Sensitivity Analysis of Zika Epidemic Model

T. O. Oluyo, M. O. Adeyemi

Abstract – In recent times, Zika fever has become a scourge to human. This is so especially because there is no specific treatment or vaccine currently available. However, we present an eight compartmental mathematical model here, which studies the dynamical spread of Zika fever within humans (host) and between humans and mosquitoes (vector), and the possible control measures. The existence of region where the model is epidemiologically feasible is established. The mathematical analysis of the model shows that there exists a disease-free equilibrium point, which is locally asymptotically stable. We carried out a sensitivity analysis of the basic reproduction number, which shows that the most sensitive parameter that must be worked upon in order to control the disease outbreak. Numerical simulation was also carried out by maple software using differential transformation method to show the effects of recovery (as a result of symptoms treatment) (γ), isolation (ρ), and vector elimination (δ_2) on the spread of Zika fever. Our numerical results showed that increasing the recovery to a very high rate has significant effect in reducing infection and isolation of infected individuals also reduces the transmission of the ZikV infection. Also, the rate of mosquito human-induced deaths, if increased, will result in the elimination of the vector (mosquitoes). The result from the sensitivity analysis showed that human birth rate and human-human transmission parameters are the most sensitive parameter to the basic reproduction number obtained. Therefore, isolation of infected individuals, screening of blood prior to transfusion and practising of protected sex will reduce the risk of human-human transmission, and as such, prevention in transmission of ZikV infection is ensured.

Keywords – *Basic reproduction number, Critical points, Isolation, Sensitivity analysis, Stability, ZikV.*

1 INTRODUCTION

ZIKA fever (or Zika virus disease) is an illness caused by the Zika virus. The disease is spread through the bite of daytime-active Aedes mosquitoes such as the A. aegypti and A. albopictus (these mosquitoes also spread dengue and chikungunya viruses) [3], [18]. The disease derives its name from ‗Zika forest' in Uganda, where the virus was first isolated from a rhesus monkey in 1947 [2], [13]. The first human cases were reported in Nigeria in 1954 [3]. The first documented outbreak among people occurred in 2007, in the Federated State of Micronesia [3], [18]. As of January 2016, the disease was occurring in 20 regions of the Americas [12]. It is estimated that about 1.5 million people have been infected by Zika in Brazil with over 3,500 cases of microcephaly reported between October 2015 and January 2016 [4], [11]. Also, it is known to have occurred in Africa, Asia and the Pacific [7]. As a result of the outbreak which started in Brazil in 2015, the World health Organization has declared Zika fever a public health emergency of international concern [13], [18].

The disease of Zika virus is transmitted from infected Aedes mosquitoes to humans through mosquito bites [1], [18]. It can also be transmitted from human to human through the blood and semen of an infected human [16], and through an infected pregnant woman to the foetus [11]. Zika is a cause of microcephaly and other severe brain defects [12]. The incubation period (the time from exposure to symptoms) of Zika virus disease is not clear, but is likely to be a few days to a week. The symptoms are similar to other arbovirus infection such as dengue, and include fever, skin rashes, conjunctivitis (red eyes), muscle and joint pain, malaise and headache. These symptoms are usually mild and usually last from 2 – 7 days [1], [3], [18].

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There is no specific treatment or vaccine currently available for Zika virus disease [1]. Prevention and control relies on reducing mosquitoes through source reduction (removal and modification of breeding sites), and reducing contacts between mosquitoes and people. Since there is no specific treatment currently, the symptoms can be treated [1]. Most people fully recover without severe complications, and hospitalization rates are low [1], [3]. Till date, disease related deaths are rare. However, there is scientific consensus that Zika virus is a cause of complications such as microcephaly (a birth defect where a baby's head and/or brain is smaller than expected) and Guillain-Barre syndrome (a neurological disorder that could lead to paralysis and death) [12], [17].

Mathematical models for transmission dynamics of mosquito-borne diseases can be useful in providing better insights into the behaviour of this disease. The models have played great roles in influencing the decision making processes regarding intervention strategies for preventing and controlling the insurgence of mosquito-borne diseases [6]. Kucharski, *et al.* [4] suggested that ZikV may exhibit similar dynamics to dengue virus in Island population, with transmission characterized by large sporadic outbreaks with a high proportion of asymptomatic or unreported cases. Perkins and his colleagues developed and applied a method that leverages highly spatially resolved data about drivers of Zika virus transmission to project that millions of infections in childbearing women and all demographic strata could occur before the first wave of the epidemic concludes and that tens of thousands of pregnancies would be affected [11]. Oluyo and Adeyemi [9] formulated a 5-compartmental model to study how to best slow or prevent the outbreak of Zika virus disease and protect vulnerable populations, which include isolation of infected individuals, among other measures. The present study extended the work done by Oluyo and Adeyemi [9] to look into which parameter(s) is/are most sensitive and must be focused on in order to control the Zika virus disease outbreak and protect vulnerable populations. This is done by carrying out a sensitivity analysis on the basic reproduction number of a full dynamic 8-compartmental model of ZikV infection.

The rest of this work is organized as follows: we give a full description of the model and show a domain where the model is epidemiologically well posed in Section 2. Section 3 provides the existence of equilibria including a derivation of the basic reproduction number and stability analysis of the equilibria. In Section 4, we perform numerical simulations of the model with graphical illustrations and their discussion, and give concluding remark in Section 5.

2. MODEL FORMULATION

To study the transmission and spread of malaria in two interacting population of humans (the host) and mosquitoes (the vector), we formulate a model which subdivides the total human population size at time t, denoted by $N_h(t)$, into susceptible humans $S_h(t)$, exposed humans $E_h(t)$, infectious humans $I_h(t)$, isolated humans $Q(t)$ and recovered humans $R(t)$. Hence, we have:

$$N_h(t) = S_h(t) + E_h(t) + I_h(t) + Q(t) + R(t). \quad .$$

The mosquito population is divided into two subclasses: susceptible mosquitoes $S_m(t)$, exposed mosquitoes $E_m(t)$ and infectious mosquitoes $I_m(t)$. Thus, the total size of the mosquito population at any time t is denoted by

$$N_m(t) = S_m(t) + E_m(t) + I_m(t). \quad .$$

The transmission of ZikV between human and mosquito is governed by some basic epidemiological parameters. Susceptible individuals are recruited into the human population either by birth or immigration at a rate β_1, and that of mosquito population at a rate β_2. When a mosquito carrying ZikV bite a susceptible human, the virus is passed onto the human and the person becomes exposed at a rate τ_1. After the viruses have completed their period of latency, exposed individuals move to the infected class $I_h(t)$ at a rate α_1. Similarly, when an uninfected mosquito bites an infectious human, it carries the virus and so moves to the exposed class $E_m(t)$ at rate α_2. The exposed mosquito then

becomes infectious and enters the infected class $I_m(t)$ after a given time at a rate τ_3. ZikV can also be transmitted from human to human through the blood and semen of an infected human. The rate of this transmission is denoted as τ_2. The fraction of births that are infected is denoted as ⁂ After some time, the infectious human recovers and moves to the recovered class $R_h(t)$. However, to reduce the rates of transmission by contacts, infected individuals may be migrated to isolated class $Q(t)$, where they recover as well and move to the recovered class. A fraction (1– ⁂ of the

recovered humans are immune permanently to the disease while ⁂ of recovered human has some immunity to the disease only for some period of time and later loses the immunity to become susceptible again.

