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Analysis of Model in Pregnant and Non-Pregnant Dengue Patients

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***Abstract*—**We used mathematical model to study the transmission of dengue disease. The model is developed in which the human population is separated into two populations, pregnant and non-pregnant humans. The dynamical analysis method is used for analyzing this modified model. Two equilibrium states are found and the conditions for stability of theses two equilibrium states are established. Numerical results are shown for each equilibrium state. The basic reproduction numbers are found and they are compared by using numerical simulations.

***Keywords*—**Basic reproductive number, dengue disease, equilibrium states, pregnancy.

I. Introduction

DENGUE disease especially known in Southeast Asia, is sweeping around the world, hitting countries with tropical and warm climates. This disease is transmitted from person to person by biting of the infected *Aedes Aegypti* mosquito[1] .

The principal mosquito vector, female *Aedes Aegypti*, is found in or near human habitations and prefers to feed on humans during the daytime. It has two peak periods of biting activity, in the morning for several hours after daybreak and in the late afternoon for several hours before dark [2]. The mosquito may feed at any time during the day. The vector breeding sites include artificial water containers such as discarded tires, uncovered water storage barrels, buckets, flower vases or pots, cans and cisterns. This disease has three forms: dengue fever(DF) or classic dengue, dengue hemorrhagic fever(DHF) and dengue shock syndrome(DSS); these depend on the characteristic of symptoms for each person. DHF and DSS are severe forms of this disease. The person who be infected with any single type of dengue virus apparently produces permanent immunity to it, but only temporary cross immunity to the others. The major problem with dengue is the fact that the disease is caused by four distinct serotypes known as DEN-1, DEN-2, DEN-3 and DEN-4. DF is characterized by sudden onset after an incubation period of 3 - 14 days (most commonly 4 - 7 days) of high fevers, severe frontal headache, and joint and muscle pain. Many patients have nausea, vomiting, and a maculopapular rash. Most patients report a nonspecific viral syndrome or a flu-like illness. Asymptomatic infections are also common. DHF is a potentially deadly complication that is characterized by high fever, hemorrhagic phenomena, often with enlargement of the liver and in severe cases, circulatory failure. The fever usually continues for 2-7 days and can be as high as 40 - 41 ^{0}C, possibly with febrile convulsions and hemorrhagic phenomena. In severe cases, the patient's condition may develop hypovolaemic shock resulting from the plasma leakage, go into a critical state of shock and die within 12-24 hours, or quickly recover following appropriate volume replacement therapy, this is called DSS .

The first reported epidemics of DF occurred in 1779-1780 in Asia, Africa and North America. After World War II, a pandemic of dengue began in Southeast Asia and has spread around the globe since then. In Southeast Asia, epidemic DHF first appeared in the 1950s, but by 1975 it had become a frequent cause of hospitalization and death among children in many countries in that region. In the 1980s, DHF began a second expansion into Asia when Sri Lanka, India and the Maldive Islands had their first major DHF epidemics, Pakistan first reported an epidemic of dengue fever in 1994. In 1998, there were more than 616,000 cases of dengue in America, of which 11,000 cases of dengue hemorrhagic fever, that's twice the number of cases recorded in the same region during the year 1995. In 2001 there were 400,000 cases of hemorrhagic in Southeast Asia, whereas, in Rio de Janeiro alone, 500,000 people were struck by a dengue outbreak in 2002 [3].

According to the present evaluations of the World Health Organization (WHO), about 50 million cases of dengue occur in the world every year, with an increasing tendency, with approximately 10,000 infant deaths due to this disease [4]. The most dengue infections occur during childhood but some adults may remain susceptible to infection. About 30 percent of dengue infection is reported in patients more than 15 years old [5]. In 1989, the first 5 reported neonates of vertical dengue infection were born in Tahiti [6]. Since then, there have been 12 additional cases reported from Thailand, Malaysia and France [6]-[13]. Some pregnant women may also be susceptible to dengue and if they experience dengue infection, they can transmit the dengue virus to their babies.

We are interested in the transmission process of pregnant and non-pregnant humans. The dynamical model is formulated to describe the transmission of this disease.

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II. Mathematical Model

To present the transmission process, we divide the human population into two classes, pregnant and non-pregnant human. Each class has constant size and it is divided into three subclasses, susceptible, infected and recovered human. The vector populations are separated into two classes because it never recovers from infection, susceptible and infected vector populations.

