But due to some factors like drug resistance and immunity system the failure of treatment is high [19]. Though the primary investigation like piezoelectic Biosensor based on ultrasensitive MEMS can play very important role in the disease control. But the disease being poor centered, economic burden is the main hurdle [12].
Different Mathematical models have been formulated for disease control using both differential equations and fractional differential differential equations [1, 27, 28]. We in this

work focuses the comprehensive model formulation and control of disease with non pharmaceutical approach. The total population is comprised of humans, sandflies and dogs. This population is divided in 11 groups. The novalities of the model includes;

- The latency or incubation of the visceral strain in human's body.
- The dormant period through which the victim pass before the appearance of PKDL strain.
- The threshold condition for global stability of disease free state, enabling to stop the new outbreaks of the disease

we, design control strategies to over come the transmission of the disease. These strategies are designed with help of sensitivity index of M_0; the reproduction number.

2. Model Formulation

In this section, we outline the development of the model.
The compartmental model of the human, reservoir, and vector populations is divided into various classes. Within the human population, subclasses include:

- H_1; The human class that is susceptible.
- H_2; The latency class of Vl.
- H_3; The PKDL Exposed class.
- H_4; The Vl Infected class.
- H_5; The PKDL infectious class.
- H_6; The Recovered class.

$H(t)$ represents the total reservoir population, which is divided into the following subclasses.

- $G_1(t)$; The susceptible reservoir,
- $G_2(t)$; the infectious of reservoir,
- $G_3(t)$; the reservoir class being recovered from infection.

$G(t)$ denotes the total vector population, which is categorized into the following classes.

- $V_1(t)$; The susceptible-vector class,
- $V_2(t)$; the infectious-vector class.

In impoverished communities, dogs, humans, and sandflies often coexist in close proximity. In these kinds of environments, sandflies interact with humans as well as reservoirs. Pathogens are transferred into human bloodstreams when an infected sandfly bites a vulnerable human in order to feed on blood. After the incubation period, the afflicted person exhibits the typical signs and symptoms of a VL infection. Some infected individuals dies due to the disease, some recover, and others appear to recover initially but later develop a complication of VL infection known as PKDL. During this phase, individuals enter an infectious stage of PKDL, characterized by the development of nodules throughout the body. When an infected sand fly feeds on the blood of a susceptible dog, it introduces the infection into the animal's bloodstream. Following the incubation period, the dog becomes infectious.

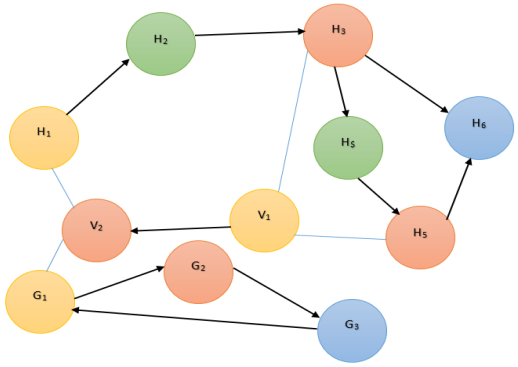

FIGURE 1. The diagram illustrates the progression of the illness, with distinct colors representing various categories or groups.

On the other hand, a vulnerable sand fly contracts the virus directly from the source if it feeds on the blood of an infected dog or human.
The interaction between the human, reservoir, and vector populations is illustrated in the flowchart depicted in the figure.

The system of differential equations governing the dynamics of human, reservoir, and vector populations is expressed as follows:

$$\begin{cases} \dot{H}_1 = B_1 - fe\frac{V_2}{H+G}H_1 - \xi_1 H_1 \\ \dot{H}_2 = fe\frac{V_2}{H+G}H_1 - l_2 H_2 - \xi_1 H_2 \\ \dot{H}_3 = l_2 H_2 - \pi_1 H_3 - \beta H_3 - \xi_1 H_3 \\ \dot{H}_4 = \pi_1 H_3 - \omega\pi_1 H_3 - l_3 H_2 - \xi_1 H_4 \\ \dot{H}_5 = l_3 H_4 - \pi_2 H_5 - \beta_1 H_5 - \beta_2 H_5 - \xi_1 H_5 \\ \dot{H}_6 = \omega\pi_1 H_3 + \pi_2 H_5 + \beta_1 H_5 - \xi_1 H_6 \\ \dot{G}_1 = B_2 + yG_3 - fe_1\frac{V_2}{H+G}G_1 - \xi_2 G_1 \\ \dot{G}_2 = fe_1\frac{V_2}{H+G}G_1 - (d+\xi_2)G_2 \\ \dot{G}_3 = dG_2 - (y+\xi_2)G_3 \\ \dot{V}_1 = B_3 - \frac{fV_1}{H+G}\left(m_2(H_3+H_5) + mG_2\right) - \xi_3 V_1 \\ \dot{V}_2 = \frac{fV_1}{H+G}\left(m_2(H_3+H_5) + mG_2\right) - \xi_3 V_2. \end{cases} \tag{2. 1}$$

Below is a table (1) displaying the values of the various parameters utilized in the model.

