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Analysis of a Mathematical Model for Dengue Disease in Pregnant Cases

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***Abstract*—**Dengue fever is an important human arboviral disease. Outbreaks are now reported quite often from many parts of the world. The number of cases involving pregnant women and infant cases are increasing every year. The illness is often severe and complications may occur. Deaths often occur because of the difficulties in early diagnosis and in the improper management of the diseases. Dengue antibodies from pregnant women are passed on to infants and this protects the infants from dengue infections. Antibodies from the mother are transferred to the fetus when it is still in the womb. In this study, we formulate a mathematical model to describe the transmission of this disease in pregnant women. The model is formulated by dividing the human population into pregnant women and non-pregnant human (men and non-pregnant women). Each class is subdivided into susceptible (S), infectious (I) and recovered (R) subclasses. We apply standard dynamical analysis to our model. Conditions for the local stability of the equilibrium points are given. The numerical simulations are shown. The bifurcation diagrams of our model are discussed. The control of this disease in pregnant women is discussed in terms of the threshold conditions.

***Keywords*—**Dengue disease, local stability , mathematical model, pregnancy.

I. Introduction

DENGUE a mosquito borne viral disease with a high capacity for epidemic outbreaks. It has become the most important arthropod-borne viral disease of human. There are four serotypes: dengue 1, 2, 3 and 4. This disease is transmitted to the human through the bite of infected *Aedes* mosquitoes, particularly *Aedes Aegypti* [1]. Infection by any of the four serotypes induces lifelong immunity against re-infection by the same serotype, but only partial and transient protection against the others. Dengue fever (DF), Dengue hemorrhagic fever (DHF) and Dengue shock syndrome (DSS) are three forms of this disease. Sequential infection by different serotypes seems to be the main trigger of DHF or DSS. Infection with dengue virus can result in a wide disease spectrum, from a mild fever to the life-threatening DHF and DSS. Symptoms of classical dengue fever, following a 5-8 day incubation period, include rash, severe headache, nausea, vomiting, chills, malaise, and rash and may include lymphadenopathy. DHF involves increased blood vessel permeability that can lead to shock and death in about 10% of the reported cases. Until now, there is no efficient vaccine to prevent this disease.

Dengue fever occurs in people of all ages. It has been estimated that there are between 50 and 100 million cases per year, with approximately 10,000 infant deaths due to this disease. DHF follows secondary dengue infections, but may sometimes follow primary infections, especially in infants. In such infants, maternally acquired dengue antibodies are presumed to enhance primary infections. About 30% of dengue cases are reported in patients older than 15 years [2]. In 1989, there have been reported cases of vertical infection in Tahiti [3]. Since then, there have been reports of increasing number of cases in Thailand, Malaysia, France and India [3]-[9].

There have been reported cases of dengue virus infection in pregnancy; they are shown in Table 1. More cases of dengue infection during pregnancy have occurred because of the increasing incidences of dengue infection among adults. An infection should be suspected when a pregnant woman is presented with similar patterns of symptoms and signs like those seen in non-pregnant human. Dengue infection during pregnancy should be of greater concern because of the possibility of increased mortality, particularly in preterm deliveries with premature babies. Where dengue fever is endemic, the dengue infection should be highly suspected in cases of febrile pregnant women, and a thorough investigation should be conducted to confirm the infection and prevent the possible maternal and fetal complications which could occur [10]. According to the CDC (The Centers for Diseases Control and Prevention (USA)), some vaccine- preventable infections lead to more severe illness in pregnant women than in non-pregnant human or can cause serious damage to the fetus.

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TABLE I
REPORTED CASES ON DENGUE DISEASE IN PREGNANCY [24]

	No of cases	Quantity	Reference
1989	9	China	[11]
1991	5	French	[3]
1994	>60	Thailand, Cuba	[4, 12]
1997	5	Thailand, Malaysia	[2, 13]
1999	22	French	[14]
2000	38	French	[15]
2001	4	Thailand, French	[5, 6, 10]
2003	27	Thailand, Bangladesh, Colombia	[16, 17, 18, 19, 20]
2004	3	Thailand	[21, 22]
2005	8	India	[8]
2006	26	Malaysia	[23]

Antibodies (also known as immunoglobulin) [25] are gamma globulin proteins that are found in blood or other bodily fluids of vertebrates, and are used by the immune system to identify and neutralize foreign objects, such as bacteria and viruses. There are vaccines that are useful in preventing infections during pregnancy. Vaccination protects against infection by stimulating the body's immune system to produce antibodies that in many cases are protective. Some infections are less common in newborn infants because they have antibodies from their mothers that prevent these infections.

Mathematical modeling of disease transmission has a long history. In 1911, an epidemiology model for malaria transmission was developed by Ross [26]. Mac Donald [27] later added a layer of biological realism to the model by providing careful interpretation and estimation of the parameter, which should go into the model. Mc Kenzie [28] has pointed out that the utility of a model depends not as much on how well a mathematical job has been accomplished but on how well a particular question has been translated. If one is interested in disease transmission, it is imperative that the model describes as closely as possible the characteristics of the disease being transmitted.

Modeling the dynamics of dengue transmission may help to improve the understanding of the interrelationships between dengue virus, vector, and host. Esteva and Vargas [29] introduced a mathematical model to provide a qualitative assessment for the problem. The model they used is based on the SIR model often used to model the dynamics of transmission for some diseases. It does not however describe the transmission of dengue in pregnant women. The purpose of this paper is to study the transmission of dengue disease in a population containing both pregnant and non-pregnant human through a mathematical model. In section 2, we introduce a mathematical model to describe the transmission of dengue disease in pregnant and non-pregnant classes. The analytical results of the model are presented in Section 3. In the last section, numerical solutions of the model are presented.