Let

$S_p^{'}(t)$ denotes the number of susceptible pregnant human population at time t,

$I_p^{'}(t)$ denotes the number of infected pregnant human population at time t,

$R_p^{'}(t)$ denotes the number of recovered pregnant human population at time t,

$S_n^{'}(t)$ denotes the number of susceptible non-pregnant human population at time t,

$I_n^{'}(t)$ denotes the number of infected non-pregnant human population at time t,

$R_n^{'}(t)$ denotes the number of recovered non-pregnant human population at time t,

$S_v^{'}(t)$ denotes the number of susceptible vector population at time t,

$I_v^{'}(t)$ denotes the number of infected vector population at time t.

The transmission model of dengue disease in pregnant and non-pregnant human are described by the following equations:

$$\frac{d}{dt}S_p^{'}(t) = \varpi(N_{tp} - S_p^{'}) - \varphi\lambda_{vn}S_p^{'}I_v^{'}\frac{a_v}{N_t + h},$$

$$\frac{d}{dt}I_p^{'}(t) = \varphi\lambda_{vn}S_p^{'}I_v^{'}\frac{a_v}{N_t + h} - (\varpi + r)I_p^{'},$$

$$\frac{d}{dt}R_p^{'}(t) = rI_p^{'} - \varpi R_p^{'},$$

$$\frac{d}{dt}S_n^{'}(t) = \varpi(N_{tn} - S_n^{'}) - \lambda_{vn}S_n^{'}I_v^{'}\frac{a_v}{N_t + h} \quad , \qquad (1)$$

$$\frac{d}{dt}I_n^{'}(t) = \lambda_{vn}S_n^{'}I_v^{'}\frac{a_v}{N_t + h} - (\varpi + r)I_n^{'},$$

$$\frac{d}{dt}R_n^{'}(t) = rI_n^{'} - \varpi R_n^{'},$$

$$\frac{d}{dt}S_v^{'}(t) = D - \theta_v S_v^{'} - \lambda_{nv}S_v^{'}\frac{a_v}{N_t + h}(\tau I_p^{'} + I_n^{'}),$$

$$\frac{d}{dt}I_v^{'}(t) = \lambda_{nv}S_v^{'}\frac{a_v}{N_t + h}(\tau I_p^{'} + I_n^{'}) - \theta_v I_v^{'}$$

with the conditions $N_{tp} = S_p^{'} + I_p^{'} + R_p^{'}$, $N_v = S_v^{'} + I_v^{'}$ and $N_{tn} = S_n^{'} + I_n^{'} + R_n^{'}$. (2)

where the parameters in the above equations are defined as

N_t is the total number of the human population,

N_v is the total number of the vector population,

N_{tp} is the total number of the pregnant human population,

N_{tn} is the total number of the non-pregnant human population,

D is the constant recruitment rate of the vector population,

ρ is the birth rate of the human population,

ϖ is the death rate of the human population,

θ_v is the death rate of the vector population,

r is the recovery rate of the human population,

h is the number of alternative hosts available as blood sources,

λ_{vp} is the transmission probability of dengue virus from vector population to pregnant human population and become infectious pregnant human population,

λ_{vn} is the transmission probability of dengue virus from vector population to non-pregnant human population and become infectious non-pregnant human population,

λ_{pv} is the transmission probability of dengue virus from infectious pregnant human population to vector population and become infectious vector population,

λ_{nv} is the transmission probability of dengue virus from infectious non-pregnant human population to vector population and become infectious vector population,

ψ is the ratio between the transmission probability from vector to pregnant and the transmission probability from vector to non- pregnant human population,

τ is the ratio between the transmission probability from pregnant human to vector and the transmission probability from non- pregnant to vector population,

a_v is the biting rate of the vector population,

c is the percentage of the human to be pregnant.

The total number of populations are assumed that constant for pregnant, non-pregnant human and vector populations. So the rates of change for the total pregnant, non-pregnant human and vector populations are equal to zero. We obtain $\rho = \varpi$ for the human population. The total number of vector population is $N_v = (D/\theta_v)$. We normalize (1) by letting

$S^p = \frac{S_p^{'}}{N_{tp}}$, $I^p = \frac{I_p^{'}}{N_{tp}}$, $R^p = \frac{R_p^{'}}{N_{tp}}$, $S^n = \frac{S_n^{'}}{N_{tn}}$, $I^n = \frac{I_n^{'}}{N_{tn}}$,

