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Zoonotic Visceral Leishmania: Modeling and Control

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Abstract

In this work we focus on the transmission dynamics of Visceral strains of leishmania, using mathematical model with two latent compartments in human. From the governing differential equations of the model, we find the reproductive number R0; the number of secondary infection and its biological interpretation. Using Routh- Hurwitz criteria on upper bound matrix, the threshold condition, for stability of the Disease Free State, is calculated. Finally we show that the disease free equilibrium is globally asymptotically stable if $R_0 <<\xi$ 11.

Keywords: Leishmaniasis; Basic reproductive number; Mathematical model; Local and global stability

Introduction

Visceral leishmaniasis is a vector-borne disease of humans and other mammals. This disease is caused by parasites of the Leishmania donovani complex. There are two main forms of visceral leishmania: (1) zoonotic visceral leishmaniasis (ZVL), which affects mainly young children and the domestic dog as its principal reservoir and (2) anthroponotic visceral leishmaniasis (AVL), this affects people of all ages, and infectious sand y transmit it from human to human via biting [1]. Visceral leishmaniasis (Vl) is severe and fatal. The average incubation period is 2-6 months; however it may vary from 10 days to one year [2,3]. Some of the patients recovered from V l, develops Post kala-Azar dermal leishmania with in the interval of 6 months to 3 years [4]. The vector latent period is assumed roughly to be 3 to 7 days [5,6].

No doubt leishmania control is challenging because the control of both sandflies and the reservoir is di cult. The failure rate of treatment is high due the two factors. Clinical structure of disease, the response of human immune system and the drug resistance acquired by the species [7].

Motivated from Hashim et al. [8] and Shillor et al. [9], the authors did not consider Homogenous population. We in our work have considered the homogenous mixing of the population. The Reproductive number so calculated, depends upon the densities of humans, reservoirs and vectors, which highlights the importance of homogenous mixing. Also we have applied new concept for calculating threshold condition, for disease free state as developed by Kamgang and Sallet [10].

In this paper, we present a mathematical model for the transmission dynamic of leishmaniasis. The model of 10 compartments includes 2 exposed classes of human infected with visceral leishmaniasis and PKDL. These exposed classes were not considered previously in the models. We find positive invariant region and use next generation matrix method to find the basic reproduction number R_0. Using upper bound matrix $A_1(X)$ of the matrix $A_1(X)$, of the infected classes, the threshold number is found. Comparing R_0 and we find three values for R_0. On the basis of these values, we discuss the dynamical behavior of the model. Finally we show the global stability of the disease free equilibrium, and the existence of endemic equilibrium.

Model Formulation

In this section we present the formulation of the model.

We divide the compartmental model of human, reservoir and vector populations into different classes. The human population consist of sub-classes, S_h; E_1; I_1; P_2; R_1; E_{12}. Here S_h represent the class of susceptible human, E_1 is the Vl infected class, E_{12} is the class recovered from Vl and exposed to PKDL. P_2 is the human class with PKDL and R_1 is the human recovered class, I_1 is the human class infectious with Vl,

The total human population N_h is

$$N_h = S_h + E_1 + I_1 + E_{12} + P_2 + R_1$$

The vector population is divided into two sub-classes $S_v(t)$ and $I_v(t)$, also the reservoir class is divided into $S_r(t)$ and $I_r(t)$.

$$N_v(t) = S_v(t) + I_v(t);\ N_r(t) = S_r(t) + I_r(t):$$

After susceptible person, being bitten by infectious vector, he/she can't transmit leishmania virus immediately. We call this person as infected (exposed). When a susceptible vector $S_v(t)$, bite the infectious person, the vector moves from susceptible compartment to the infectious compartment $I_v(t)$ [11].

The interaction of human, reservoir and vector population is represented in the flowchart as shown in Figure 1.

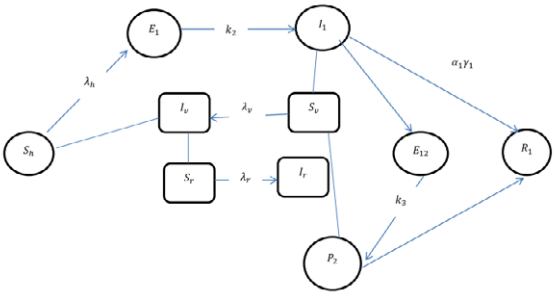

Figure 1: The interaction of human, reservoir and vector population.