II. MATHEMATICAL MODEL

We propose a new model to study the transmission of dengue virus infection by introducing pregnant and non-pregnant classes into the SIR model. We classify the human population into two groups, pregnancy and non-pregnancy. Each group is constant in size and is divided into three classes, susceptible, infectious and recovered human populations. The vector population is divided into two groups, susceptible and infectious mosquitoes, with the mosquitoes never recover from the infection. In our SIR model, the dynamic of each component of the human population is given.

$$\frac{dS'_{PH}}{dt} = \lambda N_{PH} - \mu_H S'_{PH} - \varepsilon\beta_{VNH} S'_{PH} I'_{VH} \frac{b_v}{N_T + O_h} \quad (1.1)$$

$$\frac{dI'_{PH}}{dt} = \varepsilon\beta_{VNH} S'_{PH} I'_{VH} \frac{b_v}{N_T + O_h} - (\mu_H + \gamma_{IHR}) I'_{PH} \quad (1.2)$$

$$\frac{dR'_{PH}}{dt} = \gamma_{IHR} I'_{PH} - \mu_H R'_{PH} \quad (1.3)$$

$$\frac{dS'_{NH}}{dt} = \lambda N_{NH} - \mu_H S'_{NH} - \beta_{VNH} S'_{NH} I'_{VH} \frac{b_v}{N_T + O_h} \quad (1.4)$$

$$\frac{dI'_{NH}}{dt} = \beta_{VNH} S'_{NH} I'_{VH} \frac{b_v}{N_T + O_h} - (\mu_H + \gamma_{IHR}) I'_{NH} \quad (1.5)$$

and $$\frac{dR'_{NH}}{dt} = \gamma_{IHR} I'_{NH} - \mu_H R'_{NH} \quad (1.6)$$

where S'_{PH}, I'_{PH}, and R'_{PH} are the numbers of susceptible, infectious, and recovered pregnant women, respectively; S'_{NH}, I'_{NH}, and R'_{NH} are the numbers of susceptible, infectious, and recovered non- pregnant human populations , respectively.

The parameters in our model are defined as follows:

r_p is the percentage of the women to become pregnant,

N_T is the number of human population (assumed to be constant),

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

b_v is the average rate of biting per mosquito per day ,

λ is the average constant birth rate of the human population,

μ_H is the average constant death rate of the human population,

γ_{IHR} is the constant rate at which an infected human recovers,

β_{VNH} is the transmission probability from vector to non-pregnant human,

β_{VPH} is the transmission probability from vector to pregnant women,

ε is the ratio between transmission probability from vector to pregnant women and transmission probability from vector to non-pregnant human.

The last parameter is of most interest to us in this study. We are interested in the role of this parameter in determining how the infection in pregnant women progresses.

We now add (1.1) to (1.6), (1.1) to (1.3) and (1.4) to (1.6). The six equations reduce to the following three equations

$$\frac{dN_T}{dt} = \lambda N_T - \mu_H (S'_{PH} + I'_{PH} + R'_{PH} + S'_{NH} + I'_{NH} + R'_{NH}) \tag{2.1}$$

$$\frac{dN_{PH}}{dt} = \lambda N_{PH} - \mu_H (S'_{PH} + I'_{PH} + R'_{PH}) \tag{2.2}$$

$$\frac{dN_{NH}}{dt} = \lambda N_{NH} - \mu_H (S'_{NH} + I'_{NH} + R'_{NH}) \tag{2.3}$$

where

$N_T (= S'_{PH} + I'_{PH} + R'_{PH} + S'_{NH} + I'_{NH} + R'_{NH})$ is the total human population, N_{PH} $(= S'_{PH} + I'_{PH} + R'_{PH})$ is the total number of pregnant women and $N_{NH} (= S'_{NH} + I'_{NH} + R'_{NH})$ is the number of non-pregnant human.

We assume that the total population remains constant. Therefore $\frac{dN_T}{dt} = \frac{dN_{PH}}{dt} = \frac{dN_{NH}}{dt} = 0$

with $\frac{r_p N_T}{100} = N_{PH}$, $\frac{(100 - r_p) N_T}{100} = N_{NH}$ and $N_T = N_{PH} + N_{NH}$. With the number of each human class is constant, the rate of change in each class is equal to zero. Setting the right hand side of (2.1), (2.2) and (2.3) to be zero, we obtain $\lambda = \mu_H$ (birth rate equals to the death rate). The dynamic equations of the vector population are described by

$$\frac{dS'_{VH}}{dt} = V_H - \mu_V S'_{VH} - \beta_{NHV} S'_{VH} \frac{b_v}{N_T + O_h} (\eta I'_{PH} + I'_{NH}), \tag{3.1}$$

and $$\frac{dI'_{VH}}{dt} = \beta_{NHV} S'_{VH} \frac{b_v}{N_T + O_h} (\eta I'_{PH} + I'_{NH}) - \mu_V I'_{VH}, \tag{3.2}$$

where S'_{VH} and I'_{VH} are the number of susceptibles and infectives in the vector population, respectively.

V_H is the constant recruitment rate of the vector population,

μ_V is the average constant death rate of the vector population ,

β_{NHV} is the transmission probability from non-pregnant human to vector,

β_{PHV} is the transmission probability from pregnant women to vector ,

η is the ratio between transmission probability from pregnant women to vector and the transmission probability from non-pregnant human to vector.

