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Modelling the Spread of Zika Virus with Vaccination and Vector Reduction as Control Strategies

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Abstract
Zika virus is a mosquito-borne disease transmitted to humans through the bites of infected Aedes mosquitoes. In this paper, we formulated a mathematical model for Zika virus incorporating vaccination and vector reduction as control strategies. The model exhibits two equilibria, disease free equilibrium and the endemic equilibrium. The threshold quantity (R_o) which is the basic reproduction number is computed and used to prove that the Disease Free Equillibrum is locally asymptotically stable when it is less than unity. Our numerical simulations show that the application of residual sprays (indoor & outdoor) increases mosquito death rate and reduces mosquito longevity which in turn reduces the burden of Zika virus in the population. Also, vaccination programmes are one of the important strategies for controlling Zika virus as it aids in the reduction of humans at risk of infection.

Keywords: Zika Virus, Mathematical Model, Reproduction Number, Ordinary Differential Equations.

INTRODUCTION

Zika virus (ZIKV) is a mosquito-borne epidemic transmitted to humans through the bites of infected Aedes mosquitoes. It was first discovered in a rhesus monkey population in 1947 in the Zika forest of Uganda. Historically, ZIKV was thought to cause mild symptoms in humans, including headaches, maculopapular rash, fever, malaise, conjunctivitis, and arthralgia, occurring three to twelve days after the bite from an infected mosquito. Recently, however, there have been reported increases in congenital anomalies (such as microcephaly), Guillain-Barre syndrome, and other neurological and autoimmune disorders in regions where ZIKV has been newly introduced. It is believed by researchers that ZIKV is responsible for these increases, suggesting that ZIKV is a more serious disease than initially realized (Cao-Lormeau *et al.*, 2016; World Health Organization, 2015).

The first human epidemic was recorded in 2007 in Yap, Federated States of Micronesia, Pacific region. The second epidemic dates back to October 2013, six years after the first epidemic

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occurred in the same region. Subsequently, the virus spread to several countries and is considered to be a public health emergency of global importance. Epidemiologically, ZIKV cases were only sporadically recorded in some African and Southeast Asian countries until the late 2000s. Over 19,000 suspected cases were estimated during this epidemic. In Brazil, the first autochthonous transmission occurred in the Northeastern region in 2015. ZIKV arrived in Brazil due to possible events involving foreign individuals (Gourinat *et al*., 2015; Zanluca *et al*., 2015). ZIKV incidence in Brazil and French Polynesia possibly compels World Health Organisation to declare a Public Health Emergency of International Concern in response to the clusters of microcephaly and other neurological disorders. The number of suspected cases in Brazil was estimated at 440,000 to 1,300,000 in 2015. Apart from the major outbreak in French Polynesia incident which saw 42 Guillain-Barre syndrome cases between March 2014 and May 2015 in same region, 10 cases of Guillain-Barre syndrome with microcephaly and severe brain lesions were reported. Globally ZIKV has the potential to spread across all continents; therefore, it is critical to characterize the transmission dynamics of the disease (Gourinat *et al*., 2015; Zanluca *et al*., 2015; Dupont *et al*., 2015; Dias *et al*., 2018;Bonyah and Okosun, 2016).

People with Zika virus disease usually have symptoms; mild fever, skin rashes, conjuctivities, muscle and joint pain, malaise or headache, which last for 2-7days normally. National health authorities in China reported that potential neurological and auto-immune complications of zika virus disease (Ding *et al*., 2016). The microcephaly morbidity rate of the new baby is very high if the pregnancy is infected by Zika virus (Ding *et al*., 2016).

Mathematical model is powerful tool to investigate and address the emergence of infectious diseases. One of the most popular modeling frameworks is the compartmental models. The model divides the population of interest based on their health status. The compartmental model has been employed in the study of transmission dynamics in many vector- borne diseases such as dengue fever and malaria (Supariz *et al*., 2018). The present work therefore is aimed at constructing a simple vector- borne compartmental model that incorporates vaccination and vector reduction as control strategies for ZIKV which other authors did not consider in their work.