3. MODEL ANALYSIS

3.1. **Invariant Region.** It is assumed that every parameter is nonnegative. The state variables should be nonnegative at t=0 because the model deals with live populations [3]. The

TABLE 1. Table displaying various parameter values

Notation	Parameter definition	Value/days	Resource
β_2	Reduce the mortality rate caused by PKDL	0.0006	[28]
e	The likelihood of transmission of the V_l virus from flies to humans	0.0714	[15]
m	Transmission likelihood of V_l from canines to flies	0.022	[28]
π_1	V_l treatment rate	0.03	Assumed
$1-\omega$	Vl complication rate	0.36	[11]
π_2	$PKDL-recovery$ rate due to treatment	0.033	[11]
β	The mortality rate in dogs induced by V_l	0.00181	[15]
D	The natural, periodic occurrence of dogs without prior planning	0.000274	[2]
y	The rate at which dogs lose immunity	0.00274	[2]
B_3	fly Birth rate	0.299	[14]
l_3	The latency phase of $PKDL$	0.004925925	[26]
ξ_2	Natural lifespan of dogs	0.000274	[8]
B_2	the birth rate of Dogs	0.073	[8]
f	The flies biting rate	0.2856	[9]
B_1	Natural lifespan of human	0.00004	[14]
ξ_1	Human birth rate	0.0015875	[10]
m_2	The likelihood of V_l transmission from humans to flies	0.22	[9]
l_2	The time it takes for V_l to incubate in human	0.009555	[5]
ξ_3	Flies natural mortality rate	0.189	[14]
e_1	The likelihood of V_l transmission from flies to Dogs	0.0714	[21]
β_1	$PKDL$ natural-healing rate	0.00556	[11]

general dynamics are represented by the differential equations as follows:

$$\dot{H} = B_1 - \xi_1 H - \beta H_3 - \beta_2 H_5 \quad (3.\ 2)$$
$$\dot{G} = B_2 - \xi_2 G, \quad (3.\ 3)$$
$$\dot{V} = B_3 - \xi_3 V. \quad (3.\ 4)$$

In the case when $I_1 = P_2 = 0$ and the human population is disease-free, equation (3. 2) reduces to the following form:

$$\dot{H} = B_1 - \xi_1 H. \quad (3.\ 5)$$

Nonnegative equilibrium of (3. 5) is

$$H_u = \frac{B_1}{\xi_1}. \tag{3. 6}$$

Appling the mathematical fact $(\beta + \beta_2)H \geq \beta H_3 + \beta_2(H_5)$, to the equation (3. 2) we have:

$$B_1 - \xi_1 H - (\beta + \beta_2)H \leq \dot{H} \leq B_1 - \xi_1 H. \tag{3. 7}$$

Equation (3. 7) in lower bond is:

$$\dot{H} = B_1 - \xi_1 H - (\beta + \beta_2)H. \tag{3. 8}$$

The nonnegative equilibrium of (3. 8) is:

$$H_l = \frac{B_1}{\xi_1 + \beta + \beta_2}. \tag{3. 9}$$

We take the following starting conditions to be true:

$$\begin{aligned} H(0) &= H^0. \\ G(0) &= G^0, \\ V(0) &= V^0, \end{aligned}$$

If H_u and H_l are solutions to equations (3. 5) and (3. 8) respectively, then any solution to equation (3. 2) must meet the following cond:

$$H_l \leq H \leq H_u. \tag{3. 10}$$

Examine Ω, the biologically viable zone, as provided by

$\Omega = \Bigg((H_1, H_2, H_3, H_4, H_5, H_6, G_1, G_2, G_3, V_1, V_2) \in R_+^{11}$,

$0 \leq H_1, H_2, H_3, H_4, H_5, H_6, G_1, G_2, G_3, V_1, V_2, H \leq \frac{B_1}{\xi_1}; G \leq \frac{B_2}{\xi_2}; V \leq \frac{B_3}{\xi_3} \Bigg)$.

Using the usual comparison theorem, we may obtain from equation (2)

$H \leq H(0)e^{-\xi t} + \frac{B_1}{\xi_1}\Bigg(1 - e^{-\xi_1 t}\Bigg)$.

So

$H \leq \frac{B_1}{\xi_1}$ as $t \to \infty$.

Similarly

$\Bigg[V \leq \frac{B_3}{\xi_3}$ and $G \leq \frac{B_3}{\xi_3}\Bigg] \quad as\ t \to \infty$.

Therefore, Ω constitutes a positively invariant domain, ensuring the epidemiological and mathematical well-posedness of the model [7, 28], with all trajectories being forward bounded.