The human natural and disease-induced death rates are denoted respectively as μ_1 and δ_1. The average life of mosquitoes is $1/\mu_2$, where μ_2 is the mosquito death rate and it is assumed that there is no mosquito mortality due to presence of virus. However there is an additional human-induced death for mosquitoes, denoted as δ_2. Other parameters are as given in table 2.1.

The Fig 2.1 below shows the dynamics of the model with the inflow and outflow in each compartment of both populations.

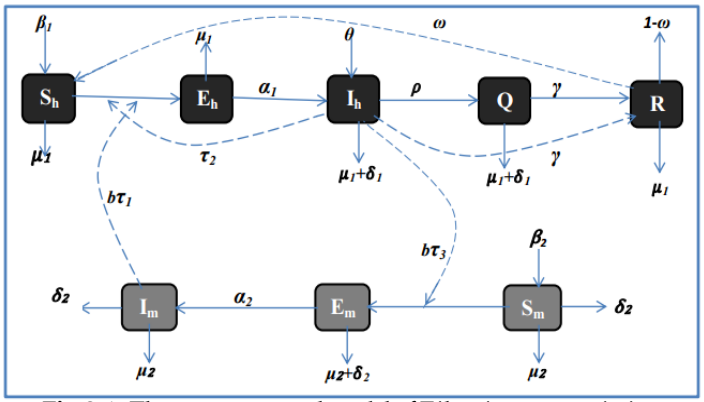

Fig 2.1: *The compartmental model of Zika virus transmission between humans and mosquitoes.*

The model is formulated as a system of coupled ordinary differential equation as:

$$\frac{dS_h}{dt} = (1-\theta I_h)\beta_1 - \mu_1 S_h - (b\tau_1 I_m + \tau_2 I_h)S_h + \varepsilon\omega R$$

$$\frac{dE_h}{dt} = (b\tau_1 I_m + \tau_2 I_h)S_h - (\mu_1 + \alpha_1)E_h$$

$$\frac{dI_h}{dt} = \alpha_1 E_h + \theta\beta_1 I_h - (\mu_1 + \delta_1 + \rho + \gamma)I_h$$

$$\frac{dQ}{dt} = \rho I_h - (\mu_1 + \delta_1 + \gamma)Q \qquad (2.1)$$

$$\frac{dR}{dt} = \gamma(I_h + Q) - \mu_1 + (1-\varepsilon)\omega + \varepsilon\omega)R$$

$$\frac{dS_m}{dt} = \beta_2 - (\mu_2 + \delta_2)S_m - b\tau_3 I_h S_m$$

$$\frac{dE_m}{dt} = b\tau_3 I_h S_m - (\mu_2 + \delta_2 + \alpha_2)E_m$$

$$\frac{dI_m}{dt} = \alpha_2 E_m - (\mu_2 + \delta_2)I_m;$$

together with the initial conditions:

$$S_h(t_0) = S_{h0}, E_h(t_0) = E_{h0}, I_h(t_0) = I_{h0}, Q(t_0) = Q_0, R(t_0) = R_0,$$
$$S_m(t_0) = S_{m0}, E_m(t_0) = E_{m0}, I_m(t_0) = I_{m0};$$

Positivity of Solution

Recall that $N_h = S_h + E_h + I_h + Q + R$ and $N_m = S_m + E_m + I_m$ represent human and mosquito population respectively, so that from the system (2.1), we have

$$\frac{dN_h}{dt} = \beta_1 - \mu_1 N_h - \delta_1(I_h + Q) \text{ and}$$
$$\frac{dN_m}{dt} = \beta_2 - (\mu_2 + \delta_2)N_m . \qquad (2.2)$$

Let $D = \{(S_h, E_h, I_h, Q, R, S_m, E_m, I_m) \in \mathbb{R}^8 : N_h \le \frac{\beta_1}{\mu_1 N_h}; N_m \le \frac{\beta_2}{(\mu_1 + \delta_2)N_m}\}$,

Then it is necessary to show that the solution of the system (2.1) is non-negative in the domain D, for all time $t > 0$, since the model represents human and mosquito populations.

The state variables and parameters used for the transmission model are described in the following table.

TABLE 1
DESCRIPTION OF VARIABLES AND PARAMETERS USED IN THE MODEL

State Variables and Parameters	Description
$S_h(t)$	Number of humans susceptible to ZikV infection at time t
$E_h(t)$	Number of humans exposed to ZikV infection at time t
$I_h(t)$	Number of infected humans at time t
$Q(t)$	Number of isolated humans at time t
$R(t)$	Number of recovered humans at time t
$S_m(t)$	Number of susceptible mosquitoes at time t
$E_m(t)$	Number of exposed mosquitoes at time t
$I_m(t)$	Number of infected mosquitoes at time t
N_h	Total human population
N_m	Total mosquitoes population
β_1, β_2	Recruitment term of the susceptible humans and mosquitoes
b	Biting rate per human per mosquito
τ_1	Probability that a bite by an infectious mosquito results in transmission of disease to human
τ_2	Rate of transmission from contact between susceptible and infected humans
$\tau 3$	Probability that a bite results in transmission of parasite to a susceptible mosquito
θ	Fraction of births that are infected
α_1, α_2	Per capita rates of progression from the exposed state to the infectious state for humans and mosquitoes respectively
ρ	Per capita rate of progression of humans from the infected state to the isolated state
γ	Recovery rate for humans from both the infectious and isolated states
ω	Per capita immunity loss rate
ε	Fraction of recovered individuals that lose their immunity
μ_1, μ_2	Human and mosquito natural death rates respectively
δ_1	Disease-induced death rate for humans
δ_2	Extra human-induced death for mosquitoes

THEOREM 2.1: *Suppose*

$S_h(0),\ E_h(0),\ I_h(0),\ Q(0),\ R(0),\ S_m(0),\ E_m(0),\ I_m(0)$

are non-negative initial conditions, then

$S_h(t),\ E_h(t),\ I_h(t),\ Q(t),\ R(t),\ S_m(t),\ E_m(t),\ I_m(t)$

are also non-negative, for all $t > 0$.

In particular, the closed set

$$D = \left\{ (S_h, E_h, I_h, Q, R, S_m, E_m, I_m) \in \mathbb{R}^8 : N_h \le \frac{\beta_1}{\mu_1 N_h};\ N_m \le \frac{\beta_2}{(\mu_1 + \delta_2) N_m} \right\}$$

is positively invariant and attracting with respect to the model equation (2.1).