MATERIALS AND METHODS

Model Formulation

In this work, we consider two populations consisting of human and vector population. The total population of human and vectors is divided into the following mutually exclusive epidemiological classes, namely, susceptible humans ($S_h(t)$), Infectious humans with Zika Virus ($I_h(t)$), Recovered humans ($R_h(t)$), Susceptible mosquitoes ($S_m(t)$) and Infectious mosquitoes ($I_m(t)$).

Let $N_h(t)$ and $N_m(t)$ denote the total number of humans and vectors at time t, respectively. Hence, we have that,

$$N_h(t) = S_h(t) + I_h(t) + R_h(t)$$

and

$$N_m(t) = S_m(t) + I_m(t)$$

The model equations are given by

$$
\begin{aligned}
\dot{S}_h &= \frac{\alpha_{mh} b_V S_h I_m}{N_h} - (\mu_h + v_h) S_h \\
\dot{I}_h &= \frac{S_h I_m}{N_h} - (\gamma + \delta_h + \mu_h) I_h \\
\dot{R}_h &= v_h S_h - \mu_h R_h \\
\dot{S}_m &= \frac{\alpha_{hm} b_V S_m I_h}{N_h} - (\mu_m + \delta_m) S_m \\
\dot{I}_m &= \frac{S_m I_h}{N_h} - (\mu_m + \delta_m) I_m
\end{aligned} \tag{1}
$$

In the above let,

$$k_1 = \mu_h + v_h, \quad k_2 = \gamma + \delta_h + \mu_h, \quad k_3 = \mu_m + \delta_m$$

expressing(1) in terms of forces of infection gives

$$
\begin{aligned}
\dot{S}_h &= \lambda_h S_h - k_1 S_h \\
\dot{I}_h &= \lambda_h S_h - k_2 I_h \\
\dot{R}_h &= v_h S_h - \mu_h R_h \\
\dot{S}_m &= \lambda_m S_m - k_3 S_m \\
\dot{I}_m &= \lambda_m S_m - k_3 I_m
\end{aligned} \tag{2}
$$

where,

$$\lambda_h = \frac{\alpha_{mh} b_V I_m}{N_h}, \quad \lambda_m = \frac{\alpha_{hm} b_V I_h}{N_h} \tag{3}$$

Parameters	Description
α_{mh}	Effective virus transmission rate from mosquito to human
α_{hm}	Effective transmission rate from human to mosquito
δ_m	Death rate of mosquito from insecticide
Λ_h	Human recruitment rate
Λ_m	Mosquito recruitment rate
γ	Recovery rate of human from infection
μ_m	Natural death rate of mosquito
μ_h	Natural death rate of human
δ_h	Death rate of human from infection
v_h	Vaccination rate of human
b_V	Mosquito biting rate

Positivity of Solutions

We assumed that the initial conditions of the model are nonnegative and we also intend to show that the solution of the model is also positive.

Lemma 2.1:

Let the initial data for the model be
$S_h(0) > 0, I_h(0) > 0, R_h(0) > 0, S_m(0) > 0, I_m(0) > 0$
then the solutions $(S_h(t), I_h(t), R_h(t), S_m(t), I_m(t))$ of the model with initial data will remain positive for all time $t > 0$

Proof: Let $t_1 = Sup\{t > 0 : S_h(0) > 0, I_h(0) > 0, R_h(0) > 0, S_m(0) > 0, I_m(0) > 0\} > 0$
From the first equation in model (1)
$\dot{S}_h \geq -(\lambda_h + k_1)S_h$
which implies
Using integrating factor method we have

$$\frac{d}{dt}\left\{S_h(t)\exp\left((k_1)t + \int_0^{t_1}\lambda_h(\tau)d\tau\right)\right\} = \Lambda_h \exp\left((k_1)t + \int_0^{t_1}\lambda_h(\tau)d\tau\right)$$

$$S_h(t_1)\exp\left((k_1)t + \int_0^{t_1}\lambda_h(\tau)d\tau\right) - S_h(0) \geq \int_0^{t_1}\Lambda_h \exp\left((k_1)t + \int_0^{t_1}\lambda_h(\tau)d\tau\right)$$

$$S_h(t_1) = S_h(0)\exp\left(-(k_1)t - \int_0^{t_1}\lambda_h(\tau)d\tau\right)$$

$$+\exp\left(-(k_1)t - \int_0^{t_1}\lambda_h(\tau)d\tau\right)\times\int_0^{t_1}\left[\Lambda_h \exp\left((k_1)t + \int_0^{t_1}\lambda_h(\tau)d\tau\right)\right]dy > 0$$