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The dynamical system for human, reservoir and vector population is given by

$$\begin{cases} \dot{S} = \Gamma_h - (\lambda_h + \mu_h)S_h \\ \dot{E_1} = \lambda_h S_h - (k_2 + \mu_h)E_1 \\ \dot{I_1} = k_2 E_1 - (\gamma_1 + \delta_1 + \mu_h)I_1 \\ \dot{E_{12}} = (1-\alpha_1)\gamma_1 I_1 - (k_3 + \mu_h)E_{12} \\ \dot{P_2} = k_3 E_{12} - (\gamma_2 + \beta_1 + \delta_2 + \mu_h)P_2 \\ \dot{R} = \alpha_1\gamma_1 I_1 + (\gamma_2 + \beta_1)P_2 - (\mu_h)R \\ \dot{S_r} = \Gamma_r - \lambda_r S_r - \mu_r S_r \\ \dot{I_r} = \lambda_r S_r - \mu_r I_r \\ \dot{S_v} = \Gamma_v - \lambda_v S_v - \mu_v S_v \\ \dot{I_v} = \lambda_v S_v - \mu_v I_v. \end{cases} \quad (1)$$

The description of the parameters is given in Table 1.

The terms of interaction λ_h, λ_r and λ_v are as under $\lambda_h = ab_2 \frac{I_v}{N_h + N_r}$ is the average rate of infection rate of human with Vl, from infectious sandfly.

λ_r is the average rate of infection of susceptible reservoir by infected sandfly.

$\lambda_r = ab\frac{I_v}{N_h + N_r}$; b is transmission probability of V l to reservoir from sandfly.

$\lambda_v = \frac{a}{N_h + N_r}\left(c_2(I_1 + P_2) + cI_r\right)$, is the average rate of infection of sandfly with Vl strain from human or reservoir. Where c_2 is the transmission probability of Vl from human in stage I_1 and P_2 to sandfly

Mathematical Analysis of the Model

In this section, we discuss invariant region, the disease free equilibrium point and reproductive number R_0, of the system (1).

Invariant region

We have assumed all the parameters as nonnegative. Since the model is concerned with living population, therefore the state variables are assumed to be nonnegative at t=0. The dynamic of overall population is given by the following differential equations.

$$\dot{N_h} = \Gamma_h - \mu_h N_h - \delta_1 I_1 - \delta_2 P_2 \quad (2)$$

$$\dot{N_r} = \Gamma_r - \mu_r N_r, \quad (3)$$

$$\dot{N_v} = \Gamma_v - \mu_v N_v. \quad (4)$$

If the human population is disease free, i.e. $I_1 = P_2 = 0$, then equation (2) reduces to the form;

$$\dot{N_h} = \Gamma_h - \mu_h N_h. \quad (5)$$

Equilibrium in this case is

$$N_{h_u} = \frac{\Gamma_h}{\mu_h}. \quad (6)$$

From equation (2) and the fact that $(\delta_1 + \delta_2)N_h \geq \delta_1 I_1 + \delta_2(p_2)$, we have

$$\Gamma_h - \mu_h N_h - (\delta_1 + \delta_2)N_h \leq \dot{N_h} \leq \Gamma_h - \mu_h N_h \quad (7)$$

