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Stability Analysis of Disease-Free Equilibrium Point for Transmission and Control of Zika Virus Fever Dynamics

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Abstract:
We give the overview of the dynamics of the transmission and control of zika virus fever in the paper. Four mediums of transmission and control are incorporated into the formulated mathematical model of the virus dynamics. The effective reproduction number is obtained from the model equations. The local stability of disease free equilibrium point of the model is analyzed using reduced, linearized Jacobian matrix if the effective reproduction number is less than one and the global stability is also analyzed using the constructed Lyapunov function if the effective reproduction number is less or equal to one. The epidemiological implication of the analysis shows that zika virus fever can be controlled.

Keywords: *Zika virus fever, effective reproduction number, disease free equilibrium, stability, mathematical model*

1. Introduction

Zika virus derives its name from zika forest in Uganda where it was first discovered in monkeyin 1947, in a female Aedes mosquito in 1948 and in human in 1952; the infection caused by zika virus is called zika virus fever which does not kill but is linked with Microcephaly and Neurological anomalies (WHO, 2016). Zika virus lives longer in the semen than in the blood or virginal fluid (CDC, 2016). The virus is transmitted through mosquito bite, sexual contact, vertical transmission and blood transfusion (ECDC, 2016). (Funk *et.al.,* 2016) worked on comparative analysis of Zika and Dengue by setting the viruses. (Kucharski *et.al.,* 2016) worked on the outbreaks of zika in French Polynesia between 2013 and 2014. Gao *et.al*., (2016) and Augusto *et.al*., (2017) modeled zika virus as mosquito borne and sexually transmitted disease. We computed effective reproduction number using next generation matrix and establish the condition for the local asymptotical stability and global asymptotical stability of the disease free equilibrium pointof our improved model equations as the aim of this paper.

2. Materials and Methods

Total female population (N_1) is split into: Susceptible female compartment (S_1), Exposed female compartment (E_1), Symptomatic female compartment (I_{11}), Asymptomatic female compartment (I_{12}) and the Removed female compartment (R_1). The male population (N_2) is similarly partitioned into sub –populations as given in equation (15); and mosquito population is split into mosquitoes without zika virus (S_3) and mosquitoes with zika virus (I_3) as in (14).