When we add (3.1) to (3.2), we get

$$\frac{d}{dt}(S'_{VH} + I'_{VH}) = V_H - \mu_V N_v, \tag{3.3}$$

where N_v is the number of the vector population and it is equal to $S'_{VH} + I'_{VH}$. We assume the number of the vector population is also constant. Then the right hand side of (3.3) is equal to zero. This gives $N_v = \frac{V_H}{\mu_V}$. We now introduce the normalized populations $S_{PH} = \frac{S'_{PH}}{N_{PH}}$, $I_{PH} = \frac{I'_{PH}}{N_{PH}}$, $R_{PH} = \frac{R'_{PH}}{N_{PH}}$, $S_{NH} = \frac{S'_{NH}}{N_{NH}}$, $I_{NH} = \frac{I'_{NH}}{N_{NH}}$, $R_{NH} = \frac{R'_{NH}}{N_{NH}}$, $S_{VH} = \frac{S'_{VH}}{(V_H/\mu_V)}$ and $I_{VH} = \frac{I'_{VH}}{(V_H/\mu_V)}$.

Then (1.1)-(1.6), (3.1) and (3.2) can be rewritten as

$$\frac{dS_{PH}}{dt} = \mu_H (1 - S_{PH}) - \varepsilon \beta_{VNH} S_{PH} I_{VH} (V_H/\mu_V) \frac{b_v}{N_T + O_h}, \tag{4.1}$$

$$\frac{dI_{PH}}{dt} = \varepsilon \beta_{VNH} S_{PH} I_{VH} (V_H/\mu_V) \frac{b_v}{N_T + O_h} - (\mu_H + \gamma_{IHR}) I_{PH}, \tag{4.2}$$

$$\frac{dS_{NH}}{dt} = \mu_H (1 - S_{NH}) - \beta_{VNH} S_{NH} I_{VH} (V_H/\mu_V) \frac{b_v}{N_T + O_h}, \tag{4.3}$$

$$\frac{dI_{NH}}{dt} = \beta_{VNH} S_{NH} I_{VH} (V_H/\mu_V) \frac{b_v}{N_T + O_h} - (\mu_H + \gamma_{IHR}) I_{NH}, \tag{4.4}$$

and $$\frac{dI_{VH}}{dt} = \beta_{NHV} (1 - I_{VH}) \frac{b_v}{N_T + O_h} (\eta I_{PH} N_{PH} + I_{NH} N_{NH}) - \mu_V I_{VH}, \tag{4.5}$$

The dynamic equations for R_{PH}, R_{NH} and S_{VH} are not needed, since $S_{PH} + I_{PH} + R_{PH} = 1$, $S_{NH} + I_{NH} + R_{NH} = 1$ and $S_{VH} + I_{VH} = 1$.

III. Analysis of the Mathematical Model

A. Equilibrium Points

The equilibrium points are obtained by setting the right hand side of (4.1)-(4.5) equal to zero. We get two equilibrium points, the disease free state $E_1 = (1,0,1,0,0)$ and the endemic disease state $E_2 = (S^*_{PH}, I^*_{PH}, S^*_{NH}, I^*_{NH}, I^*_{VH})$ where

$$S^*_{PH} = \frac{\alpha_1}{\alpha_1 + \alpha_2 I^*_{VH}}, \tag{5.1}$$

$$I^*_{PH} = \frac{\alpha_1 \alpha_2 I^*_{VH}}{(\alpha_1 + \alpha_2 I^*_{VH})(\alpha_1 + \alpha_3)}, \tag{5.2}$$

$$S^*_{NH} = \frac{\varepsilon\alpha_1}{\varepsilon\alpha_1 + \alpha_2 I^*_{VH}} \quad , \tag{5.3}$$

$$I^*_{NH} = \frac{\alpha_1\alpha_2 I^*_{VH}}{\left(\varepsilon\alpha_1 + \alpha_2 I^*_{VH}\right)(\alpha_1 + \alpha_3)} \quad , \tag{5.4}$$

And where I^*_{VH} are solutions of

$$A_1(I^*_{VH})^2 + A_2 I^*_{VH} + A_3 = 0 \tag{6.1}$$

The solutions of (6.1) are given by

$$I^*_{VH1} = \frac{-A_2 + \sqrt{A_2^2 - 4A_1A_3}}{2A_1} \quad , \tag{6.2}$$

$$\text{and } I^*_{VH2} = \frac{-A_2 - \sqrt{A_2^2 - 4A_1A_3}}{2A_1} \tag{6.3}$$

$$\text{where } A_3 = ((\frac{\alpha_1}{\alpha_2}K_3 - K_1)\varepsilon - K_2)\left(\frac{\alpha_1}{\alpha_2}\right), \tag{6.4}$$

$$A_2 = ((K_1 + K_3)\varepsilon + K_2 + K_3)\left(\frac{\alpha_1}{\alpha_2}\right) - K_1 - K_2, \tag{6.5}$$

$$\text{and } A_1 = K_1 + K_2 + K_3 \tag{6.6}$$

with $\alpha_1 = \mu_H(N_T + O_h)$, $\alpha_2 = \varepsilon\beta_{VNH}\left(V_H/\mu_V\right)b_v$

$\alpha_3 = \gamma_{IHR}(N_T + O_h)$ and $K_1 = \beta_{NHV}b_v\eta\alpha_1(\alpha_2)^2 N_{PH}$, $K_2 = \beta_{NHV}b_v\alpha_1(\alpha_2)^2 N_{NH}$, $K_3 = \mu_V(N_T + O_h)(\alpha_1 + \alpha_3)(\alpha_2)^2$.