The lower bond for equation (7) is given by

$$\dot{N_h} = \Gamma_h - \mu_h N_h - (\delta_1 + \delta_2)N_h. \quad (8)$$

The equilibrium of equation (8) is

$$N_{h_l} = \frac{\Gamma_h}{\mu_h + \delta_1 + \delta_2}. \quad (9)$$

With the initial condition

Notation		Value	Resource
c_2	Progression rate of VL in sand y(from human)	0.22	[14]
a	Sandflies biting rate	0.2856 day^{-1}	[14]
Γ_h	Recruitment rate of human	0.0015875day^{-1}	[15]
Γ_v	Recruitment rate of sandfly	0.299 day^{-1}	[16]
Γ_r	Recruitment rate of reservoir	0.073 day^{-1}	Assumed
Γ_h	Natural mortality rate of human	0.00004 day^{-1}	[16]
μ_v	Natural mortality rate of Sandflies	0.189 day^{-1}	[16]
μ_r	Natural mortality rate of Reservoirs	0.000274 day^{-1}	Assumed
γ_2	PKDL recovery rate after treatment	0.033 day^{-1}	[17]
$1-\alpha_1$	Developing PKDL rate after treatment	0.36 day^{-1}	[17]
β_1	PKDL natural healing rate	0.00556 day^{-1}	[17]
c	Progression rate of Vl in sandfly (from reseroir)	Variable	Variable
b	Progression rate of Vl in reservoir(from sandfly)	Variable	Variable
γ_1	Treatment rate of VL	variable	Assumed
δ_1	VL induced death rate	0.011 day^{-1}	[18]
k_2	$1/k_2$ is Incubation period of vl	0.006555 day^{-1}	[19]
k_3	$1/k_3$ is Incubation period of PKDL	0.004925925day^{-1}	[2,20]
δ_2	PKDL induced death rate	assumed	Assumed
b_2	Progression rate of VL in human (from sandfly)	0.0714 day^{-1}	[21]

Table 1: Description of the parameters.

$N_h(0) = N_0$. (10)

If N_u, and N_l, denote the solution of equation (5) and equation (8), then any solution of equation (2), satisfy

$N_l \le N_h \le N_u$. (11)

Consider the biological feasible region Ω given by:

$$\Omega = \left[(S_h, E_1, I_1, P_2, R_1, E_{12}, S_r, I_r, S_v, I_v) \in R_+^{10} , N_h \le \frac{\Gamma_h}{\mu_h}; N_r \le \frac{\Gamma_r}{\mu_r}; N_v \le \frac{\Gamma_v}{\mu_v} \right].$$

From equation (2), using standard comparison theorem, we have

$$N_h \le N_h(0)e^{-\mu(t)} + \frac{\Gamma_h}{\mu_h}\left(1 - e^{-\mu_h(t)}\right).$$

So

$$N_h \to \frac{\Gamma_h}{\mu_h} \quad \text{as } t \to \infty .$$

Similarly

$$\left[N_v \to \frac{\Gamma_v}{\mu_v} \text{ and } N_r \to \frac{\Gamma_r}{\mu_r} \right] \text{and } t \to \infty .$$

Hence is positively invariant domain, and the model is epidemiologically and mathematically well posed.

Let us de ne a new region G as

$$G = \{X \in \Omega; N_{h_l} \le N_h \le N_{h_u}; N_r \le \frac{\Gamma_r}{\mu_r}; N_v \le \frac{\Gamma_v}{\mu_v}\} .$$

where

$$X = (S_h, E_1, I_1, E_{12}, P_2, R_1, S_r, I_r, S_v, I_v)^T .$$

Clearly G is the sub region of Ω. In light of equation (3), equation (4) and equation (11), it is reasonable to work on G instead of Ω.

Disease free equilibrium

The disease free equilibrium of the model (1) is given by:

$$X_0 = (\frac{\Gamma_h}{\mu_h}, 0, 0, 0, 0, 0, , \frac{\Gamma_r}{\mu_r}, 0),$$

Reproductive number

The number of secondary infections occurring in completely susceptible population by introducing an infectious individual to the population is called reproductive number R_0 [12]. In order to find the basic reproductive number, we use next generation method for $R_0 = (-FV^{-1})$, [13]. Where is spectral radius? And

$$F = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & m_1 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & m_2 \\ 0 & m_3 & 0 & m_4 & m_5 & 0 \end{pmatrix}, V = \begin{pmatrix} -a_1 & 0 & 0 & 0 & 0 & 0 \\ k_2 & -a_2 & 0 & 0 & 0 & 0 \\ 0 & d_2 & -a_3 & 0 & 0 & 0 \\ 0 & 0 & k_3 & -a_4 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\mu_r & 0 \\ 0 & 0 & 0 & 0 & 0 & -\mu_v \end{pmatrix},$$