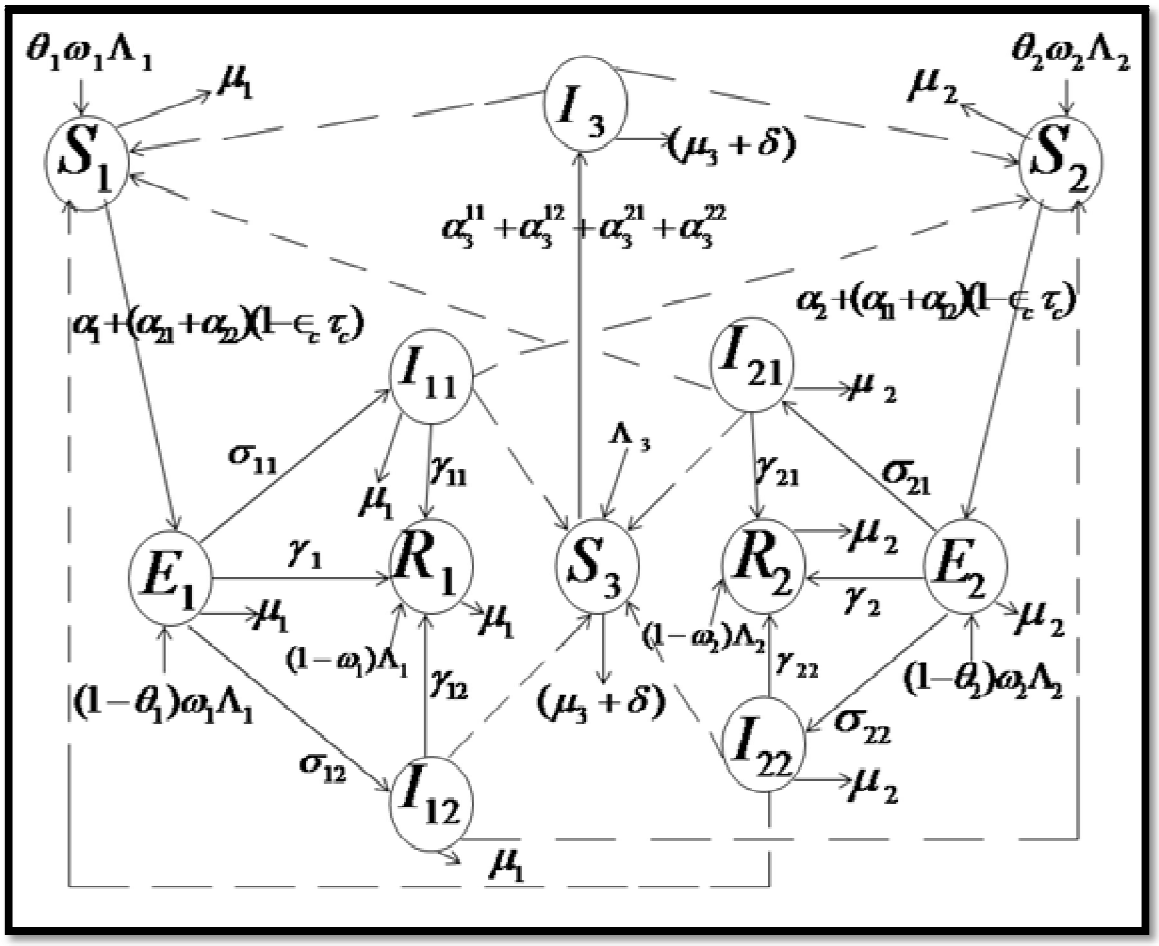

Figure 1: Model Graph

2.1. Model Equations

$$\frac{dS_1}{dt}=\theta_1\omega_1\Lambda_1-\frac{S_1}{N_1}\{\alpha_1\phi_3 I_3+\alpha_{21}\phi_{21}I_{21}(1-\epsilon_c\,\tau_c)+\alpha_{22}\phi_{22}I_{22}(1-\epsilon_c\,\tau_c)\}-\mu_1 S_1 \quad (1)$$

$$\frac{dE_1}{dt}=(1-\theta_1)\omega_1\Lambda_1+\frac{S_1}{N_1}\{\alpha_1\phi_3 I_3+\alpha_{21}\phi_{21}I_{21}(1-\epsilon_c\,\tau_c)+\alpha_{22}\phi_{22}I_{22}(1-\epsilon_c\,\tau_c)\}-(\gamma_1+\sigma_{11}+\sigma_{12}+\mu_1)E_1 \quad (2)$$

$$\frac{dI_{11}}{dt}=\sigma_{11}E_1-(\gamma_{11}+\mu_1)I_{11} \quad (3)$$

$$\frac{dI_{12}}{dt}=\sigma_{12}E_1-(\gamma_{12}+\mu_1)I_{12} \quad (4)$$

2.

$$\frac{dR_1}{dt}=(1-\omega_1)\Lambda_1+\gamma_1E_1+\gamma_{11}I_{11}+\gamma_{12}I_{12}-\mu_1R_1 \quad (5)$$

$$\frac{dS_3}{dt}=\Lambda_3-\frac{S_3}{N_3}(\alpha_3^{11}\phi_{11}I_{11}+\alpha_3^{12}\phi_{12}I_{12}+\alpha_3^{21}\phi_{21}I_{21}+\alpha_3^{22}\phi_{22}I_{22})-(\mu_3+\delta)S_3 \quad (6)$$

$$\frac{dI_3}{dt}=\frac{S_3}{N_3}(\alpha_3^{11}\phi_{11}I_{11}+\alpha_3^{12}\phi_{12}I_{12}+\alpha_3^{21}\phi_{21}I_{21}+\alpha_3^{22}\phi_{22}I_{22})-(\mu_3+\delta)S_3 \quad (7)$$