Looking at the term in square root of I^*_{VH1} and I^*_{VH2}, $A_2^2 - 4A_1A_3$ is positive for $\frac{\alpha_2K_2 + \alpha_2\varepsilon K_1}{\alpha_1K_3\varepsilon} > 1$. Since $(\frac{\alpha_1}{\alpha_2}K_3 - K_1)\varepsilon - K_2 < 0$, then A_3 is negative and A_1 is always positive. Moreover $\sqrt{A_2^2 - 4A_1A_3}$ is greater than A_2. We can easily see that $\frac{-A_2 + \sqrt{A_2^2 - 4A_1A_3}}{2A_1} > 0$ and $\frac{-A_2 - \sqrt{A_2^2 - 4A_1A_3}}{2A_1} < 0$. The solution $I^*_{VH2} = \frac{-A_2 - \sqrt{A_2^2 - 4A_1A_3}}{2A_1}$ is negative. This is physical meaningless since the infectious vector proportion must be positive. Hence the solution is defined for $R_0 > 1$ $(R_0 = \frac{\alpha_2K_2 + \alpha_2\varepsilon K_1}{\alpha_1K_3\varepsilon})$.

B. Local Asymptotical Stability

The local stability of an equilibrium point is determined from the signs of eigenvalues of the Jacobian matrix of the right hand side of the above set of differential equations.

C. Disease Free State

For the system defined by (4.1)-(4.5), the Jacobian matrix evaluated at E_1 is the 5x5 matrix given by

$$J_{E_1} = \begin{bmatrix} -\mu_H & 0 & 0 & 0 & -\varepsilon\beta_{VNH}\frac{b_v}{N_T + O_h}(V_H/\mu_V) \\ 0 & -\mu_H - \gamma_{IHR} & 0 & 0 & \varepsilon\beta_{VNH}\frac{b_v}{N_T + O_h}(V_H/\mu_V) \\ 0 & 0 & -\mu_H & 0 & -\beta_{VNH}\frac{b_v}{N_H + O_h}(V_H/\mu_V) \\ 0 & 0 & 0 & -\mu_H - \gamma_{IHR} & \beta_{NH}\frac{b_v}{N_T + O_h}(V_H/\mu_V) \\ 0 & \beta_{NHV}\frac{b_v}{N_T + O_h}\eta N_{PH} & 0 & \beta_{NHV}\frac{b_v}{N_T + O_h}N_{NH} & -\mu_V \end{bmatrix}$$

The eigenvalues are obtained by solving the characteristic equation; $\det(\mathrm{J}_{\mathrm{E}_1} - \lambda\mathrm{I}_5) = 0$ where I_5 is the identity matrix dimension 5x5. If all eigenvalues for each equilibrium state have negative real parts then that equilibrium state is locally stable. The characteristic equation for the disease free state is given by

$$\left(\lambda + \mu_H\right)\left(\lambda + \mu_H + \gamma_{IHR}\right)\left(\lambda + \mu_H\right)\left(\lambda^2 + B_1\lambda + B_0\right) = 0, \tag{7}$$

where

$$B_0 = \mu_V(\mu_H + \gamma_{IHR}) - \beta_{NHV}[\frac{b_v}{N_T + O_h}]^2\beta_{VNH}(V_H/\mu_V)(N_{NH} + \varepsilon\eta N_{HP}),$$

$B_1 = \mu_H + \mu_V + \gamma_{IHR}$.

From the characteristic (7), the first three eigenvalues are $\lambda_1 = -\mu_H$, $\lambda_2 = -\mu_H - \gamma_{IHR}$ and $\lambda_3 = -\mu_H$. The remaining eigenvalue is found by solving

$\lambda^2 + B_1\lambda + B_0 = 0$.

It can be easily seen that λ_1, λ_2 and λ_3 are always negatives. We can see that $\lambda_4 = \frac{-B_1 - \sqrt{B_1^2 - 4B_0}}{2}$ and $\lambda_5 = \frac{-B_1 + \sqrt{B_1^2 - 4B_0}}{2}$. The eigenvalue λ_4 has a negative real part. λ_5 has negative real part when

$\sqrt{B_1^2 - 4B_0} < B_1$ or $B_1^2 - 4B_0 < B_1^2$ or $B_0 > 0$. So that

$$\mu_V(\mu_H + \gamma_{IHR}) - \beta_{NHV}\beta_{VNH}(V_H/\mu_V)(\frac{b_v}{N_T + O_h})^2(N_{NH} + \varepsilon\eta N_{HP}) > 0.$$

and $\frac{\beta_{NHV}\beta_{VNH}(V_H/\mu_V)(\frac{b_v}{N_T + O_h})^2(N_{NH} + \varepsilon\eta N_{HP})}{\mu_V(\mu_H + \gamma_{IHR})} < 1$. Thus, the disease free state is locally stable state when

$$R_0 = \frac{\alpha_2(K_2 + \varepsilon K_1)}{\alpha_1\varepsilon K_3} < 1. \tag{8}$$