Here

$$m_1 = ab_2 \frac{\Gamma_h \mu_r}{\mu_r \Gamma_h + \mu_h \Gamma_r}, m_2 = ab \frac{\Gamma_r \mu_h}{\mu_r \Gamma_h + \mu_h \Gamma_r},$$

$$m_3 = ac_2 \frac{\mu_r \mu_h \Gamma_v}{\mu_v(\mu_r \Gamma_h + \mu_h \Gamma_r)}, \quad m_4 = ac_2 \frac{\mu_r \mu_h \Gamma_v}{\mu_v(\mu_r \Gamma_h + \mu_h \Gamma_r)}, m_5 = ac \frac{\mu_r \mu_h \Gamma_v}{\mu_v(\mu_r \Gamma_h + \mu_h \Gamma_r)}.$$

with

$$a_1 = k_2 + \mu_h, \quad a_2 = \gamma_1 + \delta_1 + \mu_h \quad a_3 = k_3 + \mu_h \; a_4 = \gamma_2 + \beta_1 + \delta_2 + \mu_h$$

$$d_2 = (1 - \alpha_1)\gamma_1 .$$

After simplification, we get reproduction number

$$R_0 = \left[\frac{m_2 m_5}{\mu_r \mu_v} + \frac{k_2 m_1 m_3}{a_1 a_2 \mu_v} + \frac{d_2 k_3 k_2 m_4 m_1}{\mu_v a_1 a_2 a_3 a_4} \right]^{\frac{1}{2}} .$$

We can further simplify to get $R_0 = \sqrt{R_a + R_b}$ where $R_a = R_1 R_2$, $R_b = R_3 R_4$.

$$R_1 = \frac{ab\mu_h \Gamma_v}{\mu_v(\Gamma_h \mu_r + \Gamma_r \mu_h)}, \; R_2 = \frac{ac\mu_h \Gamma_r}{\mu_v(\Gamma_h \mu_r + \Gamma_r \mu_h)},$$

$$R_3 = \frac{ab_2 \mu_r \Gamma_h}{\mu_v(\Gamma_h \mu_r + \Gamma_r \mu_h)}, \; R_4 = \frac{ac_2 \mu_r \mu_h \Gamma_v}{\mu_v(\Gamma_h \mu_r + \Gamma_r \mu_h)} \left[\frac{k_2}{a_1 a_2} (1 + \frac{d_2 k_3}{a_3 a_4}) \right].$$

The term R1 indicates that if sandfly is infectious and the reservoir is susceptible, the contact would result the transmission of Vl from sand y to reservoir. The term R_2 indicates the transmission of V_l from reservoir to sand y. So the term R_a indicate the transmission of V_l between sandfly and reservoir. Similarly the term R_b indicates the transmission of Vl between human and sand fly. The term R_a and R_b both denote the transmission of visceral strains of leishmania. There is no term representing the transmission of PKDL because it is the silent complication of V l. When a susceptible vector bites human/reservoir infected with PKDL, the vector does not transmit PKDL but transmit V_l to the next victim. So R_0 is biologically sensible.

Stability Analysis

In this section, we discuss the relation between additional threshold number and basic ξ reproductive number R_0, to find the global stability of the disease free equilibrium, and existence of endemic equilibrium of the system (1).

Proposition: The disease free equilibrium is locally asymptotically stable if $R_0<1$ and unstable if $R_0>1$.

Proof: For the proof of this result verify the reference [13].

Global stability of the disease free equilibrium

To find the global stability of the disease free equilibrium of the system (1), we state some definitions [9,10].

Definition 1: An m × m matrix, for m>2 is called irreducible if for any proper sub-set I of {1, 2,…,m}, $\exists$, $p \in I$ and $q \notin I$ such that $A_{(p,q)} \neq 0$

Definition 2: The matrix M is said to be Metzler matrix if $A_{(p,q)} \geq 0$ for $p \neq q$.

Definition 3: The compact set $M \subset \Omega$ is called stable for the dynamical system defined on Ω if for every trajectory initiated from a point in U is in W, for all t≥0. Here U and W are neighborhoods of M.