Similarly, it can be shown that all state variables of the model remain positive for all time $t > 0$ so that

$I_h(t) > 0, R_h(t) > 0, S_m(t) > 0, I_m(t) > 0$ for all time $t > 0$

Boundedness
Lemma2.2

Consider the region $D_1 = \left\{(S_h, I_h, R_h, S_m, I_m) \in \square^{\cdot} \quad \frac{\Lambda_h}{\mu_h},\ N_m \leq \frac{\Lambda_m}{\mu_m}\right\}$. It can be shown that the set D_1 is positively invariant and an attractor of all positive solution of the system (2)

Proof
The rate of change of the total human population gives
$\dot{N}_h \leq \mu_h N_h - \delta_h I_h$ (4)
By standard comparison theorem,
$\dot{N}_h \leq \mu_h N_h$
Using the integrator factor method, we have

$$N_h(t) = N_h(0)e^{-\mu_h t} + \frac{\Lambda_h}{\mu_h}\left(1 - e^{-\mu_h t}\right) \quad (5)$$

The rate of change of the total mosquito population gives

$$\dot{I}_m \quad \mu_m N_m - \delta_m N_m \tag{6}$$

By standard comparison theorem,

$$\dot{I}_m \quad \mu_m N_m$$

Using the integrator factor method, we have

In particular, $N_h(t) \le \frac{\Lambda_h}{\mu_h}$ if $N_h(0) \le \frac{\Lambda_h}{\mu_h}$ and $N_m(t) \le \frac{\Lambda_m}{\mu_m}$ if $N_m(0) \le \frac{\Lambda_m}{\mu_m}$ respectively.

Hence D_1 is a positively invariant setand the solution enters D_1 in finite time or $N_h(t) \to \frac{\Lambda_h}{\mu_h}$ and $N_m(t) \to \frac{\Lambda_m}{\mu_m}$ as $t \to \infty$. Hence it is sufficient to consider the dynamics of system (1) in D_1. In this region, the system (1) is considered as being mathematically and epidemiologically well posed.

Local Stability of Disease- Free Equilibrium (DFE) of Zika Virus Model

The system (1) has a disease-free equilibrium obtained by setting the right hand side to zero and the disease classes to zero to give

$$\xi^* = (S_h^*, I_h^*, R_h^*, S_m^*, I_m^*) = \left(\frac{\Lambda_h}{\mu_h + v_h}, 0, \frac{v_h \Lambda_h}{\mu_h(\mu_h + v_h)}, \frac{\Lambda_m}{\mu_m + v_m}, 0 \right) \tag{7}$$

The next generation operator method described by Van den Driessche and Watmough (2002) is used here to obtain the basic reproduction number. The matrices F and V for the new infection terms and the remaining transfer terms are respectively given as

$$F = \begin{pmatrix} 0 & \frac{\alpha_{mh} b_V S_h}{N_h} \\ \frac{\alpha_{hm} b_V S_m}{N_h} & \end{pmatrix}$$

$$V = \begin{pmatrix} k_2 & 0 \\ 0 & k_3 \end{pmatrix}$$

It follows that the effective reproduction number is

$$R_E = \sqrt{\frac{\alpha_{mh} b_V S_h^*}{N_h^* k_3} \cdot \frac{\alpha_{hm} b_V S_m^*}{N_h^* k_2}} \tag{8}$$

$$R_E = \sqrt{R_h . R_m}$$

$$R_h = \frac{\alpha_{mh} b_V S_h^*}{N_h^*(\gamma + \delta_h + \mu_h)} \text{ and } R_m = \frac{\alpha_{hm} b_V S_m^*}{N_h^*(\mu_m + \delta_m)} \tag{9}$$

The threshold quantity, R_E is the average number of zika virus cases generated by a typically infected individual introduced into a susceptible population. The expression R_h is the number of secondary infections in human introduced by one infectious mosquito, while the expression R_m is the number of secondary infections in mosquito introduced by one infectious human.