3.2. **Initial Rate of transmission.** The number of secondary infections that arise from the introduction of an infected individual into a completely susceptible population is called Reproduction number, denoted by M_0 in this work [6, 27, 24]. To determine the basic reproductive number, we employ the next generation method, as outlined in [18, 28]. After simplification, we get M_0

$$W = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & z_1 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & z_2 \\ 0 & z_3 & 0 & z_4 & z_5 & 0 \end{pmatrix},$$

$$P = \begin{pmatrix} -a_1 & 0 & 0 & 0 & 0 & 0 \\ l_2 & -a_2 & 0 & 0 & 0 & 0 \\ 0 & d_2 & -a_3 & 0 & 0 & 0 \\ 0 & 0 & l_3 & -a_4 & 0 & 0 \\ 0 & 0 & 0 & 0 & -(D+\xi_2) & 0 \\ 0 & 0 & 0 & 0 & 0 & -\xi_3 \end{pmatrix},$$

Here

$$\begin{aligned} z_1 &= fe\frac{B_1\xi_2}{\xi_2B_1+\xi_1B_2},\ z_2 = fe_1\frac{B_2\xi_1}{\xi_2B_1+\xi_1B_2}, \\ z_3 &= fm_2\frac{\xi_2\xi_1B_3}{\xi_3(\xi_2B_1+\xi_1B_2)},\ z_4 = fm_2\frac{\xi_2\xi_1B_3}{\xi_3(\xi_2B_1+\xi_1B_2)}, \\ z_5 &= fm\frac{\xi_2\xi_1v_c}{(D+\xi_2)\xi_3(\xi_2B_1+\xi_1B_2)} \end{aligned}$$

with
$a_1 = l_2 + \xi_1,\ a_2 = \pi_1 + \beta + \xi_1\ a_3 = l_3 + \xi_1\ a_4 = \pi_2 + \beta_1 + \beta_2 + \xi_1.$
$d_2 = (1-\omega)\pi_1.$
Following computation, we obtain M_0 as

$$M_0 = \left[\frac{z_2z_5}{(D+\xi_1)\xi_3} + \frac{l_2z_1z_3}{a_1a_2\xi_3} + \frac{d_2l_3l_2z_4z_1}{\xi_3a_1a_2a_3a_4}\right]^{\frac{1}{2}}.$$

following further simplification to get $M_0 = \sqrt{M_a + M_b}$ *where* $M_a = M_1M_2,\ M_b = M_3M_4$.

$$\begin{aligned} M_1 &= \frac{fe_1\xi_1B_3}{\xi_3(B_1\xi_2+B_2\xi_1)},\ M_2 = \frac{fm\xi_1B_2}{(D+\xi_2)\xi_3(B_1\xi_2+B_2\xi_1)}, \\ M_3 &= \frac{fe\xi_2B_1}{\xi_3(B_1\xi_2+B_2\xi_1)},\ M_4 = \frac{fm_2\xi_2\xi_1B_3}{\xi_3(B_1\xi_2+B_2\xi_1)}\left[\frac{l_2}{a_1a_2}(1+\frac{d_2l_3}{a_3a_4})\right]. \end{aligned}$$

3.3. **Sensitivity and Biological Sense of M_0.** The first term of M_0 is $M_b = M_3M_4$. Where

$$M_3 = \frac{fe\xi_2B_1}{\xi_3(B_1\xi_2+B_2\xi_1)},\ M_4 = \frac{fm_2\xi_2\xi_1B_3}{\xi_3(B_1\xi_2+B_2\xi_1)}\left[\frac{l_2}{a_1a_2}(1+\frac{d_2l_3}{a_3a_4})\right].$$

When a susceptible human comes into contact with a Vl-infected fly at a rate of f, and there's a chance of disease transmission from the fly to the human denoted by e, the Vl-infection can be transmitted from the fly to the human. This process is appropriately represented by M_3. Conversely, if a human is infected and a fly is susceptible, the direction of Vl-transmission occurs from the human to the fly, as shown by M_4. Therefore, M_b

rightly presnts the transmission of the Vl-strain between the fly and the human.
Similarly, M_a represents the mechanism through which transmission of Vl-infection occurs between the fly and reservoir. Both M_a and M_b refer to the transmission of Vl strains of leishmaniasis, making M_0 biologically significant.

3.4. **Control strategies based model.**

$$\begin{cases} \dot{H}_1 = B_1 - (f-u_1)e\frac{V_2}{H+G}H_1 - \xi_1 H_1 \\ \dot{H}_2 = (f-u_1)e\frac{V_2}{H+G}H_1 - l_2 H_2 - \xi_1 H_2 \\ \dot{H}_3 = l_2 H_2 - \pi_1 H_3 - \beta H_3 - \xi_1 H_3 \\ \dot{H}_4 = \pi_1 H_3 - \omega\pi_1 H_3 - l_3 H_2 - \xi_1 H_4 \\ \dot{H}_5 = l_3 H_4 - \pi_2 H_5 - \beta_1 H_5 - \beta_2 H_5 - \xi_1 H_5 \\ \dot{H}_6 = \omega\pi_1 H_3 + \pi_2 H_5 + \beta_1 H_5 - \xi_1 H_6 \\ \dot{G}_1 = B_2 + yG_3 - (f-u_1)e_1\frac{V_2}{H+G}G_1 - (\xi_2+u_3)G_1 \\ \dot{G}_2 = (f-u_1)e_1\frac{V_2}{H+G}G_1 - (d+\xi_2+u_3)G_2 \\ \dot{G}_3 = dG_2 - (y+\xi_2)G_3 \\ \dot{V}_1 = B_3 - \frac{(f-u_1)V_1}{H+G}\left(m_2(H_3+H_5)+mG_2\right) - (\xi_3+u_2)V_1 \\ \dot{V}_2 = \frac{(f-u_1)V_1}{H+G}\left(m_2(H_3+H_5)+mG_2\right) - (\xi_3+u_2)V_2. \end{cases} \tag{3. 11}$$

4. THRESHOLD CONDITION

In this section, we examine the stability of the disease-free equilibrium. We employ Theorem 3.1 from the referenced source [27]. Let the column vector representing all state variables be denoted as Y, with susceptible variables designated as Y_s and infected variables as M_I.

