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Effect of Control Measure on the Transmission of Leishmaniasis

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ABSTRACT

In this paper we develop a mathematical model to describe the transmission of the disease Leishmaniasis between three populations, a human host population, a reservoir host population (dogs) and vector population (sand flies). The dynamical equations of the model are analyzed using the standard method. The conditions for the stability of the model are determined. It was found that there are two equilibrium points, disease free equilibrium and endemic equilibrium. The basic reproductive number that represents the epidemic indicator is obtained from the spectral radius of the next generation matrix. It is seen that if the basic reproductive number is less than one, the disease free equilibrium is local asymptotically stable, meaning that the disease will died out but if the basic reproductive number is greater than one, the endemic equilibrium will be local asymptotically stable, meaning that the disease will persist in the community. The numerical simulations are presented to illustrate the results. In addition, we show that vector control by the use of insecticide is the best method for controlling the disease.

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INTRODUCTION

Leishmaniasis is a vector-born disease, which is considered as one of the six most important tropical diseases in the world (Neghina, Neghina, 2010). Leishmaniasis is caused by a protozoa parasite of the genus *Leishmania* which multiplies in certain vertebrate (dogs or rodent) that act as reservoir. The parasite is transmitted to humans through the bite of infected sand flies that had fed on an infected reservoir or an infected human. There are at least 20 species of Leishmania identified as being pathogenic to human. There are two basic forms of leishmaniasis, namely cutaneous leishmaniasis (CL), which causes skin sores, and visceral leishmaniasis (VL), which affects several internal organs (usually spleen, liver, and bone marrow) (CDC, 2014) depending on the species of leishmaniasis responsible and the immune response to the infection. Leishmaniasis is found in parts of the tropics, subtropics, and southern Europe. The symptoms of this disease varies among individuals with some having silent infection, i.e., without any symptoms or signs. Others develop clinical evidences of infection which are a fever, weight loss, swelling of the spleen and liver and abnormal blood tests. Patients may have low blood counts, including a low red blood cell count, a low white blood cell count, and a low platelet count (CDC, 2014).

Numerous mathematical models have been proposed and have been used to gain insight into disease transmission in a community. These date back in the classical models of Ross (1911) and Macdonald (1957). Chaves and Pascual (2006) studied monthly data of CL incidence in Costa Rica by using several approaches for non stationary time series analysis to describe of CL's cycles. ELmojtaba *et al* (2010) proposed the model of three populations, human reservoir and vector populations. Simulation results show that human treatments helps in disease control, its synergy with vector control will more likely result in the elimination of the disease. Stauch *et al* (2011) used a model to support the elimination program with basic quantifications of transmission, disease and intervention parameters. Ribas *et al* (2013) proposed a mathematical model to study of control strategies for zoonotic visceral leishmaniasis (ZVL). It found that vector control and the use of insecticide – impregnated dogs collars were efficient at reducing the prevalence of ZVL. In this paper we take the use of insecticide into account.

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II. Model Formulation:

In our model, we assume that the human, reservoir and vector population are constant. We formulate the model of leishmaniasis transmission by using basic ideas taken from epidemiology. The equations are obtained by assuming that;

1. The total human population $\overline{N}_H$ can be divided into three compartments: Susceptible human denoted by $\overline{S}_H$ as the members of the human population who may become infected. Infected human denoted by $\overline{I}_H$ as the members of the human population infected by leishmaniasis. Recover human denoted by $\overline{R}_H$ as the members of the human population who have become immune.

2. The total vector population (sand fly) $\overline{N}_F$ is divided into two compartments: Susceptible sand fly denoted by $\overline{S}_F$ as the members of the sand fly population which may become infected and infected sand fly denoted by $\overline{I}_F$ as the members of the sand fly population infected by leishmaniasis.

3. The total reservoir host (dog) population $\overline{N}_A$ is divided into two compartments: Susceptible dogs denoted by $\overline{S}_A$ as the members of the dog population which could become infected and infected dogs denoted by $\overline{I}_A$ as the members of the dog population infected by leishmaniasis.

The dynamics of the disease is depicted in the flow chart shown in Fig. 1.