The Jacobian at the disease-free equilibrium gives

$$J(\xi^*)=\begin{pmatrix} -k_1 & 0 & 0 & 0 & \frac{-\alpha_{mh}b_V S_h^*}{N_h} \\ 0 & -k_2 & 0 & 0 & \frac{\alpha_{mh}b_V S_h^*}{N_h} \\ v_h & \gamma & -\mu_h & 0 & 0 \\ 0 & \frac{-\alpha_{hm}b_V S_m^*}{N_h} & 0 & -k_3 & 0 \\ 0 & \frac{\alpha_{hm}b_V S_m^*}{N_h} & 0 & 0 & -k_3 \end{pmatrix} \quad (10)$$

The characteristic equation gives

$$(-k_1-\lambda)(-\mu_h-\lambda)(-k_3-\lambda)\left[\lambda^2+\lambda(k_2+k_3)+k_2k_3\left(1-\frac{\alpha_{mh}b_V S_h^*\alpha_{hm}b_V S_m^*}{N_h^*N_h^*k_2k_3}\right)\right]=0$$

Therefore, either

$\lambda_1=-k_1,\quad \lambda_2=-\mu_h,\quad \lambda_3=-k_3$ or

$\lambda^2+\lambda(k_2+k_3)+k_2k_3\left(1-R_E^2\right)=0$

The Jacobian stability technique requires that all eigen values be negative for local stability to hold, we now apply the Routh-Hurwitz stability criterion to show that all eigen values are negative.That is, comparing the above polynomial with $P(\lambda)=a_0\lambda^2+a_1\lambda+a_2$ gives

$a_0=1>0,\quad a_1=k_2+k_3>0,\quad a_2=k_2k_3\left(1-R_E^2\right)>0 \ \ if\ \ R_E<1$

From the Routh-Hurwitz criteria, we conclude that the DFE is LAS if $R_E<1$. The epidemiological significance of LAS of Zika virus is that small introduction of infected mosquitoes into the population cannot cause an epidemic and hence zika virus can be controlled.

Existence of Endemic Equilibrium Point (EEP) of the Model

Let the EEP of the model (1) be denoted by $\xi^{**}=(S_h^{**},I_h^{**},R_h^{**},S_m^{**},I_m^{**})$. Solving equation (1) in terms of the force of infection at steady state gives

$$S_h^{**}=\frac{\Lambda_h}{k_1+\lambda_h^{**}}\ ,\quad I_h^{**}=\frac{\lambda_h^{**}\Lambda_h}{k_2(k_1+\lambda_h^{**})}\ ,\quad R_h^{**}=\frac{\gamma\lambda_h^{**}\Lambda_h+k_2v_h\Lambda_h}{\mu_hk_2(k_1+\lambda_h^{**})}$$

$$S_m^{**}=\frac{\Lambda_m}{k_3+\lambda_m^{**}}\ ,\quad I_m^{**}=\frac{\lambda_m^{**}\Lambda_m}{k_3(k_3+\lambda_m^{**})}$$

Now,

$$\lambda_h^{**}=\frac{\alpha_{mh}b_V I_m^{**}}{N_h^{**}}\qquad \lambda_m^{**}=\frac{\alpha_{hm}b_V I_h^{**}}{N_h^{**}} \quad (11)$$

Substituting the value of I_m^{**} into (11) gives

$$\lambda_h^{**}=\frac{\alpha_{mh}b_V\lambda_m^{**}\Lambda_m}{N_h^{**}k_3(k_3+\lambda_m^{**})} \quad (12)$$

Substituting the value of λ_m^{**} into (12) gives

$$\lambda_h^{**} = \frac{\alpha_{mh} b_V \Lambda_m \alpha_{hm} b_V I_h^{**}}{N_h^{**} N_h^{**} k_3 \left(k_3 + \frac{\alpha_{hm} b_V I_h^{**}}{N_h^{**}} \right)} \tag{13}$$

Substituting the value of I_h^{**} into (13) and simplifying gives

$$\lambda_h^{**} = \frac{\alpha_{mh} b_V \Lambda_m \alpha_{hm} b_V \Lambda_h \lambda_h^{**}}{N_h^{**} k_3 \left((N_h^{**} k_2 k_3 + \alpha_{hm} b_V \Lambda_h) \lambda_h^{**} + N_h^{**} k_1 k_2 k_3 \right)} \tag{14}$$