D. Endemic Disease State

The local stability of the endemic state, E_2, is determined by looking at the signs of the eigenvalues of the Jacobian evaluated at E_2. The Jacobian matrix for this state is

$$J_{E_2}=\begin{bmatrix} -\mu_H-\beta I^*_{VH} & 0 & 0 & 0 & -\beta S^*_{PH} \\ \beta I^*_{VH} & -\mu_H-\gamma_{IHR} & 0 & 0 & \beta S^*_{PH} \\ 0 & 0 & -\mu_H-\frac{\beta}{\varepsilon}I^*_{VH} & 0 & \frac{\beta}{\varepsilon}S^*_{NH} \\ 0 & 0 & \frac{\beta}{\varepsilon}I^*_{VH} & -\mu_H-\gamma_{IHR} & \frac{\beta}{\varepsilon}S^*_{NH} \\ 0 & c_0-c_0 I^*_{VH} & 0 & d_0-d_0 I^*_{VH} & -c_0 I^*_{PH}-d_0 I^*_{NH}-\mu_V \end{bmatrix},$$

with

$$\beta=\varepsilon\beta_{VNH}\frac{b_v}{N_T+O_h}(V_H/\mu_V),$$

$$c_0=\beta_{NHV}\frac{b_v}{N_T+O_h}\eta N_{PH} \text{ and } d_0=\beta_{NHV}\frac{b_v}{N_T+O_h}N_{NH}$$

where $S^*_{PH}, I^*_{PH}, S^*_{NH}, I^*_{NH}$ and I^*_{VH} are defined in (5.1)-(5.4), (6.1) and $R_0>1$ $\left(R_0=\frac{\alpha_2 K_2+\alpha_2\varepsilon K_1}{\alpha_1 K_3\varepsilon}\right)$. (8)

The characteristic equation for the endemic state is given by

$$(\lambda+\mu_H+\gamma_{IHR})(\lambda^4+a_3\lambda^3+a_2\lambda^2+a_1\lambda+a_0)=0 \quad (9.1)$$

where

$$a_3=I^*_{VH}\beta\gamma_1+c_0 I^*_{PH}+d_0 I^*_{NH}+\gamma_{IHR}+3\mu_H+\mu_V, \quad (9.2)$$

$$a_2=\frac{1}{\varepsilon}(\beta(I^{*2}_{VH}\beta-(\varepsilon c_0+d_0))+I^*_{VH}\beta((\gamma_{IHR}+2\mu_H)\gamma_2+\varepsilon\mu_H(2\gamma_{IHR}+3\mu_H))+$$
$$d_0(\beta(I^*_{NH}(1+(\gamma_2+S^*_{NH})I^*_{VH}+R^*_{NH})+I^*_{NH}\varepsilon\gamma_3)+c_0(\hat{I}_{PH2}I^*_{VH}+R^*_{PH}+I^*_{PH}\hat{I}_{VH1})\beta$$
$$+I^*_{PH}\gamma_3)\varepsilon+(I^*_{VH}\beta\gamma_2+\varepsilon\gamma_3)\mu_V) \quad (9.3)$$

$$a_1=\frac{1}{\varepsilon}((2I^*_{VH}\beta+\mu_H\gamma_2+\gamma_4+d_0(\beta((I^*_{NH}\hat{I}_{VH2}+R^*_{NH}+S^*_{NH}\hat{I}_{VH3})\beta+$$
$$I^*_{NH}I^*_{VH}\gamma_2\gamma_{IHR})+2(\beta(R^*_{NH}+I^*_{VH}S^*_{NH}+(\varepsilon\hat{I}_{VH4}+\hat{I}_{VH1})I^*_{NH})\mu_H+3I^*_{NH}\varepsilon\mu_H^2)+$$
$$c_0(\beta((I^*_{PH}\hat{I}_{VH2}+R^*_{PH}+S^*_{PH}\hat{I}_{VH3})\beta+I^*_{NH}I^*_{VH}\gamma_2\gamma_{IHR})+2(I^*_{PH}I^*_{VH}\beta+(I^*_{PH}+$$
$$\hat{I}_{PH1}I^*_{VH}+R^*_{PH})\varepsilon\beta+I^*_{PH}\varepsilon\gamma_{IHR})\mu_H+3I^*_{PH}\varepsilon\mu_H^2)-\beta(d_0\gamma_5+c_0\gamma_6)+(I^*_{VH}\beta(I^*_{VH}\beta+$$
$$\gamma_2\gamma_{IHR})+2(I^*_{VH}\beta\gamma_2+\varepsilon\gamma_{IHR})\mu_H+3\varepsilon\mu_H^2)\mu_V))), \quad (9.4)$$

$$a_0=\frac{1}{\varepsilon}(-\beta\mu_H(d_0\gamma_7+c_0\gamma_8)+d_0(I^*_{NH}\gamma_{IHR}\hat{I}_{VH5}\hat{I}_{VH6}+\mu_H((I^*_{NH}\hat{I}_{VH2}+R^*_{NH}+\hat{I}_{VH3}S^*_{NH})\beta^2+$$
$$\beta(I^*_{NH}\hat{I}_{VH1}+R^*_{NH}+(S^*_{NH}+I^*_{NH}\varepsilon)I^*_{VH})\mu_H+I^*_{NH}\varepsilon\mu_H^2))+c_0(I^*_{PH}\gamma_{IHR}\hat{I}_{VH5}\hat{I}_{VH6}+$$
$$\mu_H((I^*_{PH}\hat{I}_{VH2}+R^*_{PH}+\hat{I}_{VH3}S^*_{PH})\beta^2+\mu_H(I^*_{PH}I^*_{VH}\beta+((I^*_{PH}\hat{I}_{VH1}+R^*_{PH}+I^*_{VH}S^*_{PH})\beta+$$
$$I^*_{PH}\mu_H)\varepsilon)))+\hat{I}_{VH5}\gamma_4+\hat{I}_{VH6}\gamma_9\mu_V) \quad (9.5)$$

with

$$\gamma_1=(1+\frac{1}{\varepsilon}),\gamma_2=(1+\varepsilon),\gamma_3=\gamma_{IHR}+3\mu_H,\gamma_4=\gamma_{IHR}+\mu_H,\gamma_5=\beta+2\mu_H,\gamma_6=\beta+2\varepsilon\mu_H,\gamma_7=\beta+\mu_H,$$
$$\gamma_8=\beta+\varepsilon\mu_H,\gamma_9=\gamma_{IHR}\varepsilon+\mu_H,\hat{I}_{PH1}=I^*_{PH}+S^*_{PH},\hat{I}_{PH2}=I^*_{PH}\beta+S^*_{PH},\hat{I}_{VH1}=1+I^*_{VH},\hat{I}_{VH2}=1+I^{*2}_{VH},$$
$$\hat{I}_{VH3}=I^{*2}_{VH}+S^*_{VH},\hat{I}_{VH4}=I^*_{VH}+\gamma_{IHR},\hat{I}_{VH5}=I^*_{VH}\beta+\mu_H,\hat{I}_{VH6}=I^*_{VH}\beta+\varepsilon\mu_H$$