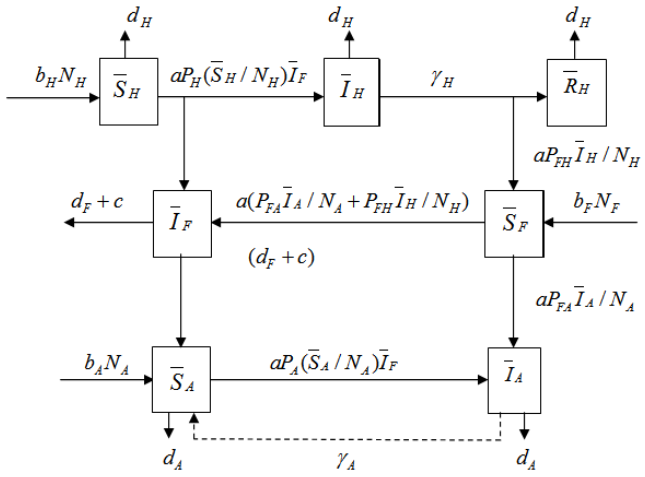

Fig. 1: Flow chart of the dynamical transmission of leishmaniasis

The dynamics of the flow chart are described by the following ordinary differential equations:

$$\frac{d\overline{S}_H}{dt} = b_H N_H - aP_H\left(\frac{\overline{S}_H}{N_H}\right)\overline{I}_F - d_H\overline{S}_H \quad (1)$$

$$\frac{d\overline{I}_H}{dt} = aP_H\left(\frac{\overline{S}_H}{N_H}\right)\overline{I}_F - (\gamma_H + d_H)\overline{I}_H \quad (2)$$

$$\frac{d\overline{R}_H}{dt} = \gamma_H\overline{I}_H - d_H\overline{R}_H \quad (3)$$

$$\frac{d\overline{S}_F}{dt} = b_F N_F - a\left(\frac{P_{FA}\overline{I}_A}{N_A} + \frac{P_{FH}\overline{I}_H}{N_H}\right)\overline{S}_F - (d_F + c)\overline{S}_F \quad (4)$$

$$\frac{d\overline{I}_F}{dt} = a\left(\frac{P_{FA}\overline{I}_A}{N_A} + \frac{P_{FH}\overline{I}_H}{N_H}\right)\overline{S}_F - (d_F + c)\overline{I}_F \quad (5)$$

$$\frac{d\overline{S}_A}{dt} = b_A N_A + \gamma_A\overline{I}_A - aP_A\left(\frac{\overline{S}_A}{N_A}\right)\overline{I}_F - d_A\overline{S}_A \quad (6)$$

$$\frac{d\overline{I}_A}{dt} = aP_A\left(\frac{\overline{S}_A}{N_A}\right)\overline{I}_F - (\gamma_A + d_A)\overline{I}_A \quad (7)$$

with $\bar{S}_H + \bar{I}_H + \bar{R}_H = N_H, \bar{S}_F + \bar{I}_F = N_F$ and $\bar{S}_A + \bar{I}_A = N_A$ (8)

Equations (3), (4) and (6) can be dropped since it is assumed that all populations are constant; $\bar{R}_H = N_H - \bar{S}_H - \bar{I}_H$, $\bar{S}_F = N_F - \bar{I}_F$ and $\bar{S}_A = N_A - \bar{I}_A$. The number of state variables reduced to four, which we pick to be S_H, I_H, I_F and I_A. The time rate of change of human population must be equal to zero, i.e. $\frac{d\bar{S}_H}{dt} + \frac{d\bar{I}_H}{dt} + \frac{d\bar{R}_H}{dt} = 0$. For this to occur, the birth rate and death rate of human population must be equal. Similarly the birth rate and death rate of dogs and sand flies must be equal to each other. Thus we have $N_H = \frac{b_H}{d_H}$, $N_A = \frac{b_A}{d_A}$ and $N_F = \frac{b_F}{c + d_F}$. If we normalized equations (1) – (7) via the new state variables:

$$S_H = \frac{\bar{S}_H}{N_H}, I_H = \frac{\bar{I}_H}{N_H}, R_H = \frac{\bar{R}_H}{N_H}, S_F = \frac{\bar{S}_F}{N_F}, I_F = \frac{\bar{I}_F}{N_F}, S_A = \frac{\bar{S}_A}{N_A} \text{ and } I_A = \frac{\bar{I}_A}{N_A} \quad (9)$$

where

S_H, I_H, R_H are the percentages of susceptible, infected, recovered humans, respectively