$R^n = \frac{R_n^{'}}{N_{tn}}$, $S^v = \frac{S_v^{'}}{(D/\theta_v)}$ and $I^v = \frac{I_v^{'}}{(D/\theta_v)}$ then

our equations become

$$\frac{d}{dt}S^p = \varpi(1-S^p) - \varphi\lambda_{vn}S^pI^v(D/\theta_v)\frac{a_v}{N_t+h},$$
$$\frac{d}{dt}I^p = \varphi\lambda_{vn}S^pI^v(D/\theta_v)\frac{a_v}{N_t+h} - (\varpi+r)I^p,$$
$$\frac{d}{dt}S^n = \varpi(1-S^n) - \lambda_{vn}S^nI^v(D/\theta_v)\frac{a_v}{N_t+h}, \quad (3)$$
$$\frac{d}{dt}I^n = \lambda_{vn}S^nI^v(D/\theta_v)\frac{a_v}{N_t+h} - (\varpi+r)I^n,$$
$$\frac{d}{dt}I^v = \lambda_{nv}(1-I^v)\frac{a_v}{N_t+h}(\tau I^pN_{tp} + I^nN_{tn}) - \theta_vI^v,$$

with the new three conditions $S^p + I^p + R^p = 1$,
$S^n + I^n + R^n = 1$ and $S^v + I^v = 1$. (4)

III. Analysis of the Mathematical Model

A. Analytical Results

We find equilibrium points by setting right hand side of all equations in (3) equal to zero. Then two equilibrium points are

i) disease free equilibrium state:

$$U_0 = (1,0,1,0,0) \quad (5)$$

ii) endemic equilibrium state

$$U_1 = (\overline{S_p}, \overline{I_p}, \overline{S_n}, \overline{I_n}, \overline{I_v}) \quad (6)$$

where

$$\overline{S_p} = \frac{D_0}{D_0 + D_1\overline{I_v}},$$
$$\overline{I_p} = \frac{D_0D_1\overline{I_v}}{(D_0 + D_1\overline{I_v})(D_1 + D_2)},$$
$$\overline{S_n} = \frac{\psi D_0}{\psi D_0 + D_1\overline{I_v}},$$
$$\overline{I_n} = \frac{D_0D_1\overline{I_v}}{(\psi D_0 + D_1\overline{I_v})(D_0 + D_2)},$$
$$\overline{I_v} = \frac{-h_1 + \sqrt{h_1^2 - 4h_2h_0}}{2h_2}$$

and $h_0 = \left(\frac{D_0}{D_1}\right)^2 \psi G_3 - \psi\left(\frac{D_0}{D_1}\right)G_1 - \left(\frac{D_0}{D_1}\right)G_2,$

$$h_1 = \frac{\psi D_0}{D_1}G_1 + \frac{D_0}{D_1}G_2 + \frac{D_0}{D_1}G_3 + \frac{\psi D_0}{D_1}G_3 - G_1 - G_2,$$
$$h_2 = G_1 + G_2 + G_3$$

such that

$$D_0 = \varpi(N_t + h), D_1 = \psi\lambda_{vn}(D/\theta_v)a_v,$$
$$D_2 = r(N_t + h)$$

and $G_1 = \lambda_{nv}a_v\tau D_0D_1^2N_{tp}$, $G_2 = \lambda_{nv}a_vD_0D_1^2N_{tn}$,
$G_3 = \theta_v(N_t + h)(D_0 + D_2)D_1^2$.

The local stability for each equilibrium point is determined by the signs of all eigenvalues. If all eigenvalues have negative real parts, then that equilibrium point is local stability. We find eigenvalues for each equilibrium point by setting

$$\det(J - kI) = 0 \quad (7)$$

where J is the Jacobian matrix of the right hand side of (3)
k is the eigenvalue
and I is the identity matrix.

Diagonalizing the jacobian for the free equilibrium point, we obtain the characteristic equation

$$(k + \varpi)(k + \varpi + r)(k + \varpi)(k^2 + g_1k + g_2) = 0 \quad (8)$$

where

$$g_2 = \varpi\theta_v + r\theta_v - \lambda_{nv}N_{tn}\left(\frac{a_v}{N_t+h}\right)^2\lambda_{vn}(D/\theta_v)$$
$$-\psi\tau\lambda_{nv}N_{tp}\left(\frac{a_v}{N_t+h}\right)^2\lambda_{vn}(D/\theta_v)$$
$$g_1 = \varpi + \theta_v + r.$$

There are five eigenvalues corresponding to (8). We denote these five eigenvalues by k_1, k_2, k_3, k_4 and k_5.