Theorem 4.1. *Let the Domain U be defined as*

$$U = \{\mathcal{M} \in \Omega; \mathcal{M}_I = 0, \mathcal{M}_s \neq 0\}.$$

Then the sub system

$$\begin{cases} \dot{H}_1 = B_1 - (f-u_1)e\frac{V_2}{H+G}H_1 - \xi_1 H_1 \\ \dot{H}_6 = \omega\pi_1 H_3 + \pi_2 H_5 + \beta_1 H_5 - \xi_1 H_6 \\ \dot{G}_1 = B_2 + yG_3 - (f-u_1)e_1\frac{V_2}{H+G}G_1 - (\xi_2+u_3)G_1 \\ \dot{G}_3 = dG_2 - (y+\xi_2)G_3 \\ \dot{V}_1 = B_3 - \frac{(f-u_1)V_1}{H+G}\left(m_2(H_3+H_5)+mG_2\right) - (\xi_3+u_2)V_1 \end{cases} \tag{4. 12}$$

is GAS at the domain U.

Proof. The above sub-system

$$\dot{\mathcal{M}}_s = \mathcal{C}_s(\mathcal{M}).(\mathcal{M}_s) + \mathcal{J}_s$$

reduces to the form:

$$\begin{cases} \dot{H}_1 = B_1 - \xi_1 H_1 \\ \dot{H}_6 = -\xi_1 H_6 \\ \dot{G}_1 = B_2 + yG_3 - (\xi_2 + u_3)G_1 \\ \dot{G}_3 = -(y + \xi_2)G_3 \\ \dot{V}_1 = B_3 - (\xi_3 + u_2)V_1 \end{cases} \tag{4. 13}$$

Here

$$C_S = \begin{pmatrix} \xi_1 & 0 & 0 & 0 & 0 \\ -0 & \xi_1 & 0 & 0 & 0 \\ 0 & 0 & (\xi_2 + u_3) & y & 0 \\ 0 & 0 & 0 & -(y + \xi_2) & 0 \\ 0 & 0 & 0 & 0 & -(\xi_3 + u_2) \end{pmatrix}, \ \mathcal{J}_s = (B_1, 0, B_1, 0, B_1)^T$$

All entries $C_{(J,J)}$ in matrix C_s are negative. Consequently, the subsystem pertaining to the non-infected human population exhibits GAS at the DFE point, which is denoted as $(\frac{B_1}{\xi_1}, 0, 0, 0, 0, 0)$.

□

The subsystem representing the infected population is:

$$\dot{\mathcal{M}}_1 \ = \ \mathcal{S}_I \left(\mathcal{M}\right) \mathcal{M}_I.$$

Where

$$\dot{\mathcal{M}}_1 = \begin{cases} \dot{H}_2 = (f - u_1)e\frac{V_2}{H+G}H_1 - l_2H_2 - \xi_1 H_2 \\ \dot{H}_3 = l_2H_2 - \pi_1 H_3 - \beta H_3 - \xi_1 H_3 \\ \dot{H}_4 = \pi_1 H_3 - \omega\pi_1 H_3 - l_3H_2 - \xi_1 H_4 \\ \dot{H}_5 = l_3H_4 - \pi_2 H_5 - \beta_1 H_5 - \beta_2 H_5 - \xi_1 H_5 \\ \dot{G}_2 = (f - u_1)e_1\frac{V_2}{H+G}G_1 - (d + \xi_2 + u_3)G_2 \\ \dot{V}_2 = \frac{(f-u_1)V_1}{H+G}\Big(m_2(H_3 + H_5) + mG_2\Big) - (\xi_3 + u_2)V_2. \end{cases} \tag{4. 14}$$

Theorem 4.2. *$\mathcal{S}_I$ is irreducible and metzler $\forall\ \mathcal{M} \in \Omega$ in the system* (4. 14)*. Moreover, certain $\overline{\mathcal{S}_I}$ exist so as*

$$\mathcal{S}_I \left(\mathcal{M}\right) \leq \overline{\mathcal{S}_I} \left(\mathcal{M}\right) for\, \mathcal{M} \in \Omega. \tag{4. 15}$$

Also

$$\overline{\mathcal{S}_I} \in \mathcal{N} = \{\mathcal{S}_I(\mathcal{M}), \mathcal{M} \in \Omega\}\ \overline{\mathcal{S}_I} = \mathcal{N}_{max\Omega}. \tag{4. 16}$$

$$\varrho(\overline{\mathcal{S}_I}) \leq 0. \tag{4. 17}$$

The modulus of stability, ϱ, represents the real component that dominates the eigenvalues of $\overline{\mathcal{S}_I}$.