$$\frac{dS_2}{dt}=\theta_2\omega_2\Lambda_2-\frac{S_2}{N_2}\{\alpha_2\phi_3 I_3+\alpha_{11}\phi_{11}I_{11}(1-\epsilon_c\,\tau_c)+\alpha_{12}\phi_{12}I_{12}(1-\epsilon_c\,\tau_c)\}-\mu_2 S_2 \quad (8)$$

$$\frac{dE_2}{dt}=(1-\theta_2)\omega_2\Lambda_2+\frac{S_2}{N_2}\{\alpha_2\phi_3 I_3+\alpha_{11}\phi_{11}I_{11}(1-\epsilon_c\,\tau_c)+\alpha_{12}\phi_{12}I_{12}(1-\epsilon_c\,\tau_c)\}-(\gamma_2+\sigma_{21}+\sigma_{22}+\mu_2)E_2 \quad (9)$$

$$\frac{dI_{21}}{dt}=\sigma_{21}E_2-(\gamma_{21}+\mu_2)I_{21} \quad (10)$$

$$\frac{dI_{22}}{dt} = \sigma_{22}E_2 - (\gamma_{22} + \mu_2)I_{22} \quad (11)$$

$$\frac{dR_2}{dt} = (1-\omega_2)\Lambda_2 + \gamma_2 E_2 + \gamma_{21}I_{21} + \gamma_{22}I_{22} - \mu_2 R_2 \quad (12)$$

$$\left.\begin{aligned} N_1 &= S_1 + E_1 + I_{11} + I_{12} + R_1 \\ N_3 &= S_3 + I_3 \\ N_2 &= S_2 + E_2 + I_{21} + I_{22} + R_2 \end{aligned}\right] \quad (13)$$

Parameter	Description
Λ_1	Number of recruitment into female population
ω_1	Proportion of births without microcephaly into female population
$(1-\omega_1)$	Proportion of female births with microcephaly
θ_1	Proportion of susceptible female births without microcephaly
$(1-\theta_1)$	Proportion of exposed female births without Microcephaly
μ_1	Natural death rate of females
Λ_2	Number of recruitment into male population
ω_2	Proportion of births without microcephaly into male population
$(1-\omega_2)$	Proportion of male births with microcephaly
θ_2	Proportion of susceptible female births without microcephaly
$(1-\theta_2)$	Proportion of exposed female births without Microcephaly
μ_2	Natural death rate of males
Λ_3	Number of recruitment into the population of mosquitoes without zika virus
μ_3	Natural death rate of mosquitoes
δ	Death rate of mosquitoes due to insecticides
α_1	Transmission rate of infection through mosquito bite to the susceptible females
α_2	Transmission rate of infection through mosquito bite to the susceptible males
α_{21}	Transmission rate of infection through sex from symptomatic infectious males to susceptible females
α_{22}	Transmission rate of infection through sex from asymptomatic infectious males to susceptible females
α_{11}	Transmission rate of infection through sex from symptomatic infectious females to susceptible males
α_{12}	Transmission rate of infection through sex from symptomatic infectious females to susceptible males
α_3^{11}	Transmission rate of virus from symptomatic infectious females to mosquitoes without virus through mosquito bite
α_3^{12}	Transmission rate of virus from asymptomatic infectious females to mosquitoes without virus through mosquitoes bite
α_3^{21}	Transmission rate of virus from symptomatic infectious males to mosquitoes without virus through mosquito bite

