

Mathematical analysis on the vertical and horizontal transmission dynamics of HIV and Zika virus co-infection

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ARTICLE INFO

MSC:
92B05
92D30
92-10
34D20

Keywords:

HIV-ZIKV co-infection
Vertical transmission
Basic reproduction number
Stability
bifurcation

ABSTRACT

The co-infection of HIV and Zika virus (ZIKV) poses a complex and understudied health challenge, requiring a comprehensive investigation into the synergistic effects, potential complications, and the impact on affected individuals. Consequently, This paper introduces a novel deterministic mathematical model that examines the transmission dynamics of HIV and Zika virus co-infection, considering both vertical and horizontal transmission. The analysis begins with two sub-models: one for HIV-only and another for ZIKV-only. Qualitative examination indicates that the HIV only sub-model achieves a globally asymptotically stable disease-free equilibrium when the associated reproduction number is below unity. In contrast, the ZIKV only sub-model exhibits a backward bifurcation phenomenon, where both stable disease-free and stable endemic equilibria co-exist when the associated reproduction number of the ZIKV only sub-model is less than unity. Thus, the backward bifurcation property makes effective control of ZIKV infection in the population difficult when the associated reproduction number is less than unity. It is shown, using the center manifold theory that the full HIV-ZIKV co-infection model undergoes the phenomenon of backward bifurcation. We carried out the sensitivity analysis of the HIV and ZIKV basic reproduction numbers to determine the parameters that positively influence the spread of the two diseases. It is also revealed that an increase in HIV infection in the population will positively influence the transmission of ZIKV. We validated the ZIKV only sub-model by fitting the ZIKV only sub-model to the confirmed cases of ZIKV data in Brazil. The outcome of the numerical simulations of HIV-ZIKV co-infection model reveals that the two diseases co-exist when their basic reproduction number surpasses one. Furthermore, increasing HIV treatment rate significantly reduces the burden of co-infection with the Zika virus.

1. Introduction

Human-Immunodeficiency Virus (HIV) is a virus that causes Acquired-Immunodeficiency Syndrome (AIDS). It targets the immune system, specifically the Cluster of Differentiation 4 (CD4) cells or *T* cells of the infected individual weakening it and making an individual incapable of resisting attack from a wide range of infections [1]. Between its identification in 1981 and 2006, AIDS had tragically claimed the lives of over 25 million individuals, while HIV had affected approximately 0.6% of the global populace [2]. In 2018, on a global scale, there were approximately 37.9 million people living with HIV/AIDS, resulting in 1.2 million deaths. Among those who were infected, approximately

62% were diagnosed and undergoing Antiretroviral Therapy (ART) [3]. The data highlights that Africa had the largest share of individuals living with HIV/AIDS globally. HIV primarily spreads through three main routes; sexual intercourse, contact with contaminated blood via transfusion, blood products, or needles, and from mother to child during pregnancy, childbirth, or breastfeeding. While homosexual contact continues to be a significant source of HIV transmission in the United States, globally, heterosexual transmission is the predominant mode of HIV propagation today [4]. The symptoms of HIV change with progression of infection. Although individuals with HIV tend to be highly contagious during the first few months after contracting the virus,

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many remain unaware of their condition until it reaches advanced stages. During the initial weeks after infection, individuals might either have no symptoms or develop flu-like symptoms such as fever, headache, rash, or a sore throat. As the infection continues to erode the immune system, individuals may experience additional indications or symptoms, including elevated body temperature, enlarged lymph nodes, diarrhea, weight loss, and persistent cough. In the absence of treatment, individuals may be at risk of developing serious health conditions like tuberculosis (TB), cryptococcal meningitis, serious bacterial infections, and cancers like lymphomas and Kaposi's sarcoma [5]. HIV/AIDS spreads predominantly in Africa through heterosexual intercourse and vertical transmission from mother to child. Mother-to-child transmission accounts for 40% of all HIV/AIDS cases [6]. In sub-Saharan Africa, more than 25 million children under 15 years old have succumbed to AIDS, with many of them contracting HIV during childbirth or through breastfeeding. Globally, HIV/AIDS poses a significant menace to future development.

Zika virus (ZIKV) is an arbovirus belonging to the genus *Flavivirus*, of the *Flaviviridae* family and was first isolated from a Rhesus monkey in the Zika forest of Uganda in 1947 [7]. Human cases were first reported in Nigeria in 1954, and since then, there have been occasional descriptions of sporadic cases in humans [7,8]. Through genetic sequencing, it was divided into two types: African and Asian [9]. In April 2007, a significant outbreak of the Asian genotype of ZIKV occurred in Yap Island and Guam, Micronesia. From 2013 to 2014, the Asian genotype triggered epidemics in various Pacific Islands, including French Polynesia, New Caledonia, Cook Islands, Tahiti, and Easter Island [10, 11]. ZIKV is a flavivirus transmitted by mosquitoes, primarily through the bites of infected *Aedes aegypti* mosquitoes. Moreover, it can also be transmitted through sexual intercourse, blood transfusions, and from an expectant mother to her developing fetus during pregnancy [12,13]. The ZIKV is spread during daylight hours when active female *Aedes aegypti* in preparation for egg laying bites and it has an extrinsic incubation period of 2–12 days [14]. Starting in 2015, several countries, including Argentina, Canada, Chile, France, Italy, New Zealand, Peru, Portugal, and the United States of America, have been researching the sexual transmission and blood transfusion aspects of the disease. In February 2016, France recorded the first case of Zika virus disease transmitted through sexual contact [15]. A significant portion of Zika virus infections show no symptoms. When symptoms do occur, they often include a rash. Sometimes with fever, itching, joint and muscle pain, redness of the eyes (conjunctivitis), and fatigue [16]. The most severe outcome of ZIKV in adults is Guillain-Barre Syndrome [17]. When pregnant women contract ZIKV, it can lead to unfavourable pregnancy outcomes, such as miscarriage, still birth, or the delivery of infants who are premature and/or affected by congenital Zika syndrome. This syndrome is defined by features like microcephaly, cerebral calcifications, ventriculomegaly, and arthrogryposis [18]. Recently, Blohm released a case report regarding the potential transmission of Zika virus via breastfeeding [19]. In 2015, rapid expansion of the Zika virus was documented in South American nations, particularly in Brazil and Colombia, as reported by PAHO/WHO [20]. In Brazil, health authorities identified the Zika virus in 14 states, while in Colombia, 9 out of 98 samples were confirmed. From October 2015 to February 2016 in Brazil, there were over 6000 documented cases of Zika virus infection, which included 139 cases of congenital microcephaly. On February 1, 2016, Zika virus epidemic was officially declared as a Public Health Emergency of International Concern (PHEIC) by the World Health Organization (WHO) [21].

In Brazil, there are approximately 900,000 people living with HIV [22], and the Pan American Health Organization (PAHO) has reported 231,725 suspected cases of Zika virus infection [23]. However, there is scarcity of information on cases where individuals are simultaneously infected with both ZIKV and HIV [24,25]. To be more precise, there is lack of substantial data on ZIKV infection in Pregnant women with HIV and the potential repercussions of such co-infection on both these

women and their babies. Furthermore, there is no available evidence to indicate whether ZIKV infection might exacerbate HIV infection or vice versa [26].

Mathematical modeling has been instrumental in the study of infectious diseases. Several mathematical models have been developed to study the transmission dynamics of HIV, HIV co-infecting with other diseases, and the transmission dynamics of Zika virus, ZIKV co-infecting with other diseases. For instance, Mushanyu J. [27] developed a deterministic mathematical model for HIV/AIDS to study how delayed diagnosis of HIV influences the spread of the disease. According to his findings, initiating motivation for HIV/AIDS treatment earlier and optimizing HIV self-testing schedules can lead to a higher number of undiagnosed individuals becoming aware of their status, ultimately reducing HIV transmission. Ayele et al. [28] proposed and analyzed a mathematical model for the transmission dynamics of HIV/AIDS. They examined how the rate of awareness and unawareness depended on media campaigns, while keeping screening and treatment rates constant. They also extended the model by including interventions like preventive measures, screening, and treatment strategies. Their conclusion was that implementing both preventive and screening strategies concurrently is the best cost-effective approach. Podder et al. [29] developed and analyzed a deterministic model for evaluating the impact of anti-retroviral drugs (ARVs), voluntary testing (using standard antibody-based and a DNA based testing methods) and condom use on the transmission dynamics of HIV in a community. They included some of the widely recognized features of HIV infection, which encompass the concept of staged progression. In this context, individuals with HIV typically transition through various infection phases, with a heightened level of contagiousness during the pre-antibody phase. Their conclusion was that using condoms as the only HIV prevention method is slightly more effective than the limited effectiveness of the standard approach involving testing and anti-retroviral therapy. Nwankwo et al. [30] introduced a mathematical model that elucidates the transmission dynamics of HIV and syphilis co-infection in a population with easily accessible treatment for syphilis. Moore et al. [31] developed and analyzed a Caputo–Fabrizio fractional derivative model for HIV/AIDS epidemic which includes an anti-retroviral treatment compartment. Omame et al. [32] developed and examined a mathematical model with non-integer order for the co-dynamics of SARS-COV-2, Dengue, and HIV. The objective was to evaluate how SARS-COV-2 infection influences the dynamics of Dengue and HIV using fractional derivatives in their analysis.

