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Stability Analysis of Zika – Malaria Co-infection Model for Malaria Endemic Region

John Amoah-Mensah[1*], I. K. Dontwi[1] and E. Bonyah[2]

[1]Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.
[2]Kumasi Technical University, Kumasi, Ghana.

Authors' contributions

This work was carried out in collaboration between all authors. Author JAM designed the study, performed the analysis, wrote the protocol and it was supervised by authors IKD and EB. All authors read and approved the final manuscript.

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Abstract

This article proposes a system of nine nonlinear dynamical model to study transmission dynamics of both Zika and Malaria in malaria-endemic areas such as Kedougou in the Southeastern part of Senegal and other parts of the world where it is possible to have co-infection of the two diseases simultaneously. The model is divided into three sub-models: Zika only, Malaria only and both Zika-Malaria to address the best possible strategy to control both diseases concurrently.
Stability analysis was performed on the model to determine the disease-free and the endemic equilibria. Sensitivity analysis on the basic reproduction number indicated that by improving the recovery rate of both diseases, the basic reproduction number can be reduced considerably. It is also confirmed from Fig. 5 that, the best approach to control or eliminate the diseases is to improve the recovery rate of both diseases simultaneously. Thus increasing recovery rates are shown to have great impact in decreasing the basic reproduction number.

Keywords: Coinfection; reproduction number; local stability; global stability; sensitivity analysis.

**Corresponding author: E-mail: amoahmensahjohn@gmail.com;*

1 Introduction

Zika disease is caused by a virus which is transmitted mostly by female Aedes aegypti mosquito [1], which is also responsible for the transmission of chikungunya and dengue fever. The disease was initially discovered in a monkey in the Zika forest of Uganda in 1947 [2]. Much attention was not given until recently when it started causing harm to expectant mothers in the Americas. Mothers in this part of the world were producing microcephaly babies (children with abnormal small head and other neurological disorders), and this forced the World Health Organization (WHO) to seek for strategies in order to control or eliminate before it gains grounds in addition to the current infectious diseases hanging on the neck of the WHO. The alarming rate of the incidence in Brazil and other parts of the world also forced the world's health body, WHO to declare the virus as the international emergency concerned. Due to unavailability of sound cure or a vaccine, the Zika disease is spreading at a faster rate than expected since it begun. Since Zika disease and our known unkind friend, malaria disease, which affects those of us in West African, has similar symptoms, if Zika is not tackled at its current locations and migrates to other parts of West Africa and other regions where malaria is endemic, it may cause great havoc to pregnant women and their families, since health officials may be mistakenly treating malaria when the actual disease will be Zika. Currently, Zika has raised its ugly head in a town in Senegal called, Kedougou. Therefore Zika may even be existing in other part of West Africa which we are not aware of because the effort has not been made to test for Zika when malaria patients report at a health facility, unlike Senegal [3].

Only female Aedes aegypti mosquito bites an infected human. It has to bite during the viremia stage that is in the first several days of infection when the virus is still circulating in the human's blood. The mosquito takes up the virus, stores it in her gut and salivary glands, and then transmits it when she bites another uninfected human [4]. As part of the mode of transmission, an individual who is infected with Zika virus can infect his or her sex partner through an exchange of fluid during vaginal sex, anal sex, and likely oral sex. There has been an evidence that Zika virus is detected in the semen and vaginal fluids according to [5].

In the light of this, it is very important to know the key parameters in the transmission of the disease and come out with the measures to combat the menace.

In another development, Malaria is an old sickness that was first concentrated by Ross in the late 1800's [6]. Malaria is a vector-borne ailment which is caused by a female Anopheles mosquito. There are four types of parasites specifically: Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale and Plasmodium malariae contaminate human.

Among the parasites, Plasmodium falciparum is considered as savage [7]. Plasmodium falciparum is known to be the sort of species that is accepted to cause human diseases in Africa [8]. The disease keeps on being a noteworthy issue in sub-Sahara Africa, Asia, Central and South America and the Middle East. Right around 40% of the total populace settles in endemic ranges [9]. The disease is caused by Plasmodium parasite and is transmitted between people through the bite of the female Anopheles mosquito. It kills around 700,000 to 2.7million individuals yearly, 75% of whom are African youngsters [10]. The parasites develop into the body of human between 10-18 days, then is passed on when the mosquito injects saliva while feeding. In the human body, intestinal sickness parasites relocate to the liver, where they develop and increase. As time goes on the parasites find its way in the blood stream and continue to develop in the red blood cells. At this stage, the infected individuals begin to show symptoms like fever, chills, sweating, migraines and other influenza-like conditions. The infection can now and again create considerably more serious responses including kidney failure and passing on, particularly if not treated for a timeframe.

2 Difference between Zika Virus and Malaria

Zika infection and Malaria are both mosquito-borne sicknesses, and since the rise of Zika first in Brazil and now reaching out to different parts of the world, a lot of inquiries are being made to get some information about the difference between Zika infection and Malaria [11]. The real disparities are the way we battle the two illnesses since they are spread by two unique sorts of mosquito species, to be specific female Anopheles

for Malaria and female Aedes aegypti for Zika virus. Female anopheles mosquito bites during the evening and at first light and can give you malaria. This can be forestalled by resting in the mosquito bug spray net. Despite what might be expected, the Aedes aegypti mosquito bites amid the daytime which makes aversion more unpredictable to manage. That notwithstanding, to keep away from being bitten by the female Aedes aegypti mosquito having the infection, the medical experts recommend that utilizing creepy crawly repellant and defensive attire can likewise help in a way [12]. Also since zika infection can be transmitted through vaginal sex, anal sex, and likely oral sex there is the need to use the condom or abstain from sex [5].

To the best of my knowledge, this work has not been done by any researcher or been published. It is in this regard that a mathematical model for the Co-infection Malaria-Zika is proposed to access the effect of Zika in the Malaria endemic region. This research has become very necessary for the researcher and the public health officials because the symptoms of both diseases sometimes confuse the medical practitioners and the victims as well.

The model in this paper is a system of ordinary nonlinear differential equations and is described, formulated and analyzed below.

The paper has been organized as follows, Section 3 deals with the description of the model, the analysis of Zika only model, Malaria only model, Co-infection Malaria - Zika model, Section 4 discusses the sensitivity analysis, Section 5 presents numerical simulation and section 6 is the conclusion.

3 Model Formulation and Description

The model in this work is developed from current existing models on both diseases. This new model subdivides human population into six compartments namely: susceptible humans S_h, infectious malaria only I_m, infectious zika only I_z, both malaria and zika infectious I_{mz}, recovered from malaria only R_m and recovered from zika only R_z.The female mosquito population is also partitioned into three compartments, that is, susceptible female mosquitoes S_m, infectious female Anopheles mosquito $I_v$and infectious female Aedes aegypti mosquito I_a. People are recruited into the human population through the rate Π_h and exit through per capital natural death rate μ_h in the six human compartments or through malaria induce death rate (η) in I_m compartment. The susceptible individual in S_h compartment gets infected with malaria when he or she is bitten by an infected mosquito in the I_v compartment. Again, the susceptible individual in S_h compartment gets infected with Zika virus when he or she is bitten by an infected Aedes aegypti mosquito in the I_a compartment. An individual in I_m compartment either moves to R_m compartment after recovered from only malaria infection or moves to I_{mz} compartment and become co-infected with Zika virus when bitten by a mosquito in I_a compartment. Also, an infected Zika virus individual (I_z) moves to I_{mz} compartment when he or she becomes co-infected with malaria after being bitten by a mosquito in I_a compartment or to R_z compartment when the zika infection subsides and becomes a Zika carrier (mild zika infection). Those in R_m compartment moves to the S_h compartment for reinfection after they have lost their immunity to malaria and individuals in R_z compartment moves to S_h compartment after they have become zika free.

Mosquitoes in either I_a or I_v compartment remain in the infectious state for life or kill by natural death or insecticides. Mosquitoes are recruited into the mosquito population through the rate Π_m and exit through per capital natural death rate (μ_m) in the three mosquito compartments [13].