Parameter	Description
α_3^{22}	Transmission rate of virus from asymptomatic infectious males to mosquitoes without virus through mosquito bite
σ_{11}	Progression rate of exposed females to the symptomatic infectious compartment
σ_{12}	Progression rate of exposed females to the asymptomatic infectious compartment
σ_{21}	Progression rate of exposed males to the symptomatic infectious compartment
σ_{22}	Progression rate of exposed males to the asymptomatic infectious compartment
γ_1	Rate of recovery from the compartment of exposed females to the removed compartment
γ_2	Rate of recovery from the compartment of exposed males to the removed compartment
γ_{11}	Rate of recovery from the compartment of symptomatic, infectious, females to the removed compartment
γ_{12}	Rate of recovery from the compartment of asymptomatic, infectious, females to the removed compartment
γ_{21}	Rate of recovery from the compartment of symptomatic, infectious, males to the removed compartment
γ_{22}	Rate of recovery from the compartment of asymptomatic, infectious, males to the removed compartment
ϕ_3	Is measuring the reduction in effectiveness of mosquito activities in transmitting virus by creating non conducive environment for the mosquitoes through the use of air conditioner
ϕ_{11}	Is measuring the reduction in effectiveness of sexual transmission through adherence to the preventive instructions
ϕ_{12}	Is measuring the reduction in effectiveness of sexual transmission through adherence to the preventive instructions
ϕ_{21}	Is measuring the reduction in effectiveness of sexual transmission through adherence to the preventive instructions
ϕ_{22}	Is measuring the reduction in effectiveness of sexual transmission through adherence to the preventive instructions
$(1-\in_c \tau_c)$	Reflects the impact of condom usage which is enhanced by public campaign (efficacy and compliance) on sexual transmission where $0<\in_c, \tau_c<1$

Table 1: Parameters of the Model

2.2. Model Reformation

To reform the model we substitute the following substitutes from (14) into the system (1) – (12)

$$\left.\begin{aligned} &\beta_1=\alpha_1\phi_3, \beta_2=\alpha_{21}\phi_{21}(1-\in_c \tau_c), \beta_3=\alpha_{22}\phi_{22}(1-\in_c \tau_c), \beta_4=\alpha_3^{11}\phi_{11}, \beta_5=\alpha_3^{12}\phi_{12}, k_6=\gamma_{21}+\mu_2 \\ &\beta_6=\alpha_3^{21}\phi_{21}, \beta_7=\alpha_3^{22}\phi_{22}, \beta_8=\alpha_2\phi_3, \beta_9=\alpha_{11}\phi_{11}(1-\in_c \tau_c), \beta_{10}=\alpha_{12}\phi_{12}(1-\in_c \tau_c), k_7=\gamma_{22}+\mu_2 \\ &k_1=\gamma_1+\sigma_{11}+\sigma_{12}+\mu_1, k_2=\gamma_{11}+\mu_1, k_3=\gamma_{12}+\mu_1, k_4=\mu_3+\delta, k_5=\gamma_2+\sigma_{21}+\sigma_{22}+\mu_2 \end{aligned}\right\} \quad (14)$$

2.3. Effective Reproduction Number (R_e)

Applying next generation matrix operator to compute the effective reproduction number as it was applied by Diekman *et.al*., (1990) and improved by Driessche(2002). The effective reproduction number is the basic reproduction number in Which control parameters are incorporated into the model equations. The basic reproduction number is the largest spectral radius of FV^{-1}

$$FV^{-1}=\left[\frac{\partial F(\varepsilon_0)}{\partial x_i}\right]\left[\frac{\partial V(\varepsilon_0)}{\partial x_i}\right]^{-1} \quad (27)$$

$$FV^{-1}=\begin{pmatrix} 0 & 0 & 0 & \frac{\theta_1\omega_1\beta_1}{k_4} & 0 & \frac{\theta_1\omega_1\beta_2}{k_6} & \frac{\theta_1\omega_1\beta_7}{k_7} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{\theta_2\omega_2\beta_9}{k_2} & \frac{\theta_2\omega_2\beta_{10}}{k_3} & \frac{\theta_2\omega_2\beta_8}{k_4} & 0 & 0 & 0 \\ 0 & \frac{\beta_4}{k_2} & \frac{\beta_5}{k_3} & 0 & 0 & \frac{\beta_6}{k_6} & \frac{\beta_7}{k_7} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix} \quad (28)$$

$$\left|FV^{-1}-\lambda I\right|=0 \text{ implies } R_e=\frac{\theta_2\omega_2\beta_8}{k_4} \quad (29)$$

Equation (29) gives the effective reproduction number of the reformed model equations.