S_F, I_F are the percentages of susceptible, infected sand flies, respectively

S_A, I_A are the percentages of susceptible, infected dogs, respectively

b_H, (d_H) is the birth (death) rate of humans

b_F, (d_F) is the birth (death) rate of sand flies

b_A, (d_A) is the birth (death) rate of dogs

P_{FH} is the probability that disease will be transmitted from the infected human to sand fly,

P_{FA} is the probability that disease will be transmitted from the infected dog to sand fly,

P_H is the probability that disease will be transmitted from infected sand fly to human,

P_A is the probability that disease will be transmitted from infected sand fly to dog,

a is the biting rate of sand fly,

c is the added death rate due to the use of insecticide,

γ_H is the recovery rate of humans,

γ_A is the recovery rate of dogs,

The reduced model becomes:

$$\frac{dS_H}{dt} = b_H - \frac{aP_H S_H I_F N_F}{N_H} - d_H S_H \quad (10)$$

$$\frac{dI_H}{dt} = \frac{aP_H S_H I_F N_F}{N_H} - (\gamma_H + d_H) I_H \quad (11)$$

$$\frac{dI_F}{dt} = a(P_{FA} I_A + P_{FH} I_H)(1 - I_F) - (d_F + c) I_F \quad (12)$$

$$\frac{dI_A}{dt} = \frac{aP_A (1 - I_A) I_F N_F}{N_A} - (\gamma_A + d_A) I_A \quad (13)$$

III. Analysis of The Model:

Equilibrium Points:

The system has two equilibrium points; a disease free equilibrium point and an endemic equilibrium point. We obtained these by setting the right hand sides of equations. (10) - (13) to zero. Doing this, we obtained

Disease Free Equilibrium Point (E_0)***:***

In the absence of the disease**, i.e.,** $I_H = I_F = I_A = 0$**,** equation (10) becomes

$$\frac{dS_H}{dt} = b_H - d_H S_H$$

The solution to this equation is $S_H = 1$. The disease free state is $E_0 = (1, 0, 0, 0)$

Endemic Equilibrium Point (E_1)***:***

In the case where the disease is present, we must have $I_H^* \neq 0, I_F^* \neq 0, I_A^* \neq 0$. This gives

$$S_H^* = \frac{b_H N_H}{aP_H I_F^* N_F + d_H N_H}$$

$$I_H^* = \frac{ab_H P_H I_F^* N_F}{\left(aP_H I_F^* N_F + d_H N_H\right)\left(\gamma_H + d_H\right)} \tag{14}$$

$$I_F^* = \frac{-Y \pm \sqrt{Y^2 - 4XZ}}{2X}$$

$$I_A^* = \frac{aP_A I_F^* N_F}{aP_A I_F^* N_F + \left(\gamma_A + d_A\right) N_A}$$

Where

$$X = -E - b_H G - L, \quad Y = E + b_H G - d_H N_H T - b_H N_A K - N_A V - d_H N_H P,$$

$$Z = d_H N_H T + b_H N_A K - d_H N_H N_A, \quad E = aP_H N_F aP_A N_F aP_{FA}\left(\gamma_H + d_H\right),$$

$$T = aP_A N_F aP_{FA}\left(\gamma_H + d_H\right), \quad G = aP_H N_F aP_A N_F aP_{FH}, \quad K = aP_H N_F aP_{FH}\left(\gamma_A + d_A\right)$$

$$L = aP_H N_F aP_A N_F \left(\gamma_H + d_H\right), \quad V = aP_H N_F \left(\gamma_H + d_H\right)\left(\gamma_A + d_A\right), \quad P = \left(\gamma_H + d_H\right)\left(\gamma_A + d_A\right)$$

Thus

$$E^* = \left(\frac{b_H N_H}{aP_H I_F^* N_F + d_H N_H}, \frac{ab_H P_H I_F^* N_F}{(aP_H I_F^* N_F + d_H N_H)(\gamma_H + d_H)}, I_F^*, \frac{aP_A I_F^* N_F}{(aP_A I_F^* N_F + (\gamma_A + d_A) N_A)}\right)$$

Basic Reproductive Number:

The basic reproductive number is obtained by the next generation matrix. In the notation of Van den Driessche and Watmough (2002), we start with

$$\frac{dX}{dt} = F - V \tag{15}$$

where F is the matrix of new infectious and V is the matrix of the transfers between the compartments in the infective equations. We obtained

$$F = \begin{bmatrix} 0 \\ \dfrac{aP_H S_H I_F N_F}{N_H} \\ a\left(p_{FA} I_A + p_{FH} I_H\right)\left(1 - I_F\right) \\ \dfrac{aP_A I_F N_F \left(1 - I_A\right)}{N_A} \end{bmatrix}, \quad V = \begin{bmatrix} d_H S_H - b_H \\ \left(\gamma_H + d_H\right) I_H \\ \left(d_F + c\right) I_F \\ \left(\gamma_A + d_A\right) I_A \end{bmatrix}$$

where $F=[\frac{\partial F_i(E_0)}{\partial X_j}]$ and $V=[\frac{\partial V_i(E_0)}{\partial X_j}]$ for all $i,j=1,2,3,4$. This are the Jacobian matrix of F and V at E_0. The basic reproductive number, R_0, is the threshold for indicating the degree of epidemiology of the disease. It can be determined by noting that

$$R_0=\rho(FV^{-1}).$$

For our model, the Jacobian matrices are

$$F=\begin{bmatrix} 0 & 0 & 0 & 0 \\ 0 & 0 & \frac{aP_HN_F}{N_H} & 0 \\ 0 & aP_{FH} & 0 & aP_{FA} \\ 0 & 0 & \frac{aP_AN_F}{N_A} & 0 \end{bmatrix}$$

and $$V=\begin{bmatrix} d_H & 0 & 0 & 0 \\ 0 & \gamma_H+d_H & 0 & 0 \\ 0 & 0 & d_F+c & 0 \\ 0 & 0 & 0 & \gamma_A+d_A \end{bmatrix}.$$

The inverse of V is

$$V^{-1}=\begin{bmatrix} \frac{1}{d_H} & 0 & 0 & 0 \\ 0 & \frac{1}{(\gamma_H+d_H)} & 0 & 0 \\ 0 & 0 & \frac{1}{(d_H+c)} & 0 \\ 0 & 0 & 0 & \frac{1}{(\gamma_A+d_A)} \end{bmatrix}$$

This leads to

$$FV^{-1}=\begin{bmatrix} 0 & 0 & 0 & 0 \\ 0 & 0 & \frac{aP_HN_F}{N_H(d_F+c)} & 0 \\ 0 & \frac{aP_{FH}}{\gamma_H+d_H} & 0 & \frac{aP_{FA}}{\gamma_A+d_A} \\ 0 & 0 & \frac{aP_AN_F}{N_A(d_F+c)} & 0 \end{bmatrix}$$

Thus,

$$\Re_0=\sqrt{\frac{a^2P_AN_FP_{FA}N_H(d_F+c)(\gamma_H+d_H)+a^2P_{FH}P_HN_FN_A(d_F+c)(\gamma_A+d_A)}{N_A(d_F+c)(\gamma_A+d_A)N_H(d_F+c)(\gamma_H+d_H)}} \quad (16)$$

Local Asymptotically Stability:

The local stability of an equilibrium point is determined from the Jacobian matrix of the ordinary differential equation (10) - (13) evaluated at E_0. The Jacobian matrix at E_0 is

$$J_0 = \begin{bmatrix} -d_H & 0 & -\frac{aP_H N_F}{N_H} & 0 \\ 0 & -(\gamma_H + d_H) & \frac{aP_H N_F}{N_H} & 0 \\ 0 & aP_{FH} & -(d_F + c) & aP_{FA} \\ 0 & 0 & \frac{aP_A N_F}{N_A} & -(\gamma_A + d_A) \end{bmatrix}$$

The eigenvalues of the J_0 are obtained by solving $\det(J_0 - \lambda I) = 0$. From this, we obtain the characteristic equation,

$$(\lambda + d_H)(\lambda^3 + \varepsilon_1\lambda^2 + \varepsilon_2\lambda + \varepsilon_3) = 0$$

where

$$\varepsilon_1 = d_F + c + \gamma_A + d_A + \gamma_H + d_H$$

$$\varepsilon_2 = (d_F + c)(\gamma_A + d_A) - M_3M_4 + (\gamma_H + d_H)(d_A + c + \gamma_A + d_A) + M_1M_2$$

$$\varepsilon_3 = (\gamma_H + d_H)((d_F + c)(\gamma_A + d_A) - M_3M_4) + M_1M_2(\gamma_A + d_A)$$

$$M_1 = \frac{aP_H N_F}{N_H},\ M_2 = aP_{FH},\ M_3 = aP_{FA},\ M_4 = \frac{aP_A N_F}{N_A}$$