Definition 4: A compact set $N \subset D$ is called an attractor for a dynamical system defined on D if there exist a nbhds X and Y of N such that for every point $X \in x$, there exists a time $t_{x,y}>0$, such that every trajectory initiated at x, belongs to Y for $t>t_{x,y}$. The largest set X is called a bassin of attraction.

If X=D the set N is then called global attractor. A set N which is both stable and a global attractor is called globally asymptotically stable.

Theorem: The set G is globally asymptotically stable for the dynamical system (1) defined on Ω.

Proof: Let

$$N_r(0) = N_r^0, \tag{12}$$

$$N_v(0) = N_v^0, \tag{13}$$

be initial conditions associated with equation (3) and equation (4). And for $\epsilon > 0$, $B_\epsilon(G)$ be defined as;

$$B_\epsilon(G) = \{X \in \Omega; N_h - \epsilon < N_h < N_{h_u} + \epsilon; N_r^0 - \epsilon < N_r < N_{r_u} + \epsilon; N_v^0 - \epsilon < N_v < N_{v_u} + \epsilon\},$$

where

$X = (S_h, E_1, I_1, E_{12}, P_2, R_1, S_r, I_r, S_v, I_v)$.

Since the collection $\{B_\epsilon(G), \epsilon > 0\}$ is a complete neighborhood system of the compact set G. So X and Y as discussed in above definitions, also belong to this collection.

Consider an arbitrary $\epsilon > 0$. The points $N_{r_u}, N_{v_u}, N_{h_l}, N_{h_u}$ are globally asymptotically stable equilibria of the dynamical system defined by equation (3), equation (4), equation (5), and equation (8) on (0, ∞).

For any initial point of the model (1), $N_h^0 \in (0,\infty), N_r^0 \in (0,\infty), N_v^0 \in (0,\infty)$ Hence there exists $t_\epsilon > 0$ so that for any $t > t_\epsilon$ we have

$$N_{h_l} - \epsilon < N_l \le N_h \le N_u < N_{h_u} + \epsilon,$$

$$N_{r_l} - \epsilon < N_r < N_{r_u}\epsilon,$$

$$N_{v_l} - \epsilon < N_v < N_{v_u} + \epsilon,$$

$$\Rightarrow X = (S_h, E_1, I_1, , E_{12}, S_r, I_r, S_v, I_v) \in B_\epsilon(G).$$

Thus G is global attractor.

Next to show that G is stable

On the basis of monotonicity of N_l, N_u, N_r, N_v, we have

$$\begin{cases} N_{h_l} - \epsilon < N_h^0 < N_{h_u} + \epsilon \\ N_{r_l} - \epsilon < N_r^0 < N_{r_l} + \epsilon \\ N_{v_l} - \epsilon < N_v^0 < \hat{N}_{v_l} + \epsilon \end{cases} \Rightarrow \begin{cases} N_{h_l} - \epsilon < N_l \le N_h \le N_u < N_{h_u} + \epsilon \\ N_r^* - \epsilon < N_r < N_r^* + \epsilon \\ N_v^* - \epsilon < N_v < N_v^* + \epsilon. \end{cases}$$

Thus we have shown that any solution of the model (1), starting from a point in $B_\epsilon(G)$, remains in $B_\epsilon(G)$. So G is stable. Thus G is globally asymptotically stable. Hence we can now study the system (1) on G, instead of Ω.

Theorem: Let a positive system be defined on set $\Omega \subseteq R^n$ and let $\varepsilon \subset \Omega$ be globally asymptotically stable. Let M be the largest invariant sub set of $\mathcal{E}$. Then M is globally asymptotically stable on Ω. Particularly if $M = \{x^*\}$ where x^* is equilibrium point of the system with basin of attraction containing $\mathcal{E}$. Then x^* is GAS for the system on Ω.

Proof: For the proof of the theorem verify the reference [9] theorem (5). To prove the global stability of the disease free equilibrium, we use theorem (4.3) of [10].