3. Results and Discussion

3.1 Local Stability of Disease-Free Equilibrium Point (ε_0)

- Theorem 1: The disease-free equilibrium point of the (1) – (12) is locally asymptotically stable if $R_e<1$ or unstable if $R_e>1$ Proof

$$J(\varepsilon_0)=\begin{pmatrix} -\mu_1 & 0 & 0 & 0 & 0 & 0 & -\beta_1 & 0 & 0 & -\beta_2 & -\beta_3 & 0 \\ 0 & -k_1 & 0 & 0 & 0 & 0 & \beta_1 & 0 & 0 & \beta_2 & \beta_3 & 0 \\ 0 & \sigma_{11} & -k_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \sigma_{12} & 0 & -k_3 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \gamma_1 & \gamma_{11} & \gamma_{12} & -\mu_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -\beta_4 & -\beta_5 & 0 & -k_4 & 0 & 0 & 0 & -\beta_6 & -\beta_7 & 0 \\ 0 & 0 & \beta_4 & \beta_5 & 0 & 0 & -k_4 & 0 & 0 & \beta_6 & \beta_7 & 0 \\ 0 & 0 & -\beta_9 & -\beta_{10} & 0 & 0 & -\beta_8 & -\mu_2 & 0 & 0 & 0 & 0 \\ 0 & 0 & \beta_9 & \beta_{10} & 0 & 0 & \beta_8 & 0 & -k_5 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \sigma_{21} & -k_6 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \sigma_{22} & 0 & -k_7 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \gamma_2 & \gamma_{21} & \gamma_{22} & -\mu_2 \end{pmatrix} \quad (30)$$

Using Gauss Jordan elimination approach, (30) implies the characteristics equation, and we obtain the respective eigenvalues:

$$\left.\begin{array}{l} \lambda_1=-\mu_1<0,\lambda_2=-k_1<0,\lambda_3=-k_1k_2<0,\lambda_4=-k_1k_3<0,\lambda_5=-k_1k_2k_3\mu_1<0,\lambda_6=-k_4<0,\lambda_{11}=k_1k_2k_3k_4k_5k_6-k_1k_2k_3k_4k_5k_7 \\ \lambda_7=-k_1k_2k_3k_4+k_3\beta_1\beta_4\sigma_{11}+k_2\beta_1\beta_5\sigma_{12},\lambda_8=-\mu_2<0,\lambda_9=-k_1k_2k_3k_4k_5<0,\lambda_{12}-k_1k_2k_3k_4k_5\mu_2k_7-k_1k_2k_3k_4k_5\gamma_{22}<0 \\ \lambda_{10}=-k_1k_2k_3k_4k_5k_6-k_3k_4\beta_2\beta_9\sigma_{11}\sigma_{21}-k_2\beta_2\beta_4\beta_9\beta_{10}\sigma_{12}\sigma_{21}-k_1k_2k_3\beta_6\beta_8\sigma_{21}+k_3\beta_2\beta_4\beta_9\sigma_{11}\sigma_{21}+k_2\beta_2\beta_5\beta_{10}\sigma_{12}\sigma_{21} \end{array}\right] \quad (31)$$

$\lambda_1,\lambda_2,\lambda_3,\lambda_4,\lambda_5,\lambda_6,\lambda_8,\lambda_9,\lambda_{12}$ are negative real numbers. If $\lambda_7<0\Rightarrow -k_1k_2k_3k_4+k_3\beta_1\beta_4\sigma_{11}+k_2\beta_1\beta_5\sigma_{12}<0$, $\Rightarrow$ $-k_5k_6k_7k_4+k_7\beta_8\beta_6\sigma_{21}+k_6\beta_8\beta_7\sigma_{22}<0$

