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# Stability Analysis of Deterministic Mathematical Model for Zika Virus

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***Authors' contributions***

*This work was carried out in collaboration between both authors. Authors MK and FSK designed the study and performed the statistical analysis and managed the analyses of the study and literature searches. Authors MK and FSK have equal contribution in writing this research paper. Both authors read and approved the final manuscript.*

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## Abstract

This research paper presents the stability analysis of infectious state of Zika Virus in many types of population in mathematical perspective. This model focus on viral activity in disease free equilibrium, in epidemic equilibrium and their $R_\circ$ of epidemic under the possibility of spread due to human interaction. The constructed mathematical model is based on the data sets obtained from three regions Brazil, Cape Verde and Colombia. Results obtained validate the given conditions.

*Keywords: Zika virus; stability analysis; numerical simulation; deterministic compartment model.*

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# 1 Introduction

## 1.1 Historical background

The most uprising viral disease nowadays is Zika Virus (ZIKV). ZIKV is transferred via mosquito bite specifically by the biting of Aedes Aegypti. This particular mosquito belongs to the family Flaviviridae and Genus Flavivirus. Chikungunya, Dengue and Yellow fever are also the off shots of this family. Despite the fact that the attack of ZIKV shows moderate disease symptoms, like that of the clinical presentation and transmission cycles in the epidemiology of Chikungunya and Dengue occurrences in urban environments.

Symptoms of Zika virus disease encompasses conjunctivitis, skin rash, fever, muscle and pains in various joints, uncomforting nuisance and headache, which can last normally between 2 to 7 days time period. There is no specific treatment for ZIKV yet but apparent symptoms are normally mild and can be treated with common pain and fever medicines, bed rest and taking plenty of water and healthy fluids.

The very first incidence of Zika virus was identified in 1947 in a specie of monkey in the African forest called Zika in Uganda. And the first isolated case was identified in humans in 1952 also in Uganda and then in United Republic of Tanzania. Zika virus has been shown intermittent disease patterns among the people of Africa and Asia. Moreover, the outbreaks reported for the first time from the Pacific in 2007 and 2013 in French Polynesia and Yap Island (i.e. Federated States of Micronesia). There were subsequent incidents of the spread of this virus to other areas of the region like Cook Islands, Easter Islands (Chile), Pacific Islands (including New Caledonia, Fiji, Samoa, Solomon Islands and Vanuatu). Zika virus has been steadily increasing its geographical domain, ever since its first appearance.

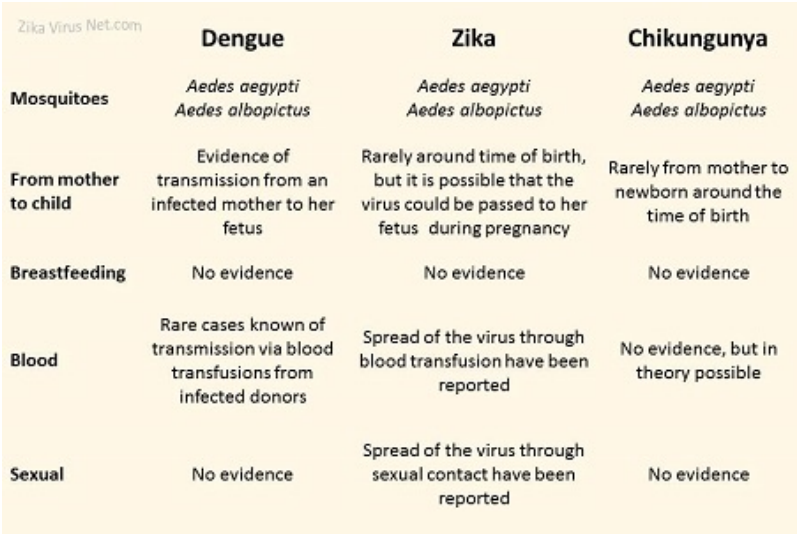
The pace of outbreaks of Zika virus epidemic in the American continents is on rise. Similarly, the spread of this monster is reported in more regions of the world that were previously completely unaffected, that includes Europe, [1]. The immunity of the Europeans population is relatively immature as contrast to Afro-Asian Populations. At the arrival of summer season in the northern hemisphere is the most suitable time when Aedes mosquitoes in Europe find optimum climate to get infected by Zika virus and later transmit this virus to tourists and then into local population through biting. Mosquito logy suggests that Aedes albopictus and Aedes Aegypti mosquito that is proven factor as a transmission vector for the spread of viruses like Dengue and Chikungunya in Europe, [2],[3] is also found to be competent for spread of Zika virus according to recently available increasing experimental and ecological evidences [4],[5],[6],[7],[8]. At this point it is relevant to cover and analyze the monthly traffic of travelers by air, arriving into the cities of Europe from the Zika affected regions of both the American continents.