From the characteristic (9.1), the first eigenvalue $\lambda_1=-\mu_H-\gamma_{IHR}$ is always negative. The other eigenvalues are found by solving $\lambda^4+a_3\lambda^3+a_2\lambda^2+a_1\lambda+a_0=0$. The signs of these eigenvalues are negatives when they satisfy the Routh-Hurwitz criteria [30] which are:

i) $a_3>0$, (10.1)

ii) $a_1>0$, (10.2)

iii) $a_0\geq 0$, (10.3)

iv) $a_3a_2a_1>a_1^2+a_3^2a_0$ (10.4)

We now map out the regions in a_3 - ε phase space, a_1 - ε phase space, a_0 - ε phase space and ($a_3a_2a_1-a_1^2-a_3^2a_0$) - ε phase space in which the four above conditions are met and $R_0>1$. These are shown in the following figures.

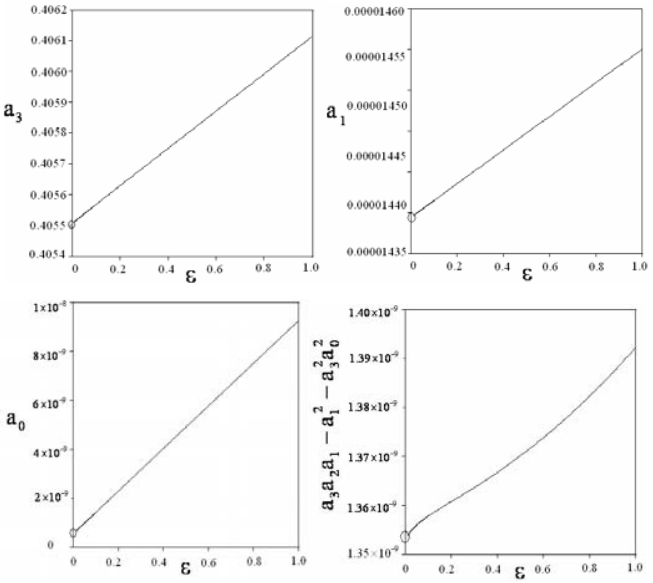


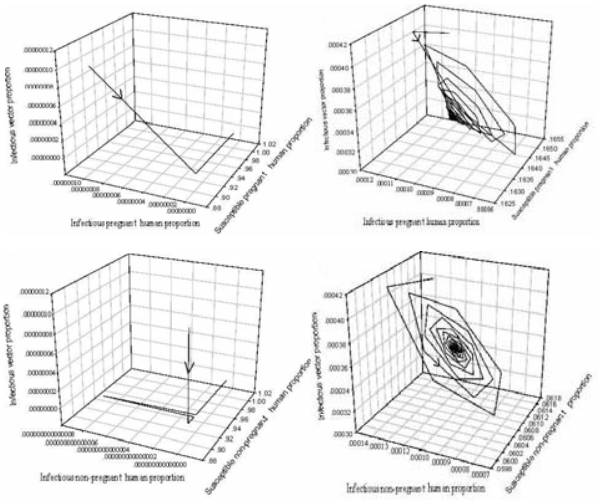
Fig. 1 The parameter space for the endemic equilibrium point which satisfies the Routh-Hurwitz criteria. The values of the other parameters are $\mu_H=0.000039139\ \text{day}^{-1}$, $\mu_V=0.071428571\ \text{day}^{-1}$, $N_T=100{,}000$, $V_H=40{,}000$ $b_v=0.33333\ \text{day}^{-1}$, $\gamma_{IHR}=0.33333\ \text{day}^{-1}$, $N_{PH}=500$, $\beta_{VNH}=0.9$, $\beta_{NHV}=0.7$, $\beta_{PHV}=0.4$, $\eta=0.5714286$, $N_{NH}=99{,}500$.

From the above figure, Routh-Hurwitz criteria (10.1) to (10.4) are satisfied for $R_0>1$. Thus, the endemic equilibrium state is locally stable when $R_0>1$.

E. Numerical Results

In this section, we consider the transmission of this disease among the pregnant and non-pregnant classes. The trajectories of the solutions when the parameter values will lead to a disease free equilibrium state and when they will lead to the endemic equilibrium state are shown in the figures. The values of the parameters used in this study are $\mu_H=0.000039139$ per day. This corresponds to a life expectancy of 70 years in human. The mean life of mosquito is 14 days and so is $\mu_V=0.071428571$ per day. R_0 is defined in (8). R_0' is the basic reproductive number