$\Rightarrow k_7\beta_8\beta_6\sigma_{21}+k_6\beta_8\beta_7\sigma_{22}<k_5k_6k_7k_4$

$$\frac{\theta_2\omega_2\beta_8}{k_4}\cdot\frac{k_7\beta_6\sigma_{21}+k_6\beta_7\sigma_{22}}{k_5k_6k_7\theta_2\omega_2}<1\Rightarrow R_e\cdot\frac{k_7\beta_6\sigma_{21}+k_6\beta_7\sigma_{22}}{k_5k_6k_7\theta_2\omega_2}<1 \text{ if and only if } R_e<1. \quad (32)$$

If $\lambda_{10} < 0$ then $-k_1k_2k_3k_4k_5k_6 - k_3k_4\beta_2\beta_9\sigma_{11}\sigma_{21} - k_2\beta_2\beta_4\beta_9\beta_{10}\sigma_{12}\sigma_{21} - k_1k_2k_3\beta_6\beta_8\sigma_{21} + k_3\beta_2\beta_4\beta_9\sigma_{11}\sigma_{21} + k_2\beta_2\beta_5\beta_{10}\sigma_{12}\sigma_{21} < 0$ (33)

Comparing $-k_3k_4\beta_2\beta_9\sigma_{11}\sigma_{21}$ and $k_3\beta_2\beta_4\beta_9\sigma_{11}\sigma_{21}$, $k_4 > \beta_4$ implies $-k_3k_4\beta_2\beta_9\sigma_{11}\sigma_{21} + k_3\beta_2\beta_4\beta_9\sigma_{11}\sigma_{21} < 0$ (34)

Comparing $-k_1k_2k_3k_4k_5k_6$ and $k_2\beta_2\beta_5\beta_{10}\sigma_{12}\sigma_{21}$, $k_1 > \beta_2, k_3 > \beta_5, k_4 > \beta_{10}, k_5 > \sigma_{12}, k_6 > \sigma_{21}$

$\Rightarrow -k_1k_2k_3k_4k_5k_6 + k_2\beta_2\beta_5\beta_{10}\sigma_{12}\sigma_{21} < 0$ (35)

Hence, (33), (34) and (35) show that $\lambda_{10} < 0$.

$\lambda_{11} = k_1k_2k_3k_4k_5k_6 - k_1k_2k_3k_4k_5k_7 < 0$, implies $k_6 < k_7$, implies $\frac{k_6}{k_7} < 1$ if and only if $k_7 > k_6$ that is $\lambda_{11} < 0$

Therefore, the model system (1) - (12) is locally asymptotically stable (LAS) at DFE if and only if $R_e < 1$. The epidemiological implication is that the outbreak can be controlled if $R_e < 1$

3.2. Global Stability Analysis of Disease-Free Equilibrium Point

- Theorem 2

The model equations (1) – (12) is globally asymptotically stable at DFE if $R_e \leq 1$

To construct Lyapunov function, we substitute for the forces of infection in the model equations.

Constructed Lyapunov function is $V = \theta_2\omega_2(E_1 + I_3 + E_2) + \frac{k_4}{k_2}I_{11} + \frac{k_4}{k_3}I_{12} + \frac{k_4}{k_6}I_{21} + \frac{k_4}{k_7}I_{22}$ (36)

The derivative of the function implies $\Rightarrow \dot{V} \leq k_4(I_{11} + I_{12} + I_3 + I_{21} + I_{22})(4\Lambda_2.R_e - 1)$

$\Rightarrow \dot{V} \leq 0$, if and only if, $R_e \leq 1$, and equality is achieved at $I_{11} = I_{12} = I_3 = I_{21} = I_{22} = 0$.

Therefore, invoking La Salle's invariance principle on the derivative of the Lyapunov function shows that the system (1) – (12) is globally asymptotically stable at the DFE if $R_e \leq 1$

4. Conclusion

With reference to the control measures incorporated into the model equations, the epidemiological implication of Local Asymptotical Stability (LAS) Analysis and Global Asymptotical Stability (GAS) Analysis of the system (1) – (12) at the disease free equilibrium point (ε_0) show that the outbreak of zika virus fever can be controlled locally if and only if $R_e < 1$ and globally if and only if $R_e \leq 1$.

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