From the characteristic equation, we see that one of eigenvalue is $\lambda_1 = -d_H < 0$. The other three are the solution of the characteristic equation $\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0$. The roots of this equation will be negative if three coefficients satisfied with the Routh-Hurwitz criteria (Allen,2006).

1) $\varepsilon_1 > 0$
2) $\varepsilon_3 > 0$
3) $\varepsilon_1\varepsilon_2 > \varepsilon_3$

Disease Endemic Equilibrium Point:

To determine the stability of the endemic equilibrium point, E_1, we examine the eigenvalues of Jacobian matrix at E_1, which is

$$J_1 = \begin{bmatrix} -\left(\frac{aP_H {I_F}^* N_F}{N_H} + d_H\right) & 0 & -\frac{aP_H {S_H}^* N_F}{N_H} & 0 \\ \frac{aP_H {I_F}^* N_F}{N_H} & -(\gamma_H + d_H) & \frac{aP_H {S_H}^* N_F}{N_H} & 0 \\ 0 & aP_{FH}(1 - {I_F}^*) & -\left(a\left(P_{FA}{I_A}^* + P_{FH}{I_H}^*\right) + d_F + c\right) & aP_{FA}(1 - {I_F}^*) \\ 0 & 0 & \frac{aP_A N_F(1 - {I_A}^*)}{N_A} & -\left(\frac{aP_A {I_F}^* N_F}{N_A} + \gamma_A + d_A\right) \end{bmatrix}$$

Where ${S_H}^*, {I_H}^*, {I_F}^*, {I_A}^*$ are given by equations (15). The characteristic equation of Jacobian matrix at E_1, given by equations (10)- (14) , becomes,

$$\lambda^4 + \omega_1\lambda^3 + \omega_2\lambda^2 + \omega_3\lambda + \omega_4 = 0$$

where

$$\omega_1 = a_1 + a_3 + a_6 + a_9, \quad \omega_2 = a_1\left(a_3 + a_6 + a_9\right) + a_9\left(a_3 + a_6\right) + a_3a_6 + a_7a_8 + a_4a_5$$

$$\omega_3 = a_1\left(a_9\left(a_3 + a_6\right)\right) + a_3a_6 + a_7a_8 + a_4a_5 + a_3a_6a_9 + a_7a_8a_3 + a_4a_5a_9 - a_2a_4a_5$$

$$\omega_4 = a_1\left(a_3a_6a_9 + a_7a_8a_3 + a_4a_5a_9\right) - a_2a_4a_5a_9$$

$$a_1 = M_1{I_F}^* + d_H, \quad a_2 = M_1{I_F}^*, \quad a_3 = \gamma_H + d_H, \quad a_4 = M_2\left(1 - {I_F}^*\right), \quad a_5 = M_1{S_H}^*$$

$$a_6 = M_3{I_A}^* + M_2{I_H}^* + d_H + c, \quad a_7 = M_4\left(1 - {I_A}^*\right), \quad a_8 = M_3\left(1 - {I_F}^*\right), \quad a_9 = M_4{I_F}^* + \gamma_A + d_A$$

The fourth eigenvalue of $\lambda^4 + \omega_1\lambda^3 + \omega_2\lambda^2 + \omega_3\lambda + \omega_4 = 0$ will have negative real part if they satisfy the Routh - Hurwitz criteria (Marsden and McCracken , 1976).

IV. Numerical Results:

The value of parameters used in the numerical simulation are given in Table 1.

Table 1: Parameter values used in numerical simulations at disease free state.