Total population of humans and mosquitoes are

$$N_h = S_h + I_m + I_z + I_{mz} + R_m + R_z \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (1)$$

and

$$N_m = S_m + I_v + I_a \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (2)$$

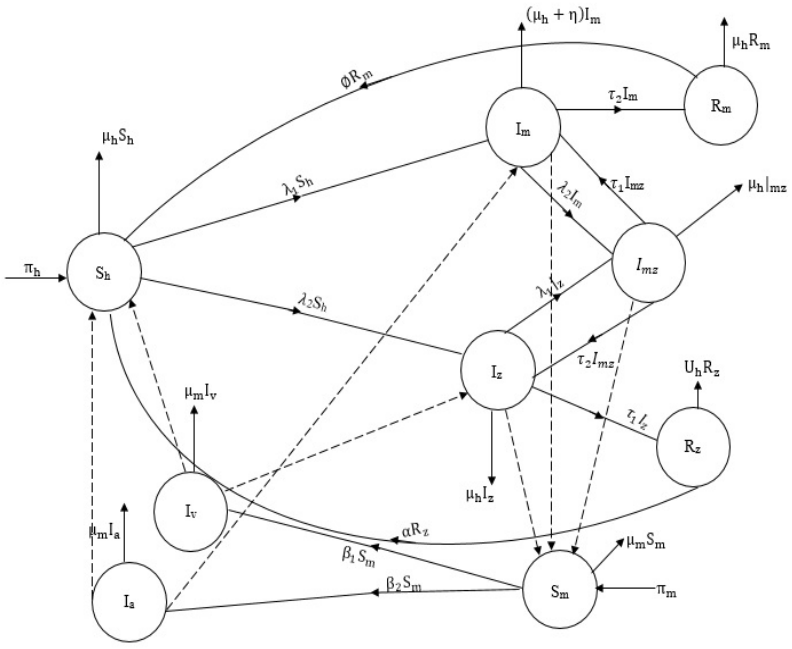

Fig. 1. Flowchart of the model

Putting all the assumptions together, the co-infection model for Malaria-Zika is given as (3) below:

$$\left.\begin{aligned}
\frac{dS_h}{dt} &= \Pi_h + \phi R_m + \alpha R_z - \mu_h S_h - \lambda_1 S_h - \lambda_2 S_h \\
\frac{dI_m}{dt} &= \lambda_1 S_h - \lambda_2 I_m - (\mu_h + \eta + \tau_2) I_m + \tau_1 I_{mz} \\
\frac{dI_z}{dt} &= \lambda_2 S_h - \lambda_1 I_z - (\mu_h + \tau_1) I_z + \tau_2 I_{mz} \\
\frac{dI_{mz}}{dt} &= \lambda_2 I_m + \lambda_1 I_z - (\mu_h + \tau_1 + \tau_2) I_{mz} \\
\frac{dR_m}{dt} &= \tau_2 I_m - (\mu_h + \phi) R_m \\
\frac{dR_z}{dt} &= \tau_1 I_z - (\mu_h + \alpha) R_z \\
\frac{dS_m}{dt} &= \Pi_m - \mu_m S_m - \beta_1 S_m - \beta_2 S_m \\
\frac{dI_m}{dt} &= \beta_1 S_m - \mu_m I_v \\
\frac{dI_a}{dt} &= \beta_2 S_m - \mu_m I_a
\end{aligned}\right\} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (3)$$

With the force of infection

$$\lambda_1 = \frac{\beta_h I_v}{N_h}, \lambda_2 = \frac{\sigma_z I_a}{N_h}, \beta_1 = \frac{\beta_v (I_m + I_{mz})}{N_h}, \beta_2 = \frac{\sigma_a (I_z + I_{mz})}{N_h} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (4)$$

In this area, we present the basic results concerning the model (3). The following theorem portrays the region within which the model will be examined in the subsequent sections.

Theorem 1: If the initial state variables are non-negative i.e.

$$\begin{pmatrix} S_h(t) \geq 0, I_m(t) \geq 0, I_z(t) \geq 0, I_{mz}(t) \geq 0, R_m(t) \geq 0, R_z(t) \geq 0, S_m(t) \geq 0, I_v(t) \geq 0, \\ I_a(t) \geq 0, \end{pmatrix}$$

then they remain so i.e.

$$(S_h(t) \geq 0, I_m(t) \geq 0, I_z(t) \geq 0, I_{mz}(t) \geq 0, R_m(t) \geq 0, R_z(t) \geq 0, S_m(t) \geq 0, I_v(t) \geq 0, I_a(t) \geq 0)$$

for all future times. Moreover $\lim_{t \leftarrow \infty} sup\, N_h(t) \leq \frac{\Pi_h}{\mu_h}$ and $\lim_{t \leftarrow \infty} sup\ N_m(t) \leq \frac{\Pi_m}{\mu_m}$. Again, if $N_h(0) \leq \frac{\Pi_h}{\mu_h}$ and $N_m(0) \leq \frac{\Pi_m}{\mu_m}$ then $N_h(t) \leq \frac{\Pi_h}{\mu_h}$ and $N_m(t) \leq \frac{\Pi_m}{\mu_m}$.

More importantly, the region $\Omega = \Omega_h \times \Omega_m$ with

$\Omega_h = \left\{(S_h, I_m, I_z, I_{mz}, R_m, R_z) \epsilon R_+^6 | N_h = S_h + I_m + I_z + I_{mz} + R_m + R_z \leq \frac{\Pi_h}{\mu_h}\right\}$ and
$\Omega_m = \left\{(S_m, I_v, I_a) \epsilon R_+^3 | N_m = S_m + I_v + I_a \leq \frac{\Pi_m}{\mu_m}\right\}$

is positively invariant. The theorem 1 above indicates that the model (3) is biologically and epidemiologically well-posed in the region and thus, the dynamics of the model can be sufficiently studied in Ω. [14].

The co-infection model (3) above can be divided into sub-models namely Zika only model and Malaria only model. The sub-models are given as:

Zika only mode

$$\left.\begin{aligned} \frac{dS_h}{dt} &= \Pi_h + \alpha R_z - \mu_h S_h - \lambda_2 S_h \\ \frac{dI_z}{dt} &= \lambda_2 S_h - (\mu_h + \tau_1) I_z \\ \frac{dR_z}{dt} &= \tau_1 I_z - (\mu_h + \alpha) R_z \\ \frac{dS_m}{dt} &= \Pi_m - \mu_m S_m - \beta_2 S_m \\ \frac{dI_a}{dt} &= \beta_2 S_m - \mu_m I_a \end{aligned}\right\} \ldots (5)$$

and Malaria only mode

$$\left.\begin{aligned} \frac{dS_H}{dt} &= \Pi_h + \phi R_m - \mu_h S_h - \lambda_1 S_h \\ \frac{dI_m}{dt} &= \lambda_1 S_h - (\mu_h + \eta + \tau_2) I_m \\ \frac{dR_m}{dt} &= \tau_2 I_m - (\phi + \mu_h) R_m \\ \frac{dS_m}{dt} &= \Pi_m - \mu_m S_m - \beta_1 S_m \\ \frac{dI_v}{dt} &= \beta_1 S_m - \mu_m I_v \end{aligned}\right\} \ldots . (6)$$

With force of infection

$\lambda_2 = \frac{\sigma_z I_a}{N_h}$ *and* $\beta_2 = \frac{\sigma_a I_z}{N_h}$ $\qquad$ $\lambda_1 = \frac{\beta_h I_v}{N_h}$ *and* $\beta_1 = \frac{\beta_1 I_m}{N_h}$

3.1 Stability of the disease free-equilibrium (DFE)

Disease-free equilibrium (DFE) is the steady state solution where there is no infection or disease in the population. In the subsequent section, we present the various sub-models and their disease-free state.

3.1.1 Stability of the disease free-equilibrium (DFE) of Zika only model

The disease-free equilibrium of Zika only model is obtained when the right-hand side of equation (5) is set to zero and the infectious compartment also set to zero. Thus $I_z = R_z = I_a = 0$.

The (DFE) of Zika only model (5) is given as

$$E_{zv} = (S_h^* , I_z^* , R_z^* , S_m^* , I_a^*) = \left(\frac{\Pi_h}{\mu_h} , 0 , 0 , \frac{\Pi_m}{\mu_m}, 0 \right) \dots\dots\dots\dots\dots (7)$$

3.1.2 Basic reproduction number for Zika only

Using the next generation matrix method, the basic reproduction number can be defined as the average number of secondary infectious cases produced by a single infective individual in a population where everyone is susceptible. Applying the next generation matrix method of [15] the basic reproduction number of the Zika only model is the spectral radius of the matrix $\mathcal{F}_z V_z^{-1}$. Where $\boldsymbol{\mathcal{F}_z}$ and V_z are the transmission and transition matrices respectively given by

$$\mathcal{F}_z = \begin{bmatrix} 0 & \frac{\sigma_z \Pi_h}{\mu_h} \\ \frac{\sigma_a \Pi_m}{\mu_m} & 0 \end{bmatrix} \text{ and } V_z = \begin{bmatrix} (\mu_h + \tau_1) & 0 \\ 0 & \mu_m \end{bmatrix}$$

The basic reproduction number of Zika only is denoted by (R_{zv}) and is given as

$$R_{zv} = \sqrt{\frac{\sigma_a \sigma_z \Pi_m \mu_h}{(\mu_h + \tau_1)\Pi_h \mu_m^2}} \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots (8)$$

3.1.3 Local stability of disease free equilibrium point for Zika virus

Theorem2: The disease-free equilibrium point is locally asymptotically stable if $\Re_{zv} < 1$ and unstable if $\Re_{zv} > 1$.

$$J(E_{zv}) = \begin{bmatrix} -B_1 & 0 & B_2 & 0 & B_3 \\ 0 & -B_4 & 0 & 0 & B_3 \\ 0 & B_5 & -B_6 & 0 & 0 \\ 0 & -B_7 & 0 & -B_8 & 0 \\ 0 & B_7 & 0 & 0 & -B_8 \end{bmatrix} \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots (9)$$

$B_1 = \mu_h, B_2 = \alpha, B_3 = \sigma_z, B_4 = (\mu_h + \tau_1), B_5 = \tau_1, B_6 = (\mu_h + \alpha), B_7 = \frac{\sigma_a \Pi_m \mu_h}{\Pi_h \mu_m}, B_8 = \mu_m$

The diagonal entries -B_1,-$B_6$and$-B_8$, are the three eigenvalues of the Jacobian matrix [16]. Therefore, excluding their columns and corresponding rows lead to

$$J(E_{zv}) = \begin{bmatrix} -B_4 & B_3 \\ B_7 & -B_8 \end{bmatrix} \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots (10)$$

The eigenvalues of the Jacobian (10) is the characteristic equation of $|J - \lambda I = 0|$

$$J-\lambda I=\begin{vmatrix}-(B_4+\lambda) & B_3\\ B_7 & -(B_8+\lambda)\end{vmatrix}=0$$

$$\Rightarrow \lambda^2+(\mu_h+\mu_m+\tau_1)\lambda+\mu_m(\mu_h+\tau_1)[1-R_{zv}^2]=0 \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (11)$$

If $\Re_{zv}<1$ then all the coefficients of equation (11) are positive. Therefore, using Routh-Hurwitz criterion, if all the coefficients of the (11) are positive then, all the roots of the characteristic polynomial (11) have negative real parts. Hence the disease-free equilibrium of Zika only model is locally asymptotically stable $\Re_{zv}<1$.