Equation (14) can be expressed as

$$\lambda_h^{**} (A_1 \lambda_h^{**} + A_2) = 0$$

Either λ_h^{**}=0, or $A_1 \lambda_h^{**} + A_2 = 0$ (15)

Where

$$A_1 = N_h^{**} k_3 (N_h^{**} k_2 k_3 + \alpha_{hm} b_V \Lambda_h) > 0$$

$$A_2 = N_h^{**2} k_1 k_2 k_3^2 \left(1 - \frac{\alpha_{mh} b_V \Lambda_m \alpha_{hm} b_V \Lambda_h}{N_h^{**} k_2 k_3 N_h^{**} k_1 k_3} \right)$$

$$A_2 = N_h^{**2} k_1 k_2 k_3^2 \left(1 - R_E^2 \right)$$

$$A_2 < 0 \ \ if \ \ R_E > 1$$

So system (1) has a unique (stable) endemic equilibrium if $R_E > 1$ since $\lambda_h^{**} > 0 \quad for \quad R_E > 1$

Local Stability of Endemic Equilibrium Point (EEP) of the Zika Virus Model

The Jacobian expressed in terms of forces of infection gives

$$J(\xi^{**}) = \begin{pmatrix} -(\lambda_h^{**} + k_1) & 0 & 0 & 0 & 0 \\ \lambda_h^{**} & -k_2 & 0 & 0 & 0 \\ v_h & \gamma & -\mu_h & 0 & 0 \\ 0 & 0 & 0 & -(\lambda_m^{**} + k_3) & 0 \\ 0 & 0 & 0 & \lambda_m^{**} & -k_3 \end{pmatrix} \tag{16}$$

Expressing in terms of upper triangular matrix gives

$$J(\xi^{**}) = \begin{pmatrix} -(\lambda_h^{**} + k_1) & 0 & 0 & 0 & 0 \\ 0 & -k_2 & 0 & 0 & 0 \\ 0 & 0 & -\mu_h & 0 & 0 \\ 0 & 0 & 0 & -(\lambda_m^{**} + k_3) & 0 \\ 0 & 0 & 0 & 0 & -k_3 \end{pmatrix}$$

The eigen values are;

$\lambda_1 = -(\lambda_h^{**} + k_1)$, $\lambda_2 = -k_2 < 0$, $\lambda_3 = -\mu_h < 0$, $\lambda_4 = -(\lambda_m^{**} + k_3)$, $\lambda_5 = -k_3 < 0$

from (15)

$$\lambda_h^{**} = \frac{-A_2}{A_1} = \frac{N_h^{**} k_1 k_2 k_3 \left(R_E^2 - 1\right)}{(N_h^{**} k_2 k_3 + \alpha_{hm} b_V \Lambda_h)} \tag{17}$$

$$\lambda_1 = -\left(\frac{N_h^{**} k_1 k_2 k_3 \left(R_E^2 - 1\right)}{(N_h^{**} k_2 k_3 + \alpha_{hm} b_V \Lambda_h)} + k_1 \right) < 0 \text{ if } R_E > 1$$

$$\lambda_4 = -(\lambda_m^{**} + k_3)$$

But $\lambda_m^{**} = \dfrac{\alpha_{hm} b_V \Lambda_h \lambda_h^{**}}{N_h^{**} k_2 (k_1 + \lambda_h^{**})} = \dfrac{\dfrac{\alpha_{hm} b_V \Lambda_h N_h^{**} k_1 k_2 k_3 \left(R_E^2 - 1\right)}{(N_h^{**} k_2 k_3 + \alpha_{hm} b_V \Lambda_h)}}{N_h^{**} k_2 \left(k_1 + \dfrac{N_h^{**} k_1 k_2 k_3 \left(R_E^2 - 1\right)}{(N_h^{**} k_2 k_3 + \alpha_{hm} b_V \Lambda_h)} \right)} > 0 \text{ if } R_E > 1$

Hence, $\lambda_4 = -(\lambda_m^{**} + k_3) < 0$

We conclude that the EEP of the Zika virus model is LAS if $R_E > 1$.