## 1.2 Mathematical background

Many researchers showed interest in the study epidemic situations mathematically. Many mathematical models have been created for analyzing Dengue epidemic, such as [9],[10],[11],[12],[13], [14]. Some of these mathematical models were based on novel approach and some of these were verified using real life data. Various methods have been adopted to study the numerical solutions of epidemic models such as VIM, HPM, PIA etc,[15],[16].

Above discussed models have been analyzed for dengue and other epidemic SIR conditions. In [17] for the first time a mathematical model was provided for Zika virus transmission in French Polynesia Island populations. But in their work one of the very important parameter was neglected. Since Zika virus is the only such virus among this class of virus that can be transmitted through human interaction such as blood transfusion or sexual transmission See Fig 1. Therefore in this paper, the

presented model is based on more realistic parameters and this model will give more insight into epidemic areas under varying situations.



| Zika Virus Net.com | Dengue | Zika | Chikungunya |
|---|---|---|---|
| **Mosquitoes** | *Aedes aegypti* *Aedes albopictus* | *Aedes aegypti* *Aedes albopictus* | *Aedes aegypti* *Aedes albopictus* |
| **From mother to child** | Evidence of transmission from an infected mother to her fetus | Rarely around time of birth, but it is possible that the virus could be passed to her fetus during pregnancy | Rarely from mother to newborn around the time of birth |
| **Breastfeeding** | No evidence | No evidence | No evidence |
| **Blood** | Rare cases known of transmission via blood transfusions from infected donors | Spread of the virus through blood transfusion have been reported | No evidence, but in theory possible |
| **Sexual** | No evidence | Spread of the virus through sexual contact have been reported | No evidence |

**Fig. 1. Transmission comparison between Dengue, Zika and Chikungunya. Picture courtesy by http://www.zikavirusnet.com /transmission.html**

## 2 Mathematical Formulation

In order to depict epidemic conditions of Zika virus mathematically a compartmental model was considered. Since a deterministic model provide a vast insight into the epidemic situation than stochastic one, therefore the considered model in this work is deterministic.

For human population SEIR structured model is assumed and for vector population SIR structured model is considered. Let the size of human population be $T^H$ with classifications Susceptible $S^H$, Exposed $E^H$, Infected $I^H$ and Recovered $R^H$. Similarly for vector population the size be $T^Z$ with classifications Susceptible $S^Z$, Infected $I^Z$ only since recovered population is not a real concept among vectors, once a mosquito gets infected it will survive with it or die. It implies that $T^H = S^H + E^H + I^H + R^H$ also $T^Z = S^Z + E^Z + I^Z$. Assumed in this case Zika vectors exposed and susceptible situation is almost same i.e. $T^Z = S^Z + I^Z$. In this compartmental model, flow from one compartment to other compartment for each species depends on the level of contact with the other species. The populations of humans and mosquitoes are assumed to be in a steady state so that in general, recruitment equals deaths. Also in this model, no vaccination case is assumed.