Parameter	Values
N_H	5,000
N_F	5,000
N_A	5,000
d_H	0.000042 d^{-1}
γ_H	0.003288 d^{-1}
a	0.071429
P_H	0.3
P_A	0.25
P_{FH}	0.25
P_{FA}	0.25
d_F	0.071429 d^{-1}
C	1.0
d_A	0.002792 d^{-1}
γ_A	0.013699 d^{-1}

Stability of the disease free state: Using the values of parameters listed in Table 1. We find the eigenvalues and basic reproductive number to be:

$$\lambda_1 = -0.000042, \lambda_2 = -1.072090, \lambda_3 = -0.016134, \lambda_4 = -0.002964,$$

$$R_0 = 0.125368, \Re_0 = 0.354074$$

Since all of the eigenvalues are negative and the basic reproductive number is less than one, the equilibrium state will be the disease free state, E_0 as seen in Fig. 2.

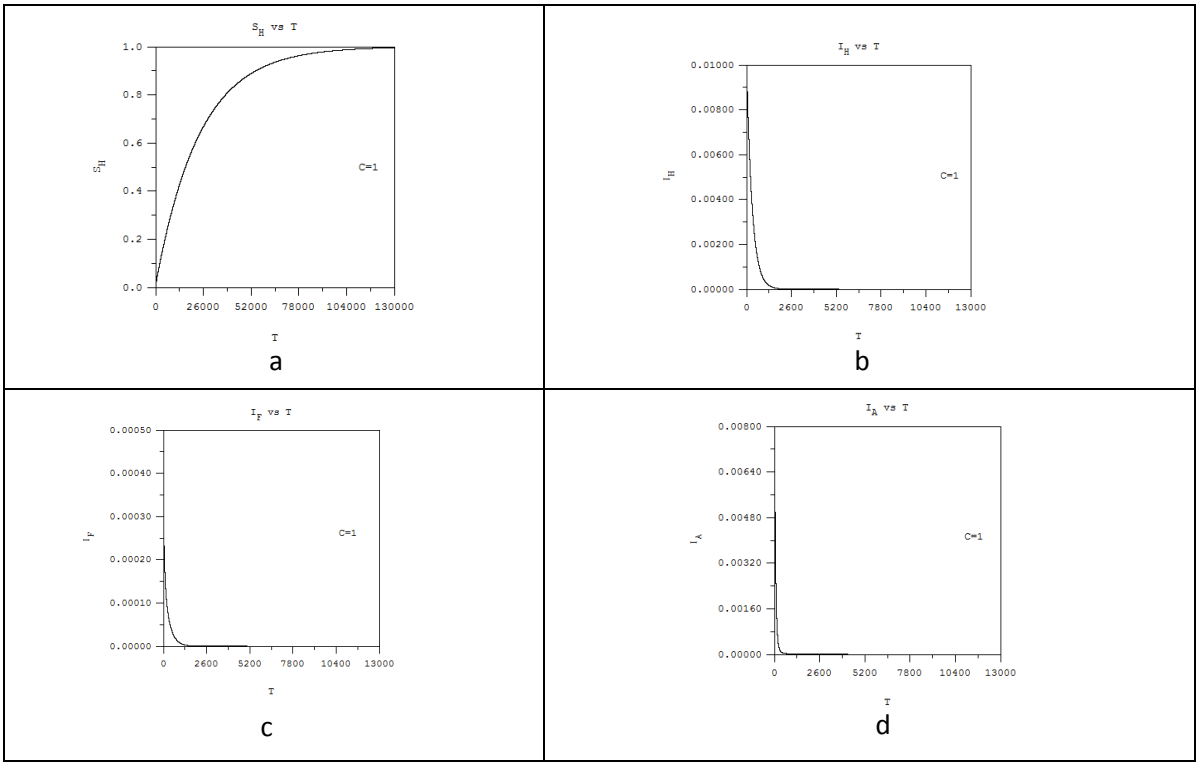

Fig. 2: The time series of (a) the susceptible human population, (b) infected human population, (c) infected san flies population and (d) infected dogs population. As is seen, all the state variables approach their disease free state values $E_0 = (1, 0, 0, 0)$.