NUMERICAL RESULTS AND DISCUSSIONS

Our numerical simulations examine the effects of different variations of our control strategies on the transmission of Zika virus using Maple Software.

Variables	Description	Values	References
$S_h(0)$	Susceptible human	3000	Assumed
$I_h(0)$	Infectious human	500	Assumed
$R_h(0)$	Recovered human	200	Assumed
$S_m(0)$	Susceptible mosquito	11000	Assumed
$I_m(0)$	Infectious mosquito	300	Assumed
Parameters	**Description**	**Values**	**References**
α_{mh}	Effective virus transmission rate from mosquito to human	0.33	Agusto et al., (2017)
α_{hm}	Effective transmission rate from human to mosquito	0.33	Agusto et al., (2017)
δ_m	death rate from of mosquito from insecticide	(0,1)	
Λ_h	Human recruitment rate	78	Estimated
Λ_m	Mosquito recruitment rate	807	Estimated
γ	Recovery rate of human from infection	0.118	Agusto et al., (2017)
μ_m	natural death rate of mosquito	0.0714	Adamu et al., (2017)
μ_h	natural death rate of human	0.02043	Andrawus&Eguda (2017)
δ_h	Death rate of human from infection	0.5	Adamu et al., (2017)
v_h	vaccination rate of human	(0,1)	
b_V	Mosquito biting rate	0.5	Agusto et al., (2017)