Biswas et al. [33] developed and analyzed a deterministic Zika virus mathematical model, wherein they considered both the vector and sexual transmission route with the effect of human awareness and vector control in the absence of disease-induced death. Thorough examination of their model showed that when the transmission likelihood per biting of a susceptible mosquito with infected humans exceeds the critical threshold, the model displays the phenomenon of backward bifurcation. They concluded that the increase in sexual transmission rate simultaneously triggers and upsurge the density of the exposed and infected populations. Agosto et al. [34] developed and analyzed a mathematical model for ZIKV with human vertical transmission of ZIKV. They examined the human populations, which included both the adults and new borns, in addition to the vector population. Their results suggest that employing personal protection is a more effective control measure than reducing mosquito populations. Ali et al. [35] developed a model for Zika virus, considering both mosquito and human transmission, while incorporating human awareness in the host population. They determined that leveraging human awareness and employing bilinear incidence would enhance the efficiency of eliminating Zika virus infection. Ibrahim et al. [36] introduced a mathematical model for ZIKV, incorporating vertical transmission to the fetus during early pregnancy to enhance the estimation of microcephaly risk. Their model included distinct compartments for infants affected by microcephaly, accounted for asymptomatic carriers, considered the

impact of seasonality and incorporated transmission through sexual contact. Omame et al. [37] presented a model for SARS-COV-2 and Zika co-dynamics incorporating incident co-infection by susceptible individuals. The results from their simulation revealed that SARS-COV-2 prevention could greatly reduce the burden of Co-infections with Zika. Jose et al. [38] formulated a deterministic mathematical model for the transmission dynamics of Dengue fever and Zika virus co-infection. They incorporated the sexual route of transmission for ZIKV and thoroughly analyzed their model.

Zika virus infection could have negative consequences for individuals living with HIV, especially pregnant women and their Infant. To the best of the author's knowledge, no mathematical model has been designed and analyzed to specifically examine the dynamics of HIV and Zika virus co-infection, and also the impact of one disease on the other. Consequently, in this study, we carefully formulated a new deterministic mathematical model that captures transmission dynamics of HIV and ZIKV co-infection. We incorporated vertical transmission for both HIV and ZIKV in our model, as both diseases can be passed from a mother to her child during pregnancy and child-birth. It is crucial to highlight that this marks the inaugural inclusion of vertical transmission in a Zika virus model co-infecting with other diseases. Furthermore, we considered both the human to human and vector to human route for the horizontal transmission of ZIKV. We then investigate the impact of HIV on ZIKV infection. Thus, this study encompasses all the possible route of HIV and ZIKV transmission, which is comprehensive in capturing the full dynamics of the two diseases and their co-infection. The rest of the paper is organized as follows: the model formulation and basic properties of the model are described in Section 2, the model analysis in Section 3, the numerical simulations in Section 4, and Section 5 is the concluding remarks.

2. Model formulation

The total human population at time t , denoted by $N_h(t)$, is divided into sixteen mutually exclusive compartment of Susceptible individuals $S_h(t)$, exposed individuals to ZIKV only $E_Z(t)$, individuals infected with ZIKV only $I_Z(t)$, treated individuals with ZIKV only $T_Z(t)$, recovered individuals from ZIKV only $R_Z(t)$, individuals exposed to HIV only $E_H(t)$, individuals infected with HIV only but not showing clinical symptoms of AIDS $I_H(t)$, individual infected with HIV only showing clinical symptoms of AIDS $A(t)$, treated individuals with HIV only (showing and not showing symptoms of AIDS) $T_H(t)$, exposed individuals to both HIV and ZIKV $E_{HZ}(t)$, individuals infected with ZIKV that are exposed to HIV $H_1(t)$, infected individuals with HIV (not showing clinical symptoms of AIDS) that are exposed to ZIKV $H_2(t)$, individuals infected with HIV (showing clinical symptoms of AIDS) that are exposed to ZIKV $H_3(t)$, individuals co-infected with both HIV (not showing clinical symptoms of AIDS) and ZIKV $I_{HZ}(t)$, individuals co-infected with both HIV (showing clinical symptoms of AIDS) and ZIKV $I_{AZ}(t)$, and treated individuals with both HIV (showing and not showing symptoms of AIDS) and ZIKV $T_{HZ}(t)$, so that

$$N_h(t) = S_h(t) + E_Z(t) + I_Z(t) + T_Z(t) + R_Z(t) + E_H(t) + I_H(t) + A(t) + T_H(t) + E_{HZ}(t) + H_1(t) + H_2(t) + H_3(t) + I_{HZ}(t) + I_{AZ}(t) + T_{HZ}(t).$$

The total mosquito population (vector) at time t , denoted by $N_m(t)$, is subdivided into susceptible mosquitoes $S_m(t)$, exposed mosquitoes to ZIKV $E_m(t)$, and infected mosquitoes to ZIKV $I_m(t)$, so that

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

The susceptible human population is recruited at a constant rate Λ_h , in which a fraction β_H were born infected with HIV infection, a fraction β_Z were born infected with ZIKV infection, and a fraction β_{HZ} were born with both HIV and ZIKV coinfection from the parents. Susceptible

individuals acquire HIV infection following effective contact with HIV infected individuals at the rate λ_H , given by

$$\lambda_H = \frac{\alpha_H (I_H + \eta_1 (A + H_3) + \eta_2 T_H + H_2 + I_{HZ} + \eta_3 I_{AZ} + \eta_4 T_{HZ})}{N_h}.$$

where α_H is the transmission probability of HIV from infected individuals to susceptible individuals, η_1 and η_3 are the modification parameters that accounts for increased level of infectiousness from HIV infectious individuals showing clinical symptoms of AIDS ($A(t)$) and individuals co-infected with both HIV (showing clinical symptoms of AIDS) and ZIKV ($I_{AZ}(t)$). This is due to the fact that individuals showing clinical symptoms of AIDS experience a higher disease viral load in contrast to individuals with HIV infection not showing clinical symptoms of AIDS. η_2 and η_4 are modification parameters that accounts for reduced transmission from Treated individuals with HIV only infection ($T_H(t)$) and Treated individuals with both HIV and ZIKV coinfection ($T_{HZ}(t)$), this is because individuals undergoing treatment for HIV infection are informed about their HIV status and have heightened awareness on various ways to curb the spread of HIV infection.

Similarly, susceptible individuals acquire ZIKV infection through sexual interaction, blood transmission with infected individuals and effective contact with infected mosquitoes at the rate λ_Z , given by

$$\lambda_Z = \frac{\alpha_Z (I_Z + H_1 + I_{HZ} + I_{AZ})}{N_h} + \frac{\alpha_{mZ} \omega I_m}{N_h}.$$

where α_Z is the transmission probability of ZIKV from infected individuals to susceptible individuals, α_{mZ} is the transmission probability of ZIKV from infected mosquitoes to susceptible individuals, and ω is the mosquito biting rate. It is pertinent to note that the conservation laws of bites (i.e., the total number of bites made by mosquitoes equals the total number of bites received by the human hosts) has been applied. The consequence of the application of such law is that the infection rate for both humans and mosquitoes is normalized by the total human population, $N_h(t)$ [35]. Individuals with ZIKV-only infection may recover and become susceptible again at the rate κ_Z . Natural death occurs in all the human sub-population at the rate μ_h . Susceptible individuals who come in contact with infected individuals and mosquitoes with ZIKV infection are transferred to the exposed class $E_Z(t)$ at the rate λ_Z , and then progressed to being infectious at the rate ψ_Z . Exposed individuals to ZIKV can acquire HIV infection following effective contact with HIV infected individuals (they moved to $E_{HZ}(t)$ class at the rate λ_H). Infectious individuals with ZIKV-only infection are treated at the γ_Z , and may die from the disease at the rate δ_Z . Infectious individuals with ZIKV infection $I_Z(t)$ can acquire HIV infection at the rate $\theta \lambda_H$ (where $0 < \theta < 1$, accounts for decrease in sexual activity by ZIKV infected individuals due to ill health). Treated individuals with ZIKV infection $T_Z(t)$ may die from the disease at the rate $\phi_Z \delta_Z$ (where ϕ_Z is the parameter that accounts for disease-induced death while undergoing treatment), and they recover from the disease at the rate τ_Z (see Table 1).

Susceptible individuals who come in contact with HIV infected individuals, transitioned to the exposed compartment $E_H(t)$ at the rate λ_H , and progressed to HIV infectious class $I_H(t)$ at the rate ψ_H . Exposed individuals to HIV can acquire ZIKV infection following effective contact with individuals and mosquitoes infected with ZIKV infection (they moved to $E_{HZ}(t)$ class at the rate λ_Z). HIV infectious individuals progressed to showing clinical symptoms of AIDS at the rate ρ_1 . Furthermore, we assumed that HIV infectious individuals can be exposed to ZIKV infection at the rate $\epsilon_1 \lambda_Z$ (where $0 < \epsilon_1 < 1$, accounts for increased susceptibility to ZIKV infection due to HIV infection). The AIDS compartment $A(t)$ is generated by HIV infectious individuals showing clinical symptoms of AIDS at the rate ρ_1 , and can be exposed to ZIKV infection at the rate $\epsilon_2 \lambda_Z$ (where $0 < \epsilon_2 < 1$, accounts for increased susceptibility to ZIKV infection due to AIDS). HIV infectious individuals showing clinical symptoms of AIDS dies from the disease at

the rate δ_H . The treated individuals with HIV-only infection $T_H(t)$ class is generated by treatment rates q_1 and q_2 of HIV infected individuals not showing and showing clinical symptoms of AIDS respectively, and can be exposed to ZIKV infection while receiving treatment at the rate $\epsilon_3\lambda_Z$ (where $0 < \epsilon_3 < 1$, accounts for increased susceptibility to ZIKV infection due to HIV/AIDS infection). Furthermore, treated individuals with HIV-only infection dies from the disease at the rate $\phi_H\delta_H$ (where ϕ_H is the parameter that accounts for disease-induced death while undergoing treatment). The population of HIV infectious individuals (not showing clinical symptoms of AIDS) that are exposed to ZIKV $H_2(t)$ is increased by treated HIV infectious individuals that are exposed to ZIKV infection at the rate $f\epsilon_3\lambda_Z$ (where $0 < f < 1$, is a fraction of HIV treated individuals not showing clinical symptoms AIDS).