$k_1 = -\varpi, k_2 = -\varpi - r, k_3 = -\varpi$ and

$k_4 = \frac{-g_1 - \sqrt{g_1^2 - 4g_2}}{2}$ have negative real parts. The one eigenvalue $k_5 = \frac{-g_1 + \sqrt{g_1^2 - 4g_2}}{2}$, k_5 has negative real part when $-g_1 + \sqrt{g_1^2 - 4g_2} < 0$.

So $\sqrt{g_1^2 - 4g_2} < g_1$ or $g_1^2 - 4g_2 < g_1^2$. Then we have $g_2 > 0$,

$$\varpi\theta_v + r\theta_v - \lambda_{nv}N_{tn}\left(\frac{a_v}{N_t+h}\right)^2\lambda_{vn}(D/\theta_v)$$
$$-\psi\tau\lambda_{nv}N_{tp}\left(\frac{a_v}{N_t+h}\right)^2\lambda_{vn}(D/\theta_v) > 0 \text{ or}$$
$$R_A = \frac{D_1(G_2 + \psi G_1)}{D_0\psi G_3} < 1.$$

Therefore the disease free equilibrium point is local stability for $R_A < 1$.

The correspondent eigenvalues for the endemic equilibrium point are found by solving the characteristic equation; which is in the form

$$(k+\varpi+r)(k^4+\eta_3 k^3+\eta_2 k^2+\eta_1 k+\eta_0)=0 \quad (9)$$

The first eigenvalue is $k_1=-\varpi-r$, the other eigenvalue k_2, k_3, k_4 and k_5 are found by solving $k^4+\eta_3 k^3+\eta_2 k^2+\eta_1 k+\eta_0=0$. By using Routh-Hurwitz criteria, the endemic equilibrium point is locally stable if the following conditions are satisfied;

i) $\eta_3>0$,

ii) $\eta_1>0$,

iii) $\eta_0\geq 0$,

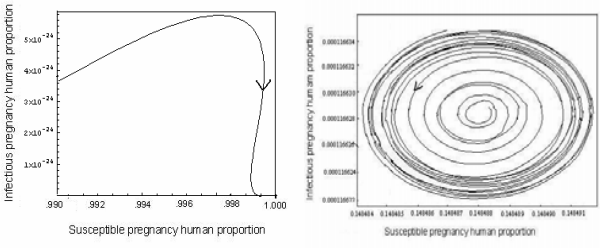
iv) $\eta_3\eta_2\eta_1>\eta_1^{\,2}+\eta_3^2\eta_0$.

We check the above conditions by using MATHEMATICA, we found that U_1 is locally stable for $R_A>1$. The basic reproductive number of the disease is given by $R_A^{'}=\sqrt{R_A}$, which gives the average number of secondary cases that one case can produce if introduced into a susceptible human. Thus the outbreak of dengue disease in the endemic region can be reduced when the basic reproductive number $(R_A^{'})$ is greater than one.

B. Numerical Results

Numerical solutions are presented for comparing the transmission of dengue disease for the free and endemic stables. The values of most of the parameters are determined by the real life observations. They are $\varpi=0.0000457$ per day, corresponding to a life expectancy of 60 years; $\theta_v=0.0714286$ per day , corresponding to a mosquito mean life of 14 days; $a_v=0.33$, one bite providing enough blood meal for three days; $\lambda_{vp}=0.4$, $\lambda_{vn}=0.8$, $\lambda_{pv}=0.4$ and $\lambda_{nv}=0.8$ which were chosen arbitrarily. We assume that $\lambda_{vn}>\lambda_{vp}, \lambda_{nv}>\lambda_{pv}$ and there is no alternative host $(h=0)$.

The numerical solutions of (3) are shown in following figures.



(1a) (1b)

Fig. 1 Numerical solutions of (3), demonstrate the solution trajectories, projected onto (S^p, I^p)

(1a) for $R_A<1$ with the parameters are

$\varpi=0.0000457\,\text{day}^{-1}$, $\theta_v=0.0714286\ \text{day}^{-1}$,

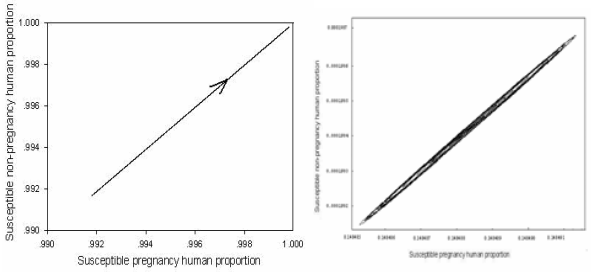
$a_v=0.33\ \text{day}^{-1}$, $\lambda_{vp}=0.4, \lambda_{vn}=0.8, \lambda_{pv}=0.4$,

$\lambda_{nv}=0.8, \psi=0.5, \tau=0.5$, $r=0.33\ \text{day}^{-1}$,

$N_t=100,000$, $D=2,000$, $N_{tn}=99,000$,

$N_{tp}=1,000$, $R_A=0.181769$, $R_A^{'}=0.426344$.