Contact rates are calculated by using formula $\gamma_{ZH} = T_{ZH} \times \beta_I$, $\gamma_{HH} = T_{HH} \times \beta_H$ and $\gamma_{HZ} = T_{HZ} \times \beta_S$. Parameters and their values used in this model have been shown in Tab. 2.Also

$$Fractional\,Recovery\,Rate = \frac{1}{Human\,Infection\,Duration}. \tag{2.1}$$

**Table 1. Parameter discussion**

| Description | Parameter | Value |
|---|---|---|
| Transmission probability H to Z | $T_{HZ}$ | 0.75 [18] |
| Transmission probability H to H | $T_{HH}$ | 0.25 |
| Transmission probability Z to H | $T_{ZH}$ | 0.75 [18] |
| Bites per $S^Z$ per/day | $\beta_S$ | 0.5 [18] |
| Interaction of two H/day | $\beta_H$ | 0.5 |
| Bites per infectious Z/day | $\beta_I$ | 1.5 [18] |
| Effective contact rate Z to H | $\gamma_{ZH}$ | 1.125 |
| Effective contact rate H to H | $\gamma_{HH}$ | 1.125 |
| Effective contact rate H to Z | $\gamma_{HZ}$ | 0.375 |
| Zika vector carrying capacity | $K_Z$ | 20000 [18] |
| Average human life span | $L_H$ | 25000 days [18] |
| Average Zika vector life span | $L_Z$ | 4 days [18] |
| Intrinsic incubation period of Zika $V$ | $P_{IN}$ | 12 days [19] |
| Extrinsic incubation period of Zika $V$ | $P_{EX}$ | 10 days [20] |
| Human infection duration | $\alpha$ | 3 days [18] |

The population of Susceptible humans and Infectious vectors can be written as $s_h(t) = \frac{S^H}{T^H}$ and $i_Z(t) = \frac{I^Z}{T^Z}$ and $\gamma_{ZH}$ is the contact rate between Zika vector and human populations, so the number of new cases will be given as $S^H I^Z \frac{\gamma_{ZH}}{T^H}$. Similarly other factors can be formed. Then the system of differential equations is

$$\frac{dS^H}{dt} = \frac{T^H}{L_H} - S^H\Big(I^Z\frac{\gamma_{ZH}}{T^H}\Big) + \gamma_{HH}S^H\frac{I^H}{T^H} - \frac{S^H}{L_H} \tag{2.2a}$$

$$\frac{dE^H}{dt} = \frac{S^H I^Z\gamma_{ZH}}{T^H} - E^H\Big(\frac{1}{P_{IN}} + \frac{1}{L_H}\Big) - \gamma_{HH}S^H\frac{I^H}{T^H} \tag{2.2b}$$

$$\frac{dI^H}{dt} = \frac{E^H}{P_{IN}} - I^H\Big(\frac{1}{\alpha} + \frac{1}{L_H}\Big) + \gamma_{HH}S^H\frac{I^H}{T^H} \tag{2.2c}$$

$$\frac{dR^H}{dt} = \frac{I^H}{\alpha} - \frac{R^H}{L_H} + \gamma_{HH}S^H\frac{I^H}{T^H} \tag{2.2d}$$

$$\frac{dS^Z}{dt} = \frac{T^Z K_Z}{L_Z} - S^Z\Big(\frac{I^H\gamma_{HZ}}{P_{EX}T^H} + \frac{K_Z}{L_Z}\Big) \tag{2.2e}$$

$$\frac{dI^Z}{dt} = S^Z\Big(\frac{I^H\gamma_{HZ}}{T^H P_{EX}}\Big) - \frac{I^Z K_Z}{L_Z} \tag{2.2f}$$

Since $T^Z = S^Z + I^Z$ or $S^Z = T^Z - I^Z$. For human population $T^H = S^H + E^H + I^H + R^H$ or $R^H = T^H - S^H - E^H - I^H$ , the above system of equations reduces to

$$\frac{dS^H}{dt} = \frac{T^H}{L_H} - S^H\Big(I^Z\frac{\gamma_{ZH}}{T^H}\Big) + \gamma_{HH}S^H\frac{I^H}{T^H} - \frac{S^H}{L_H} \tag{2.3a}$$

$$\frac{dE^H}{dt} = \frac{S^H I^Z\gamma_{ZH}}{T^H} - E^H\Big(\frac{1}{P_{IN}} + \frac{1}{L_H}\Big) - \gamma_{HH}S^H\frac{I^H}{T^H} \tag{2.3b}$$