Exposed individuals to both HIV and ZIKV infections $E_{HZ}(t)$, ZIKV infectious individuals that are exposed to HIV $H_1(t)$, and HIV infectious individuals (not showing clinical symptoms of AIDS) that are exposed to ZIKV $H_2(t)$ all progressed to being Infected with both HIV (not showing clinical symptoms of AIDS) and ZIKV coinfection $I_{HZ}(t)$ at the rates ψ_{HZ} , ϑ , and ξ_1 respectively. Similarly, HIV infectious individuals, showing clinical symptoms of AIDS that are exposed to ZIKV $H_3(t)$ progressed to being Infected with both HIV (showing clinical symptoms of AIDS) and ZIKV coinfection $I_{AZ}(t)$ at the rate ξ_2 . Furthermore, Infectious individuals with both HIV (not showing clinical symptoms of AIDS) and ZIKV coinfection $I_{HZ}(t)$ progressed to HIV (showing clinical symptoms of AIDS) and ZIKV coinfection $I_{AZ}(t)$ class at the rate ρ_2 . The rates δ_{HZ} and δ_{AZ} are the disease-induced death rate for Infectious individuals with both HIV (not showing clinical symptoms of AIDS) and ZIKV coinfection $I_{HZ}(t)$, and Infectious individuals with both HIV (showing clinical symptoms of AIDS) and ZIKV coinfection $I_{AZ}(t)$ respectively.

The treated class of individuals with both HIV (showing and not showing clinical symptoms of AIDS) and ZIKV $T_{HZ}(t)$, is generated by treatments of Infectious individuals with both HIV (not showing clinical symptoms of AIDS) and ZIKV coinfection $I_{HZ}(t)$, and Infectious individuals with both HIV (showing clinical symptoms of AIDS) and ZIKV coinfection $I_{AZ}(t)$ at the rates γ_{HZ} and γ_{AZ} respectively. The disease-induced death rates in the treated class $T_{HZ}(t)$ is given by $\phi_{HZ}\delta_{HZ}$ and $\phi_{AZ}\delta_{AZ}$ (where ϕ_{HZ} accounts for both HIV (not showing clinical symptoms of AIDS) and ZIKV co-infection diseased-induced death rate while receiving treatment in $T_{HZ}(t)$, and ϕ_{AZ} accounts for both HIV (showing clinical symptoms of AIDS) and ZIKV co-infection diseased-induced death rate while receiving treatment in $T_{HZ}(t)$ class). Furthermore, individuals in $T_{HZ}(t)$ class recovers from only ZIKV infection at the rate v . The population of the susceptible mosquitoes is generated at a constant rate Λ_m , and susceptible mosquitoes acquires ZIKV infection through effective contact with infected humans with ZIKV at the rate λ_m , given by

$$\lambda_m = \frac{\alpha_m\omega(I_Z + H_1 + I_{HZ} + I_{AZ})}{N_h}$$

where α_m is the transmission probability of ZIKV from infected individuals to susceptible mosquitoes, and ω is the mosquito biting rate. Susceptible mosquitoes moved to the exposed class $E_m(t)$, and progressed to being infectious at the rate ψ_m . Furthermore, natural death rate of mosquitoes occurs at the μ_m .

From the above assumptions and formulations, we can represent the HIV-ZIKV co-infection model with the following set of non-linear differential equations

$$\begin{aligned} \frac{dS_h}{dt} &= (1 - \beta_Z I_Z - \beta_H I_H - \beta_{HZ} I_{HZ}) \Lambda_h - \lambda_Z S_h \\ &\quad - \lambda_H S_h - \mu_h S_h + \kappa_Z R_Z \\ \frac{dE_Z}{dt} &= \lambda_Z S_h - \lambda_H E_Z - (\psi_Z + \mu_h) E_Z \\ \frac{dI_Z}{dt} &= \psi_Z E_Z + \beta_Z \Lambda_h I_Z - \theta \lambda_H I_Z - (\gamma_Z + \delta_Z + \mu_h) I_Z \\ \frac{dT_Z}{dt} &= \gamma_Z I_Z - (\tau_Z + \phi_Z \delta_Z + \mu_h) T_Z \\ \frac{dR_Z}{dt} &= \tau_Z T_Z + \nu T_{HZ} - (\kappa_Z + \mu_h) R_Z \\ \frac{dE_H}{dt} &= \lambda_H S_h - \lambda_Z E_H - (\psi_H + \mu_h) E_H \\ \frac{dI_H}{dt} &= \psi_H E_H + \beta_H \Lambda_h I_H - \epsilon_1 \lambda_Z I_H - (\rho_1 + q_1 + \mu_h) I_H \\ \frac{dA}{dt} &= \rho_1 I_H - \epsilon_2 \lambda_Z A - (q_2 + \delta_H + \mu_h) A \\ \frac{dT_H}{dt} &= q_1 I_H + q_2 A - \epsilon_3 \lambda_Z T_H - (\phi_H \delta_H + \mu_h) T_H \\ \frac{dE_{HZ}}{dt} &= \lambda_H E_Z + \lambda_Z E_H - (\psi_{HZ} + \mu_h) E_{HZ} \\ \frac{dH_1}{dt} &= \theta \lambda_H I_Z - (\vartheta + \delta_Z + \mu_h) H_1 \\ \frac{dH_2}{dt} &= \epsilon_1 \lambda_Z I_H + f \epsilon_3 \lambda_Z T_H - (\xi_1 + \mu_h) H_2 \\ \frac{dH_3}{dt} &= \epsilon_2 \lambda_Z A + (1 - f) \epsilon_3 \lambda_Z T_H - (\xi_2 + \delta_H + \mu_h) H_3 \\ \frac{dI_{HZ}}{dt} &= \psi_{HZ} E_{HZ} + \vartheta H_1 + \xi_1 H_2 + \beta_{HZ} \Lambda_h I_{HZ} \\ &\quad - (\gamma_{HZ} + \rho_2 + \delta_{HZ} + \mu_h) I_{HZ} \\ \frac{dI_{AZ}}{dt} &= \xi_2 H_3 + \rho_2 I_{HZ} - (\gamma_{AZ} + \delta_{AZ} + \mu_h) I_{AZ} \\ \frac{dT_{HZ}}{dt} &= \gamma_{HZ} I_{HZ} + \gamma_{AZ} I_{AZ} - (v + \phi_{HZ} \delta_{HZ} + \phi_{AZ} \delta_{AZ} + \mu_h) T_{HZ} \\ \frac{dS_m}{dt} &= \Lambda_m - \lambda_m S_m - \mu_m S_m \\ \frac{dE_m}{dt} &= \lambda_m S_m - (\psi_m + \mu_m) E_m \\ \frac{dI_m}{dt} &= \psi_m E_m - \mu_m I_m \end{aligned} \tag{1}$$

where

$$\begin{aligned} \lambda_Z &= \frac{\alpha_Z(I_Z + H_1 + I_{HZ} + I_{AZ})}{N_h} + \frac{\alpha_{mz}\omega I_m}{N_h}, \\ \lambda_m &= \frac{\alpha_m\omega(I_Z + H_1 + I_{HZ} + I_{AZ})}{N_h}, \text{ and} \\ \lambda_H &= \frac{\alpha_H(I_H + \eta_1(A + H_3) + \eta_2 T_H + H_2 + I_{HZ} + \eta_3 I_{AZ} + \eta_4 T_{HZ})}{N_h} \end{aligned}$$

It is important to highlight some of the main assumptions in the model formulation

1. Infection of both diseases can be transmitted from parents to offspring during pregnancy. (see [4,12,13])
2. There is no recovery from HIV/AIDS infection [4].
3. Disease-induced death occurs only to HIV infected individuals showing clinical symptoms of AIDS.
4. The mixing of people is homogeneous, indicating that everyone has equal chance of contracting the infection when they have sufficient contact with infectious people (see Fig. 1).

Table 1
Description of the model variables and parameters.

Variable	Description
S_h	Susceptible individuals
E_Z	Exposed individuals to ZIKV only
I_Z	Infected individual with ZIKV only
T_Z	Treated individuals with ZIKV only
R_Z	Recovered individuals from ZIKV only
E_H	Exposed individuals to HIV only
I_H	Infected individuals with HIV only
A	HIV infected individuals, showing clinical symptoms of AIDS
T_H	Treated individuals with HIV only
E_{HZ}	Exposed individuals to both HIV and ZIKV
H_1	ZIKV infected individuals that are exposed to HIV
H_2	HIV infected individuals that are exposed to ZIKV
H_3	HIV infected individuals, showing clinical symptoms of AIDS that are exposed to ZIKV
I_{HZ}	Infected individuals with both HIV and ZIKV
I_{AZ}	Infected individuals with both AIDS symptoms and ZIKV
T_{HZ}	Treated individuals with both HIV and ZIKV
S_m	Susceptible mosquitoes
E_m	Exposed mosquitoes
I_m	Infected mosquitoes
Parameter	Description
$A_h (A_m)$	Recruitment rate for humans (mosquitoes).
$\mu_h (\mu_m)$	Natural death rate for humans (mosquitoes).
$\beta_Z, \beta_H, \beta_{HZ}$	Fraction of individuals that are infected with ZIKV, HIV, both HIV and ZIKV from birth.
ω	Mosquito biting rate.
α_H	Transmission probability of HIV from infected individuals to susceptible individuals.
α_Z	Transmission probability of ZIKV from infected individuals to susceptible individuals.
α_m	Transmission probability of ZIKV from infected individuals to susceptible mosquitoes.
α_{mZ}	Transmission probability of ZIKV from infected individuals to susceptible individuals.
ψ_Z	Progression rate from E_Z to I_Z .
ψ_H	Progression rate from E_H to I_H .
ψ_{HZ}	Progression rate from E_{HZ} to I_{HZ} .
ψ_m	Progression rate from E_m to I_m .
δ_Z	ZIKV-only induced death rate.
δ_H	HIV-only induced death rate.
γ_Z	Treated rate of infectious individuals with ZIKV-only.
τ_Z	Recovery rate of treated individuals with ZIKV-only.
ρ_1	Progression rate from I_H to A .
ρ_2	Progression rate from I_{HZ} to I_{AZ} .
q_1 and q_2	Treatment rate for I_H and A .
γ_{HZ} and γ_{AZ}	Treatment rate for I_{HZ} and I_{AZ} .
ϑ	Progression rate from H_1 to I_{HZ} .
ξ_1	Progression rate from H_2 to I_{HZ} .
ξ_2	Progression rate from H_3 to I_{AZ} .
η_1	Modification parameter that accounts for increased level of infectiousness from A and H_3 .
η_2	Modification parameter that accounts for reduced transmission from T_H .
η_3	Modification parameter that accounts for increased level of infectiousness from I_{AZ} .
η_4	Modification parameter that accounts for reduced transmission from T_{HZ} .
θ	Modification parameter that accounts for decrease in sexual activity by individuals with ZIKV symptoms (due to ill health).
$\epsilon_1, \epsilon_2, \epsilon_3$	Modification parameters that accounts for increased susceptibility to ZIKV infection due to HIV infection.
f	Fraction of treated HIV infectious individuals not showing clinical symptoms of AIDS that are exposed to ZIKV.
δ_{HZ} and δ_{AZ}	Disease-induced death rate of I_{HZ} and I_{AZ} .
ϕ_Z	Modification parameter that accounts for reduction of ZIKV-only induced death in T_Z class.
ϕ_H	Modification parameter that accounts for reduction of HIV-only induced death in T_H class.
ϕ_{HZ}	Modification parameter that accounts for reduction of I_{HZ} diseased-induced death rate in T_{HZ} class.
ϕ_{AZ}	Modification parameter that accounts for reduction of I_{AZ} diseased-induced death rate in T_{HZ} class.
κ_Z	The rate at which recovered individuals from ZIKV infection becomes susceptible again.
ν	ZIKV recovery rate from T_{HZ} .