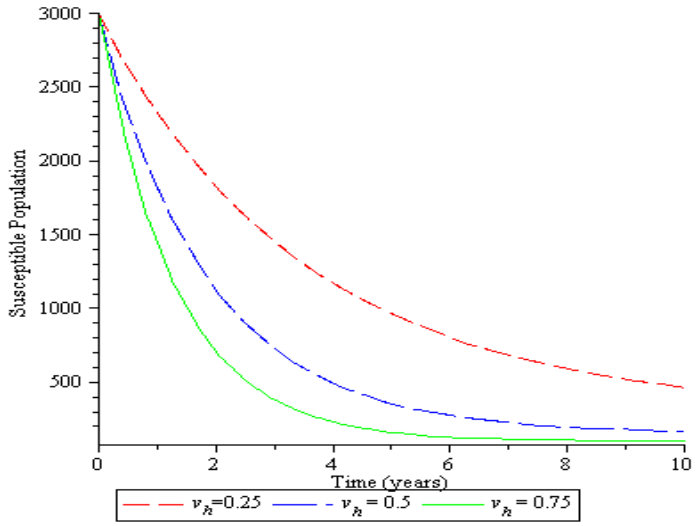

Figure 1: The Effect of Varying Vaccination Rates on the Susceptible Population

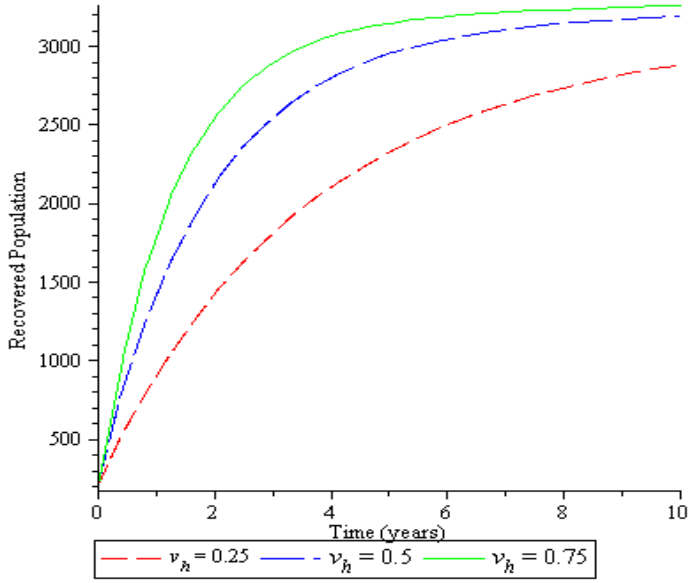

Figure 2: The Effect of Varying Vaccination Rates on the Recovered Population

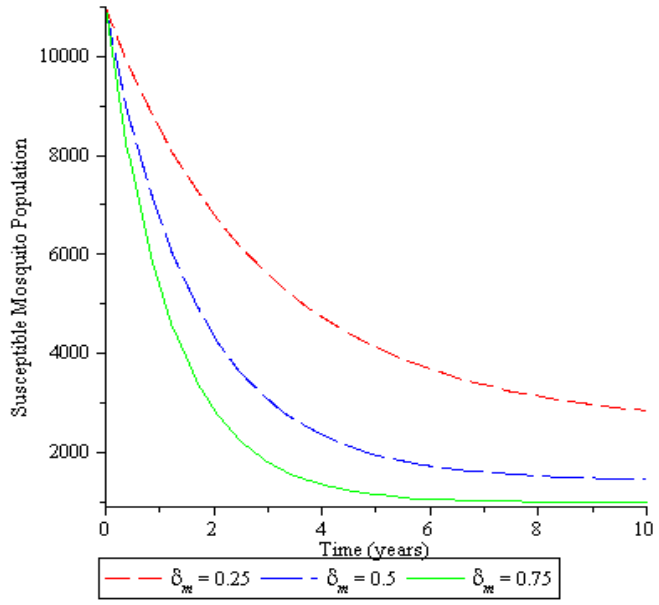

Figure 3: The Effect of Varying Vector-Reduction Rates on the Susceptible Mosquito Population

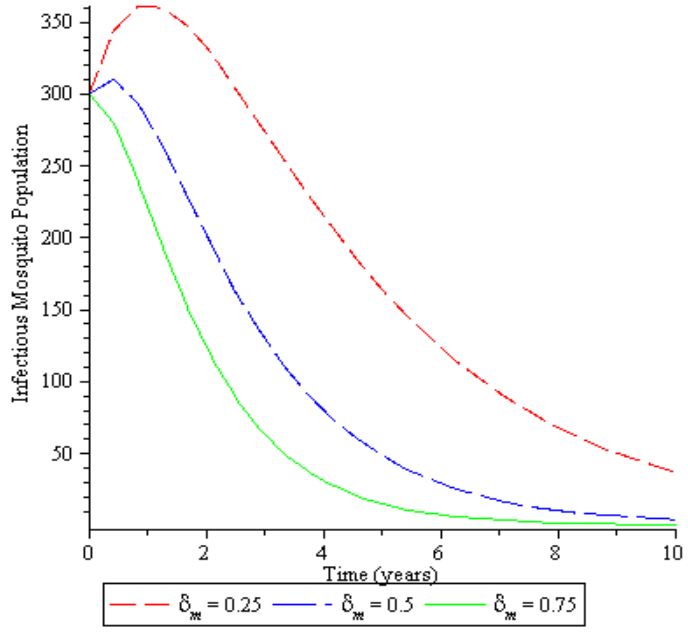

Figure 4: The Effect of Varying Vector-Reduction Rates on the Infectious Mosquito Population

Figure 1 indicates that the higher the vaccination rate the lower the population of those at risk of Zika virus infection. Figure 2 shows that increase in the vaccination rate, increases the population of those who are immune to Zika virus infection. Hence vaccination plays a vital role in the dynamics of Zika virus in the population. Figure 3 shows that application of residual sprays (indoor & outdoor) increases mosquito death rate and reduces mosquito longevity which in turn reduces the burden of Zika virus in the population.In figure 4, the population of Infectious mosquito increases, reaching a maximum and then falls. This maximum is higher in the case of lower vector reduction rates. In the case of high pesticide control through residual sprays, the burden of Zika virus reduces drastically within a shorter period.

CONCLUSION

In this paper, a mathematical model for Zika virus was formulated and analysed in order to gain a better understanding of its transmission pattern in the population. It was proved that the disease free equilibrium pointis locally asymptotically stable if the control reproduction number is less than unity and the endemic equilibrium point is locally asymptotically stable if the control reproduction number is greater than unity. Our analysis shows that if only small number of infectious individuals is introduced into the society then they cannot cause an epidemic if the effective reproduction number can be brought below unity and hence Zika virus can be controlled. Numerical simulations show that the exposure rate of humans to mosquitoes can be greatly reduced through effective application of residual sprays which in turn reduces the burden of Zika virus in the population.However, in the Zika virus dynamics, vaccination programmes play a vital role in controlling Zika virus as it reducesthe risk of infection.

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