$$\frac{dI^H}{dt} = \frac{E^H}{P_{IN}} - I^H\Big(\frac{1}{\alpha} + \frac{1}{L_H}\Big) + \gamma_{HH}S^H\frac{I^H}{T^H} \tag{2.3c}$$

$$\frac{dI^Z}{dt} = (T^Z - I^Z)\Big(\frac{I^H\gamma_{HZ}}{T^H P_{EX}}\Big) - \frac{I^Z K_Z}{L_Z} \tag{2.3d}$$

The system is defined on the domain $D = \{(S^H, E^H, I^H, I^Z)|0 \leq I^Z \leq T^Z, 0 \leq I^H < T^H, 0 \leq S^H, 0 \leq E^H\}$. First equilibrium point becomes $(T^H, 0, 0, 0)$ which clearly states no disease situation. For the second equilibrium point the considered population is of infected humans and Zika vectors. Since a suspected person does not exist in sub-infected system or they exist in the no disease situation only therefore $S^H = T^H$, then the system reduces to sub-infected system i.e.

$$\frac{dE^H}{dt} = I^Z\gamma_{ZH} - E^H\Big(\frac{1}{P_{IN}} + \frac{1}{L_H}\Big) - \gamma_{HH}I^H \tag{2.4a}$$

$$\frac{dI^H}{dt} = \frac{E^H}{P_{IN}} - I^H\Big(\frac{1}{\alpha} + \frac{1}{L_H}\Big) + \gamma_{HH}I^H \tag{2.4b}$$

$$\frac{dI^Z}{dt} = (T^Z - I^Z)\big(\frac{I^H\gamma_{HZ}}{T^H P_{EX}}\big) - \frac{I^Z K_Z}{L_Z} \tag{2.4c}$$

Therefore we get two equilibrium points for this sub-infected system i.e. $(0, 0, T^Z)$ and $(E^{H*}, I^{H*}, I^{Z*}) = \Big( - \rho - \rho^*, \omega(-\rho - \rho^*), \dfrac{T^Z}{1 - \dfrac{\rho}{\omega(\rho + \rho^*)}}\Big)$. First equilibrium point shows the end of the epidemic stage i.e. if all mosquitoes become infected then human survival will become very much difficult. Whereas $(E^{H*}, I^{H*}, I^{Z*})$ shows the epidemic stage very clearly.

For estimating the effects of outbreaks in emerging infectious diseases, basic reproduction number is the most vital quantity in mathematical modeling. $R_\circ$ is basically the average number of new infectious cases caused by single infected individual in susceptible human population. There is hardly any research work done without calculating $R_\circ$ related to epidemic models.

To find out the basic reproduction number $R_\circ$, NGM method is being used here, for more detail see [21]. The next generation matrix is calculated by the formula $K = -E^t T\Sigma^{-1}E$ where $\Sigma$ is the transition matrix and $T$ represents the transmission matrix. $R_\circ$ can be calculated by using formula

$$R_\circ = \big(\frac{\alpha\gamma_{ZH}L_H^2}{L_H^2 + \alpha P_{IN} + L_H M}\big), \tag{2.5}$$

where $M = \alpha + P_{IN}(1 - \alpha\gamma_{HH})$. $R_\circ > 1$ represents that the disease free equilibrium point is unstable whereas $R_\circ < 1$ shows the local asymptotically stable behavior of equilibrium point.

# 3 Numerical Simulation

Three different populations have been considered here. This mathematical model is applied on each of these three cases in order to verify the validity of this work. The data collected for this simulation has been provided by World Health Organization (WHO) [22]. The real life data dramatically matches the results obtained through this mathematical work. Therefore this model shall be helpful in future predictions with precision.

## 3.1 Case I

First case under discussion is of Colombia. The initial conditions have been assumed by considering the total population of Colombia as $T^H = 48481280$. World Health Organization's situation report from 1st October, 2015 to 13th February, 2016 suggests that the infected cases of Colombia are $I^H = 100000$ till now. Other initial values have been calculated using $T^H = S^H + E^H + I^H + R^H$ is $S^H = 38705024$, $E^H = 9676256$.