2.1. Basic properties of the HIV- ZIKV co-infection model

2.1.1. Positivity of solution

It is important to show that all the state variables of the HIV-ZIKV Co-infection Model (1) are non-negative for all time $t > 0$, for the model to be biologically meaningful in a feasible region Δ , given by

$$\Delta = \Delta_h \cup \Delta_m \subset \mathfrak{R}_+^{16} \times \mathfrak{R}_+^3 \tag{2}$$

where,

$$\Delta_h = \left\{ (S_h, E_Z, I_Z, T_Z, R_Z, E_H, I_H, A, T_H, E_{HZ}, H_1, H_2, H_3, I_{HZ}, I_{AZ}, T_{HZ}) \in \mathfrak{R}_+^{16} : N_h \leq \frac{A_h}{\mu_h} \right\}$$

and

$$\Delta_m = \left\{ (S_m, E_m, I_m) \in \mathfrak{R}_+^3 : N_m \leq \frac{A_m}{\mu_m} \right\}.$$

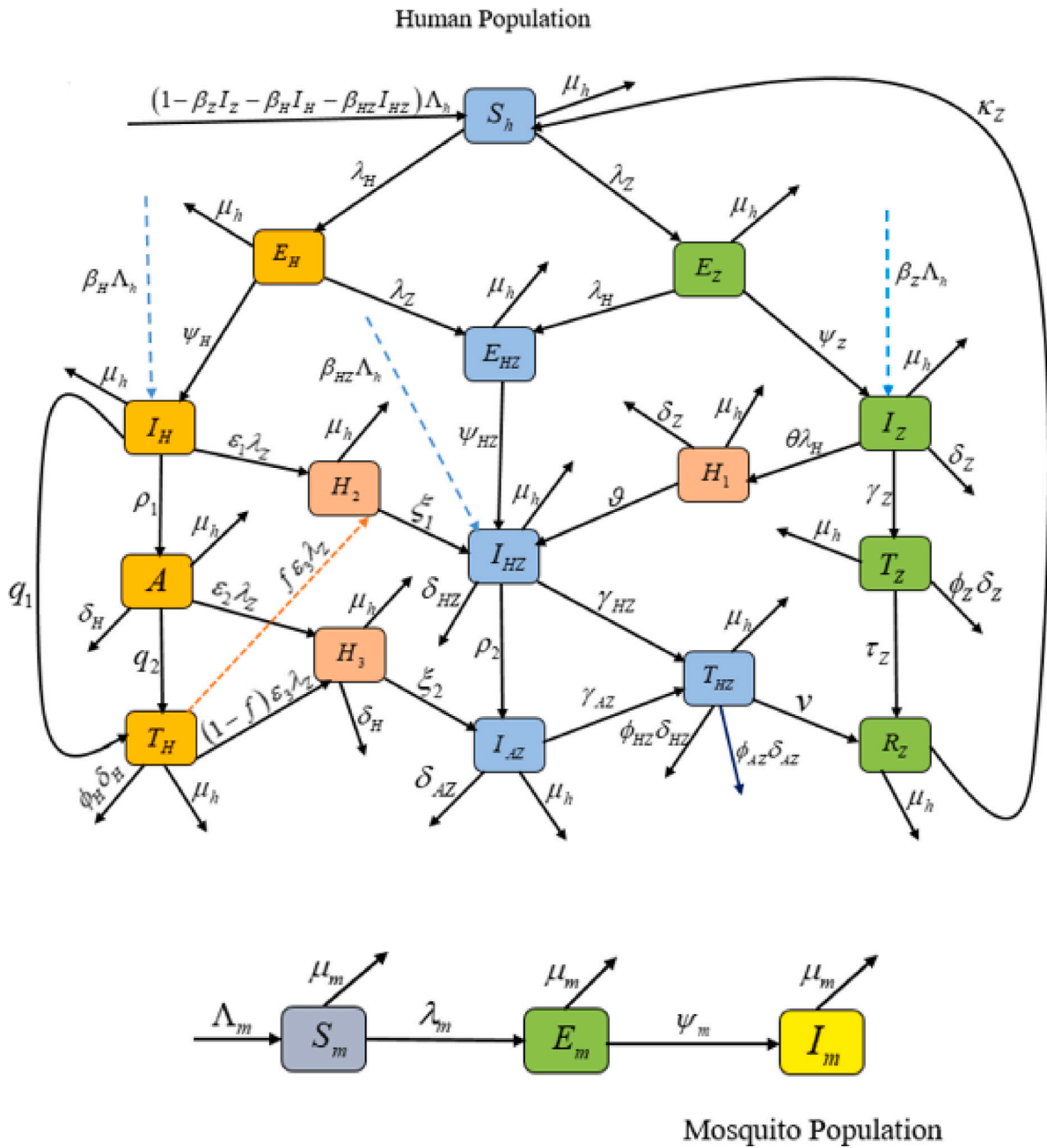


Fig. 1. Flowchart of the HIV-ZIKV co-infection model.

Theorem 1. Let the initial data for the HIV-ZIKV co-infection model (1) be $S_h(0) > 0, E_Z(0) \geq 0, I_Z(0) \geq 0, T_Z(0) \geq 0, R_Z(0) \geq 0, E_H(0) \geq 0, I_H(0) \geq 0, A(0) \geq 0, T_H(0) \geq 0, E_{HZ}(0) \geq 0, H_1(0) \geq 0, H_2(0) \geq 0, H_3(0) \geq 0, I_{HZ}(0) \geq 0, I_{AZ}(0) \geq 0, T_{HZ}(0) \geq 0, S_m(0) > 0, E_m(0) \geq 0, I_m(0) \geq 0$. Then the solution $(S_h, E_Z, I_Z, T_Z, R_Z, E_H, I_H, A, T_H, E_{HZ}, H_1, H_2, H_3, I_{HZ}, I_{AZ}, T_{HZ}, S_m, E_m, I_m)$ of the HIV-ZIKV co-infection model (1) are positive for all time $t > 0$.

Proof. Let $t_f = \sup \{t > 0 : (S_h > 0, E_Z > 0, I_Z > 0, T_Z > 0, R_Z > 0, E_H > 0, I_H > 0, A > 0, T_H > 0, E_{HZ} > 0, H_1 > 0, H_2 > 0, H_3 > 0, I_{HZ} > 0, I_{AZ} > 0, T_{HZ} > 0, S_m > 0, E_m > 0, I_m > 0) \in [0, t]\}$. Thus, $t_f > 0$.

From the first equation of the HIV-ZIKV co-infection model (1), we have that

$$\frac{dS_h}{dt} = (1 - \beta_Z I_Z - \beta_H I_H - \beta_{HZ} I_{HZ}) \Lambda_h - \lambda_Z S_h - \lambda_H S_h - \mu_h S_h + \kappa_Z R_Z$$

Solving the above equation, we obtained

$$\begin{aligned} \frac{d}{dt} \left\{ S_h(t) \left[\exp \left(\int_0^t \lambda_Z(r) dr + \lambda_H(r) dr + \mu_h t \right) \right] \right\} \\ = ((1 - \beta_Z I_Z - \beta_H I_H - \beta_{HZ} I_{HZ}) \Lambda_h + \kappa_Z R_Z) \times \\ \exp \left(\int_0^t \lambda_Z(r) dr + \lambda_H(r) dr + \mu_h t \right). \end{aligned}$$

Integrating the above equation at the range $[0, t_f]$, we have

$$\begin{aligned} \left\{ S_h(t_f) \exp \left[\int_0^{t_f} \lambda_Z(r) dr + \lambda_H(r) dr + \mu_h t_f \right] \right\} - S_h(0) \\ = ((1 - \beta_Z I_Z - \beta_H I_H - \beta_{HZ} I_{HZ}) \Lambda_h + \kappa_Z R_Z) \end{aligned}$$

$$\times \int_0^{t_f} \exp \left[\int_0^x \lambda_Z(r) dr + \lambda_H(r) dr + \mu_h x \right] dx.$$

So that

$$\begin{aligned} S_h(t_f) = & S_h(0) \exp \left[- \left(\int_0^{t_f} \lambda_Z(r) dr + \lambda_H(r) dr + \mu_h t_f \right) \right] \\ & + \exp \left[- \left(\int_0^{t_f} \lambda_Z(r) dr + \lambda_H(r) dr + \mu_h t_f \right) \right] \\ & \times \left((1 - \beta_Z I_Z - \beta_H I_H - \beta_{HZ} I_{HZ}) \Lambda_h + \kappa_Z R_Z \right) \\ & \times \int_0^{t_f} \exp \left[\int_0^x \lambda_Z(r) dr + \lambda_H(r) dr + \mu_h x \right] dx > 0. \end{aligned}$$

Similarly, it can be shown that $E_Z > 0, I_Z > 0, T_Z > 0, R_Z > 0, E_H > 0, I_H > 0, A > 0, T_H > 0,$