Proof: Suppose

$\{S_h(0),\ E_h(0),\ I_h(0),\ Q(0),\ R(0),\ S_m(0),\ E_m(0),\ I_m(0)\}$

is a set of non-negative initial conditions, and that the maximum interval of existence of the corresponding solution is $[0, t_{max}]$. Let

$$t^* = Sup\{0 < t < t_{\max} : S_h, E_h, I_h, Q, R, S_m, E_m, I_m > 0, \forall [0, t]\}.$$

We need to show that each of the variables $S_h, E_h, I_h, Q, R, S_m, E_m, I_m > 0$, for all $t \ge 0$.

First, we show that $S_h > 0$, for all $t \ge 0$.

Suppose this is not true; let $\exists\ t^* > 0$ such that

$S_h(t^*) = 0,\ S_h'(t^*) \le 0$ and $S_h, E_h, I_h, Q, R, S_m, E_m, I_m > 0$ for $0 < t < t^*$. Then from (2.1),

$$S_h'(t^*) = \left(1 - \theta I_h(t^*)\right)\beta_1 - \left(\mu_1 + b\tau_1 I_m + \tau_2 I_h\right) S_h(t^*) + \varepsilon\omega R(t^*)$$

$$= \left(1 - \theta I_h(t^*)\right)\beta_1 + \varepsilon\omega R(t^*) > 0.$$

This is a contradiction. Hence, $S_h(t) > 0$, for all $t > 0$.

It can be shown in a similar way that all the other variables too are non-negative at t^*.

Now from (2.1), we have $\frac{dN_h}{dt} \le \beta_1 - \mu_1 N_h$ and $\frac{dN_m}{dt} \le \beta_2 - (\mu_2 + \delta_2) N_m$.

It follows that $\frac{dN_h}{dt} < 0$, if $N_h(t) > \frac{\beta_1}{\mu_1}$;

and $\frac{dN_m}{dt} < 0$, if $N_m(t) > \frac{\beta_2}{\mu_2 + \delta_2}$.

Thus by the standard comparison theorem in (Lakshmickantham *et al.*, 1999) [5], we have

$$N_h(t) \le N_h(0) e^{\mu_1(t)} \frac{\beta_1}{\mu_1}\left(1 - e^{-\mu_1(t)}\right);\ \text{and}$$

$$N_m(t) \le N_m(0) e^{(\mu_2 + \delta_2)(t)} + \frac{\beta_2}{\mu_2 + \delta_2}\left(1 - e^{-(\mu_2 + \delta_2)(t)}\right).$$

In particular, $N_h(t) \le \frac{\beta_1}{\mu_1}$, if $N_h(0) \le \frac{\beta_1}{\mu_1}$;

and $N_m(t) \le \frac{\beta_2}{\mu_2 + \delta_2}$, if $N_m(0) \le \frac{\beta_2}{\mu_2 + \delta_2}$.

Therefore D is positively invariant.

Furthermore, if $N_h(0) > \frac{\beta_1}{\mu_1}$ and $N_m(0) > \frac{\beta_2}{\mu_2 + \delta_2}$, then either the solution enters D in finite time or $N_h(t)$ approaches $\frac{\beta_1}{\mu_1}$ and $N_m(t)$ approaches $\frac{\beta_2}{\mu_2 + \delta_2}$, and the infection variables $I_h + Q$ approaches 0.

Thus D is attracting (i.e. all solutions $\mathbb{R}_+^8$ eventually enters D).

Hence, the model (2.1) is both epidemiologically feasible and mathematically well posed.

3. MATHEMATICAL ANALYSIS OF THE MODEL

In this section we carry out qualitative analysis of the model (2.1) to investigate existence and stability of the steady states.

3.1. Existence of Disease-Free Equilibrium Point, E_0

Disease-free equilibrium points are steady-state solutions where there is no ZikV infection (i.e. $I_h = I_m = 0$), while the steady-state solution of the system (2.1) is obtained by setting

$$\frac{dS_h}{dt} = \frac{dE_h}{dt} = \frac{dI_h}{dt} = \frac{dQ}{dt} = \frac{dR}{dt} = \frac{dS_m}{dt} = \frac{dE_m}{dt} = \frac{dI_m}{dt} = 0 \text{ in (2.1).}$$

Thus, the disease-free equilibrium point, E_0, for the ZikV model (2.1) yields

$$E_0 = \left(\frac{\beta_1}{\mu_1}, 0, 0, 0, 0, \frac{\beta_2}{\mu_2 + \delta_2}, 0, 0 \right) \qquad (2.4)$$

3.2. Derivation of Basic Reproduction Number, R_0

An important notion in epidemiological models is the basic reproduction number, usually denoted by R_0. It is a threshold value that is often used to measure the spread of a disease. It is defined as the number of secondary infections in humans that arise as a result of a single infected individual being introduced in a fully susceptible population. When $R_0 < 1$, it implies that on average an infectious individual infects less than one person throughout his/her infectious period and in this case the disease is wiped out. On the other hand, when $R_0 > 1$, then on average every infectious individual infects more than one individual during his/her infectious period and the disease persists in the population.

The derivation of basic reproduction number is essential in order to assess the local stability of the system (2.1). To do this, we employ the method of next generation matrix described by (Driessche and Watmough [15].

We have the transmission and transition matrices to be given respectively as

$$\mathcal{F} = \begin{pmatrix} (b\tau_1 I_m + \tau_2 I_h) S_h \\ \theta\beta I_h \\ 0 \\ b\tau_3 I_h S_m \\ 0 \end{pmatrix} \text{ and } \mathcal{V} = \begin{pmatrix} (\mu_1 + \alpha_1) E_h \\ (\mu_1 + \delta_1 + \gamma + \rho) I_h - \alpha_1 E_h \\ (\mu_1 + \delta_1 + \gamma) Q - \rho I_h \\ (\mu_2 + \delta_2 + \alpha_2) E_m \\ (\mu_2 + \delta_2) I_m - \alpha_2 E_m \end{pmatrix}.$$

The Jacobian matrices for $\mathcal{F}$ and $\mathcal{V}$ at DFE (E_0) are evaluated as follows:

$$F = D\mathcal{F}\big|_{E_0} = \begin{pmatrix} 0 & \frac{\beta_1\tau_2}{\mu_1} & 0 & 0 & \frac{b\beta_1\tau_1}{\mu_1} \\ 0 & \theta\beta_1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{b\beta_2\tau_3}{\mu_2 + \delta_2} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}, \quad \text{and}$$

$$V = D\nu|_{E_0} = \begin{pmatrix} \mu_1 + \alpha_1 & 0 & 0 & 0 & 0 \\ -\alpha_1 & \mu_1 + \delta_1 + \gamma + \rho & 0 & 0 & 0 \\ 0 & -\rho & \mu_1 + \delta_1 + \gamma & 0 & 0 \\ 0 & 0 & 0 & \mu_2 + \delta_2 + \alpha_2 & 0 \\ 0 & 0 & 0 & -\alpha_2 & \mu_2 + \delta_2 \end{pmatrix}.$$

$$F.V^{-1} = \begin{pmatrix} \frac{\beta_1\tau_2\alpha_1}{\mu_1(\mu_1+\alpha_1)(\mu_1+\delta_1+\gamma+\rho)} & \frac{\beta_1\tau_2}{\mu_1(\mu_1+\delta_1+\gamma+\rho)} & 0 & \frac{b\beta_1\tau_2\alpha_2}{\mu_1(\mu_2+\delta_2)(\mu_2+\delta_2+\alpha_2)} & \frac{b\beta_1\tau_1}{\mu_1(\mu_2+\delta_2)} \\ \frac{\theta\beta_1\alpha_1}{(\mu_1+\alpha_1)(\mu_1+\delta_1+\gamma+\rho)} & \frac{\theta\beta_1}{\mu_1+\delta_1+\gamma+\rho} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ \frac{b\beta_2\tau_3\alpha_1}{(\mu_1+\alpha_1)(\mu_1+\delta_1+\gamma+\rho)(\mu_2+\delta_2)} & \frac{b\beta_2\tau_3}{(\mu_1+\delta_1+\gamma+\rho)(\mu_2+\delta_2)} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