3.1.4 Global stability of disease free equilibrium of Zika virus

Theorem 3: The DFE $\left(E_{zv}\right)$ of system of equation (5) is globally asymptotically stable if $\Re_{zv}<1$ and unstable if $\Re_{zv}>1$

Proof: We start the proof by applying the theorem on page 246 of Castillo – Chavez et al. [17]. We divide (5) into two sub-models, that is, the infectious class and un-infectious class which is denoted as χ and γ respectively. The variables χ and γ are defined as, $\chi=(I_z,I_a)$and

$\gamma=(S_h,R_z,S_m)$ respectively. Therefore, the model (5) can be written as

$$\left.\begin{aligned}\frac{d\chi}{dt}&=R(\chi,\gamma)\\ \frac{d\gamma}{dt}&=S(\chi,\gamma)\end{aligned}\right\} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (12)$$

The two valued functions $R(\chi,\gamma)$and $S(\chi,\gamma)$ are given by

$$\left.\begin{aligned}R(\chi,\gamma)&=\begin{matrix}\lambda_2S_h-(\mu_h+\tau_1)I_z\\ \beta_2S_m-\mu_mI_a\end{matrix}\\ S(\chi,\gamma)&=\begin{matrix}\Pi_h+\alpha R_z-\mu_hS_h-\lambda_2S_h\\ \tau_1I_z-(\mu_h+\alpha)R_z\\ \Pi_m-\mu_mS_m-\beta_2S_m\end{matrix}\end{aligned}\right\} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (13)$$

Now consider the reduced system

$$\left.\begin{aligned}\frac{dS_h}{dt}&=\Pi_h+\alpha R_z-\mu_hS_h\\ \frac{dR_z}{dt}&=-(\mu_h+\alpha)R_z\\ \frac{dS_h}{dt}&=\Pi_m-\mu_mS_m\end{aligned}\right. \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (14a)$$

$$\frac{d\gamma}{dt}=S(\chi,0)\begin{pmatrix}\Pi_h-\mu_hS_h\\ 0\\ \Pi_m-\mu_mS_m\end{pmatrix} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (14b)$$

Obviously, $\gamma^* = (S_h^*, R_z^*, S_m^*) = \left(\frac{\Pi_h}{\mu_h}, 0, \frac{\Pi_m}{\mu_m}\right)$ is a globally asymptotically stable equilibrium point for the reduced system $\frac{d\gamma}{dt} S(\chi, 0)$ .To show this, solve the second equation of equation (14a) to obtain $\{R_z t) e^{-(\mu_h+\alpha)t}\}$; it turns to zero as $t \longrightarrow \infty$. In the same way, the last equation in equation (14a) gives $S_m(t) = \frac{\Pi_m}{\mu_m} + \left[S_m(0) - \frac{\Pi_m}{\mu_m}\right] e^{\mu_h t} \rightarrow \frac{\Pi_m}{\mu_m}$ as $t \longrightarrow \infty$. Finally, the first equation of (14a) gives $S_h(t) = \frac{\Pi_h}{\mu_h} - \left\{\frac{\Pi_h}{\mu_h} + \left[S_h(0) - \frac{\Pi_h}{\mu_h}\right]\right\} e^{\mu_h t} \rightarrow \frac{\Pi_h}{\mu_h}$ as $t \longrightarrow \infty$. Hence the convergence of the solution of (14) is global in Ω. Clearly $R(\chi, \gamma)$ satisfies the following two conditions given as H2 in [17] namely

1). $R(\chi, \gamma) = 0$ and
2). $R(\chi, \gamma) = A\chi - \hat{R}(\chi, \gamma), \hat{R}(\chi, \gamma), \geq 0$ on Ω where

$$A = D_\chi R(\chi^*, 0) = \begin{pmatrix} -(\mu_h + \tau_1) & \sigma_z \\ \frac{\sigma_a S_m}{N_h} & -\mu_m \end{pmatrix} \text{ and } R(\chi, \gamma) = \begin{pmatrix} \widehat{R_1}(\chi, \gamma) \\ \widehat{R_2}(\chi, \gamma) \end{pmatrix} = \begin{pmatrix} \sigma_z I_a \left(\mathbf{1} - \frac{S_m}{N_h}\right) \\ \sigma_a I_z \left(\mathbf{1} - \frac{S_m}{N_h}\right) \end{pmatrix}$$

It is obvious that $R(\chi, \gamma)$ satisfies the two conditions given as H2 and in Castillo – Chavez et al. [17] on page 246, namely,

1). $R(\chi, \gamma) = 0$ and
2). $R(\chi, \gamma) = A\chi - \hat{R}(\chi, \gamma), \hat{R}(\chi, \gamma), \geq 0$

Since the terms in $\hat{R}(\chi, \gamma)$ are non-negative and the conditions H2 given in [17] also satisfied, we can conclude that the disease-free equilibrium of Zika model only is globally stable.

3.2 Stability analysis on disease free equilibrium of malaria only model below

The malaria only model of the DFE is obtained by setting the right-hand side of equation (6) to zero and also to set infectious class to zero. The (DFE) of the Malaria only model is given as

$$E_{ma} = (\ S_h^*\ ,\ I_m^*\ ,\ R_m^*\ ,\ S_m^*\ ,\ I_v^*\ ) = \left(\ \frac{\Pi_h}{\mu_h},\ 0\ ,\ 0,\ \frac{\Pi_m}{\mu_m},\ 0\ \right) \ldots\ldots\ldots\ldots\ldots\ldots\ldots (15)$$

3.2.1 Basic reproduction number for malaria

Again, using the next generation matrix method as applied in zika only model, the basic reproduction number of the malaria only model is the spectral radius of the matrix $\mathcal{F}_m V_m^{-1}$ Where $\mathcal{F}_m$and V_m are the transmission and transition matrices respectively given by

$$\mathcal{F}_m = \begin{bmatrix} 0 & \beta_h \\ \frac{\beta_v \Pi_m \mu_h}{\Pi_h \mu_m} & 0 \end{bmatrix} \text{and } V_m = \begin{bmatrix} 0(\mu_h + \eta + \tau_2) & 0 \\ 0 & \mu_m \end{bmatrix}$$

The basic reproduction number of malaria only is denoted by R_{ma} is given as

$$R_{ma} = \sqrt{\frac{\beta_h \beta_v \Pi_m \mu_h}{(\mu_h + \eta + \tau_2)\Pi_h \mu_m^2}} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (16)$$

3.2.2 Local stability of disease free equilibrium point for malaria only model

Theorem 4: The disease-free equilibrium point of Malaria only is locally asymptotically stable if $\Re_{\text{ma}} < 1$ and unstable if $\Re_{\text{ma}} > 1$.

$$J(E_{zv}) = \begin{bmatrix} -C_1 & 0 & C_2 & 0 & C_3 \\ 0 & -C_4 & 0 & 0 & C_3 \\ 0 & C_5 & -C_6 & 0 & 0 \\ 0 & -C_7 & 0 & -C_8 & 0 \\ 0 & C_7 & 0 & 0 & -C_8 \end{bmatrix} \quad \dots\dots\dots\dots\dots\dots\dots\dots\dots (17)$$

$$C_1 = \mu_h, C_2 = \phi, C_3 = \beta_h, C_4 = (\mu_h + \eta + \tau_2), C_5 = \tau_2, C_6 = (\mu_h + \phi\ ), C_7 = \frac{\beta_v \Pi_m \mu_h}{\Pi_h \mu_m}, C_8 = \mu_m$$

The diagonal entries $-C_1$, $-C_6$ and $-C_8$ are the three of the eigenvalues of the Jacobian matrix [16]. Therefore, excluding their columns and corresponding rows leads to

$$J(E_{ma}) = \begin{bmatrix} -C_4 & C_3 \\ C_7 & -C_8 \end{bmatrix} \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots (18)$$

The eigenvalues of the Jacobian (18) is the characteristic equation of $|J - \lambda I = 0|$

$$J - \lambda I = \begin{vmatrix} -(C_4 + \lambda) & C_3 \\ C_7 & -(C_8 + \lambda) \end{vmatrix} = 0$$

$$\Rightarrow \lambda^2 + (\mu_h + \eta + \tau_2 + \mu_m)\lambda + \mu_m(\mu_h + \eta + \tau_2)[1 - R_{ma}^2] = 0 \dots\dots\dots (19)$$

If $R_{ma} < 1$, then all the coefficients of equation (19) are positive. Therefore, using Routh-Hurwitz criterion, if all the coefficients of equation (19) are positive then, all the roots of the characteristic polynomial (19) have negative real parts. Hence the disease-free equilibrium of Malaria only model is locally asymptotically stable if $R_{ma} < 1$.