$E_{HZ} > 0, H_1 > 0, H_2 > 0, H_3 > 0, I_{HZ} > 0, I_{AZ} > 0, T_{HZ} > 0, S_m > 0, E_m > 0, I_m > 0.$ □

2.1.2. Invariant region

Lemma 1. *The region $\Delta = \Delta_h \cup \Delta_m \subset \mathfrak{R}_+^{16} \times \mathfrak{R}_+^3$ is positively invariant and attracts all solution in \mathfrak{R}_+^{19} .*

Proof. By adding all the equations of the Human and mosquito compartments of the HIV-ZIKV co-infection model (1), the rate of change of the total human and mosquito population are given by

$$\begin{aligned} \frac{dN_h}{dt} = & \Lambda_h - \mu_h N_h - \delta_Z (I_Z + H_1) - \delta_H (A + H_3) - \phi_H \delta_H T_H \\ & - (\phi_{HZ} \delta_{HZ} + \phi_{AZ} \delta_{AZ}) T_{HZ} \\ & - \delta_{HZ} I_{HZ} - \delta_{AZ} I_{AZ}, \end{aligned}$$

and

$$\frac{dN_m}{dt} = \Lambda_m - \mu_m N_m. \tag{3}$$

Thus, whenever $N_h > \frac{\Lambda_h}{\mu_h}$ and $N_m > \frac{\Lambda_m}{\mu_m}$, then $\frac{dN_h}{dt} < 0$ and $\frac{dN_m}{dt} < 0$. considering that the right-hand side of Eq. (3) are bounded by $\Lambda_h - \mu_h N_h$ and $\Lambda_m - \mu_m N_m$, using the comparison theorem from [39], it can be shown that

$$\begin{aligned} N_h(t) & \leq N_h(0) e^{-\mu_h t} - \frac{\Lambda_h}{\mu_h} (1 - e^{-\mu_h t}), \\ N_m(t) & \leq N_m(0) e^{-\mu_m t} - \frac{\Lambda_m}{\mu_m} (1 - e^{-\mu_m t}). \end{aligned} \tag{4}$$

It follows that $N_h(t) \leq \frac{\Lambda_h}{\mu_h}$ and $N_m(t) \leq \frac{\Lambda_m}{\mu_m}$, if $N_h(0) \leq \frac{\Lambda_h}{\mu_h}$ and $N_m(0) \leq \frac{\Lambda_m}{\mu_m}$. Thus, the closed region Δ is positively invariant and attracts all the solutions in \mathfrak{R}_+^{19} . Hence, the HIV-ZIKV co-infection model (1) is both epidemiologically and mathematically well-defined in the region Δ . Therefore, it is satisfactory to examine the dynamics of the HIV-ZIKV co-infection model (1) in the region Δ [40]. □

3. Model analysis

In this section, we shall analyze the HIV-ZIKV co-infection model (1) qualitatively. For simplification of the analysis, it is comparative to split the HIV-ZIKV co-infection model (1) into sub-models.

3.1. HIV only sub-model

The HIV only sub-model is obtained by setting the ZIKV and the co-infection compartments to zero (i.e. $E_Z = I_Z = T_Z = R_Z = E_{HZ} = H_1 = H_2 = H_3 = I_{HZ} = I_{AZ} = T_{HZ} = S_m = E_m = I_m = 0$) in the full

HIV-ZIKV co-infection model (1), given by

$$\begin{aligned} \frac{dS_h}{dt} & = (1 - \beta_H I_H) \Lambda_h - \lambda_H S_h - \mu_h S_h \\ \frac{dE_H}{dt} & = \lambda_H S_h - (\psi_H + \mu_h) E_H \\ \frac{dI_H}{dt} & = \psi_H E_H + \beta_H \Lambda_h I_H - (\rho_1 + q_1 + \mu_h) I_H \\ \frac{dA}{dt} & = \rho_1 I_H - (q_2 + \delta_H + \mu_h) A \\ \frac{dT_H}{dt} & = q_1 I_H + q_2 A - (\phi_H \delta_H + \mu_h) T_H. \end{aligned} \tag{5}$$

where

$$\lambda_H = \frac{\alpha_H (I_H + \eta_1 A + \eta_2 T_H)}{N_h}.$$

It can be shown that the region

$$\Delta_1 = \left\{ (S_h, E_H, I_H, A, T_H) \in \mathfrak{R}_+^5 : S_h + E_H + I_H + A + T_H \leq \frac{\Lambda_h}{\mu_h} \right\}$$

is positively-invariant. Thus, the dynamics of the HIV only sub-model will be considered in Δ_1 .

3.1.1. HIV only disease-free equilibrium point (HDFE)

The disease-free equilibrium for HIV only sub-model represents a stable state where in which the population is free from HIV infections. This is obtained by setting $E_H = I_H = A = T_H = 0$ and equating the right hand side of the HIV only sub-model (5) to zero. Therefore, the HIV only disease-free equilibrium is given by

$$e_0^H = (S_h^*, E_H^*, I_H^*, A^*, T_H^*) = \left(\frac{\Lambda_h}{\mu_h}, 0, 0, 0, 0 \right) \tag{6}$$

3.1.2. The basic reproduction number of HIV only sub-model

The HIV basic reproduction number denoted by (R_{0H}), is a crucial parameter that regulates the transmission of HIV within a population. It is described as the number of secondary infections generated when a single HIV infected individual is introduced to a population entirely vulnerable to the virus. Understanding R_{0H} aids in predicting how quickly the disease might spread within the population and assists in implementing measures to control or prevent its transmission. When R_{0H} exceeds 1, it signifies that the disease could cause an outbreak, while an R_{0H} below 1 suggests the disease may not sustain transmission in the population. The HIV basic reproduction number can be computed using the next generation operator method described in [41]. Following the approach in [41], the non-negative matrix F and the non-singular matrix V for the new infection and the remaining transition terms respectively, at the HDFE is given by

$$\begin{aligned} F & = \begin{bmatrix} 0 & \alpha_H & \alpha_H \eta_1 & \alpha_H \eta_2 \\ 0 & \beta_H \Lambda_h & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}, \text{ and} \\ V & = \begin{bmatrix} (\psi_H + \mu_h) & 0 & 0 & 0 \\ -\psi_H & (\rho_1 + q_1 + \mu_h) & 0 & 0 \\ 0 & -\rho_1 & (q_2 + \delta_H + \mu_h) & 0 \\ 0 & -q_1 & -q_2 & (\phi_H \delta_H + \mu_h) \end{bmatrix} \end{aligned}$$

Hence, it follows from [41] that, $R_{0H} = \rho(FV^{-1})$, where ρ is the spectral radius or largest eigenvalue of the matrix FV^{-1} .

Thus,

$$R_{0H} = \frac{\alpha_H \psi_H (B_3 B_4 + \eta_1 \rho_1 B_4 + \eta_2 (q_1 B_3 + q_2 \rho_1))}{B_1 B_2 B_3 B_4} + \frac{\beta_H \Lambda_h}{B_2} \tag{7}$$

where

$$B_1 = \psi_H + \mu_h, B_2 = \rho_1 + q_1 + \mu_h, B_3 = q_2 + \delta_H + \mu_h, \text{ and } B_4 = \phi_H \delta_H + \mu_h.$$

It is worth emphasizing that the basic reproduction number for HIV (R_{0H}) consist of both the HIV horizontal basic reproduction number and the HIV vertical basic reproduction number, that is

$$R_{0H} = R_{0H}^H + R_{0H}^V$$

where $R_{0H}^H = \frac{\alpha_H \psi_H (B_3 B_4 + \eta_1 \rho_1 B_4 + \eta_2 (q_1 B_3 + q_2 \rho_1))}{B_1 B_2 B_3 B_4}$ is the horizontal basic reproduction number, and $R_{0H}^V = \frac{\beta_H \Lambda_h}{B_2}$ is the vertical basic reproduction number.

3.1.3. Local stability of the HDFE

Theorem 2. *The disease-free equilibrium (ℓ_0^H) of the HIV only sub-model (5) is locally asymptotically stable if $R_{0H} < 1$, and unstable if $R_{0H} > 1$.*

Proof. We obtained the Jacobian matrix of the HIV only sub-model (5) evaluated at the disease-free equilibrium (ℓ_0^H), given by

$$J(\ell_0^H) = \begin{bmatrix} -\mu_h & 0 & -\beta_H \Lambda_h - \alpha_H & -\alpha_H \eta_1 & -\alpha_H \eta_2 \\ 0 & -B_1 & \alpha_H & \alpha_H \eta_1 & \alpha_H \eta_2 \\ 0 & \psi_H & \beta_H \Lambda_h - B_2 & 0 & 0 \\ 0 & 0 & \rho_1 & -B_3 & 0 \\ 0 & 0 & q_1 & q_2 & -B_4 \end{bmatrix}$$

where

$$B_1 = \psi_H + \mu_h, B_2 = \rho_1 + q_1 + \mu_h, B_3 = q_2 + \delta_H + \mu_h, \text{ and } B_4 = \phi_H \delta_H + \mu_h.$$

The eigenvalues of the Jacobian matrix $J(\ell_0^H)$ are $\lambda_1 = -\mu_h$ and the roots of the characteristic polynomial below

$$P(\lambda) = \lambda^4 + m_1 \lambda^3 + m_2 \lambda^2 + m_3 \lambda + m_4 \tag{8}$$

where

$$\begin{aligned} m_1 &= B_1 + B_2 + B_3 + B_4 - \beta_H \Lambda_h, \\ m_2 &= B_1 (B_2 + B_3 + B_4) + B_2 (B_3 + B_4) \\ &\quad + B_3 B_4 - \alpha_H \psi_H - \beta_H \Lambda_h (B_1 + B_3 + B_4), \\ m_3 &= B_1 B_2 (B_3 + B_4) + B_3 B_4 (B_1 + B_2) \\ &\quad - \alpha_H \psi_H (\eta_1 \rho_1 + \eta_2 q_1 + B_3 + B_4) - \\ &\quad \beta_H \Lambda_h (B_1 B_3 + B_1 B_4 + B_3 B_4), \\ m_4 &= B_1 B_2 B_3 B_4 (1 - R_{0H}). \end{aligned}$$

By applying the Routh–Hurwitz criterion [42,43], which states that all roots of the polynomial (8) have negative real parts if and only if $m_1 > 0, m_2 > 0, m_3 > 0, m_4 > 0$, and $m_1 m_2 m_4 > m_3^2 + m_1^2 m_4$. For all this conditions to be satisfied, then $R_{0H} < 1$. Therefore, by Routh–Hurwitz criterion, the disease-free equilibrium of the HIV only sub-model (5) is locally asymptotically stable when $R_{0H} < 1$.