Proof. Let's rewrite (4. 14) subsystem as follows:

$$\dot{\mathcal{M}}_1 \ = \ \mathcal{S}_I \left(\mathcal{MS}\right) \mathcal{M}_I$$

$$\mathcal{S}_I(\mathcal{M}) = \begin{pmatrix} -U_1 & 0 & 0 & 0 & 0 & N_1 \\ l_2 & -U_2 & 0 & 0 & 0 & 0 \\ 0 & (1-\omega)\pi_1 & -U_3 & 0 & 0 & 0 \\ 0 & 0 & l_3 & -U_4 & 0 & 0 \\ 0 & 0 & 0 & 0 & -U_5 & N_2 \\ 0 & N_3 & 0 & N_4 & N_5 & -(\xi_3+u_2) \end{pmatrix},$$

$$N_1 = \frac{(f-u_1)eH_1}{H+G}, N_2 = \frac{(f-u_1)e_1G_1}{H+G}, N_3 = \frac{(f-u_1)m_2V_1}{H+G}$$

$$N_4 = \frac{(f-u_1)m_2V_1}{H+G}, N_5 = \frac{(f-u_1)mV_1}{H+G}$$

Given that the diagonal entries $S(i,j)$ for $i=j$ are negative, and the entries $S(i,j)$ for $i \neq j$ are non-negative, the matrix $\mathcal{S}_I(\mathcal{M})$ is both metzler and irreducible for all $\mathcal{M} \in \Omega$. □

Theorem 4.3. *There is always an upper bound matrix $\overline{\mathcal{S}_I}$ for the matrix $\overline{\mathcal{S}_I}$ of equation* (4)*, such that*

$$\mathcal{S}_I(\mathcal{M}) \leq \overline{\mathcal{M}_I}(\mathcal{M}) \; for \; \mathcal{M} \in \Omega. \tag{4. 18}$$

Also

$$\overline{\mathcal{S}_I} \in \mathcal{N} = \{\mathcal{S}_I(\mathcal{M}), \mathcal{M} \in \Omega\} \; \overline{\mathcal{S}_I} = \mathcal{N}_{max_\Omega}. \tag{4. 19}$$

$$\varrho(\overline{\mathcal{S}_I}) \leq 0. \tag{4. 20}$$

The spectral radius of $\overline{\mathcal{S}_I}$ is denoted by ϱ.

Proof. Let's rewrite (4. 14) subsystem as follows:

$$\dot{\mathcal{M}}_1 = \mathcal{S}_I(\mathcal{M})\mathcal{M}_I$$

$$\mathcal{S}_I(\mathcal{M}) = \begin{pmatrix} -U_1 & 0 & 0 & 0 & 0 & \frac{(f-u_1)eH_1^0}{H_l+G_l} \\ l_2 & -U_2 & 0 & 0 & 0 & 0 \\ 0 & (1-\omega) & & & & \\ pi_1 & -U_3 & 0 & 0 & 0 & \\ 0 & 0 & l_3 & -U_4 & 0 & 0 \\ 0 & 0 & 0 & 0 & -U_5 & \frac{(f-u_1)e_1G_1^0}{H_l+G_l} \\ 0 & \frac{(f-u_1)m_2V_1^0}{H_l+G_l} & 0 & \frac{(f-u_1)m_2V_1^0}{H_l+G_l} & \frac{(f-u_1)mV_1^0}{H_l+G_l} & -(\xi_3+u_2) \end{pmatrix},$$

It follows that for any $\mathcal{M} \in \Omega$, the matrix $\mathcal{S}_I(\mathcal{M})$ is irreducible and metzler since the diagonal entries are negative and the off-diagonal elements are non-negative.
Let the upper bound of the matrix $\mathcal{S}_I(\mathcal{M})$ be shown by $\overline{\mathcal{S}_I}(\mathcal{M})$.

$$\overline{\mathcal{S}_I}(\mathcal{M}) = \begin{pmatrix} -U_1 & 0 & 0 & 0 & 0 & x_1 \\ l_2 & -U_2 & 0 & 0 & 0 & 0 \\ 0 & (1-\omega)\pi_1 & -U_3 & 0 & 0 & 0 \\ 0 & 0 & l_3 & -U_4 & 0 & 0 \\ 0 & 0 & 0 & 0 & -U_5 & x_2 \\ 0 & x_3 & 0 & x_4 & x_5 & -(\xi_3+u_2) \end{pmatrix},$$