For this let

$$X = (S_h, R_1, S_v, S_r, E_1, I_1, E_{12}, P_2, I_r, I_v)^T.$$

Now for global asymptotic stability of the disease free equilibrium of the system(1) on smaller set G, we decompose X as, Xs and XI of noninfected and infected, humans reservoirs and sandies, such that

$$X_s = (S_h, R_1, S_r, S_v)^T,$$

$$X_I = (E_1, I_1, E_{12}, P_2, I_r, I_v)^T.$$

So the model can now be written as

$$\dot{X} = A(X) + E_X \rightarrow \begin{cases} X_s = A_S(X)X_s + E_S \\ X_I = A_I(X)X_I \end{cases}$$

where

$$A_S = \begin{pmatrix} -(\mu_h + \lambda_h) & 0 & 0 & 0 \\ 0 & -\mu_h & 0 & 0 \\ 0 & 0 & -(\mu_r + \lambda_r) & 0 \\ 0 & 0 & 0 & -(\mu_v + \lambda_v) \end{pmatrix}$$

$$E_S = (\Gamma_h, \gamma_1\alpha_1 I_1 + (\gamma_2 + \beta_1)P_2, \Gamma_r, \Gamma_v)^T.$$

And the matrix $A_1(X)$ is given by

$$A_I(X) = \begin{pmatrix} -a_1 & 0 & 0 & 0 & 0 & \frac{ab_2 S_h}{N_h + N_r} \\ k_2 & -a_2 & 0 & 0 & 0 & 0 \\ 0 & d_2 & -a_3 & 0 & 0 & 0 \\ 0 & 0 & k_3 & -a_4 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\mu_r & \frac{abS_r}{N_h + N_r} \\ 0 & \frac{ac_2 S_v}{N_h + N_r} & 0 & \frac{ac_2 S_v}{N_h + N_r} & \frac{acS_r}{N_h + N_r} & -\mu_v \end{pmatrix}$$

We restrict the domain of the system (1) from G to G, to ensure the irre-ducibility of $A_1(X)$, such that $\bar{G} = \{X; X \in G, X_S \neq 0\}$.

The set $\bar{G}$ is positively invariant because only the initial point of any trajectory can have $X_s = 0$, Putting $\dot{S}_h = \dot{R}_1 = \dot{S}_r = \dot{S}_v = 0$, in the system (1), we have $S_h > 0,\ R_1 > 0,\ S_r > 0,\ S_v > 0$.

So all of the diagonal entries of $A_1(X)$ are nonnegative, hence $A_1(X)$ is metzler and irreducible $\forall X \in \bar{G}$.

Since diagonal entries of A_s are negative. So we state the following result

Proposition: Let X_s^0 be the non-infected class of the total population, then

$$X_s^0 = (S_h^0, R_1^0, S_r^0, S_v^0) = \left(\frac{\Gamma_h}{\mu_h}, , 0, \frac{\Gamma_r}{\mu_r}, \frac{\Gamma_v}{\mu_v}\right)$$

is globally asymptotically stable equilibrium point of the system (1) reduced to the sub-domain $\{X \in \bar{G}; X_I = 0\}$.

Corollary: The system (14) is globally asymptotically stable if there exist a matrix $\bar{A}_I$ such that

$$A_I(X) \le \bar{A}_I X \in \bar{G}. \tag{15}$$

and if

$$A_I(\bar{X}) = \bar{A}_I \text{ for some } \bar{X} = (\bar{X}_s, \bar{X}_I) \text{ then } \bar{X}_I = 0, \tag{16}$$

$$\alpha(\bar{A}_I) \le 0 \tag{17}$$

Where α is stability modulus or the largest real part of the eigen values of $\bar{A}_I$

Proof:

Since

$$\frac{1}{N_h+N_r}\le\frac{1}{N_{h_l}+N_r}.$$

So the upper bond of $A_I(X)$ denoted by $\overline{A}_I$ is given by

$$\overline{A_I}(X)=\begin{pmatrix} -a_1 & 0 & 0 & 0 & 0 & \frac{ab_2S_h^0}{N_{h_l}+N_r}\\ k_2 & -a_2 & 0 & 0 & 0 & 0\\ 0 & 0 & d_2 & -a_3 & 0 & 0\\ 0 & 0 & -k_3 & -a_4 & 0 & 0\\ 0 & 0 & 0 & 0 & -\mu_r & \frac{ab_2S_r^0}{N_{h_l}+N_r}\\ 0 & \frac{ac_2S_v^0}{N_{h_l}+N_r} & 0 & \frac{ac_2S_v^0}{N_{h_l}+N_r} & \frac{acS_v^0}{N_{h_l}+N_r} & -\mu_v \end{pmatrix},$$

and

Clearly $A_I(X)\le\overline{A_I}(X)$ as $\frac{1}{N_h+N_r}\le\frac{1}{N_{h_l}+N_r}$