From a Biological perspective, Theorem 2 implies that if the basic reproduction number is below one, it is possible to eradicate HIV from the population, as long as the initial sizes of the sub-populations of the HIV only sub-model fall within the basin of attraction of ℓ_0^H . This means that a small deviations from this disease-free state will diminish over time, and the system will converge back to the disease-free equilibrium. To ensure that HIV elimination is not affected by the initial sub-population sizes, it is pertinent to establish the global asymptotic stability of the HDFE. \square

3.1.4. Global stability of the HDFE

Theorem 3. *The disease-free equilibrium of the HIV only sub-model (5) is globally asymptotically stable whenever $R_{0H} \leq 1$.*

Proof. Considering the Lyapunov function as follows

$$\begin{aligned} \mathcal{L} &= \left(\frac{\psi_H (B_3 B_4 + \eta_1 B_4 \rho_1 + \eta_2 (B_3 q_1 + q_2 \rho_1))}{B_2 - \beta_H \Lambda_h} \right) E_H \\ &\quad + \left(\frac{B_1 (B_3 B_4 + \eta_1 B_4 \rho_1 + \eta_2 (B_3 q_1 + q_2 \rho_1))}{B_2 - \beta_H \Lambda_h} \right) I_H \\ &\quad + B_1 (\eta_1 B_4 + \eta_2 q_2) A + \eta_2 B_1 B_3 T_H. \end{aligned} \tag{9}$$

where

$$B_1 = \psi_H + \mu_h, B_2 = \rho_1 + q_1 + \mu_h, B_3 = q_2 + \delta_H + \mu_h, \text{ and } B_4 = \phi_H \delta_H + \mu_h.$$

With Lyapunov derivative (where a dot represents differentiation with respect to time)

$$\begin{aligned} \dot{\mathcal{L}} &= \left(\frac{\psi_H (B_3 B_4 + \eta_1 B_4 \rho_1 + \eta_2 (B_3 q_1 + q_2 \rho_1))}{B_2 - \beta_H \Lambda_h} \right) \dot{E}_H \\ &\quad + \left(\frac{B_1 (B_3 B_4 + \eta_1 B_4 \rho_1 + \eta_2 (B_3 q_1 + q_2 \rho_1))}{B_2 - \beta_H \Lambda_h} \right) \dot{I}_H \\ &\quad + B_1 (\eta_1 B_4 + \eta_2 q_2) \dot{A} + \eta_2 B_1 B_3 \dot{T}_H. \\ \dot{\mathcal{L}} &= \left(\frac{\psi_H (B_3 B_4 + \eta_1 B_4 \rho_1 + \eta_2 (B_3 q_1 + q_2 \rho_1))}{B_2 - \beta_H \Lambda_h} \right) \\ &\quad \times \left(\frac{\alpha_H (I_H + \eta_1 A + \eta_2 T_H) S_h}{N_h} - B_1 E_H \right) + \\ &\quad \left(\frac{B_1 (B_3 B_4 + \eta_1 B_4 \rho_1 + \eta_2 (B_3 q_1 + q_2 \rho_1))}{B_2 - \beta_H \Lambda_h} \right) \\ &\quad \times (\psi_H E_H + \beta_H \Lambda_h I_H - B_2 I_H) + \\ &\quad B_1 (\eta_1 B_4 + \eta_2 q_2) (\rho_1 I_H - B_3 A) + \eta_2 B_1 B_3 (q_1 I_H + q_2 A - B_4 I_H). \\ \dot{\mathcal{L}} &= \left(\frac{\psi_H (B_3 B_4 + \eta_1 B_4 \rho_1 + \eta_2 (B_3 q_1 + q_2 \rho_1))}{B_2 - \beta_H \Lambda_h} \right) \\ &\quad \times \left(\frac{\alpha_H (I_H + \eta_1 A + \eta_2 T_H) S_h}{N_h} \right) - B_1 B_3 B_4 I_H - \\ &\quad \eta_1 B_1 B_3 B_4 A - \eta_2 B_1 B_3 B_4 T_H. \end{aligned}$$

Note that $S_h(t) \leq N_h(t)$ in the region Δ_1 for all $t > 0$, so that

$$\begin{aligned} \dot{\mathcal{L}} &\leq \frac{(I_H + \eta_1 A + \eta_2 T_H) (\alpha_H \psi_H (B_3 B_4 + \eta_1 B_4 \rho_1 + \eta_2 (B_3 q_1 + q_2 \rho_1)))}{B_2 - \beta_H \Lambda_h} \\ &\quad - B_1 B_3 B_4 (I_H + \eta_1 A + \eta_2 T_H). \\ \dot{\mathcal{L}} &\leq \frac{(I_H + \eta_1 A + \eta_2 T_H)}{B_2 - \beta_H \Lambda_h} (\alpha_H \psi_H (B_3 B_4 + \eta_1 B_4 \rho_1 + \eta_2 (B_3 q_1 + q_2 \rho_1))) \\ &\quad + \beta_H \Lambda_h B_1 B_3 B_4 - B_1 B_2 B_3 B_4. \\ \dot{\mathcal{L}} &\leq \frac{(I_H + \eta_1 A + \eta_2 T_H) B_1 B_2 B_3 B_4}{B_2 - \beta_H \Lambda_h} \\ &\quad \times \left(\frac{\alpha_H \psi_H (B_3 B_4 + \eta_1 B_4 \rho_1 + \eta_2 (B_3 q_1 + q_2 \rho_1))}{B_1 B_2 B_3 B_4} + \frac{\beta_H \Lambda_h}{B_2} - 1 \right). \\ \dot{\mathcal{L}} &\leq \frac{(I_H + \eta_1 A + \eta_2 T_H) B_1 B_2 B_3 B_4}{B_2 - \beta_H \Lambda_h} (R_{0H} - 1). \end{aligned} \tag{10}$$

Hence, since all the HIV only sub-model parameters are non-negative, it follows that $\dot{\mathcal{L}} \leq 0$ for $R_{0H} \leq 1$ with $\dot{\mathcal{L}} = 0$ if and only if $I_H = A = T_H = 0$. Thus, \mathcal{L} is a Lyapunov function on Δ_1 . Therefore, by LaSalle’s invariance principle [44], every solution to the HIV only sub-model (5), with initial conditions in Δ_1 , approaches the HIV-only disease-free equilibrium point (ℓ_0^H) as $t \rightarrow \infty$. \square

Hence, the epidemiological importance of the results mentioned above is that $R_{0H} \leq 1$ is the necessary and sufficient condition for

the eradicating of HIV infection from the population. It means that any small perturbation in the system will not only lead to a temporary return to the disease-free state (local Stability) but will ensure that the entire trajectory of the system converges to the disease-free equilibrium over time, regardless of the initial conditions. Furthermore, the global asymptotic stability indicates a robust and sustainable control of the disease, offering the potential for long-term eradication without the risk of recurrent outbreaks.

3.1.5. Existence of a positive endemic equilibrium point of the HIV only sub-model

In this section, we explore the possibility of the existence of an endemic equilibrium point. The endemic equilibrium point is a positive steady state where HIV infection persist in the population. At this equilibrium point, the HIV only sub-model infected variables are non-zero (i.e. $E_H \neq 0, I_H \neq 0, A \neq 0$, and $T_H \neq 0$). To investigate the endemic equilibrium point, the HIV only sub-model equations are solved in terms of the 'force of infection', given by

$$\lambda_H^{**} = \frac{\alpha_H (I_H^{**} + \eta_1 A^{**} + \eta_2 T_H^{**})}{N_h^{**}}, \tag{11}$$

where

$$N_h^{**} = S_h^{**} + E_H^{**} + I_H^{**} + A^{**} + T_H^{**}, \tag{12}$$

with

$$\begin{aligned} S_h^{**} &= \frac{\Lambda_h B_1 (B_2 - \beta_H \Lambda_h)}{B_1 B_2 (\lambda_H^{**} + \mu_h) + \beta_H \Lambda_h (\lambda_H^{**} \psi_H - B_1 (\lambda_H^{**} + \mu_h))}, \\ E_H^{**} &= \frac{\lambda_H^{**} \Lambda_h (B_2 - \beta_H \Lambda_h)}{B_1 B_2 (\lambda_H^{**} + \mu_h) + \beta_H \Lambda_h (\lambda_H^{**} \psi_H - B_1 (\lambda_H^{**} + \mu_h))}, \\ I_H^{**} &= \frac{\lambda_H^{**} \Lambda_h \psi_H}{B_1 B_2 (\lambda_H^{**} + \mu_h) + \beta_H \Lambda_h (\lambda_H^{**} \psi_H - B_1 (\lambda_H^{**} + \mu_h))}, \\ A^{**} &= \frac{\lambda_H^{**} \Lambda_h \psi_H \rho_1}{B_3 (B_1 B_2 (\lambda_H^{**} + \mu_h) + \beta_H \Lambda_h (\lambda_H^{**} \psi_H - B_1 (\lambda_H^{**} + \mu_h)))}, \\ T_H^{**} &= \frac{\lambda_H^{**} \Lambda_h \psi_H (B_3 q_1 + q_2 \rho_1)}{B_3 B_4 (B_1 B_2 (\lambda_H^{**} + \mu_h) + \beta_H \Lambda_h (\lambda_H^{**} \psi_H - B_1 (\lambda_H^{**} + \mu_h)))}. \end{aligned} \tag{13}$$

Substituting Eqs. (12) and (13) into Eq. (11), we obtained

$$\Phi(\lambda_H^{**}) = W_1 \lambda_H^{**2} + W_2 \lambda_H^{**} \tag{14}$$

where

$$\begin{aligned} W_1 &= \Lambda_h (B_3 B_4 (B_2 + \psi_H - \beta_H \Lambda_h) + \psi_H (B_4 \rho_1 + q_1 B_3 + q_2 \rho_1)), \\ W_2 &= \Lambda_h B_1 B_2 B_3 B_4 (1 - R_{0H}). \end{aligned}$$

Solving the quadratic Eq. (14), gives the roots $\lambda_H^{**} = -\frac{B_1 B_2 B_3 B_4 (1 - R_{0H})}{B_3 B_4 (B_2 + \psi_H - \beta_H \Lambda_h) + \psi_H (B_4 \rho_1 + q_1 B_3 + q_2 \rho_1)} < 0$ and $\lambda_H^{**} = 0$ whenever $R_{0H} < 1$. Furthermore, the root $\lambda_H^{**} = -\frac{B_1 B_2 B_3 B_4 (1 - R_{0H})}{B_3 B_4 (B_2 + \psi_H - \beta_H \Lambda_h) + \psi_H (B_4 \rho_1 + q_1 B_3 + q_2 \rho_1)} > 0$ if $R_{0H} > 1$, this confirm the existence of a unique positive endemic equilibrium when $R_{0H} > 1$. This result is summarized below.