Stability of the endemic state: Using the values of parameter listed in Table 1. except for the value of c (which we chose to be equal to 0.0001). This low values means that we are no longer attempting to control the number of sand flies present by the use of insecticide. With this change in control

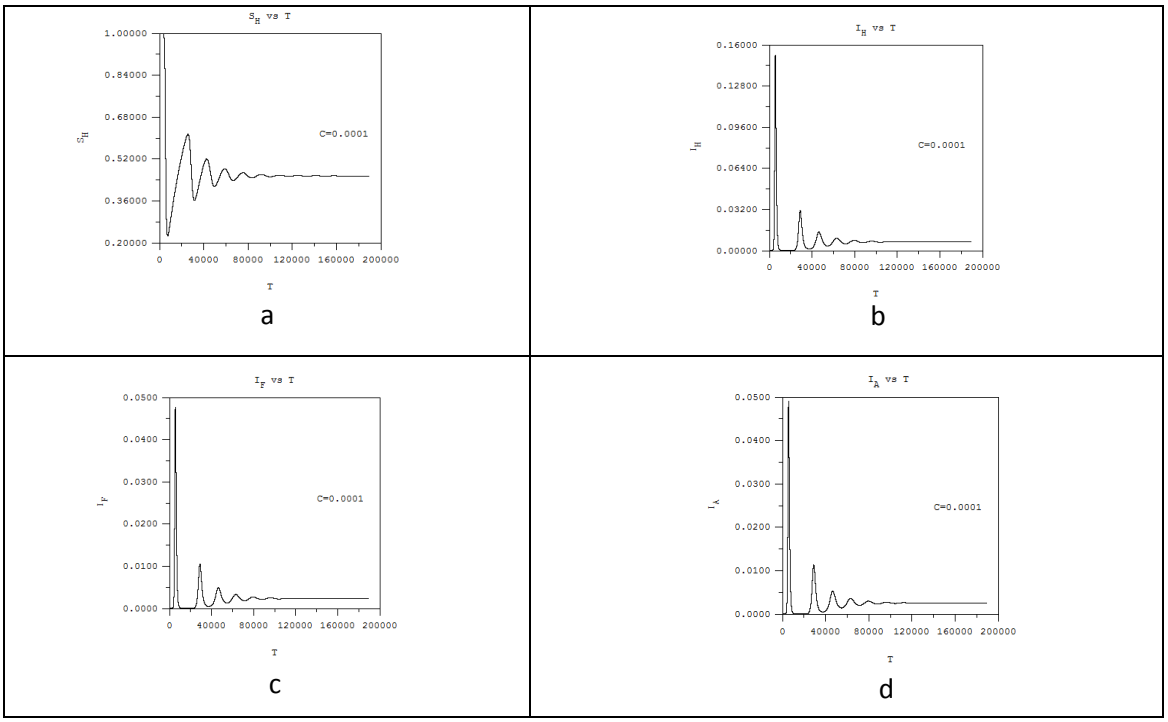

Fig. 3: The time series of (a) the susceptible human population, (b) infected human population, (c) infected sand flies population and (d) infected dogs population. Only the value of c has been changed to c = 0.0001. All the state variables approach to endemic state values $E_1(0.455447,\ 0.006868,\ 0.002344,\ 0.002541)$.

practice, the eigenvalues and basic reproductive number become greater than one and the outcome is quite different:

$$\lambda_1 = -0.017776, \lambda_2 = -0.0000004$$

$$\lambda_3 = -0.00121306 - 0.167065\,\mathrm{i}, \lambda_4 = -0.00121306 + 0.167065\,\mathrm{i}$$

$$R_0 = 2.24598, \Re_0 = 1.498$$

Since all of the eigenvalues are to be negative and the basic reproductive number is greater than one, the equilibrium state will be the endemic state, E_1 as demonstrated in Fig. 3.

V. Discussion and Conclusion:

In this paper we proposed a transmission model of Leismaniasis by take into account the use of insecticide as the vector control measure to reduce the number of sand flies. From Fig. 2, we can see that when control mechanisms are in place and setting c = 1, the basic reproductive number $\Re_0 = 0.354074$ which less than one. The percentage of infected human, infected dogs and infected sand flies will approach zero. When we change the value of c to 0.0001 (stopping the control measures to kill the sand flies) the basic reproductive number $\Re_0 = 1.498$ which is greater than one. Then the disease will persist in the human, sand flies and dogs population and approach the endemic state values as seen in Fig. 3. It is possible to eradicate the disease from the community if we can make $\Re_0$ less than one by using insecticide treated bed-net (Bern *et al*. 2000) and dog collars to prevent the dog from being infested by the sand flies or by directly killing the sand flies. We can concluded that if we have a campaign to use insecticide to reduce the number of sand flies, we can eradicate the disease

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