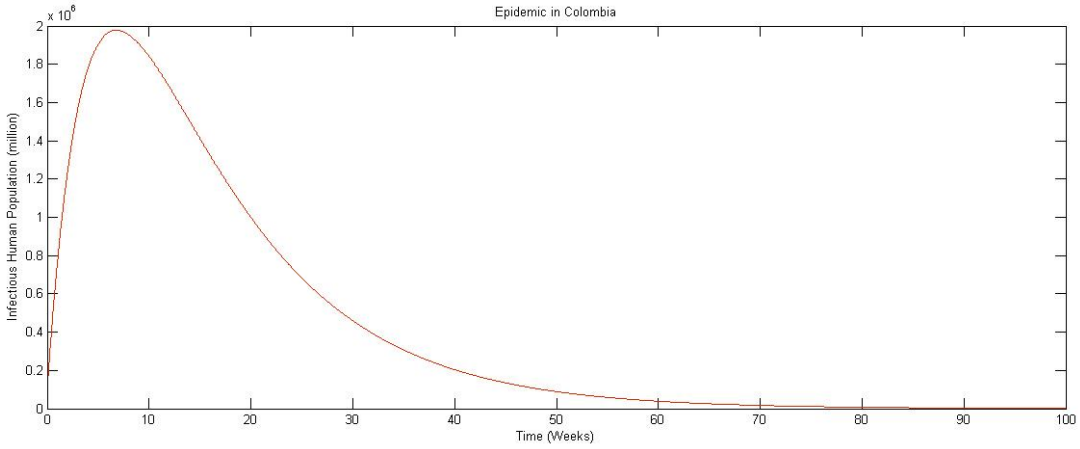



**Fig. 2. First peak of epidemic of $I^H$ in Colombia from 1st October, 2015 to 13th February, 2016**

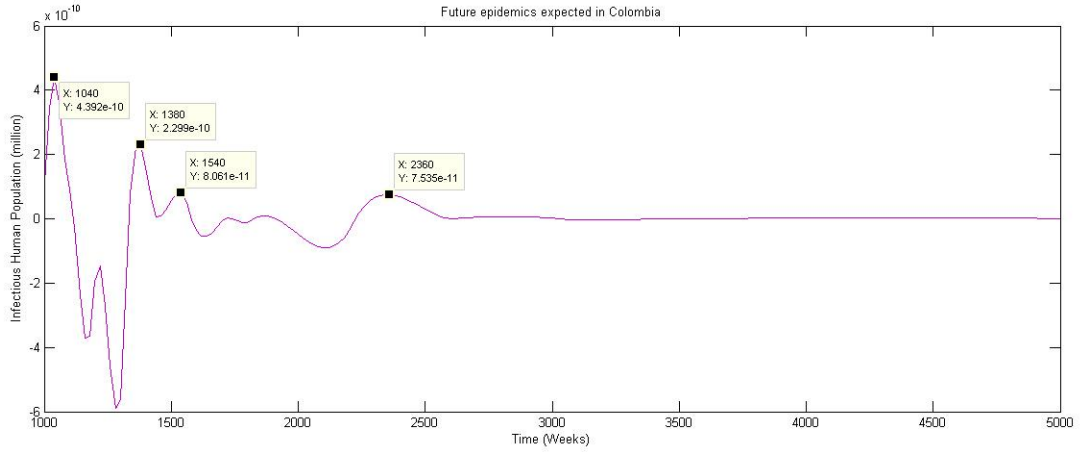



**Fig. 3. Future predictions for $I^H$ of Zika epidemics in Colombia after 13th February, 2016**

## 3.2 Case II

Second case is Cape Verde, since it is a tourism place, so epidemic can get worse and due to the human exposure to open areas, it is very likely for mosquitoes that have grown in these areas can easily transmit their virus to human and animals. World Health Organization's situation report from 1st October, 2015 to 7th February, 2016 suggests that the infected cases of Cabo Verde are $S^H = 7325$. Other initial values have been calculated using $T^H = S^H + E^H + I^H + R^H$ since $T^H = 498897$, $I^H = 122893$, $E^H = 368679$.