Now, the basic reproduction number, which equals $\rho(F.V^{-1})$, is obtained as the spectra radius (i.e. the dominant eigenvalue) of the product $F.V^{-1}$ thus:

$$R_0 = \frac{1}{2}\left\{ \left[\frac{\beta\tau\alpha}{\mu_1(\mu_1+\alpha_1)(\mu_1+\delta_1+\gamma+\rho)} + \frac{\theta\beta}{\mu_1+\delta_1+\gamma+\rho} \right] + \sqrt{\left[\frac{\beta\tau\alpha}{\mu_1(\mu_1+\alpha_1)(\mu_1+\delta_1+\gamma+\rho)} + \frac{\theta\beta}{\mu_1+\delta_1+\gamma+\rho} \right]^2 + \frac{4b^2\beta\beta\tau\tau\alpha\alpha}{\mu_1(\mu_1+\delta_1+\gamma+\rho)(\mu_2+\delta_2)}} \right\}$$

(2.5)

3.3. Stability of Disease-free Equilibrium Point

Theorem 3.1: *If* $\left(\theta\beta_1 + \frac{\beta_1\tau_2\alpha_1}{\mu_1(\mu_1+\alpha_1)}\right) < (\mu_1+\delta_1+\gamma+\rho)$, *then the disease-free equilibrium is locally asymptotically stable. Otherwise, it is unstable.*

Proof: The stability of the disease-free equilibrium is determined by the eigenvalues of the Jacobian matrix of the full system (2.1), evaluated at the disease-free equilibrium point, given by:

$$J\big|_{E_0} = \begin{pmatrix}
-\mu_1 & 0 & -\left(\theta\beta_1 + \frac{\beta_1\tau_2}{\mu_1}\right) & 0 & \varepsilon\omega & 0 & 0 & -\frac{b\beta_1\tau_1}{\mu_1} \\
0 & -(\mu_1+\alpha_1) & \frac{\beta_1\tau_2}{\mu_1} & 0 & 0 & 0 & 0 & \frac{b\beta_1\tau_1}{\mu_1} \\
0 & \alpha_1 & -(\mu_1+\delta_1+\gamma+\rho-\theta\beta_1) & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & \rho & -(\mu_1+\delta_1+\gamma) & 0 & 0 & 0 & 0 \\
0 & 0 & \gamma & \gamma & -(\mu_1+(1-\varepsilon)\omega+\varepsilon\omega) & 0 & 0 & 0 \\
0 & 0 & -\frac{b\beta_2\tau_3}{\mu_2+\delta_2} & 0 & 0 & -(\mu_2+\delta_2) & 0 & 0 \\
0 & 0 & \frac{b\beta_2\tau_3}{\mu_2+\delta_2} & 0 & 0 & 0 & -(\mu_2+\delta_2+\alpha_2) & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & \alpha_2 & -(\mu_2+\delta_2)
\end{pmatrix}$$

This matrix can be reduced into an upper triangular matrix as

$$\begin{pmatrix}
-\mu_1 & 0 & -\left(\theta\beta_1 + \frac{\beta_1\tau_2}{\mu_1}\right) & 0 & \varepsilon\omega & 0 & 0 & -\frac{b\beta_1\tau_1}{\mu_1} \\
0 & -(\mu_1+\alpha_1) & \frac{\beta_1\tau_2}{\mu_1} & 0 & 0 & 0 & 0 & \frac{b\beta_1\tau_1}{\mu_1} \\
0 & 0 & -\left[\mu_1+\delta_1+\gamma+\rho-\left|\theta\beta_1+\frac{\beta_1\tau_2\alpha_1}{\mu_1}\right|\right] & 0 & 0 & 0 & 0 & \frac{b\beta_1\tau_1\alpha_1}{\mu_1} \\
0 & 0 & 0 & -(\mu_1+\delta_1+\gamma) & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & -(\mu_1+(1-\varepsilon)\omega+\varepsilon\omega) & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & -(\mu_2+\delta_2) & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & -(\mu_2+\delta_2+\alpha_2) & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & -(\mu_2+\delta_2)
\end{pmatrix}$$

whose eigenvalues are obtained to be:

$$\lambda_1 = -\mu_1,\ \lambda_2 = -(\mu_1+\delta_1+\gamma),\ \lambda_3 = -(\mu_1+\alpha_1),\ \lambda_4 = -(\mu_2+\delta_2),\ \lambda_5 = -(\mu_2+\delta_2),$$
$$\lambda_6 = -(\mu_2+\delta_2+\alpha_2),\ \lambda_7 = -(\mu_1+\omega),\ \lambda_8 = -\left[\mu_1+\delta_1+\gamma+\rho-\left(\theta\beta_1+\frac{\beta_1\tau_2\alpha_1}{\mu_1(\mu_1+\alpha_1)}\right)\right].$$

Now if $\left(\theta\beta_1 + \frac{\beta_1\tau_2\alpha_1}{\mu_1(\mu_1+\alpha_1)}\right) < (\mu_1+\delta_1+\gamma+\rho)$, then all the eigenvalues are real, distinct and negative. Hence, the disease-free

$$\left(1 - \frac{\beta \tau \alpha}{\mu_1(\mu_1+\alpha_1)} \right) < 1 \quad 1$$

equilibrium is locally asymptotically stable. Otherwise, the disease-free equilibrium is unstable. This completes the proof.

3.4. Existence of Endemic Equilibrium Point, E_e

In addition to the disease-free equilibrium point E_0, we shall show that the model (2.1) has an endemic equilibrium point, E_e. The endemic equilibrium point is a positive steady state solution where the disease persists in the population (i.e. if $I_h \neq I_m \neq 0$).