3.2.3 Global stability on DFE malaria only $\left(E_{ma}\right)$

Here in this section, we try to prove the global stability of the disease-free equilibrium.

Theorem 5: The DFE$(E_{ma}\ )$of system of equation (6) is globally asymptotically stable if $R_{ma} < 1$ and unstable if $R_{ma} > 1$

Proof: The model (6) is now written as

$$\left.\begin{aligned} \frac{dW}{dt} &= E(V, W) \\ \frac{dV}{dt} &= F(V, W) \end{aligned}\right\} \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots (20)$$

Where $W = (I_m, I_v)$ and $V = S_h, R_m, S_m$

The two valued functions $E(V, W)$ (dimension 2) and $F(V, W)$ (dimension 3) are given by

$$E(V, W) = \begin{pmatrix} \lambda_1 S_h - (\mu_h + \eta + \tau_2) I_m \\ \beta_1 S_m - \mu_m I_v \end{pmatrix} \quad \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots (21a)$$

$$F(V,W)=\begin{pmatrix}\Pi_h+\phi R_m-\mu_h S_h-\lambda_1 S_h\\ \tau_2 I_m-(\mu_h+\phi)R_m\\ \Pi_m-\mu_m S_m-\beta_1 S_m\end{pmatrix} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (21b)$$

Where T is transpose. The reduced form of the system: $\frac{dV}{dt}=F(V,0)$

$$\left.\begin{aligned}\frac{dS_h}{dt}&=\Pi_h+\phi R_m-\mu_h S_h\\ \frac{dR_m}{dt}&=-(\mu_h+\phi)R_m\\ \frac{dS_m}{dt}&=\Pi_m-\mu_m S_m\end{aligned}\right\} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (22)$$

$V^*=(S_h^*,R_m^*,S_m^*)=\left(\frac{\Pi_h}{\mu_h},0,\frac{\Pi_m}{\mu_m}\right)$ is a globally asymptotically stable equilibrium point for the reduced system. $\frac{dV}{dt}=F(V,0)$ Therefore, $R_m(t)=R_m(0)e^{-(\mu_h+\alpha)t}$; it turns to zero as $t\to\infty$.

In $S_h(t)=\frac{\Pi_h}{\mu_h}+\frac{\phi}{\mu_h}\{R_m(0)e^{-(\mu_h+\phi)t}\}-\left\{\frac{\Pi_h}{\mu_h}+\left[S_h(0)-\frac{\Pi_h}{\mu_h}\right]\right\}e^{\mu_h t}\to\frac{\Pi_h}{\mu_h}$ as $t\longrightarrow\infty$. Hence the convergence of the solution (22) is global in Ω. Clearly $E(V,W)$ satisfies the following two conditions given as H2 in [17] namely.

1). $E(V,W)=0$ and
2). $E(V,W)=AW-\hat{E}(V,W),\hat{E}(V,W)\geq 0\ on\ \Omega$ where

$$A=D_W E(V^*,0)=\begin{pmatrix}-(\mu_h+\eta+\tau_2) & \beta_h\\ \frac{\beta_v S_m}{N_h} & -\mu_h\end{pmatrix}$$

and

$$\hat{E}(V,W)=\begin{pmatrix}\widehat{E_1}(V,W)\\ \widehat{E_2}(V,W)\end{pmatrix}=\begin{pmatrix}\beta_h I_v\left(1-\frac{S_h}{N_h}\right)\\ \beta_v I_m\left(1-\frac{S_m}{N_h}\right)\end{pmatrix}$$

Since the terms in $\hat{E}(V,W)$are nonnegative and the conditions H2 given in [17] above also satisfied, we can conclude that, the disease-free equilibrium of malaria is globally asymptotically stable.

3.3 Stability of the disease free-equilibrium of the co-infection model malaria-Zika

Disease free equilibrium (DFE) state of the co-infection model is given as

$$E_{mz}^*=\left(\ \frac{\Pi_h}{\mu_h},\ 0\ ,\ 0\ ,\ 0\ ,\ 0\ ,\ 0\ ,\ \frac{\Pi_m}{\mu_m}\ ,\ 0\ ,\ 0\ \right)\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (23)$$

The basic reproduction number (R_{mz}) of co-infection model is also given by

$$R_{mz}=\max\left\{\sqrt{\frac{\beta_h\beta_v\Pi_m\mu_h}{(\mu_h+\eta+\tau_2)\Pi_h\mu_m^2}}\ ,\sqrt{\frac{\sigma_a\sigma_z\Pi_m\mu_h}{(\mu_h+\tau_1)\Pi_h\mu_m^2}}\right\}$$

Representing

$$R_{ma} = \sqrt{\frac{\beta_h \beta_v \Pi_m \mu_h}{(\mu_h + \eta + \tau_2)\Pi_h \mu_m^2}} \quad \text{and} \quad R_{zv} = \sqrt{\frac{\sigma_a \sigma_z \Pi_m \mu_h}{(\mu_h + \tau_1)\Pi_h \mu_m^2}} \qquad \ldots\ldots\ldots\ldots (24)$$

3.3.1 Local stability of the DFE of the co-infection model malaria-Zika

Theorem 6: The disease-free equilibrium point is locally asymptotically stable if $R_0 < 1$ ($R_{ma} < 1 \; and \; R_{zv} < 1$) and unstable if $R_0 > 1$ ($R_{ma} > 1 \; and \; R_{zv} > 1$)

Proof

The Jacobian matrix of the system (3) at the disease-free equilibrium is given by for the matrix

$$\mathrm{J} = \begin{bmatrix} -A_1 & 0 & 0 & 0 & A_2 & A_3 & 0 & -A_4 & -A_5 \\ 0 & -A_6 & 0 & A_7 & 0 & 0 & 0 & A_4 & 0 \\ 0 & 0 & -A_8 & A_9 & 0 & 0 & 0 & 0 & A_5 \\ 0 & 0 & 0 & -A_{10} & 0 & 0 & 0 & 0 & 0 \\ 0 & A_9 & 0 & 0 & -A_{11} & 0 & 0 & 0 & 0 \\ 0 & 0 & A_7 & 0 & 0 & -A_{12} & 0 & 0 & 0 \\ 0 & -A_{13} & -A_{14} & -A_{15} & 0 & 0 & -A_{16} & 0 & 0 \\ 0 & A_{13} & 0 & A_{13} & 0 & 0 & 0 & -A_{16} & 0 \\ 0 & 0 & A_{14} & A_{14} & 0 & 0 & 0 & 0 & -A_{16} \end{bmatrix} \qquad \ldots\ldots\ldots\ldots (25)$$

$A_1 = \mu_h, A_2 = \phi, A_3 = \alpha, A_4 = \beta_h, A_5 = \sigma_z, A_6 = (\mu_h + \eta + \tau_2), A_7 = \tau_1, A_8 = (\mu_h + \tau_1), A_9 = \tau_2$
$A_{10} = (\mu_h + \tau_1 + \tau_2), A_{11} = (\mu_h + \phi), A_{12} = (\mu_h + \alpha), A_{13} = \frac{\beta_v \Pi_m \mu_h}{\Pi_h \mu_m}, A_{14} = \frac{\sigma_a \Pi_m \mu_h}{\Pi_h \mu_m},$
$A_{15} = \frac{(\beta_v + \sigma_a)\Pi_m \mu_h}{\Pi_h \mu_m}, A_{16} = \mu_m$

Since$-A_1, -A_{11} - A_{12}$and $-A_{16}$are diagonal entries, then they form the first four eigenvalues of the Jacobian matrix [18]. This leads to

$$J = \begin{bmatrix} -A_6 & 0 & A_7 & A_4 & 0 \\ 0 & -A_8 & A_9 & 0 & A_5 \\ 0 & 0 & -A_{10} & 0 & 0 \\ A_{13} & 0 & A_{13} & -A_{16} & 0 \\ 0 & A_{14} & A_{14} & 0 & -A_{16} \end{bmatrix} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (26)$$

Using elementary [19] row transformation on (26), we have

$$\mathrm{J} = \begin{bmatrix} -A_6 & 0 & A_7 & A_4 & 0 \\ 0 & -A_8 & A_9 & 0 & A_5 \\ 0 & 0 & -A_{10} & 0 & 0 \\ 0 & 0 & 0 & A_4 A_{10} A_{13} - A_6 A_{10} A_{16} & 0 \\ 0 & 0 & 0 & 0 & A_5 A_{10} A_{14} - A_8 A_{10} A_{16} \end{bmatrix} \ldots\ldots\ldots\ldots\ldots (27)$$