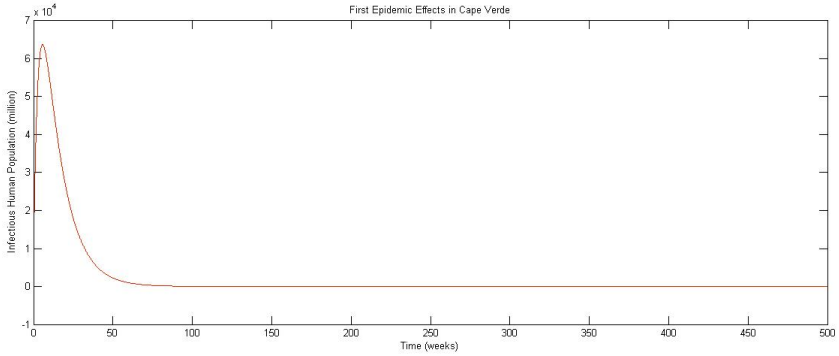



**Fig. 4. First peak of $I^H$ during first epidemic i.e. from 1st October, 2015 to 7th February, 2016 in Cabo Verde**

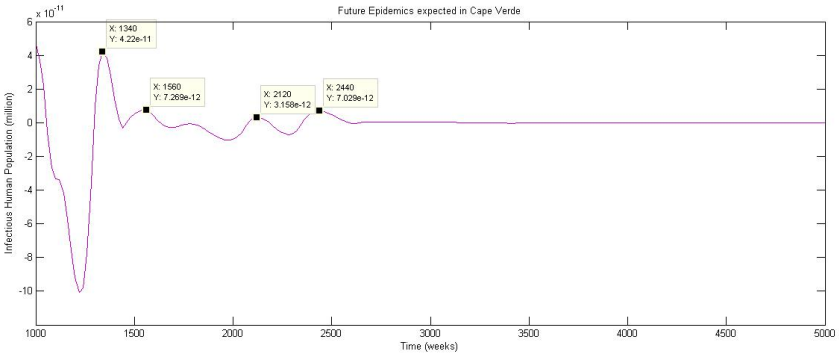



**Fig. 5. Future predictions for $I^H$ of Zika epidemics in Cabo Verde after 7th February, 2016**

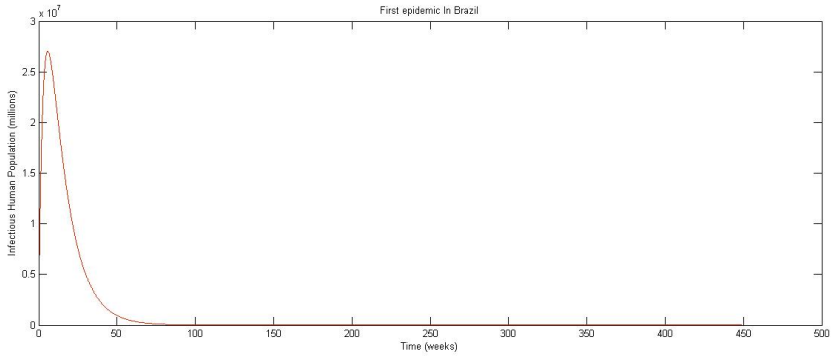



**Fig. 6. Behavior of $I^H$ during first Zika epidemics in Brazil**

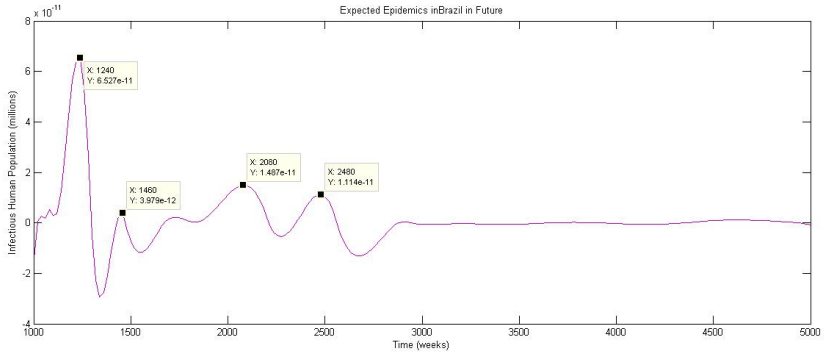



**Fig. 7. Upcoming situation of $I^H$ among future epidemics in Brazil**

## 3.3 Case III

Brazil is the worlds worst effected area. Right now, the situation is not an epidemic but being a tourist place therefore an abrupt spread of epidemic can not be over ruled. Data collected from [23] suggests that $T^H = 202033670$, $S^H = 40146734$, $E^H = 160586936$ and $I^H = 1300000$.

The Jacobian matrix for System Eq.(2.2a)-Eq.(2.2f) is

$$J = \begin{pmatrix} -\frac{1}{P_{IN}} - \frac{1}{L_H} & -\gamma_{HH} & \gamma_{ZH} \\ \frac{1}{P_{IN}} & -\frac{1}{\alpha} - \frac{1}{L_H} + \gamma_{HH} & 0 \\ 0 & \frac{T^Z \gamma_{HZ}}{T^H P_{EX}} - \frac{I^Z \gamma_{HZ}}{T^H P_{EX}} & -\frac{I^H \gamma_{HZ}}{T^H P_{EX}} - \frac{K_Z}{L_Z} \end{pmatrix}. \tag{3.1}$$

The Jacobian matrix for evaluated general equilibrium point with dissipated Zika virus is given as

$$J^*_{(T^H,0,0,0)} = \begin{pmatrix} -\frac{1}{P_{IN}} - \frac{1}{L_H} & -\gamma_{HH} & \gamma_{ZH} \\ \frac{1}{P_{IN}} & -\frac{1}{\alpha} - \frac{1}{L_H} + \gamma_{HH} & 0 \\ 0 & \frac{T^Z \gamma_{HZ}}{T^H P_{EX}} & -\frac{K_Z}{L_Z} \end{pmatrix}. \tag{3.2}$$