Where

$$\begin{aligned}
x_1 &= (f-u_1)e\frac{B_1\xi_2(\xi_1+\beta+\beta_2)}{\xi_1(B_1\xi_2+B_2(\xi_1+\beta+\beta_2)},\\
x_2 &= (f-u_1)e_1\frac{B_2\xi_2(\xi_1+\beta+\beta_2)}{\xi_2(B_1\xi_2+B_2(\xi_1+\beta+\beta_2)},\\
x_3 &= (f-u_1)m_2\frac{B_3\xi_2(\xi_3+\beta+\beta_2)}{\xi_2(B_1\xi_2+B_2(\xi_1+\beta+\beta_2)},\\
x_4 &= (f-u_1)m_2\frac{B_3\xi_2(\xi_3+\beta+\beta_2)}{\xi_2(B_1\xi_2+B_2(\xi_1+\beta+\beta_2)},\\
x_5 &= (f-u_1)m\frac{B_3\xi_2(\xi_3+\beta+\beta_2)}{\xi_2(B_1\xi_2+B_2(\xi_1+\beta+\beta_2)},\\
U_1 &= (l_2+\xi_1),\ U_2=(\pi_1+\beta+\xi_1),\ U_3=(l_3+\xi_1),\\
U_4 &= (\pi_2+\beta_1+\beta_2+\xi_1),\ U_5=(D+\xi_2+u_3)
\end{aligned}$$

Since the Jacobian matrix of the subsystem represented by (4. 14) at the Disease-Free Equilibrium (DFE) differs from the matrix $\overline{\mathcal{S}_I}$, it indicates that the upper bound is not reached within Ω. This establishes a sufficient condition for the global stability of the DFE. □

Next we prove a_5 or (4. 20).

Theorem 4.4. *The axiom a_5 ; $\varrho(\bar{S}_I) \leq 0$ is satisfied by the metzler matrix if $\xi < 1$, where ξ, is supplied by:*

$$\xi = \frac{B_2B_3f^2e_1m(D+\xi_2)\xi_2((\xi_1+\beta+\beta_2))^2}{(B_1\xi_2+B_2(\xi_1+\beta+\beta_2))^2\xi_2^2\xi_3^2}+\frac{f^2em_2l_2B_1B_3(D+\xi_2)\xi_2((\xi_1+\beta+\beta_2))^2}{(B_1\xi_2+B_2(\xi_1+\beta+\beta_2))^2(l_2+\xi_1)(\pi_1+\beta+\xi_1)}+\frac{f^2em_2B_1B_3l_2l_3(1-\omega)(D+\xi_2)\xi_2((\xi_1+\beta+\beta_2))^2}{(B_1\xi_2+B_2(\xi_1+\beta+\beta_2))^2(l_2+\xi_1)(\pi_1+\delta_1+\xi_1)(l_3+\xi_1)(\pi_2+\beta_1+\beta_2+\xi_1)\xi_1\xi_3}$$

Proof. We employ the subsequent breakdown of the matrix $\overline{B_I}$.

$\overline{B_I} = \begin{pmatrix} M & N \\ O & P \end{pmatrix}$,

where

$$M=\begin{pmatrix} -U_1 & 0 & 0 & 0 \\ l_2 & -U_2 & 0 & 0 \\ 0 & (1-\omega)\pi_1 & -U_3 & 0 \\ 0 & 0 & l_3 & -U_4 \end{pmatrix},$$

$$O=\begin{pmatrix} 0 & 0 & 0 & 0 \\ 0 & N_3 & 0 & N_4 \end{pmatrix},$$

$$N=\begin{pmatrix} 0 & N_1 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \end{pmatrix}, P=\begin{pmatrix} -U_5 & N_2 \\ N_5 & -(\xi_3+u_2) \end{pmatrix}.$$

The matrix $\overline{\mathcal{B}_I}$ is stable if

- M is stable
- $P - OM^{-1}N$ is stable.

The matrix M is metzler stable because

- For $i \neq j$ $M_{(i,j)}$ are non negative.
- The eigenvalues of M are negative.

Next, if we denote $P - OM^{-1}N$ as D, then the stability of D ensures the stability of $\overline{\mathcal{B}_I}$. From Routh-Hurwitz theory ([20]), we understand that in our specific case:
$\varrho(\bar{B}_I) \leq 0 \; only \; if$

$$\frac{B_2B_3f^2e_1m(D+\xi_2)\xi_2((\xi_1+\beta+\beta_2))^2}{(B_1\xi_2+B_2(\xi_1+\beta+\beta_2))^2\xi_2^2\xi_3^2}+\frac{f^2em_2l_2B_1B_3(D+\xi_2)\xi_2((\xi_1+\beta+\beta_2))^2}{(B_1\xi_2+B_2(\xi_1+\beta+\beta_2))^2(l_2+\xi_1)(\pi_1+\beta+\xi_1)}+$$
$$\frac{f^2em_2B_1B_3l_2l_3(1-\omega)(D+\xi_2)\xi_2((\xi_1+\beta+\beta_2))^2}{(B_1\xi_2+B_2(\xi_1+\beta+\beta_2))^2(l_2+\xi_1)(\pi_1+\delta_1+\xi_1)(l_3+\xi_1)(\pi_2+\beta_1+\beta_2+\xi_1)\xi_1\xi_3}$$
$$< 1$$