Hence

$$|J - \lambda I = 0| = \begin{vmatrix} -(A_6 + \lambda_1) & 0 & A_7 & A_4 & 0 \\ 0 & -(A_8 + \lambda_2) & A_9 & 0 & A_5 \\ 0 & 0 & -(A_{10} + \lambda_3) & 0 & 0 \\ 0 & 0 & 0 & (A_4 A_{10} A_{13} - A_6 A_{10} A_{16} + \lambda_4) & 0 \\ 0 & 0 & 0 & 0 & (A_5 A_{10} A_{14} - A_8 A_{10} A_{16} + \lambda_5) \end{vmatrix} = 0 \qquad \ldots\ldots\ldots\ldots (28)$$

$\Rightarrow (A_6+\lambda_1)(A_8+\lambda_2)(A_{10}+\lambda_3)(A_4A_{10}A_{13}-A_6A_{10}A_{16}+\lambda_4)(A_5A_{10}A_{14}-A_8A_{10}A_{16}+\lambda_5) == 0$
$\Rightarrow (A_6+\lambda_1)=0, (A_8+\lambda_2)=0, (A_{10}+\lambda_3)=0, (A_4A_{10}A_{13}-A_6A_{10}A_{16}+\lambda_4)=0$ or
$(A_5A_{10}A_{14}-A_8A_{10}A_{16}+\lambda_5)=0$

Which implies

$$(A_6+\lambda_1)=0 \Rightarrow \lambda_1=-(\mu_h+\eta+\tau_2)$$
$$(A_8+\lambda_2)=0 \Rightarrow \lambda_2=-(\mu_h+\tau_1)$$
$$(A_{10}+\lambda_3)=0 \Rightarrow \lambda_3=-(\mu_h+\tau_1+\tau_2)$$
$$(A_4A_{10}A_{13}-A_6A_{10}A_{16}+\lambda_4)=0 \Rightarrow \lambda_4=\mu_m(\mu_h+\eta+\tau_2)(\mu_h+\tau_1+\tau_2)(1-R_{ma}^2)$$
$$(A_5A_{10}A_{14}-A_8A_{10}A_{16}+\lambda_5)=0 \Rightarrow \lambda_5=\mu_m(\mu_h+\tau_1+\tau_2)[(\mu_h+\tau_1)(1-R_{zv}^2)]$$

Finally, since all the eigenvalues of the Jacobian matrix of equation (26) are negative or have negative real parts when $R_0<1$ ($R_{ma}<1$ *and* $R_{zv}<1$)therefore the disease-free equilibrium point is locally asymptotically stable when $R_0<1$.We now consider the global stability of disease- free equilibrium.

The summary of the results of the stability of the various sub-models are established in the following theorem.

Theorem 7:

1. The disease-free equilibrium of the Zika only model (5) is locally asymptotically stable if $R_{zv}<1$and unstable $R_{zv}>1$
2. The disease-free equilibrium of the Malaria only model (6) is locally asymptotically stable if $R_{ma}<1$and unstable if $R_{ma}>1$
3. The disease-free equilibrium of the Zika- Malaria model (3) is locally asymptotically stable if $R_0<1$ ($R_{ma}<1$ *and* $R_{zv}<1$) and $R_0>1$ ($R_{ma}>1$ *and* $R_{zv}>1$)

Theorem 8: The DFE$\left(E_{mz}\right)$of system of equation (3) is globally asymptotically stable if $R_{mz}<1$and unstable if $R_{mz}>1$

Proof: Using the theorem on page 246 of Castillo-Chavez et al. [17] to prove the theorem 8. To do this, we let $A=(I_m, I_{mz}, I_{mz}, I_v, I_a)$ and $B=(S_h, R_m, R_z, S_m)$. The model (3) is now written as:

$$\left.\begin{aligned}\frac{dA}{dt}&=\chi(A,B)\\ \frac{dB}{dt}&=\gamma(A,B)\end{aligned}\right\} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (29)$$

Where

$$\chi(A,B)=\begin{bmatrix}\frac{\beta_h I_v}{N_h}S_h-\frac{\sigma I_a}{N_h}I_m-(\mu_h+\eta+\tau_2)I_m+\tau_1 I_{mz}\\ \frac{\sigma I_a}{N_h}S_h-\frac{\beta_h I_v}{N_h}I_z-(\mu_h+\tau_1)I_z+\tau_2 I_{mz}\\ \frac{\sigma I_a}{N_h}I_m+\frac{\beta_h I_v}{N_h}I_z-(\mu_h+\tau_1+\tau_2)I_{mz}\\ \frac{\beta_v(I_m+I_{mz})}{N_h}S_m-\mu_m I_v\\ \frac{\sigma_a(I_z+I_{mz})}{N_h}S_m-\mu_m I_a\end{bmatrix} \ldots\ldots\ldots\ldots\ldots (30a)$$

$$\gamma(A,B)=\begin{bmatrix}\Pi_h+\alpha R_m+\phi R_z-\mu_h S_h-\lambda_1 S_h-\lambda_2 S_h\\ \tau_2 I_m-(\mu_h+\phi)R_m\\ \tau_1 I_z-(\mu_h+\alpha)R_z\\ \Pi_m-\mu_m S_m-\beta_1 S_m-\beta_2 S_m\end{bmatrix} \dots\dots\dots\dots\dots (30b)$$

The reduced form of the system: $\frac{dB}{dt}=\gamma(0,B)$ is given as (30b)

$$B^*=(\ S_h^*\ ,\ R_m^*\ ,\ R_z^*\ ,\ S_m^*\ )=\left(\ \frac{\Pi_h}{\mu_h}\ ,\ 0\ ,\ 0\ ,\ \frac{\Pi_m}{\mu_m}\ \right)\dots\dots\dots(31)$$

is globally asymptotically stable equilibrium point for the reduced form of the system $\frac{dB}{dt}=\gamma(0,B)$. Therefore,

$$S_h(t)=\Pi_h+\phi\{R_m(0)e^{-(\mu_h+\phi)t}\}+\alpha\{R_z(0)e^{-(\mu_h+\alpha)t}\}-\mu_h\left\{\frac{\Pi_h}{\mu_h}+\left[S_h(0)-\frac{\Pi_h}{\mu_h}\right]\right\}e^{\mu_h t}\to\frac{\Pi_h}{\mu_h}$$

as t→ ∞. Hence the convergence of the solution of (31) is global in Ω.Therefore $\chi(A,B)$ must satisfy the following two conditions given as H2 in [17] namely:

1. $\chi(0,B)=0$ and

2. $\chi(A,B)=TA-\chi(A,B),\chi(A,B)\geq 0\ on\ \Omega\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots(32)$

$$T=D_A\chi(0,B^*)=\begin{pmatrix}U_1&0&U_2&U_3&U_4\\0&U_5&U_6&U_7&U_8\\U_9&U_7&U_{10}&U_7&U_4\\U_{11}&0&U_{11}&0&0\\0&U_{12}&U_{12}&0&0\end{pmatrix}$$

$$U_1=-\left(\mu_h+\eta+\tau_2+\frac{\sigma_z I_a}{N_h}\right),U_2=\tau_1,U_3=\beta_h,U_4=\frac{\sigma_z I_m}{N_h},U_5=-\left(\frac{\beta_h I_z}{N_h}+\mu_h+\tau_1\right)$$

$$,U_6=\tau_2,U_7=-\frac{\beta_h I_z}{N_h},U_8=\sigma_z,U_9=\frac{\sigma_z I_a}{N_h},U_{10}=-(\mu_h+\tau_1+\tau_2),U_{11}=\frac{\beta_v S_m}{N_h},U_{12}=\frac{\sigma_a S_m}{N_h}$$

$At\ \ I_m=I_z=I_{mz}=I_v=I_a=0$

$$T=D_A\chi(0,B^*)=\begin{pmatrix}-(\mu_h+\eta+\tau_2)&0&\tau_1&\beta_h&0\\0&-(\mu_h+\tau_1)&\tau_2&0&\sigma_a\\0&0&-(\mu_h+\eta+\tau_2)&0&0\\\frac{\beta_v S_m}{N_h}&0&\frac{\beta_v S_m}{N_h}&0&0\\0&\frac{\sigma_a S_m}{N_h}&\frac{\sigma_a S_m}{N_h}&0&0\end{pmatrix}$$

$$\hat{\chi}(A,B)=\begin{pmatrix}\widehat{\chi_1}(A,B)\\\widehat{\chi_2}(A,B)\\\widehat{\chi_3}(A,B)\\\widehat{\chi_4}(A,B)\\\widehat{\chi_5}(A,B)\end{pmatrix}=\begin{pmatrix}\beta_h I_v\left(\mathbf{1}-\frac{S_h}{N_h}\right)+\lambda_2 I_m\\\lambda_2 I_a\left(\mathbf{1}-\frac{S_h}{N_h}\right)+\lambda_1 I_z\\-(\lambda_1 I_z+\lambda_2 I_m)\\\frac{\beta_v(I_m+I_{mz})}{N_h}\left(\mathbf{1}-\frac{S_m}{N_m}\right)\\\frac{\sigma_a(I_z+I_{mz})}{N_h}\left(\mathbf{1}-\frac{S_m}{N_m}\right)\end{pmatrix}$$

Since $\widehat{\chi_3}(A,B) < 0$ and does not completely satisfy the two conditions stated in equation (32), the disease-free equilibrium may not globally asymptotically stable.