Eigen values for all above studied cases at first equilibrium point are $\lambda_1 = -5000$, $\lambda_2 = -0.0417227$ and $\lambda_3 = 0.166723$. The stability theory of non linear systems, states that if the Eigen values are real and have different signs as in this case then non linear system usually have its equilibrium point a saddle. This means when $t \to \infty$ three solutions approach the equilibrium point and when $t \to -\infty$ three more solutions approach equilibrium point. Such solutions are called separatrix. Then $J^*_{(E^{H*},I^{H*},I^{Z*})}$ is equal to

$$\begin{pmatrix} -\frac{1}{P_{IN}} - \frac{1}{L_H} & -\gamma_{HH} & \gamma_{ZH} \\ \frac{1}{P_{IN}} & -\frac{1}{\alpha} - \frac{1}{L_H} + \gamma_{HH} & 0 \\ 0 & \frac{T^Z \gamma_{HZ}}{T^H P_{EX}} - \frac{T^Z \gamma_{HZ}}{T^H P_{EX}(1 - \frac{\rho}{\omega(\rho+\rho^*)})} & -\frac{\omega(-\rho-\rho^*)\gamma_{HZ}}{T^H P_{EX}} - \frac{K_Z}{L_Z} \end{pmatrix}. \tag{3.3}$$

# 4 Conclusions

An epidemic model encompasses three most important stages i.e. to understand dynamic properly, to formulate the study accurately and to predict the future circumstances. In this paper, the Zika virus epidemic has been understood appropriately and then has been formulated with accuracy. Three different country's population Zika epidemic is discussed in this paper to show the accuracy of this mathematical model. From this model and parameters according to the environment, one can easily predict the upcoming epidemic and can take necessary precautions. Third stage is left for future work.

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# Competing Interests

Authors have declared that no competing interests exist.

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