Let $E_e = \left(S_h^*, E_h^*, I_h^*, Q^*, R^*, S_m^*, E_m^*, I_m^*\right)$ (2.6)

be a nontrivial equilibrium of the model equation (2.1); i.e. all components of E_e are positive. By setting

$\frac{dS_h}{dt} = \frac{dE_h}{dt} = \frac{dI_h}{dt} = \frac{dQ}{dt} = \frac{dR}{dt} = \frac{dS_m}{dt} = \frac{dE_m}{dt} = \frac{dI_m}{dt} = 0$ in (2.1),

and solving simultaneously, we obtained:

$$S_h^* = \frac{1}{\mu}\left\{\beta_1 - \left[\theta\beta_1 + \frac{(\mu_1+\alpha_1)(\mu_1+\delta_1+\gamma+\rho-\theta\beta_1)}{\alpha_1} - \frac{\varepsilon\omega\gamma(\mu_1+\delta_1+\gamma+\rho)}{(\mu_1+\delta_1+\gamma)\left(\mu_1+(1-\varepsilon)\omega+\varepsilon\omega\right)}\right]\right\} I_h^*$$

$$E_h^* = \frac{\mu_1+\delta_1+\gamma+\rho-\theta\beta_1}{\alpha_1} I_h^*$$

$$Q^* = \frac{\rho}{\mu_1+\delta_1+\gamma} I_h^*$$

$$R^* = \frac{\gamma(\mu_1+\delta_1+\gamma+\rho)}{(\mu_1+\delta_1+\gamma)\left(\mu_1+(1-\varepsilon)\omega+\varepsilon\omega\right)} I_h^*$$

$$S_m^* = \frac{1}{\mu_2+\delta_2}\left[\beta_2 - \frac{(\mu_2+\delta_2+\alpha_2)(\mu_2+\delta_2)}{\alpha_2}\right] I_m^*$$

$$E_m^* = \frac{\mu_2+\delta_2}{\alpha_2} I_m^*,$$

where

$$I_h^* = \frac{(\mu_2+\delta_2)(\mu_2+\delta_2+\alpha_2)\left[\beta_2 - 2\right]}{b\tau_3\left\{(\mu_2+\delta_2)^2\left[\beta_2-2\right]-1\right\}\left[\beta_2(\mu_2+\delta_2)\alpha_2 - 2(\mu_2+\delta_2+\alpha_2)\right]}$$

$$I_m^* = \frac{\beta_2}{\mu_2+\delta_2}\left[\frac{\alpha_2}{\beta_2(\mu_2+\delta_2)\alpha_2 - 2(\mu_2+\delta_2+\alpha_2)}\right]$$

Hence, an endemic equilibrium point,

$E_e = \left(S_h^*, E_h^*, I_h^*, Q^*, R^*, S_m^*, E_m^*, I_m^*\right)$ exist and it is unique.

3.5. Sensitivity Analysis of the Reproduction Number

Sensitivity analysis is an important notion in epidemiology. It shows how important each parameter is to disease transmission. Such information is crucial both to experimental design, and to data assimilation and reduction of complex nonlinear model [10]. Sensitivity Analysis is commonly used in determining the responsiveness of model prediction to parameter values, since there are usually errors in data collection and presumed parameter values. It is used to determine parameters that have high impact on the R_0 and that should be targeted by intervention strategies. Sensitivity indices allows us to measure the relative changes in a variable when a parameter changes.

The normalized forward sensitivity index of R_0 that depends differentially on a parameter p is defined by

$$\chi_p^{R_0} = \frac{\partial R_0}{\partial p} \cdot \frac{p}{R_0}.$$

Given this explicit formula for R0, we can easily derive an analytical expression for the sensitivity of R_0 with respect to each parameter that comprises it. The obtained values are given in table 2 and fig. 2 below, which represent the sensitivity index for the base line parameter values in table 3 From the index table and chart, it was revealed that the most sensitive parameters are: human recruitment rate,

TABLE 2
SENSITIVITY INDICES OF R_0

PARAMETERS	SIGNS	VALUES
b	+	0.0926720783
β_1	+	0.9853663962
β_2	+	0.0146336039
θ	+	0.0016342850
α_1	+	0.0237044593
α_2	+	0.0075812647
τ_1	+	0.0146336039
τ_2	+	0.9705693638
τ_3	+	0.0146336039
μ_1	–	0.9672929948
μ_2	–	0.0197096481
γ	–	0.4821272413
ρ	–	0.4908931910
δ_1	–	0.0002454466
δ_2	–	0.0571388244

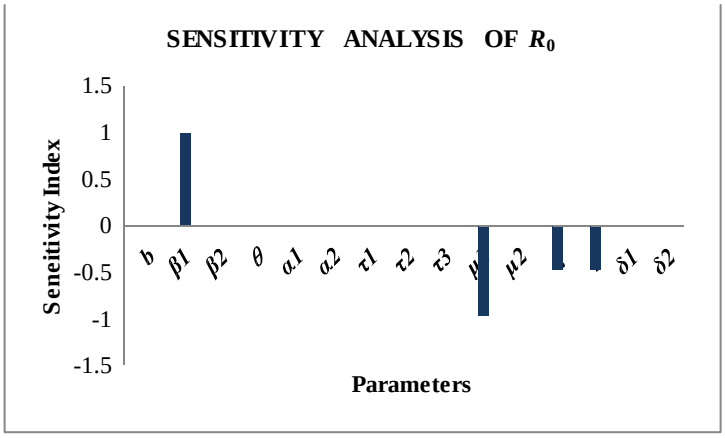

Fig. 3.1: Sensitivity Indices of R_0

human-human transmission rate and human death rate. Other parameters like recovery and isolation rates are also sensitive to the reproduction number. By a way of illustration, $\chi_{\tau_2}^{R_0} = +0.97$ means that increasing (or decreasing) τ_2 by 10% increases (or decreases) R_0 by 9.7%; while $\chi_{\rho}^{R_0} = -0.49$ means that increasing (or decreasing) ρ by 10% decreases (or increases) R_0 by 4.9%.

4. NUMERICAL RESULTS AND DISCUSSION

The numerical simulation for the model was carried out by maple software using differential transformation method to show the effects of isolation, recovery and vector elimination on the spread of zika virus disease.

We used some of the parameter values compatible with mosquito-borne diseases as given in the table 3 below, and by considering the initial conditions:

$S_h(0) = 500, E_h(0) = 250, I_h(0) = 150, Q(0) = 100, R(0) = 50,$

$S_m(0) = 750, E_m(0) = 400, I_m(0) = 150.$

TABLE 3

PARAMETER VALUES USED FOR THE MODEL

Parameters	Description	Values	Source
β_1	Recruitment term of the susceptible humans	0.01547	[4]
β_2	Recruitment term of the susceptible mosquitoes	0.07	[8]
b	Biting rate per human per mosquito	0.12	[8]
τ_1	Probability that a bite by an infectious mosquito results in transmission of disease to human	0.40	[11]
τ_2	Transmission coefficient from contact between susceptible and infected humans	0.25	Assumed
τ_3	Probability that a bite results in transmission of parasite to a susceptible mosquito	0.35	[11]
θ	Fraction of births that are infected	0.001	[11]
α_1	Progression rate from the exposed state to the infectious state for humans	0.20	Estimated
α_2	Progression from the exposed state to the infectious state for mosquitoes	0.20	Estimated
ρ	Per capital rate of progression of humans from the infected state to the isolated state	0.20	Assumed
γ	Per capital recovery rate for humans from the infectious and isolated states to the susceptible state	$(\frac{1}{4}+\frac{1}{7})^{-1}$	[4]

ω	Per capita immunity loss rate	0.30	Assumed
μ_1	Human natural death rate	0.00493	[4]
μ_2	Mosquito natural death rate	0.115	[11]
δ_2	Disease-induced death rate for humans	0.0001	Assumed
δ_1	Extra human-induced death for mosquitoes	0.10	Assumed

4.1. Presentation of Results

The results are given in Fig 4.1 – Fig 4.8 to illustrate the system's behaviour for different values of the model's parameters.