And

$A_I(X)=\overline{A_I}(X)$ only if; $S_h=S_h^0, R_1=R_1^0, S_r=S_r^0, S_v=S_v^0$

Thus H_4 of theorem (4.3) holds [10], equivalently equation (15) and equation (16), hold.

To show that H_5 or equation (18) holds, we state the following theorem.

Theorem: The metzler matrix satisfy the axiom $H_5;\alpha(\overline{A}_I)\le 0$ if the basic reproductive number R_0 satisfy the inequality; $R_0\le\xi$, where ξ, is the additional threshold number given by

$$\xi=\frac{a^2b_2c_2\mu_r(\mu_h+\delta_1+\delta_2)^2\Gamma_v\Gamma_r}{\mu_h\mu_v^2(\mu_r\Gamma_h+(\mu_h+\delta_1+\delta_2)\Gamma_r)^2}\left(\frac{k_2}{a_2a_1}(1+\frac{d_2k_3}{a_2a_3})\right)$$

$$+\frac{a^2bc(\mu_h+\delta_1+\delta_2)^2\Gamma_v\Gamma_r}{\mu_v^2(\mu_r\Gamma_h+(\mu_h+\delta_1+\delta_2)\Gamma_r)^2}$$

Proof: We decompose the matrix $\overline{A_I}$ in the blocks such that

$$\overline{A_I}=\begin{pmatrix} L & M\\ P & Q\end{pmatrix},$$

where L, M, P,Q are 3×3 sub-matrices. The matrix $\overline{A_I}$ is stable if S and $Q-PL^{-1}M$ are metzler stable. Here S is metzler stable, because all its off diagonal entries are nonnegative, and all the eigen values are negative.

Let

$$Y=Q-PL^{-1}M$$

Then $\overline{A_I}$ is stable if Y is stable.

And Y is stable if $det(Y)\ge 0$

This means that $\alpha(\overline{A_I})\le 0$ only if

$$\frac{n_2n_5}{\mu_r\mu_v}+\frac{k_2n_1n_3}{a_1a_2\mu_v}+\frac{d_2k_2k_3n_1n_4}{a_1a_2a_3a_4\mu_v}-1<0,\Rightarrow\frac{n_2n_5}{\mu_r\mu_v}+\frac{k_2n_1n_3}{a_1a_2\mu_v}+\frac{d_2k_2k_3n_1n_4}{a_1a_2a_3a_4\mu_v}<1,$$

where

$$n_1=\frac{ab_2S_h^0}{N_{h_l}+N_r},\ n_2=\frac{abS_r^0}{N_{h_l}+N_r},n_3=\frac{ac_2S_v^0}{N_{h_l}+N_r},\ n_4=\frac{ac_2S_v^0}{N_{h_l}+N_r}\ \ n_5=\frac{acS_v^0}{N_{h_l}+N_r},$$

At the disease free equilibrium,

$$S_r=S_r^0=\frac{\Gamma_r}{\mu_r},S_h=S_h^0=\frac{\Gamma_h}{\mu_h},R_1=R_1^0=\frac{\Gamma_h}{\mu_h},$$

$$N_{h_l}+N_r=\frac{\Gamma_h\mu_r+\Gamma_r(\mu_h+\delta_1+\delta_2)}{\mu_r(\mu_h+\delta_1+\delta_2+\delta_3)}.$$

By putting these values in above equation, we have

$$\frac{a^2bc(\mu_h+\delta_1+\delta_2)^2\Gamma_v\Gamma_r}{\mu_v^2(\Gamma_h\mu_r+\Gamma_r\mu_h+\delta_1+\delta_2)^2}+\frac{a^2b_2c_2(\mu_h+\delta_1+\delta_2)\mu_r^2\Gamma_h\Gamma_v}{\mu_v^2(\Gamma_h\mu_r+\Gamma_r\mu_h+\delta_1+\delta_2)^2}\left[\frac{k_2}{a_2a_2}(1+\frac{d_2k_3}{a_3a_4})\right]\ge 1$$

We take this value as ξ. Thus H_5 or equation(17) holds, if $\xi\ge 1$. Also $R_0<\xi$. So using theorem (4.3) of [10], we claim the following result.