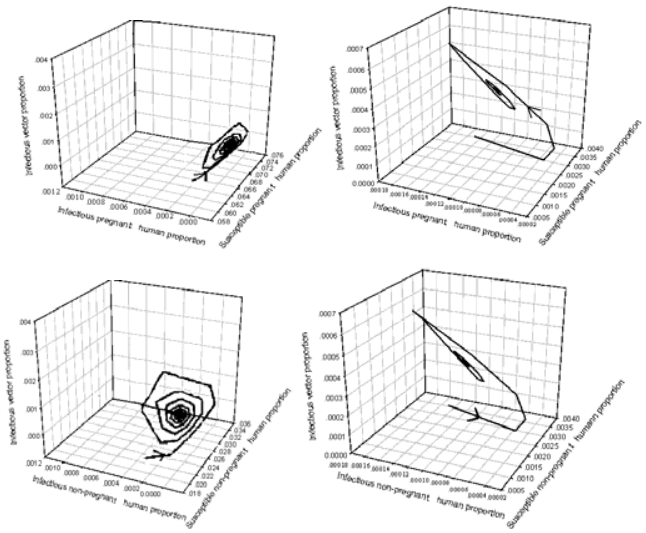
determined from the square root of R_0 [29]. We assume that the number of the non-pregnant human is greater than the number of the pregnant women and there is no alternative host. We have taken the ratio ε and η to be less than one. The trajectories of the numerical solutions of (4.1)-(4.5) are shown in the following figures.



2a) 2b)

Fig. 2 Numerical solutions demonstrate the solution trajectories, projected into two 3D space (S_{PH}, I_{PH}, I_{VH}), (S_{NH}, I_{NH}, I_{VH}) respectively. The value of parameters are $\mu_H = 0.000039139\ \text{day}^{-1}$, $\mu_V = 0.071428571\ \text{day}^{-1}$, $b_v = 0.33333\ \text{day}^{-1}$, $\gamma_{IHR} = 0.33333\ \text{day}^{-1}$, $\beta_{VNH} = 0.9$, $\beta_{VPH} = 0.3$, $\beta_{NHV} = 0.7$, $\beta_{PHV} = 0.4$, $\varepsilon = 0.33333$, $\eta = 0.5714286$, $N_T = 100{,}000$, $N_{NH} = 99{,}500$, $N_{PH} = 500$. 2a) $R_0 < 1$, $V_H = 2{,}000$, $R_0 = 0.209476$, $R_0' = 0.457685$. The fractions of populations $(S_{PH}, I_{PH}, S_{NH}, I_{NH}, I_{VH})$ approach to the disease free state $(1,0,1,0,0)$. 2b) $R_0 > 1$, $V_H = 40{,}000$, $R_0 = 4.18953$, $R_0' = 2.04683$. The trajectory of the five state variable solution $(S_{PH}, I_{PH}, S_{NH}, I_{NH}, I_{VH})$ spirals into the endemic disease equilibrium state $(0.162904, 0.000110251, 0.060917, 0.0000982777, 0.000359141)$.

Fig. 2 shows the trajectories of the solutions of (4.1) – (4.5) in the 3D (S_{PH}, I_{PH}, I_{VH}) space and the (S_{NH}, I_{NH}, I_{VH}) for two values of R_0. We now look at the trajectory of the solutions when the threshold numbers are different. We show these trajectories in Fig. 3.



3a) 3b)

Fig. 3 Numerical solutions demonstrate the solution trajectories, projected onto the 3D space for different values of the ratio ε. The values of parameters are the same as those used to generate the curves in Fig. 2, except for the ratio between transmission probability of the virus from the vector to pregnant women and that from the vector to the non-pregnant human. 3a) For $\varepsilon = 0.375$, $R_0 = 9.31117$, $R_0' = 3.05142$. The trajectories of the five component solution $(S_{PH}, I_{PH}, S_{NH}, I_{NH}, I_{VH})$ appears to spiral into the equilibrium state $(0.0698949, 0.000109197, 0.0274079, 0.000114185, 0.000372021)$ 3b) The trajectory when $\varepsilon = 0.888889$, $R_0 = 104.905$, $R_0' = 10.2423$. The trajectories here spiral to the new equilibrium state $(0.00273964, 0.000117081, 0.00243598, 0.000117117, 0.000381617)$.

Note that R_0 is the threshold condition, if it is less than one then the disease free state will be locally stable. But if this number is more than one, the endemic disease state will be locally stable. $R_0' = \sqrt{R_0}$ is the basic reproductive number of this disease.

IV. Discussion and Conclusion

In this study, we are interested in the transmission of dengue disease in pregnant and non-pregnant classes. The threshold number is defined by R_0 where

$$R_0 = \frac{\alpha_2(K_2 + \varepsilon K_1)}{\alpha_1 \varepsilon K_3} = \frac{\beta_{VNH}\beta_{NHV} b_v^2 N_{NH}(V_H/\mu_v)}{\mu_v (N_T + O_h)^2 (\mu_H + \gamma_{IHR})} + \frac{\beta_{VPH}\beta_{PHV} b_v^2 N_{PH}(V_H/\mu_v)}{\mu_v (N_T + O_h)^2 (\mu_H + \gamma_{IHR})} \quad (11)$$

The square root of the second term of this number is the number of secondary infective pregnant women. To see how this term arises, we first note that

$(\frac{b_v(V_H/\mu_v)}{(N_T+O_h)})(\frac{1}{(\mu_H+\gamma_{IHR})})$ is the number of times that the susceptible mosquitoes will bite an infected pregnant women. Of these, only a fraction of them will end up as a special class of infectious mosquito. The number of infectious mosquitoes in the class will be the number of bites multiplied by the probability that the bite will end up as an infection which is β_{PHV}. Of these mosquitoes, only a faction of them $\frac{b_v}{\mu_v}\cdot(\frac{N_{PH}}{N_T+O_h})$ will bite a pregnant woman. In turn, only a fraction (β_{VPH}) of these pregnant women will become infectious. The number of secondary infectious pregnant women will be the product of $(\frac{b_v(V_H/\mu_v)}{(N_T+O_h)})(\frac{1}{(\mu_H+\gamma_{IHR})})$ times β_{PHV} times $\frac{b_v}{\mu_v}\cdot(\frac{N_{PH}}{N_T+O_h})$ times β_{VPH}. This is just the second term in (11). For a disease to be capable of invading and establishing itself in a host population, the full threshold number R_0 must be greater than one. Otherwise, every successive generation will get smaller until no population is left .