(1b) for $R_A>1$, $D=30,000$ but the other parameters are same as in Fig. (1a). $R_A=2.72653, R_A^{'}=1.65122$. The solutions oscillate to the endemic equilibrium point $\overline{S_p}=0.148488$, $\overline{I_p}=0.000116629$.

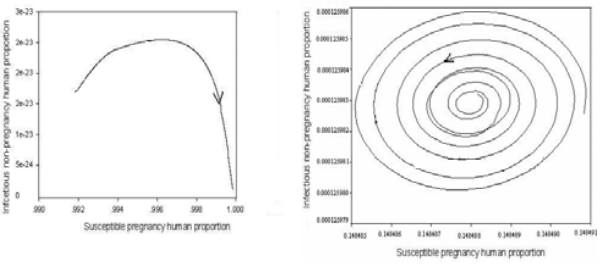


(2a) (2b)

Fig. 2 Numerical solutions of (3), demonstrate the solution trajectories, projected onto (S^p, S^n)

(2a) for $R_A<1$ with the parameters are same as Fig. 1a)

(2b) for $R_A>1$ with the parameters are same as Fig. (1b) . The solutions oscillate to the endemic equilibrium point $\overline{S_p}=0.148488$, $\overline{S_n}=0.0801984$.

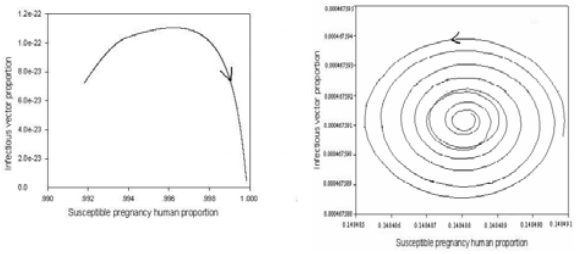


(3a) (3b)

Fig. 3 Numerical solutions of (3), demonstrate the solution trajectories, projected onto (S^p, I^n)

(3a) for $R_A<1$ with the parameters are same as Fig. (1a)

(3b) for $R_A>1$ with the parameters are same as Fig. (1b) . The solutions oscillate to the endemic equilibrium point $\overline{S_p}=0.148488$, $\overline{I_n}=0.000125983$



(4a) (4b)

Fig. 4 Numerical solutions of (3), demonstrate the solution trajectories, projected onto (S^p, I^v)

(4a) for $R_A < 1$ with the parameters are same as Fig. (1a)

(4b) for $R_A > 1$ with the parameters are same as Fig. (1b) . The solutions oscillate to the endemic equilibrium point

$$\overline{S_p} = 0.148488\,,\ \overline{I_v} = 0.000467591$$

In general, small R_A's result in long periods while large R_A's result in short periods. Next section we will compare the numerical solution behaviors for the different basic reproductive number.

IV. Discussion and Conclusion

The number of secondary infections, which can result from one primary infection, is defined from the square root of the basic reproduction number (R_A):