Theorem 4. The HIV only sub-model (5) has a unique positive endemic equilibrium whenever $R_{0H} > 1$, and no endemic equilibrium otherwise.

3.2. ZIKV only sub-model

In similar reasoning, the ZIKV only sub-model is obtained by setting the HIV and co-infection compartments to zero (i.e. $E_H = I_H = A = T_H = E_{HZ} = H_1 = H_2 = H_3 = I_{HZ} = I_{AZ} = T_{HZ} = 0$) in the full

HIV-ZIKV co-infection model (1), given by

$$\begin{aligned} \frac{dS_h}{dt} &= (1 - \beta_Z I_Z) \Lambda_h - \lambda_Z S_h - \mu_h S_h + \kappa_Z R_Z \\ \frac{dE_Z}{dt} &= \lambda_Z S_h - (\psi_Z + \mu_h) E_Z \\ \frac{dI_Z}{dt} &= \psi_Z E_Z + \beta_Z \Lambda_h I_Z - (\gamma_Z + \delta_Z + \mu_h) I_Z \\ \frac{dT_Z}{dt} &= \gamma_Z I_Z - (\tau_Z + \phi_Z \delta_Z + \mu_h) T_Z \\ \frac{dR_Z}{dt} &= \tau_Z T_Z - (\kappa_Z + \mu_h) R_Z \\ \frac{dS_m}{dt} &= \Lambda_m - \lambda_m S_m - \mu_m S_m \\ \frac{dE_m}{dt} &= \lambda_m S_m - (\psi_m + \mu_m) E_m \\ \frac{dI_m}{dt} &= \psi_m E_m - \mu_m I_m. \end{aligned} \tag{15}$$

where

$$\lambda_Z = \frac{\alpha_Z I_Z}{N_h} + \frac{\alpha_{mZ} \omega I_m}{N_h}, \text{ and } \lambda_m = \frac{\alpha_m \omega I_Z}{N_h}.$$

Similarly, for the ZIKV only sub-model, it can be shown that the region

$$A_2 = \left\{ (S_h, E_Z, I_Z, T_Z, R_Z, S_m, E_m, I_m) \in \mathfrak{R}_+^8 : N_h \leq \frac{\Lambda_h}{\mu_h}, N_m \leq \frac{\Lambda_m}{\mu_m} \right\}$$

is positively-invariant. Thus, the dynamics of the ZIKV only sub-model will be considered in A_2 .

3.2.1. ZIKV only disease-free equilibrium point (ZDFE)

The ZIKV only disease-free equilibrium is a steady state where there is absence of ZIKV infection in the population. This is achieved by setting $E_H = I_H = A = T_H = S_m = E_m = I_m = 0$ and equating the right hand side of the ZIKV only sub-model (15) to zero. Therefore, the ZIKV only disease-free equilibrium is given by

$$e_0^Z = (S_h^*, E_Z^*, I_Z^*, T_Z^*, R_Z^*, S_m^*, E_m^*, I_m^*) = \left(\frac{\Lambda_h}{\mu_h}, 0, 0, 0, 0, \frac{\Lambda_m}{\mu_m}, 0, 0 \right) \tag{16}$$

3.2.2. The basic reproduction number of ZIKV only sub-model

The ZIKV basic reproduction number denoted by (R_{0Z}) , is a crucial parameter that regulates the transmission of ZIKV within a population. It is described as the number of secondary infections generated when a single ZIKV infected individual is introduced to a population entirely vulnerable to the virus. Understanding R_{0Z} aids in predicting how quickly the disease might spread within the population and assists in implementing measures to control or prevent its transmission. When R_{0Z} exceeds 1, it signifies that the disease could cause an outbreak, while an R_{0H} below 1 suggests the disease may not sustain transmission in the population. The ZIKV basic reproduction number can be computed using the next generation operator method described in [41]. Following the approach in [41], the non-negative matrix F and the non-singular matrix V for the new infection and the remaining transition terms respectively, at the ZDFE is given by

$$F = \begin{bmatrix} 0 & \alpha_Z & 0 & 0 & \alpha_{mZ} \omega \\ 0 & \beta_Z \Lambda_h & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{\alpha_m \omega \Lambda_m \mu_h}{\Lambda_h \mu_m} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}, \text{ and } V = \begin{bmatrix} D_1 & 0 & 0 & 0 & 0 \\ -\psi_Z & D_2 & 0 & 0 & 0 \\ 0 & -\gamma_Z & D_3 & 0 & 0 \\ 0 & 0 & 0 & D_5 & 0 \\ 0 & 0 & 0 & -\psi_m & \mu_m \end{bmatrix}$$

where

$$D_1 = \psi_Z + \mu_h, D_2 = \gamma_Z + \delta_Z + \mu_h, D_3 = \tau_Z + \phi_Z \delta_Z + \mu_h, \\ D_4 = \kappa_Z + \mu_h, \text{ and } D_5 = \psi_m + \mu_m.$$

So that

$$FV^{-1} = \begin{bmatrix} \frac{\alpha_Z \psi_Z}{D_1 D_2} & \frac{\alpha_Z}{D_2} & 0 & \frac{\alpha_m \omega \psi_m}{\mu_m D_5} & \frac{\alpha_m \omega}{\mu_m} \\ \frac{\beta_Z \Lambda_h \psi_Z}{D_1 D_2} & \frac{\beta_Z \Lambda_h}{D_2} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ \frac{\alpha_m \omega \Lambda_m \mu_h \psi_Z}{\Lambda_h \mu_m D_1 D_2} & \frac{\alpha_m \omega \Lambda_m \mu_h}{\Lambda_h \mu_m D_2} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

Hence, it follows from [41] that, $R_{0Z} = \rho(FV^{-1})$, where ρ is the spectral radius or largest eigenvalue of the matrix FV^{-1} .

Thus, the characteristic polynomial of the matrix FV^{-1} is given by

$$\lambda^3 (\lambda^2 - \chi_1 \lambda - \chi_2) \tag{17}$$

where

$$\chi_1 = \frac{\alpha_Z \psi_Z + \beta_Z \Lambda_h D_1}{D_1 D_2}, \text{ and } \chi_2 = \frac{\alpha_m \alpha_m \omega^2 \Lambda_m \mu_h \psi_m \psi_Z}{D_1 D_2 D_5 \Lambda_h \mu_m^2}.$$

The quadratic equation of the above characteristic polynomial (17) is $P(\lambda) = \lambda^2 - \chi_1 \lambda - \chi_2$, with $\chi_1 > 0$, and $\chi_2 > 0$. Hence, the solution of $P(\lambda) = 0$ gives a unique positive root, which is the largest eigenvalue and the basic reproduction number of the ZIKV only sub-model, given by

$$R_{0Z} = \frac{1}{2} \left(\chi_1 + (4\chi_2 + \chi_3)^{\frac{1}{2}} \right) \tag{18}$$

where

$$\chi_1 = \frac{\alpha_Z \psi_Z + \beta_Z \Lambda_h D_1}{D_1 D_2}, \chi_2 = \frac{\alpha_m \alpha_m \omega^2 \Lambda_m \mu_h \psi_m \psi_Z}{D_1 D_2 D_5 \Lambda_h \mu_m^2}, \text{ and } \\ \chi_3 = \frac{\alpha_Z^2 \psi_Z^2 + 2\beta_Z \Lambda_h D_1 \alpha_Z \psi_Z + \beta_Z^2 \Lambda_h^2 D_1^2}{D_1^2 D_2^2}.$$

Again, $P(0) = -\chi_2 < 0$ and $P(1) = 1 - (\chi_1 + \chi_2)$. Therefore, we define $R_{0Z}^{hm} = \chi_1 + \chi_2$, that is

$$R_{0Z}^{hm} = \frac{\alpha_Z \psi_Z + \beta_Z \Lambda_h D_1}{D_1 D_2} + \frac{\alpha_m \alpha_m \omega^2 \Lambda_m \mu_h \psi_m \psi_Z}{\Lambda_h \mu_m^2 D_1 D_2 D_5} \tag{19}$$

So that

$$R_{0Z}^{hm} = R_{0Z}^h + R_{0Z}^m$$

where

$$R_{0Z}^h = \frac{\alpha_Z \psi_Z + \beta_Z \Lambda_h D_1}{D_1 D_2} \text{ consist of the vertical and horizontal transmission from humans, and } \\ R_{0Z}^m = \frac{\alpha_m \alpha_m \omega^2 \Lambda_m \mu_h \psi_m \psi_Z}{\Lambda_h \mu_m^2 D_1 D_2 D_5} \text{ is the contribution from mosquito transmission.}$$

Again, from the relation $P(1) = 1 - R_{0Z}^{hm}$, we have the following observations;

- (i) When $R_{0Z}^{hm} = 1$ then $P(1) = 0$, thus the positive root of the equation $P(\lambda) = 0$ is one ($R_{0Z} = 1$).
- (ii) When $R_{0Z}^{hm} < 1$ then $P(1) > 0$, so the positive root of the equation lies between 0 and 1 as $P(0) < 0$, thus $R_{0Z} < 1$.
- (iii) When $R_{0Z}^{hm} > 1$ then $P(1) < 0$ again $P(0) < 0$, so the positive root $P(\lambda) = 0$ is greater than one (that is $R_{0Z} > 1$).