Let $\xi = \frac{B_2B_3f^2e_1m(D+\xi_2)\xi_2((\xi_1+\beta+\beta_2))^2}{(B_1\xi_2+B_2(\xi_1+\beta+\beta_2))^2\xi_2^2\xi_3^2}+\frac{f^2em_2l_2B_1B_3(D+\xi_2)\xi_2((\xi_1+\beta+\beta_2))^2}{(B_1\xi_2+B_2(\xi_1+\beta+\beta_2))^2(l_2+\xi_1)(\pi_1+\beta+\xi_1)}+$
$\frac{f^2em_2B_1B_3l_2l_3(1-\omega)(D+\xi_2)\xi_2((\xi_1+\beta+\beta_2))^2}{(B_1\xi_2+B_2(\xi_1+\beta+\beta_2))^2(l_2+\xi_1)(\pi_1+\delta_1+\xi_1)(l_3+\xi_1)(\pi_2+\beta_1+\beta_2+\xi_1)\xi_1\xi_3}$.
Next, we have demonstrated that, for $\xi < 1$, the assumption a_5 or (4. 20) is met. □

In the preceding discussion, we have validated all the assumptions outlined in Theorem 3.1 of the referenced work [27].
We make the following theorem based on the results presented above:

Theorem 4.5. *: The Disease-Free Equilibrium (DFE) of the given system will achieve global asymptotic stability if the parameters utilized in the model adhere to the condition $\xi < 1$, where ξ is as defined previously.*

5. Strategies for control derived from sensitivity analysis

Various parameter within the model exert distinct impacts on the disease transmission. The influence of parameter K on phenomenon Z is term as the sensitivity of Z wrt K [18].

$$\Upsilon_Z^K = \frac{\partial Z}{\partial K}\frac{K}{Z}.$$

5.1. **Control strategies.** Based on sensitivity indexes, we identify five parameters for intervention. The intervention in the parameter means an increase or decrease in the value of the parameter on whether their sensitivity index is positive or negative. As a result, M_0, the initial rate of disease transmission, decreases. The following criteria were chosen for the intervention: f signifies the sand fly bite rate; m indicates the chance of the visceral strain being transmitted from dogs to sand flies; B_3 represents the fly birth rate; ξ_2 represents

TABLE 2. Parameters's sensitivity indices

Parameter	Value	index	Parameter	Value	index
f	0.2856	1	B_3	0.299	0.5
e	0.0714	$+0.0936$	m	0.22	$+0.4064$
m_2	0.22	$+0.0936$	l_2	0.009555	$+0.00039009$
l_3	0.004925925	$+0.00075372$	ξ_3	0.189	-1.0000
ξ_1	0.00004	$+0.0348$	ξ_2	0.000274	-0.4105
α_1	0.64	-0.0365	β	0.011	-0.0234
β_2	0.011	-0.0208	D	0.000274	-0.3530
B_1	0.0015875	-0.0361	B_2	0.073	-0.4639
β_1	0.00556	-0.0105	π_1	0.033	-0.0623
π_2	0.033	-0.0623	e_2	0.0714	$+0.4064$

the natural dog expiry rate; and ξ_3 represents the natural sand fly death rate. These interventions are carried out in appropriate proportions, leading to the proposal of four control strategies, as outlined in Table (3).

TABLE 3. Control strategies

$Strategy$	f	B_1	m	ξ_3	ξ_2
$Strategy-1$	0.1721	0.113	0.005	0.022	0.0007
$Strategy-2$	0.1921	0.103	0.001	0.102	0.000971
$Strategy-3$	0.2663	0.00001	0.00003	0.205	0.0099

5.2. **Numerical simulation.** We used ODE 45 to produce numerical simulations. The graphs generated with help of simulations are presented in figures (2) to (7). The figures shows the comparisons of the control strategies. To ensurer the global stability of the disease free state, perturbations were made in the infected classes (H_2, H_3, H_4, H_5, G_2, and V_2). The results shows that after perturbation all the state variables are attracted by the state of disease-free equilibrium.

5.3. **Conclusions:** This study presents a mathematical model of visceral leishmaniasis, including post-kala-azar dermal leishmaniasis (PKDL), considering homogeneously mixed populations of sandflies, dogs, and humans. Based on sensitivity indexes of parameters, we select five key parameters for intervention and propose three control strategies, the details shown in Table (3).
In our approach, we consider three different strategies for controlling the spread of the disease. In $Strategy-1$, we utilize the actual parameter values without any intervention.

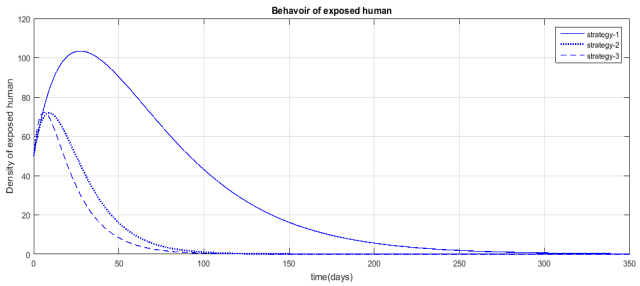

FIGURE 2. The duration required to eliminate individuals from $V_l$exposed human population.