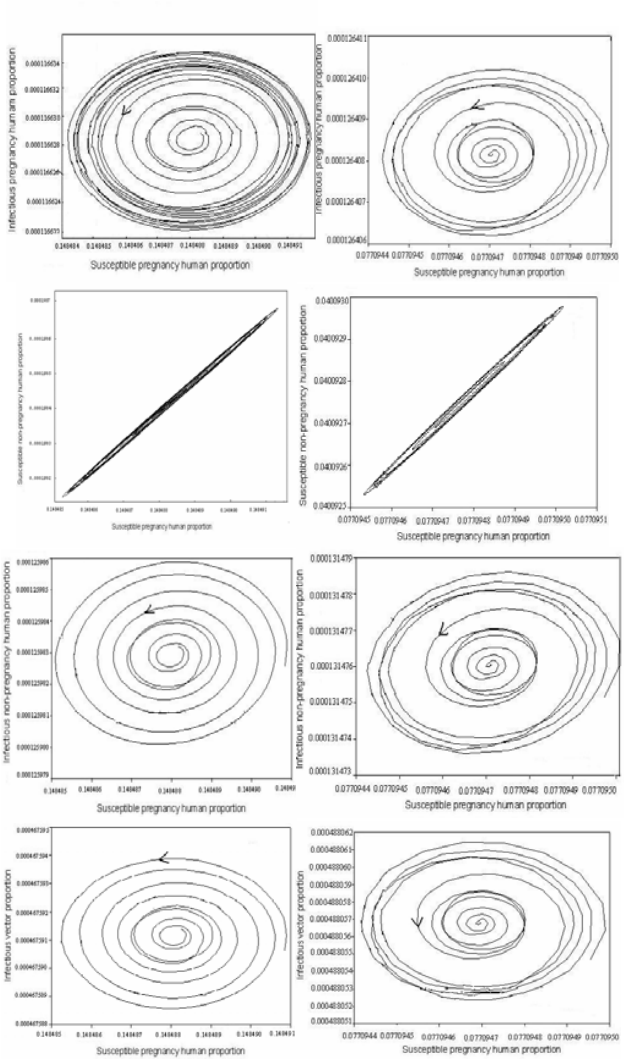
$$R_A = \frac{D_1(G_2 + \psi G_1)}{D_0 \psi G_3}$$

$$= \frac{\lambda_{vp}\lambda_{pv}a_v^2 N_{tp}(D/\theta_v)}{\theta_v(N_t + h)^2(\varpi + r)} + \frac{\lambda_{vn}\lambda_{nv}a_v^2 N_{tn}(D/\theta_v)}{\theta_v(N_t + h)^2(\varpi + r)}.$$

We can see that from Fig. 1a), 2a), 3a) and 4a), the proportion $(S^p, I^p, S^n, I^n, I^v)$ approaches to the free equilibrium value $(1,0,1,0,0)$. From Fig. (1b), (2b), (3b), and (4b) the proportion $(S^p, I^p, S^n, I^n, I^v)$ spirals to the endemic equilibrium value (0.148488, 0.000116629, 0.0801984, 0.000125983, 0.000467591).

This disease will be capable of invading and establishing itself when $R_A' = \sqrt{R_A}$ is more than one. If this number is less than one, then every successive generation will diminish in size until its number approaches zero.

Moreover, we compare the solution trajectory when the basic reproductive numbers are difference. We show in Fig. 5.



(5a) (5b)

Fig. 5 Numerical solutions of the system (3) demonstrate the solution trajectories, projected onto $(S^p, I^p), (S^p, S^n), (S^p, I^n), (S^p, I^v)$ -plane.

(5a) $R_A = 2.72653, R_A' = 1.65122$. The period of oscillation is about 3 years . The fractions of populations oscillate to the endemic disease equilibrium point

$$S^p = 0.148488\,,$$

$$I^p = 0.000116629\,,\ S^n = 0.0801984\,,$$

$$I^n = 0.000125983,\ I^v = 0.000467591\,.$$

(5b) $R_A = 5.45306,\ R_A' = 2.33518$. The period of oscillation is about 2 years . The fractions of populations oscillate to the endemic disease equilibrium point $S^p = 0.0770947$,

$$I^p = 0.000126408,\ S^n = 0.0400928\,,$$

$$I^v = 0.000488057\,.$$

The basic reproductive number of the disease for Fig. 5(a) and Fig. 5(b) equals to 1.65122 and 2.33518, respectively. Periods of the oscillations as the simulations approach the endemic equilibrium point are estimated by means of the solutions of the linearized system, obtain 3 years for Fig. 5(a) and 2 years for Fig. 5(b). As we see, the periods of fluctuation in the proportion of each class are shorter in the small basic reproduction number.

If the basic reproductive rate is higher, this means that one case can produce the greater number of secondary cases, and then the period of oscillation is shorter. The endemic equilibrium point for the fractions of susceptible pregnant and non-pregnant humans decrease. The endemic equilibrium points for the fractions of infectious pregnant, non-pregnant humans and infectious vector increase. These subsequent behaviors occur since there are enough susceptible pregnant and non-pregnant to be infected from infectious vector. Application of an ultra low volume (ULV) amount of insecticides (the standard method used to control the spread of dengue disease and other arthropod-borne disease) could reduce the basic reproductive rate to below one. The value of the basic reproductive rate would return to the above one value once the application is stopped and since the endemic state is locally stable, the disease would return.

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