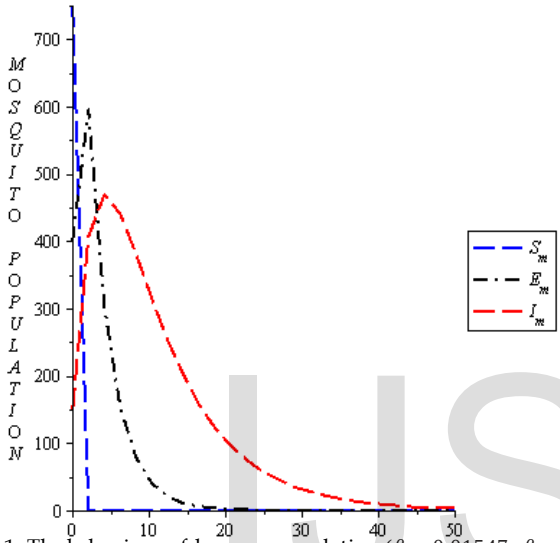

Fig. 4.1: The behaviour of human population ($\beta_1 = 0.01547$, $\beta_2 = 0.05$, $\theta = 0.001$, $\mu_1 = 0.00493$, $\mu_2 = 0.115$, $\delta_1 = 0.0001$, $\delta_2 = 0.1$, $\gamma = 11/56$, $\tau_1 = 0.4$, $\tau_2 = 0.25$, $\tau_3 = 0.35$, $\rho = 0.2$, $b = 0.12$, $\alpha_1 = 0.2$, $\alpha_2 = 0.2$, $\omega = 0.3$, $\phi = 0.5$).

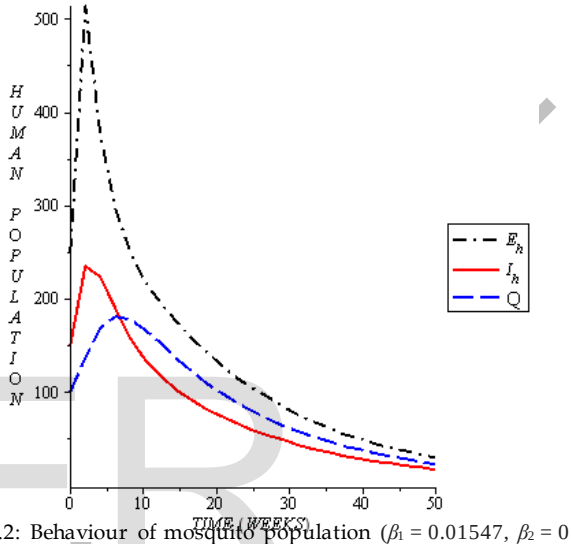

Fig. 4.2: Behaviour of mosquito population ($\beta_1 = 0.01547$, $\beta_2 = 0.05$, $\theta = 0.001$, $\mu_1 = 0.00493$, $\mu_2 = 0.115$, $\delta_1 = 0.0001$, $\delta_2 = 0.1$, $\gamma = 11/56$, $\tau_1 = 0.4$, $\tau_2 = 0.25$, $\tau_3 = 0.35$, $\rho = 0.2$, $b = 0.12$, $\alpha_1 = 0.2$, $\alpha_2 = 0.2$, $\omega = 0.3$, $\phi = 0.5$).

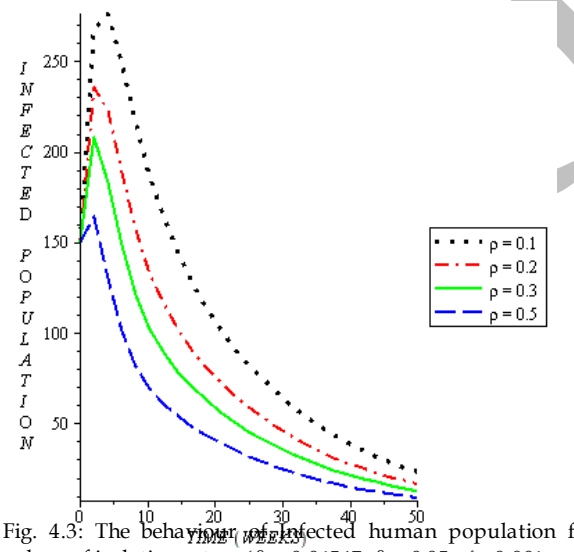

Fig. 4.3: The behaviour of infected human population for varied values of isolation rate, ρ ($\beta_1 = 0.01547$, $\beta_2 = 0.05$, $\theta = 0.001$, $\mu_1 = 0.00493$, $\mu_2 = 0.115$, $\delta_1 = 0.0001$, $\delta_2 = 0.1$, $\gamma = 11/56$, $\tau_1 = 0.4$, $\tau_2 = 0.25$, $\tau_3 = 0.35$, $b = 0.12$, $\alpha_1 = 0.2$, $\alpha_2 = 0.2$, $\omega = 0.3$, $\phi = 0.5$).

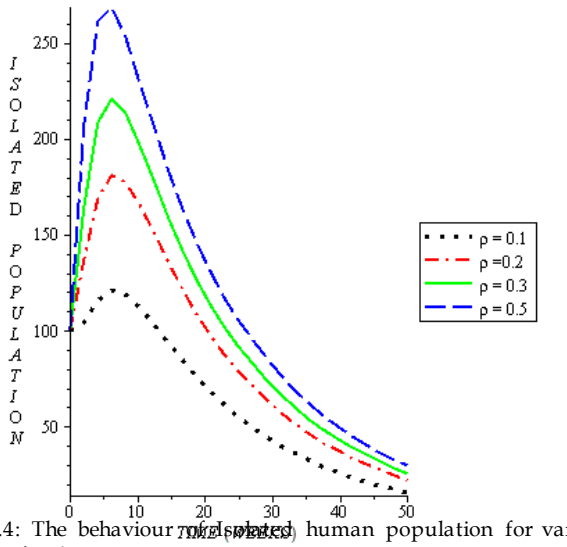

Fig. 4.4: The behaviour of isolated human population for varied values of isolation rate, ρ ($\beta_1 = 0.01547$, $\beta_2 = 0.05$, $\theta = 0.001$, $\mu_1 = 0.00493$, $\mu_2 = 0.115$, $\delta_1 = 0.0001$, $\delta_2 = 0.1$, $\gamma = 11/56$, $\tau_1 = 0.4$, $\tau_2 = 0.25$, $\tau_3 = 0.35$, $b = 0.12$, $\alpha_1 = 0.2$, $\alpha_2 = 0.2$, $\omega = 0.3$, $\phi = 0.5$).