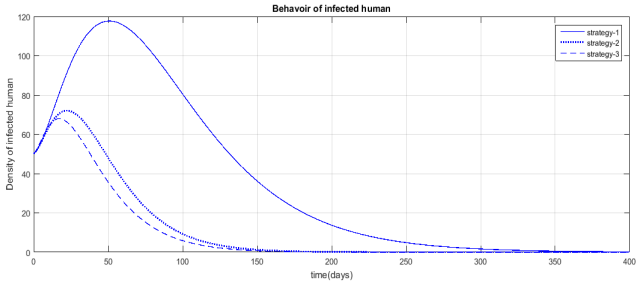

FIGURE 3. Contrasting the impacts of different control strategies on the population of infected human population.

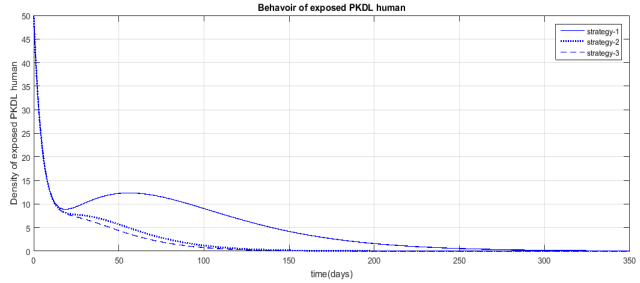

FIGURE 4. Contrasting the effects of various control strategies on the population of exposed individuals with PKDL Exposed population.

However, $Strategy - 2$ and $Strategy - 3$ uses the values of the parameters after bing intervened.

Our analysis focuses on the role of the exposed class, which serves as a gateway for disease transmission. With $Strategy-3$, we observe that the density of this class decreases to zero within a period of 110 days, as depicted in (2). Similarly, the density of the infectious class

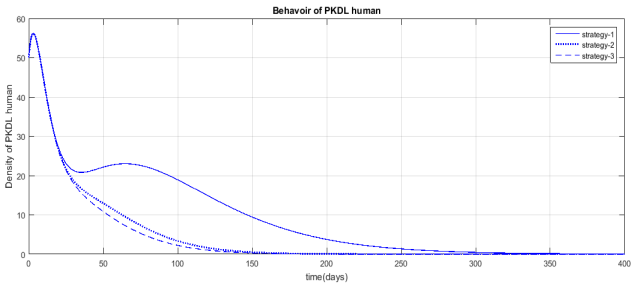

FIGURE 5. contrasting the impacts of different control strategies on the population of infected individuals with PKDL.

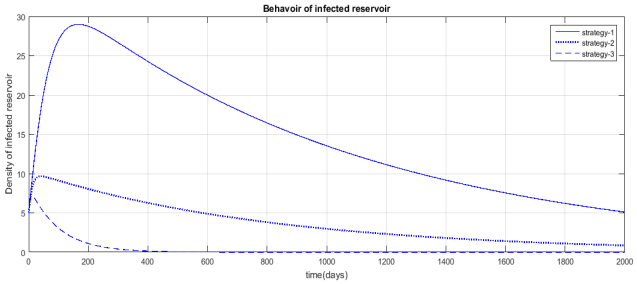

FIGURE 6. Comparing the impacts of different control strategies on the population of infected reservoirs.

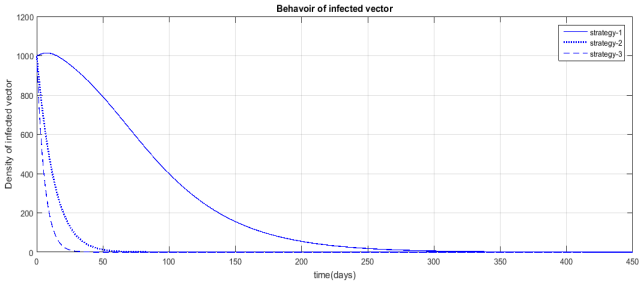

FIGURE 7. Comparing the impacts of various control strategies on the population of infected vectors.

reaches zero within 175 days with $Strategy-3$, as illustrated in (3). (4) demonstrates that by implementing $Strategy-3$, we can reduce the density of the exposed PKDL class to zero within 145 days. Additionally, the density of the PKDL infectious class diminishes to zero within 170 days, as indicated in (5).
Furthermore, we recognize the significant roles played by the reservoir and sandflies classes

TABLE 4. The duration of infection removal using various tactics

$T.E_i$	$Strategy-1$	$Strategy-2$	$Strategy-3$
$T.H_2$	350	130	110
$T.H_3$	400	190	175
$T.H_4$	400	160	145
$T.H_5$	400	180	170
$T.G_2$	$*$	$*$	470
$T.V_2$	350	72	35

Let's denote $T.E_i$ as the time taken to elimination E_i.

in disease transmission. Employing $Strategy-3$, we achieve elimination of these classes within 470 days and 35 days, respectively, as depicted in (6) and (7).
$Strategy-3$ emerges as the optimal choice for eradicating Leishmaniasis entirely. With the threshold value, ξ, calculated to be less than one based on the parameter values in use, the likelihood of new disease outbreaks is eliminated. Consequently, the disease-free state achieved through this strategy is globally asymptotically stable.

Competing interests:
The authors declare that they have no competing interests

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