Theorem: If the parameters of the model satisfy the condition $\alpha(\overline{A_I})\le 0$, then the disease free equilibrium of the system (1) is globally asymptotically stable.

Simulation results of the model

In the Figure 2 below, we have reduced the treatment rate of both Vl infected and PKDL infected humans, in the sense that we have used drugs other than sodium stibogluconate (expensive medicine) or that the hospital is far away or that the case is not properly diagnosed leading to wrong treatment. No mass awareness program is lunched for vector control. Taking $\gamma_1=\gamma_2$=0:023, a=0:2856 (normal); and α_1=0:064.

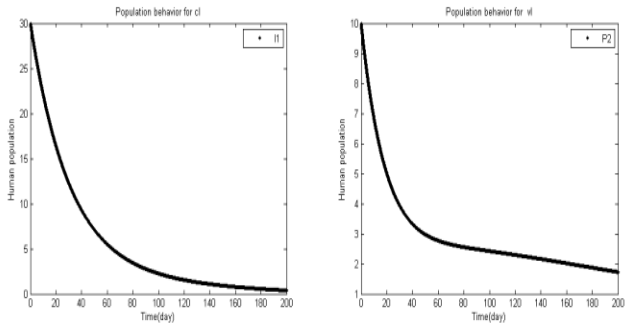

Figure 2: Population behavior graph 1.

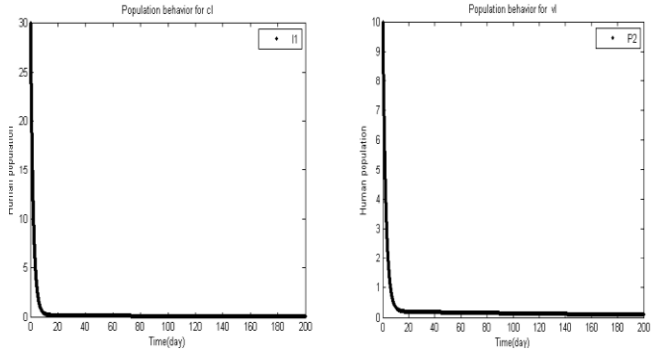

Figure 3: Population behavior graph 2.

The graph shows that it takes long time to eradicate the diseases.

In Figure 3 we have increased the treatment rate for both Vl and PKDL and also a proper arrangement for vector control. Taking γ_1=0:5, γ_2=0:4, biting of sandfly a=0.1856 medicine effectiveness α_1=0:74. The graph shows that with in short time the disease can be eradicated.

Conclusion

In this work a mathematical model of leishmania transmission was presented. The novelty of the model is, the homogenous mixing of human, reservoir and vector. The basic reproduction number R_0 so calculated, depends upon the density of human, vectors and reservoirs, which highlights the importance of homogenous mixing. R0 is most sensitive to a; b and c and can have value greater than 1 (endemic state), if a; sand y biting rate, b; transmission probability of either strain in reservoir from sand y and c, transmission probability of either strain in sand y from reservoir, were not controlled. For this, different measures to control phlebotomine sandfies, like residual spraying of dwellings and animal shelters, insecticide treated nets; application of repellents/insecticides to skin or to fabrics and impregnated dog collars may be taken. Sand y is susceptible to all the major insecticidal groups. In ZVL foci, where dogs are the unique domestic reservoir, a reduction in Leishmania transmission would be expected if we could combine an effective mass treatment of infected dogs with a protection of both healthy and infected dogs from the sand y bites. Since sand y can y up to the range of 1km, so leishmania transmission in dogs can be controlled, if they were kept away at least by 1km, from villages and cities. The disease can be controlled in human within a short time, however in reservoir class; the disease control takes long time. It is suggested to cull PCR+ dogs; this strategy gives imminent results in disease control.

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