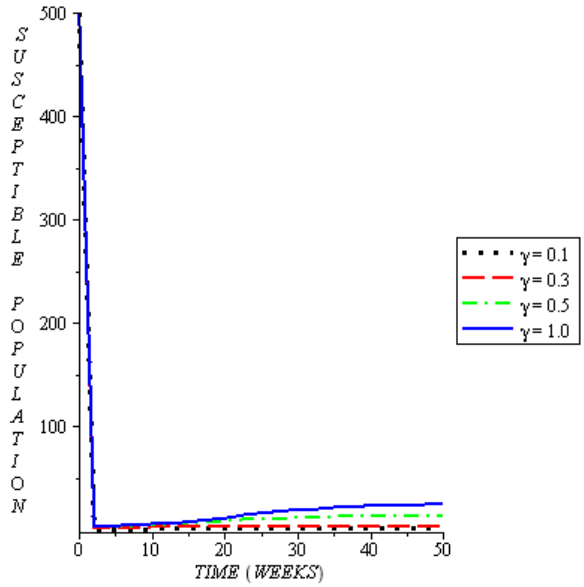

Fig. 4.5: The behaviour of Susceptible human population for varied values of recovery rate, γ ($\beta_1 = 0.01547$, $\beta_2 = 0.05$, $\theta = 0.001$, $\mu_1 = 0.00493$, $\mu_2 = 0.115$, $\delta_1 = 0.0001$, $\delta_2 = 0.1$, $\tau_1 = 0.4$, $\tau_2 = 0.25$, $\tau_3 = 0.35$, $\rho = 0.2$, $b = 0.12$, $\alpha_1 = 0.2$, $\alpha_2 = 0.2$, $\omega = 0.3$, $\gamma = 0.5$).

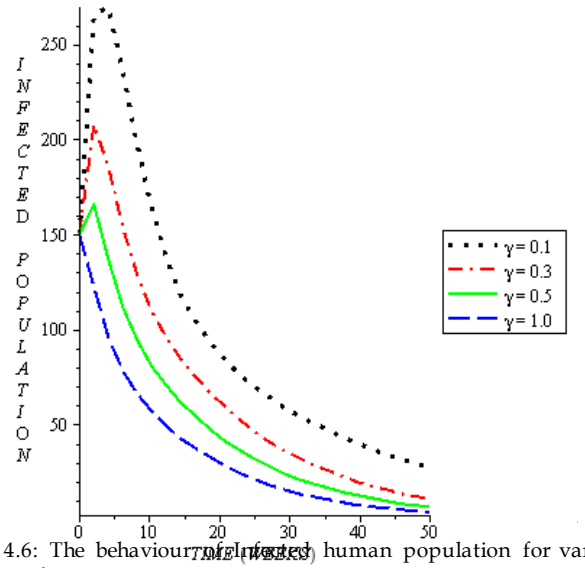

Fig. 4.6: The behaviour of Infected human population for varied values of recovery rate, γ ($\beta_1 = 0.01547$, $\beta_2 = 0.05$, $\theta = 0.001$, $\mu_1 = 0.00493$, $\mu_2 = 0.115$, $\delta_1 = 0.0001$, $\delta_2 = 0.1$, $\tau_1 = 0.4$, $\tau_2 = 0.25$, $\tau_3 = 0.35$, $\rho = 0.2$, $b = 0.12$, $\alpha_1 = 0.2$, $\alpha_2 = 0.2$, $\omega = 0.3$, $\gamma = 0.5$).

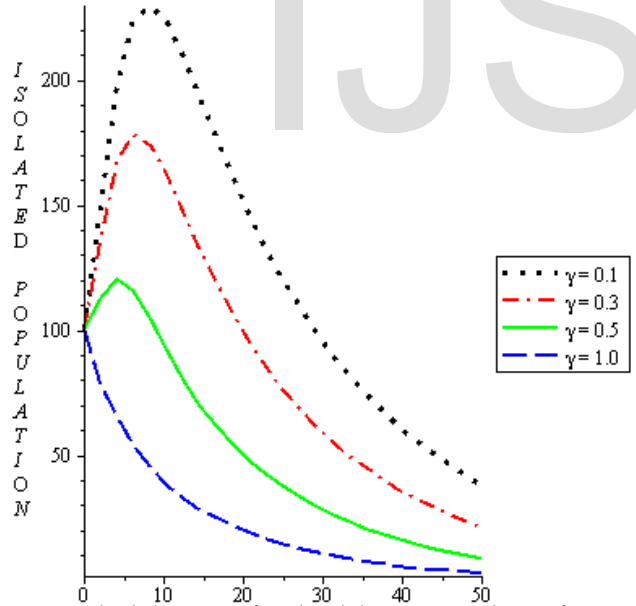

Fig. 4.7: The behaviour of Isolated human population for varied values of recovery rate, γ ($\beta_1 = 0.01547$, $\beta_2 = 0.05$, $\theta = 0.001$, $\mu_1 = 0.00493$, $\mu_2 = 0.115$, $\delta_1 = 0.0001$, $\delta_2 = 0.1$, $\tau_1 = 0.4$, $\tau_2 = 0.25$, $\tau_3 = 0.35$, $\rho = 0.2$, $b = 0.12$, $\alpha_1 = 0.2$, $\alpha_2 = 0.2$, $\omega = 0.3$, $\gamma = 0.5$).

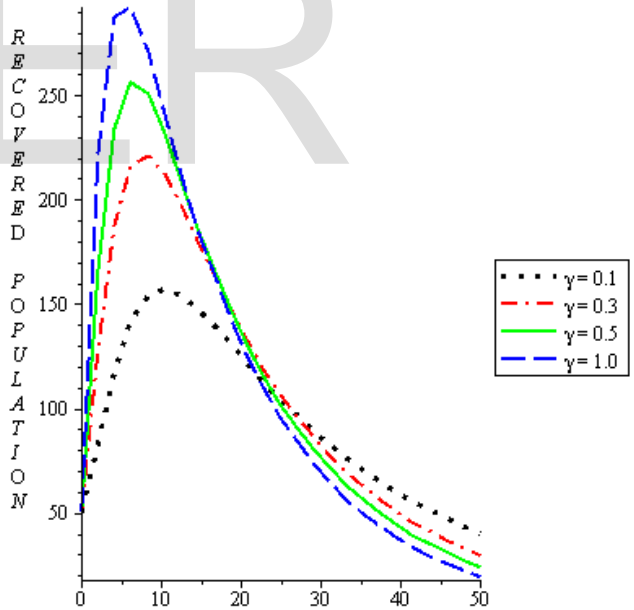

Fig. 4.8: The behaviour of Recovered human population for varied values of recovery rate, γ ($\beta_1 = 0.01547$, $\beta_2 = 0.05$, $\theta = 0.001$, $\mu_1 = 0.00493$, $\mu_2 = 0.115$, $\delta_1 = 0.0001$, $\delta_2 = 0.1$, $\tau_1 = 0.4$, $\tau_2 = 0.25$, $\tau_3 = 0.35$, $\rho = 0.2$, $b = 0.12$, $\alpha_1 = 0.2$, $\alpha_2 = 0.2$, $\omega = 0.3$, $\gamma = 0.5$).