Fig. 2 shows $(S_{PH}, I_{PH}, S_{NH}, I_{NH}, I_{VH})$ moving towards their equilibrium state. We see the trajectory approaching the disease free equilibrium state $(1,0,1,0,0)$ when $R_0 < 1$. When $R_0 > 1$, we see the trajectory is spiraling into the equilibrium endemic disease state $(0.162904, 0.000110251, 0.060917, 0.0000982777, 0.000359141)$. Using the numerical values for the various parameters which give $R_0 > 1$ in the expressions for the a_i's, (9.2) – (9.5), the characteristic equation becomes a 4th order numerical polynomial equation which can be solved by the program *mathematica* . The solution of this equation is a complex number, meaning that the eigenvalues are complex. For the imaginary part, the program finds that the complex part of the eigenvalue is approximately 0.005946. This corresponds to a period of oscillation of $2\pi/0.005946$ days or approximately 2.89511 years. The numerical solutions of $(S_{PH}, I_{PH}, S_{NH}, I_{NH}, I_{VH})$ for $R_0 > 1$ when $\varepsilon = 0.375$ and $\varepsilon = 0.88889$ are shown in Fig.3. We see the trajectories spiraling toward the different endemic disease states $(0.0698949, 0.000109197, 0.0274079, 0.000114185, 0.000372021)$ and $(0.00273964, 0.000117081, 0.00243598, 0.000117117, 0.000381617)$, for the two values of ε, respectively. The imaginary part of the two eigenvalues are approximately 0.00900892 and 0.029841. These imaginary values correspond to periods of oscillation of approximately 1.91079 years and 0.576863 years.

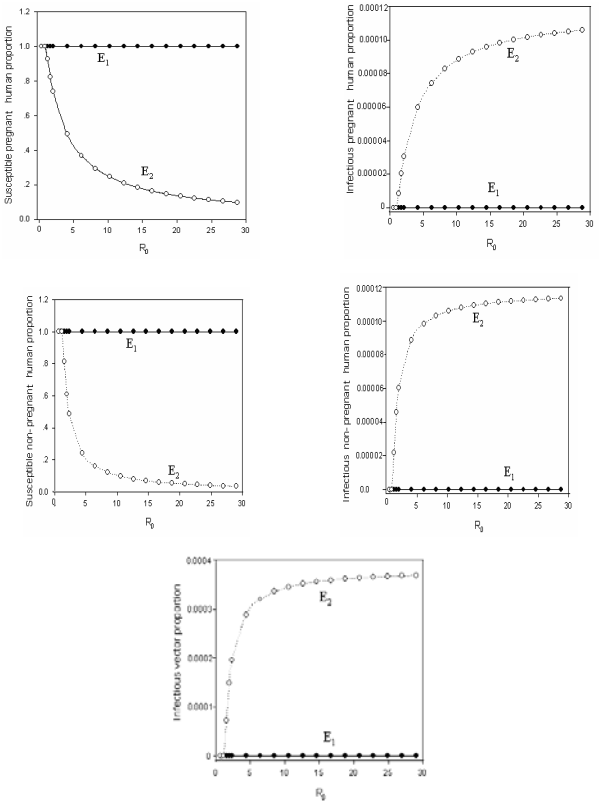


Fig. 4 Bifurcation diagrams of the solutions of equations (4a)-(4e) for the different values of R_0. ⟐ denote the stable solutions while ⟐ denote the unstable solutions. The values of the parameters used in the calculations are:

$\mu_H = 0.000039139\ \text{day}^{-1}$,

$\mu_V = 0.071428571\ \text{day}^{-1}$, $b_v = 0.33333\ \text{day}^{-1}$,

$\gamma_{IHR} = 0.33333\ \text{day}^{-1}$, $\beta_{VNH} = 0.9$, $\beta_{VPH} = 0.3$,

$\beta_{NHV} = 0.7$, $\beta_{PHV} = 0.4$, $\varepsilon = 0.33333$, $\eta = 0.5714286$,

$N_T = 100{,}000$, $N_{NH} = 99{,}500$, $N_{PH} = 500$,

$V_H = 40{,}000$, $\alpha_1 = 3.91389$, $\alpha_2 = 56{,}000$, $\alpha_3 = 33{,}333.33$,

$K_1 = 8.18265\times10^{11}$, $K_2 = 2.84961\times10^{14}$, $K_3 = 2.92237\times10^{18}$.

The bifurcation diagrams of (4.1)-(4.5) are shown in the Fig. 4. We can see that, when $R_0 < 1$, E_1 will be stable and for $R_0 > 1$, E_2 will be stable. If the threshold number is greater than one, the normalized susceptible pregnant and non-pregnant human populations decrease. The normalized infectious pregnant human, non-pregnant human and infectious vector populations increase. This subsequent behavior occurs since there are enough susceptible pregnant human and non-pregnant human to be infected from infectious vector.

The ultimate goal of any control effort would be the reduction of R_0 to a value below one [29,31,32,33]. If we

can reduce the second term of the threshold number as defined in (11), then the number of women during their pregnancies will be decreased. Consequently, the infants will be not infected with dengue virus from vertical transmission. This will reduce the outbreaks of dengue disease in neonates.

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