3.4 Endemic equilibrium point (EEP)

Endemic equilibrium point is the steady state solution where the disease is present in the population. In the same way, as we did for disease-free equilibrium, the endemic equilibrium of the co-infection model is sub-divided into Zika only model and Malaria only model.

3.4.1 Endemic equilibrium point of Zika only model

The endemic equilibrium point of the Zika virus only model is given by

$$E_{zv}^{**} = S_h^{**},\ I_z^{**},\ R_z^{**}\ ,\ S_m^{**}\ ,\ \ I_a^{**}\ \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots.(33)$$

where

$$\left.\begin{aligned}
S_h^{**} &= \frac{N_h\sigma_a\sigma_z\Pi_h\Pi_m\mu_m(\mu_h+\alpha)^2 - R_{zv}^2\mu_m^2\Pi_h^2N_h\tau_1\alpha(\mu_h+\alpha) + \Pi_h^2\mu_m^2(R_{zv}^2-1)(\mu_h+\alpha)\tau_1\alpha}{\sigma_a\sigma_z\Pi_h\Pi_m\mu_m(\mu_h+\alpha)^2(R_{zv}^2-1) + N_h\sigma_a\sigma_z\Pi_h\mu_m\mu_h(\mu_h+\alpha) - R_{zv}^2\mu_m^2\mu_h^2\tau_1\alpha}\\
I_{zv}^{**} &= \frac{(R_{zv}^2-1)(\alpha+\mu_h)\Pi_h\mu_m\mu_h}{\sigma_a\sigma_z\Pi_h\mu_h(\mu_h+\alpha) - R_{zv}^2\mu_m\mu_h\tau_1\alpha}\\
R_{zv}^{**} &= \frac{(R_{zv}^2-1)\Pi_h^2\mu_m^2\tau_1}{\sigma_a\sigma_z\Pi_h\mu_h(\mu_h+\alpha) - R_{zv}^2\mu_m^2\Pi_h\tau_1\alpha}\\
S_m^{**} &= \frac{\sigma_a\sigma_z\Pi_m^2(\mu_h+\alpha) - R_{zv}^2\mu_m^2\Pi_h\Pi_m\tau_1\alpha - \mu_m^2(R_{zv}^2-1)(\mu_h+\alpha)\sigma_a\Pi_h\Pi_m\mu_h}{\sigma_a\sigma_z\Pi_m\mu_h(\mu_h+\alpha)^2 - R_{zv}^2\mu_m^2\Pi_h(\mu_h+\alpha)\tau_1\alpha}\\
I_a^{**} &= \frac{\sigma_a\Pi_h\Pi_m\mu_m\mu_h(R_{zv}^2-1)(\mu_h+\alpha)}{\sigma_a\sigma_z\Pi_m\mu_m\mu_h(\mu_h+\alpha) - R_{zv}^2\mu_m^2\mu_h\tau_1\alpha}
\end{aligned}\right\}\ldots.(34)$$

Theorem 9: There exists a unique endemic equilibrium point for Zika only model (5) when $R_{zv} > 1$

3.4.2 Global stability of endemic equilibrium of Zika only model

Theorem 10: If $R_{zv} > 1$ then the unique endemic equilibrium E_{zv}^{**} of model (5) is globally stable in the interior of Ω.

Proof:

The global stability of the endemic equilibrium can be determined by constructing a common quadratic Lyapunov function $L(t)$ of the form [20].

$$\begin{aligned}V(S_h,I_z,R_z,S_m,I_a) = \frac{1}{2}\{(S_h-S_h^{**}) + (I_z-I_z^{**}) + (R_z-R_z^{**})\}^2\\
+\frac{1}{2}\{(S_m-S_m^{**}) + (I_a-I_a^{**})\}^2 \ldots\ldots\ldots\ldots\ldots(35)\end{aligned}$$

Differentiate equation (35) to give (36)

$$\frac{\partial V}{\partial t} = [(S_h - S_h^{**}) + (I_z - I_z^{**}) + (R_z - R_z^{**})]\frac{d}{dt}[S_h + I_z + R_z] + [(S_m - S_m^{**}) + (I_a - I_a^{**})]\frac{d}{dt}[S_m + I_a]$$
$$= -[(S_h - S_h^{**}) + (I_z - I_z^{**}) + (R_z - R_z^{**})][\mu_h(S_h - S_h^{**}) + \mu_h(I_z - I_z^{**}) + \mu_h(R_z - R_z^{**})]$$
$$-[(S_m - S_m^{**}) + (I_a - I_a^{**})][\mu_h(S_m - S_m^{**}) + \mu_h(I_a - I_a^{**})] \quad \dots\dots\dots\dots\dots (36)$$

Let $A_1 = S_h - S_h^{**}, A_2 = I_z - I_z^{**}, A_3 = R_z - R_z^{**}, A_4 = S_m - S_m^{**}, A_5 = I_a - I_a^{**}$
$A_6 = A_1 + A_2 + A_3 \; and \; A_7 = A_4 + A_5$

Substitute them in (36) gives

$$\frac{\partial V}{\partial t} = -[\mu_h A_6^2 + \mu_m A_7^2]$$
$$\frac{\partial V}{\partial t} = -[\mu_h A_6^2 + \mu_m A_7^2] \leq 0 \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots (37)$$

It can be seen that $\frac{\partial V}{\partial t} \leq 0$. Also, $\frac{\partial V}{\partial t} = 0$ if and only if $S_h = S_h^{**}, I_z = I_z^{**}, R_z = R_z^{**}$, $S_m = S_m^{**}$ and $I_a = I_a^{**}$. Therefore, the largest invariant set in $\{(S_h, I_z, R_z, S_m, I_a) \in \Omega: V^1 = 0\}$ is the singletonE_{zv}^{**},where E_{zv}^{**} is the endemic equilibrium. LaSalle's invariant principle [21] then implies that $E^{**}$is globally asymptotically stable in the interior of Ω .

3.5 Endemic equilibrium point of malaria only model

The endemic equilibrium point for Malaria only model is given as

$$E_{ma}^{**} = S_h^{**}, \; I_m^{**}, \; R_m^{**}, \; S_m^{**}, \; I_v^{**} \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots (38)$$

where

$$\left.\begin{aligned}
S_h^{**} &= \frac{(\phi + \mu_h)\{N_h\beta_h\beta_v\Pi_h\Pi_m\mu_h(\phi + \mu_h) - R_{ma}^2\Pi_h^2\mu_m^2\phi\tau_2 N_h + \Pi_h^2\mu_m^2(R_{ma}^2 - 1)\tau_2\alpha N_h\}}{\beta_h\beta_v\Pi_h\Pi_m\mu_h(R_{ma}^2 - 1)(\phi + \mu_h)^2 + \beta_h\beta_v\Pi_m\mu_m\mu_h N_h(\phi + \mu_h) - R_{ma}^2\mu_m^2\Pi_h\mu_h\tau_2\phi N_h} \\
I_m^{**} &= \frac{(R_{ma}^2 - 1)(\phi + \mu_h)\Pi_h^2\mu_m^2}{\beta_h\beta_v\Pi_m\mu_h(\phi + \mu_h) - R_{ma}^2\mu_m^2\Pi_h\tau_2\phi} \\
R_{ma}^{**} &= \frac{\Pi_h^2\mu_m^2(R_{ma}^2 - 1)\tau_2}{\beta_h\beta_v\Pi_m\mu_h(\phi + \mu_h) - R_{ma}^2\mu_m^2\Pi_h\tau_2\phi} \\
S_m^{**} &= \frac{\beta_h\beta_v\Pi_m^2\mu_h(\phi + \mu_h) - R_{ma}^2\mu_m^2\Pi_h\Pi_m\tau_2\phi - \mu_m^2(R_{ma}^2 - 1)(\phi + \mu_h)\beta_v\Pi_h\Pi_m\mu_h}{\beta_h\beta_v\Pi_m\mu_h(\phi + \mu_h)^2 - R_{ma}^2\mu_m^2\Pi_h(\phi + \mu_h)\tau_2\phi} \\
I_v^{**} &= \frac{\beta_v\Pi_h\Pi_m(R_{ma}^2 - 1)(\phi + \mu_h)}{\beta_h\beta_v\Pi_m(\phi + \mu_h) - R_{ma}^2\mu_m\Pi_h\tau_2\phi}
\end{aligned}\right\} \dots . (39)$$

Theorem 11: There exists a unique endemic equilibrium point for Malaria only model (6) when $R_{ma} > 1$.

3.5.1 Global stability of endemic equilibrium of malaria model only

Theorem 12: If $R_{ma} > 1$ then the unique endemic equilibrium E_{ma}^{**} of Malaria only model (6) is globally stable in the interior of Ω .