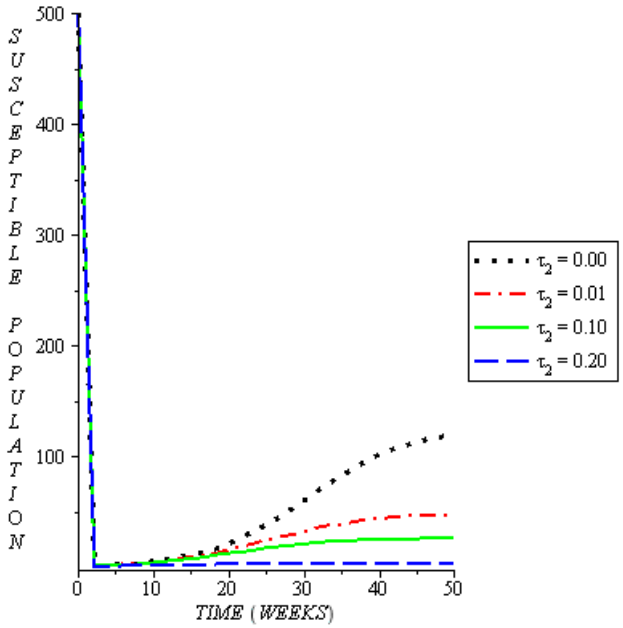

Fig. 4.9: The behaviour of Susceptible human population for varied values of human-human transmission rate, τ_2 (β_1 = 0.01547, β_2 = 0.05, = 0.001, μ_1=0.00493, μ_2 = 0.115, δ_1 = 0.0001, δ_2 = 0.1, γ =11/56, τ_1 = 0.4, τ_3 = 0.35, ρ = 0.2, b = 0.12, α_1 = 0.2, α_2 = 0.2, ω = 0.3, = 0.5).

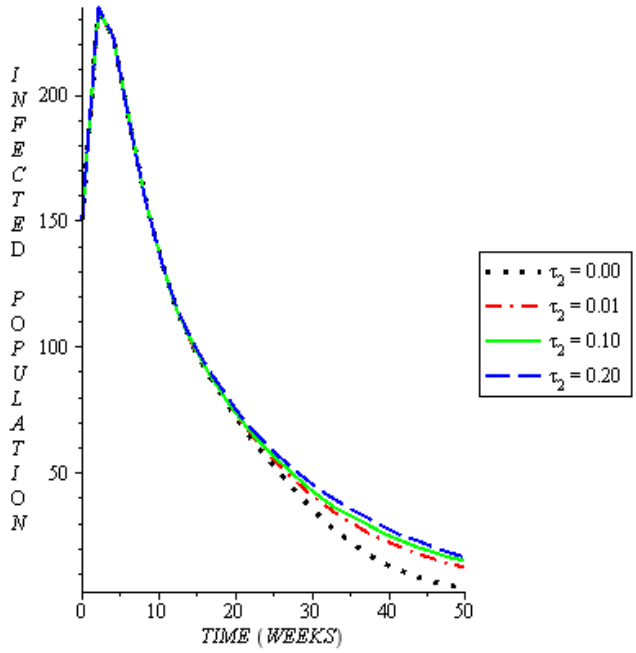

Fig. 4.10: The behaviour of Infected human population for varied values of human-human transmission rate, τ_2 (β_1 = 0.01547, β_2 = 0.05, = 0.001, μ_1=0.00493, μ_2 = 0.115, δ_1 = 0.0001, δ_2 = 0.1, γ =11/56, τ_1 = 0.4, τ_3 = 0.35, ρ = 0.2, b = 0.12, α_1 = 0.2, α_2 = 0.2, ω = 0.3, = 0.5).

4.2. Discussion on Results

Fig 4.1 and fig 4.2 show the behaviour of the solution for the selected parameter values; fig 4.1 shows the behaviour of the human population, and it is observed from the plot that there is decline in the exposed, the infected and isolated population. This implies that the disease will, at a point in time, be wiped out from the population. From fig 4.2 which shows the behaviour of the mosquito population, it can be seen that the population goes very close to zero. So, if we can work on reducing mosquitoes through source reduction (removal and modification of breeding sites), then the entire mosquito population can be eliminated, which will lead to total elimination of the Zika virus disease.

It can be observed from fig 4.3 and fig 4.4, which show the effect of isolation rate, that there is decline in infection with increase in the rate of isolation, but an increas e is seen in the isolated population as the isolation rate increases. Individuals in isolation can therefore be taken care of by treating their symptoms accordingly.

Fig 4.5 – fig 4.8 are the plots that show the effect of recovery rate, γ. From fig 4.5, it is observed that the susceptible population increases as recovery rate increases. Fig 4.6 and fig 4.7 show that there is decline in infected and isolated populations as treatment/recovery increases. The fig 4.6 and fig 4.7 further show that the infected and isolated populations decrease drastically and tend to zero for a high rate of recovery. It should be noted that individuals of the isolated population are still infectious, and they differs from the infected individual in that they are isolated to prevent their contact both with susceptible humans and mosquitoes [9]. This control measure, among others will stop/prevent outbreak of Zika virus disease. The plot in fig 4.8 shows a great deal of increase in the number of recovered individuals as recovery rate increases, as expected. However at a point, a decrease was noted in the plot. This decrease can be attributed to the fact that treatment of ZikV symptoms does not confer permanent immunity to all individuals treated. Some times after recovery, immunity is lost at a rate ω and some fraction ω of recovered individuals move to the respective susceptible

class again, while the remaining fraction (1-ω), having recovered permanently are removed from the system.

The result from our sensitivity analysis carried out in section 3 showed that one of the most sensitive parameters is the human-human transmission rate, τ_2. This is further illustrated in fig 4.9 and fig 4.10, where increase in τ_2 increases infection but decreases the susceptible population.

5. CONCLUSION

In this paper, we have formulated and analysed a compartmental model for ZikV transmission (in human and mosquito populations) and control (with isolation and symptoms treatment). The human population was divided into five compartments, while the mosquito population was divided into three compartments. We established a region where the model is epidemiologically feasible and mathematically well-posed. The existence and stability of a disease-free equilibrium point were determined. It was also shown that an endemic equilibrium point exists and it is unique.

The numerical simulations were performed to see the effects of isolation, recovery (as a result of symptoms treatment), and human-human transmission rate on the spread of the disease. Our results showed that isolation of infected individuals reduces the transmission of the ZikV infection. Also, increasing the recovery to a very high rate has significant effect of reducing infection. To aid recovery, individuals in both infected and isolated classes should get plenty of rest, drink enough fluid to prevent dehydration, and treat fever and pain with common medicines such as acetaminophen (Tylenol®) and paracetamol [1]. Also, Practices like protected sex, screening of blood prior to blood transfusion and of course isolation of infected individuals will help reduce τ_2 and hence reduction in ZikV infection.

These control measures will greatly reduce the transmission of the ZikV infection. However, efforts should be intensified in developing vaccine for ZikV disease as this would facilitate the stimulation of the immune system in producing antibodies against ZikV infection.

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