Proof:

The global stability of the endemic equilibrium can be determined by constructing a common quadratic Lyapunov function $L(t)$ of the form [20].

$$V(S_h, I_m, R_m, S_m, I_v) = \frac{1}{2}\{(S_h - S_h^{**}) + (I_m - I_m^{**}) + (R_m - R_m^{**})\}^2 + \frac{1}{2}\{(S_m - S_m^{**}) + (I_v - I_v^{**})\}^2 \quad \ldots\ldots\ldots\ldots (40)$$

Differentiate equation (40) to give (41)

$$\frac{\partial V}{\partial t} = [(S_h - S_h^{**}) + (I_m - I_m^{**}) + (R_m - R_m^{**})]\frac{d}{dt}[S_h + I_m + R_m]$$
$$+[(S_m - S_m^{**}) + (I_v - I_v^{**})]\frac{d}{dt}[S_m + I_v]$$
$$= -[(S_h - S_h^{**}) + (I_m - I_m^{**}) + (R_m - R_m^{**})][\mu_h(S_h - S_h^{**}) + (\mu_h + \eta)(I_m - I_m^{**}) + \mu_h(R_m - R_m^{**})] -$$
$$[(S_m - S_m^{**}) + (I_v - I_v^{**})][\mu_m(S_m - S_m^{**}) + \mu_m(I_v - I_v^{**})]$$

Let $B_1 = S_h - S_h^{**}, B_2 = I_m - I_m^{**}, B_3 = R_m - R_m^{**}, B_4 = S_m - S_m^{**}, B_5 = I_v - I_v^{**}$ and also

$$B_6 = B_1 + B_2 + B_3, B_7 = B_4 + B_5$$
$$\frac{\partial V}{\partial t} = [B_1 + B_2 + B_3][\mu_h(B_1 + B_2 + B_3) + \eta B_2] \quad + [B_4 + B_5][\mu_m(B_4 + B_5)] \ldots\ldots\ldots\ldots (41)$$
$$\frac{\partial V}{\partial t} = [\mu_h B_6 + \eta B_2 B_6 + \mu_m B_7]$$

It is observed that $\frac{\partial V}{\partial t} \leq 0$. Also, $\frac{\partial V}{\partial t} = 0$ if and only if $S_h = S_h^{**}, I_m = I_m^{**}, R_m = R_m^{**}$, $S_m = S_m^{**}$ *and* $I_v = I_v^{**}$

Therefore, the endemic equilibrium of malaria only model is globally asymptotically stable with reference to the section 3.4.2 above.

3.6 Existence of endemic equilibrium point of the Coinfection malaria and Zika virus

Obtaining an explicit expression from Endemic equilibrium point of the co-infection model (Malaria and Zika virus) is not forthcoming due to the complex nature of the equations involved. Therefore, we assume that the endemic equilibrium may exist as

$E_{mz}^{**} = S_h^{**}, I_m^{**}, I_z^{**}, I_{mz}^{**}, R_m^{**}, R_z^{**} S_m^{**}, I_v^{**}, I_a^{**}$. Let's now determine the global stability of the endemic equilibrium as follows

Theorem 13: If $R_{mz} > 1$ then the unique endemic equilibrium E_{mz}^{**} of System (3) is globally stable in the interior of Ω .

Proof:

The global stability of the endemic equilibrium can be determined by constructing a common quadratic Lyapunov function $L(t)$ of the form

$$V(S_h, I_m, I_z, I_{mz}, R_m, R_z, S_m, I_v, I_a)$$
$$= \frac{1}{2}\{(S_h - S_h^{**}) + (I_m - I_m^{**}) + +(I_z - I_z^{**}) + (I_{mz} - I_{mz}^{**}) + (R_m - R_m^{**}) + (R_z - R_z^{**})\}^2$$
$$+ \frac{1}{2}\{(S_m - S_m^{**}) + (I_v - I_v^{**}) + (I_a - I_a^{**})\}^2 \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (42)$$

The equation (42) is differentiated to give (43)

$$\frac{\partial V}{\partial t} = [(S_h - S_h^{**}) + (I_m - I_m^{**}) + +(I_z - I_z^{**}) + (I_{mz} - I_{mz}^{**}) + (R_m - R_m^{**}) + (R_z - R_z^{**})]$$
$$\frac{d}{dt}[S_h + I_m + I_z + I_{mz} + R_m + R_z] + [(S_m - S_m^{**}) + (I_v - I_v^{**}) + (I_a - I_a^{**})]\frac{d}{dt}[S_m + I_v + I_a]$$
$$= -[(S_h - S_h^{**}) + (I_m - I_m^{**}) + (I_z - I_z^{**}) + (I_{mz} - I_{mz}^{**}) + (R_m - R_m^{**}) + (R_z - R_z^{**})]$$
$$[\mu_h(S_h - S_h^{**}) + \mu_h(I_m - I_m^{**}) + \mu_h(I_z - I_z^{**}) + \mu_h(I_{mz} - I_{mz}^{**}) + \mu_h(R_m - R_m^{**}) + \mu_h(R_m - R_m^{**}) + \eta(I_m - I_m^{**})] - [(S_m - S_m^{**}) + (I_v - I_v^{**}) + (I_a - I_a^{**})]$$
$$[\mu_m(S_m - S_m^{**}) + \mu_m(I_v - I_v^{**}) + \mu_m(I_a - I_a^{**})] \ldots\ldots\ldots\ldots\ldots\ldots (43)$$

Let

$C_1 = S_h - S_h^{**}, C_2 = I_m - I_m^{**}, C_3 = I_z - I_z^{**}, C_4 = I_{mz} - I_{mz}^{**}, C_5 = R_m - R_m^{**}, C_6 = R_z - R_z^{**}, C_7 = S_m - S_m^{**}, C_8 = I_v - I_v^{**}, C_9 = I_a - I_a^{**}$ and also $C_{10} = C_1 + C_2 + C_3 + C_4 + C_5 + C_6$
$C_{11} = C_7 + C_8 + C_9$

Substitute them into equation (44) gives

$$\frac{\partial V}{\partial t} = -[\mu_h C_{10}^2 + \mu_m C_{11}^2 + \eta C_2 C_{10}] \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (44)$$

It can be seen that $\frac{\partial V}{\partial t} \leq 0$ and $\frac{\partial V}{\partial t} = 0$ if and only if

$S_h = S_h^{**}, I_m = I_m^{**}, I_z = I_z^{**}, I_{mz} = I_{mz}^{**}, R_m = R_m^{**}, R_z = R_z^{**}, S_m = S_m^{**}, I_v = I_v^{**}, I_a = I_a^{**}$. Therefore, the endemic equilibrium of the co-infection Zika - Malaria model is globally asymptotically stable with reference to the section 3.4.2 above.

We now move on to sensitivity analysis.

4 Sensitivity Analysis of the Co-infection Model Parameters

We now perform sensitivity analysis on the parameters of the model to determine which parameter will increase or decrease the basic reproduction number (R_0) when it is increased by a small margin. It is computed using the normalized forward sensitivity index. In terms of differentiable expression, it is defined as follows

$S = \frac{\partial R_0}{\partial \tau_1} \times \frac{\tau_1}{R_0}$ where τ_1 is the parameter under consideration

Positive sensitivity index means an increase in that parameter will lead to corresponding increase in the basic reproduction number (R_0). However, negative sensitivity index means an increase in negative parameter will lead to a decrease in (R_0).Using the parameters in Table 1 below, we compute the sensitivity indices for the parameters in the model (3) and the result is stated in Table 2.

Table 1. Description of variables and parameters of Malaria and Zika

Parameter	Interpretation	Values	Source
σ_a	The probability of female aedes aegypti mosquito getting infected with zika virus	0.406	Assumed
β_v	Probability of female Anopheles mosquito getting infected with malaria parasite	0.09	[22]

Parameter	Interpretation	Values	Source
β_h	Probability of human getting infected with malaria	0.034	Assumed
σ_z	Probability of human getting infected by zika virus	0.45	Assumed
τ_1	Recovery rate for zika virus only.	0.0181	Assumed
τ_2	Recovery rate of malaria only	0.00136	Assumed
μ_h	Natural death rate for human	0.00004	[23]
μ_m	Natural death rate for mosquitoes	0.067	Assumed
η	Malaria induced death rate	0.05	Assumed
Π_h	Human beings are recruited into their population	800	Assumed
ϕ	Progression from R_m to S_h	0.000137	Assumed
α	Progression from R_z to S_h	0.0055	Assumed

Table 2. Sensitivity indices of model parameters to R_{ma} and R_{zv}

R_{ma}	Parameter values	Sensitivity index	R_{zv}	Parameter values	Sensitivity index
τ_2	0.00136	-0.0126	μ_m	0 .067	-0.8343
Π_h	800	-0.4521	τ_1	0.0181	-0.4497
μ_h	0.00004	0.4816	Π_h	800	-0.4836
μ_m	0 .067	-0.3089	μ_h	0.00004	0.4822
β_h	0.034	0.4893	σ_a	0.406	0.4866
η	0.05	-0.4315	Π_m	1000	0.6281
β_v	0.09	0.4816	σ_z	0.45	0.4851
Π_m	1000	0.4839			

From the table, the most positive sensitivity index for malaria is $\beta_h$and most negative isτ_2. Also, the most positive sensitivity index for zika is Π_m and most negative is τ_1. Now, 10% and 15% an increase in β_h and $\Pi_m$arameters respectively will cause an increase in R_{ma}andR_{zv} by 5% and7% respectively.

5 Numerical Simulation

Using the following initial values,

$$S_h(0) = 19900\ ,\ I_m(0) = 1500\ ,\ I_z(0) = 140\ ,\ I_{mz}(0) = 170\ ,\ R_m(0) = 100\ ,$$
$$R_z(0) = 20\ ,\ S_m(0) = 30000\ ,\ I_v(0) = 33400\ ,\ I_a(0) = 6200$$

and values in Table 1 above, the numerical solution of the model 3 is given below in Figs. 2 and 3 respectively.

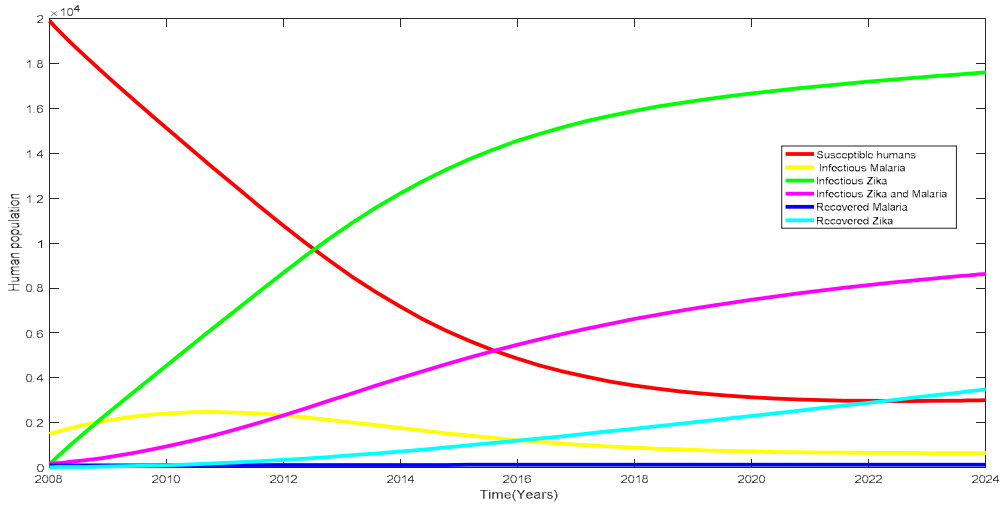

Fig. 2. The plot of numerical solution of the model with time

Fig. 2, represents the initial behavior of the model. As time increases from 2008, the susceptible human drops while those of infectious zika, infectious malaria and recovered zika increase. Also malaria infectious increases to its peak at 2011 and begins to drop gradually. However, the recovered malaria trajectory remains low throughout the period.

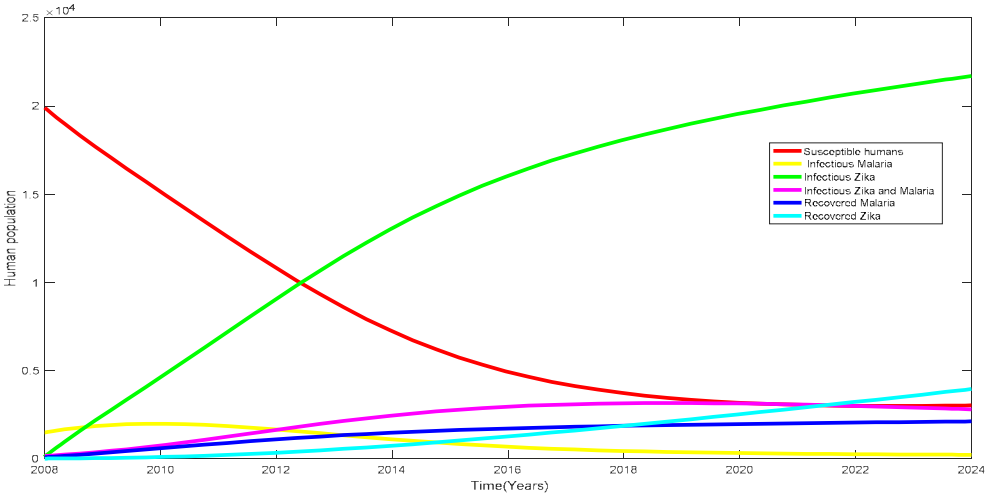

Fig. 3. Graph of increasing the most negative sensitive index value in malaria only model

As the most negative value (μ_m) of the sensitivity index in malaria only model increases, the recovery rate of malaria also increases while the malaria infection and the co-infection trajectories decrease. However, the dynamics of other trajectories remain the same.

From the model, it is found that whenever the recovery rate of malaria only is increased, the malaria and the co-infection situation also improved but not zika only.

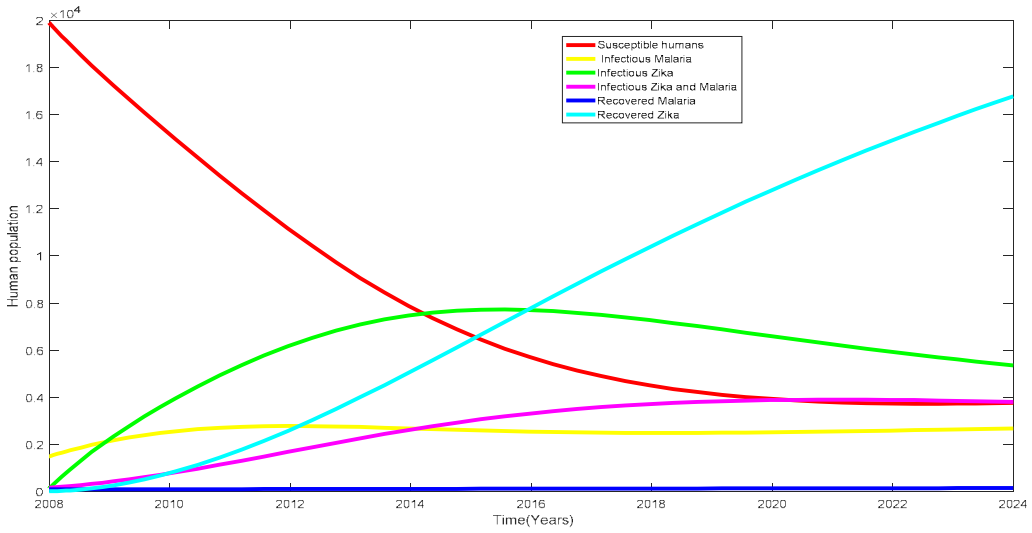

Fig. 4. Plot of increasing the most negative parameter in zika only model

From Fig. 4, it is shown that increasing the recovery rate of zika only leads to an improvement in the trajectories of infectious zika, recovered zika and co-infection. However, there is little improvement in the trajectory of susceptible humans. Surprisingly, malaria infection increased and the recovery remains the same.

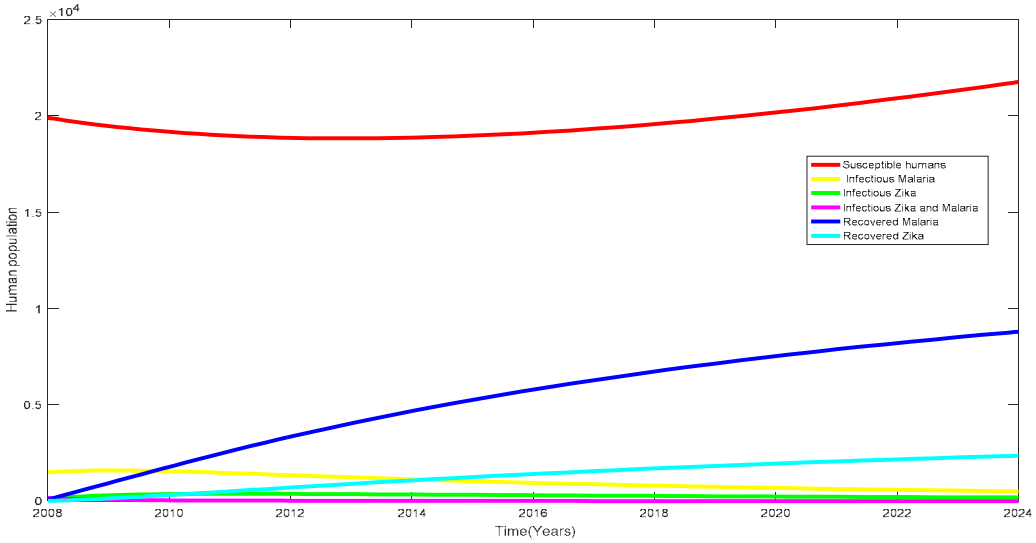

Fig. 5. Plot of increasing the most negative values of both sub-models

In improving the recovery rates in both sub-models exhibit great improvement in all the trajectories except recovered Zika which looks almost the same as it was at the beginning of the epidemic. From the five (5) figures above, the best strategy to control the Malaria- Zika co-infection is to improve upon the recovery rates of both infections simultaneously.

6 Conclusion

In this article, co-infection model was formulated to study the transmission dynamics of both Malaria and Zika virus diseases in a Malaria-endemic region like Kedougou in Senegal and other parts of the world that may have the epidemic of Zika-Malaria co-infection in future. Also stability analysis was performed on the model to determine the disease-free and the endemic equilibria. Sensitivity analysis on the basic reproduction number indicated that by improving the recovery rate of both diseases, the basic reproduction number can be reduced considerably. It is also confirmed from Fig. 5 that, the best approach to control or eliminate the diseases is to improve the recovery rate of both disease simultaneously.

Competing Interests

Authors have declared that no competing interests exist.

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