Hence, from the above observations, one can conclude that $R_{0Z}^{hm} = 1 (< 1, > 1)$ if and only if $R_{0Z} = 1 (< 1, > 1)$. Since the two threshold parameter R_{0Z} and R_{0Z}^{hm} are equivalent [33,38]. We shall be using R_{0Z}^{hm} as the ZIKV basic reproduction number in the subsequent sections of the ZIKV only sub-model.

3.2.3. Local stability of ZDFE

Theorem 5. The disease-free equilibrium (ℓ_0^Z) of the ZIKV only sub-model (15) is locally asymptotically stable if $R_{0Z}^{hm} < 1$, and unstable if $R_{0Z}^{hm} > 1$.

Proof. We obtained the Jacobian matrix of the ZIKV only sub-model (15) evaluated at the disease-free equilibrium (ℓ_0^Z), given by

$$J(\ell_0^Z) = \begin{bmatrix} -\mu_h & 0 & -(\beta_Z \Lambda_h + \alpha_Z) & 0 & \kappa_Z & 0 & 0 & -\alpha_m \omega \\ 0 & -D_1 & \alpha_Z & 0 & 0 & 0 & 0 & \alpha_m \omega \\ 0 & \psi_Z & \beta_H \Lambda_h - D_2 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \gamma_Z & -D_3 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -\tau_Z & -D_4 & 0 & 0 & 0 \\ 0 & 0 & -\frac{\alpha_m \omega \Lambda_m \mu_h}{\Lambda_h \mu_m} & 0 & 0 & -\mu_m & 0 & 0 \\ 0 & 0 & \frac{\alpha_m \omega \Lambda_m \mu_h}{\Lambda_h \mu_m} & 0 & 0 & 0 & -D_5 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \psi_m & -\mu_m \end{bmatrix}$$

where

$$D_1 = \psi_Z + \mu_h, D_2 = \gamma_Z + \delta_Z + \mu_h, D_3 = \tau_Z + \phi_Z \delta_Z + \mu_h, \\ D_4 = \kappa_Z + \mu_h, \text{ and } D_5 = \psi_m + \mu_m.$$

The eigenvalues of the Jacobian matrix $J(\ell_0^Z)$ are $\lambda_1 = -\mu_h, \lambda_2 = -D_3, \lambda_3 = -D_4, \lambda_4 = -\mu_m$ and the roots of the characteristic polynomial below

$$G(\lambda) = \lambda^4 + a_1 \lambda^3 + a_2 \lambda^2 + a_3 \lambda + a_4 \tag{20}$$

where

$$a_1 = D_1 + D_2 + D_5 + \mu_m - \beta_Z \Lambda_h, \\ a_2 = D_1 (D_2 + D_5 + \mu_m) + D_2 (D_5 + \mu_m) + D_5 \mu_m - \alpha_Z \psi_Z \\ - \beta_Z \Lambda_h (D_1 + D_5 + \mu_m), \\ a_3 = D_1 D_2 D_5 + D_2 D_5 \mu_m + D_1 \mu_m (D_2 + D_5) \\ - \beta_Z \Lambda_h (D_1 D_5 + D_1 \mu_m + D_5 \mu_m) - \alpha_Z \psi_Z (D_5 + \mu_m), \\ a_4 = D_1 D_2 D_5 \mu_m (1 - R_{0Z}^{hm}).$$

Now, by applying the Routh–Hurwitz criterion [42,43], which states that all roots of the polynomial (20) have negative real parts if and only if $a_1 > 0, a_2 > 0, a_3 > 0, a_4 > 0$, and $a_1 a_2 a_4 > a_3^2 + a_1^2 a_4$. For all this conditions to be satisfied, then $R_{0Z}^{hm} < 1$. Therefore, by Routh–Hurwitz criterion, the disease-free equilibrium of the ZIKV only sub-model (15) is locally asymptotically stable when $R_{0Z}^{hm} < 1$. □

3.2.4. Endemic equilibrium ZIKV only sub-model

Similarly, just like the HIV only sub-model, we shall investigate the possibility of the existence of ZIKV endemic equilibrium point in this section. The endemic equilibrium point is a positive steady state where ZIKV infection persist in the population. At this equilibrium point, the ZIKV only sub-model infected variables are non-zero (i.e. $E_Z \neq 0, I_Z \neq 0, T_Z \neq 0, E_m \neq 0$, and $I_m \neq 0$). To investigate the endemic

equilibrium point, the ZIKV only sub-model equations are solved in terms of the ‘forces of infection’, given by

$$\lambda_Z^{**} = \frac{\alpha_Z I_Z^{**}}{N_h^{**}} + \frac{\alpha_{mZ} \omega I_m^{**}}{N_h^{**}}, \text{ and } \lambda_m^{**} = \frac{\alpha_m \omega I_Z^{**}}{N_h^{**}} \tag{21}$$

where

$$N_h^{**} = S_h^{**} + E_Z^{**} + I_Z^{**} + T_Z^{**} + R_Z^{**} \tag{22}$$

with

$$\begin{aligned} S_h^{**} &= \frac{\Lambda_h D_1 D_3 D_4 (D_2 - \beta_Z \Lambda_h)}{D_3 D_4 (D_1 D_2 (\lambda_Z^{**} + \mu_h) + \beta_Z \Lambda_h (\lambda_Z^{**} \psi_Z - D_1 (\lambda_Z^{**} + \mu_h))) - \lambda_Z^{**} \psi_Z \gamma_Z \tau_Z \kappa_Z}, \\ E_Z^{**} &= \frac{\lambda_Z^{**} \Lambda_h D_3 D_4 (D_2 - \beta_Z \Lambda_h)}{D_3 D_4 (D_1 D_2 (\lambda_Z^{**} + \mu_h) + \beta_Z \Lambda_h (\lambda_Z^{**} \psi_Z - D_1 (\lambda_Z^{**} + \mu_h))) - \lambda_Z^{**} \psi_Z \gamma_Z \tau_Z \kappa_Z}, \\ I_Z^{**} &= \frac{\lambda_Z^{**} \Lambda_h \psi_Z D_3 D_4}{D_3 D_4 (D_1 D_2 (\lambda_Z^{**} + \mu_h) + \beta_Z \Lambda_h (\lambda_Z^{**} \psi_Z - D_1 (\lambda_Z^{**} + \mu_h))) - \lambda_Z^{**} \psi_Z \gamma_Z \tau_Z \kappa_Z}, \\ T_Z^{**} &= \frac{\lambda_Z^{**} \Lambda_h \psi_Z \gamma_Z D_4}{D_3 D_4 (D_1 D_2 (\lambda_Z^{**} + \mu_h) + \beta_Z \Lambda_h (\lambda_Z^{**} \psi_Z - D_1 (\lambda_Z^{**} + \mu_h))) - \lambda_Z^{**} \psi_Z \gamma_Z \tau_Z \kappa_Z}, \\ R_Z^{**} &= \frac{\lambda_Z^{**} \Lambda_h \psi_Z \gamma_Z \tau_Z}{D_3 D_4 (D_1 D_2 (\lambda_Z^{**} + \mu_h) + \beta_Z \Lambda_h (\lambda_Z^{**} \psi_Z - D_1 (\lambda_Z^{**} + \mu_h))) - \lambda_Z^{**} \psi_Z \gamma_Z \tau_Z \kappa_Z}, \\ S_m^{**} &= \frac{\Lambda_m}{\lambda_m^{**} + \mu_m}, E_m^{**} = \frac{\lambda_m^{**} \Lambda_m}{D_5 (\lambda_m^{**} + \mu_m)}, I_m^{**} = \frac{\lambda_m^{**} \Lambda_m \psi_m}{D_5 \mu_m (\lambda_m^{**} + \mu_m)}. \end{aligned} \tag{23}$$

where

$$\begin{aligned} D_1 &= \psi_Z + \mu_h, D_2 = \gamma_Z + \delta_Z + \mu_h, D_3 = \tau_Z + \phi_Z \delta_Z + \mu_h, \\ D_4 &= \kappa_Z + \mu_h, \text{ and } D_5 = \psi_m + \mu_m. \end{aligned}$$

Substituting Eqs. (22) and (23) into Eq. (21), we obtained

$$f(\lambda_Z^{**}) = \lambda_Z^{**} (Q_1 \lambda_Z^{**2} + Q_2 \lambda_Z^{**} + Q_3) = 0 \tag{24}$$

where

$$\begin{aligned} Q_1 &= \Lambda_h^2 \mu_m (D_3 D_4 D_5 (\alpha_m \omega \psi_Z + \mu_m (D_2 - \beta_Z \Lambda_h) + \mu_h \psi_Z) \\ &\quad + \mu_m \psi_Z \gamma_Z D_5 (D_4 + \tau_Z)) (D_3 D_4 (D_2 - \beta_Z \Lambda_h) \\ &\quad + \psi_Z (D_3 D_4 + \gamma_Z (\tau_Z + D_4))), \\ Q_2 &= \Lambda_h^2 \mu_m D_1 D_3 D_5 (D_2 - \beta_Z \Lambda_h) (\psi_Z D_3 D_4 (\alpha_m \omega \\ &\quad + 2\mu_m) + 2\mu_m D_3 D_4 (D_2 - \beta_Z \Lambda_h) + \\ &\quad 2\mu_m \psi_Z \gamma_Z (\tau_Z + D_4)) - \alpha_Z \Lambda_h^2 \mu_m \psi_Z D_3 D_4 D_5 (D_3 D_4 (\psi_Z (\alpha_m \omega + \mu_m) \\ &\quad + \mu_m (D_2 - \beta_Z \Lambda_h)) + \\ &\quad \mu_m \psi_Z \gamma_Z (\tau_Z + D_4)) - \alpha_m \alpha_{mZ} \omega^2 \Lambda_h \Lambda_m \psi_Z \psi_m D_3 D_4 (D_3 D_4 (D_1 D_2 \\ &\quad + \beta_Z \Lambda_h (\psi_Z - D_1)) - \psi_Z \tau_Z \kappa_Z), \\ Q_3 &= \Lambda_h^2 \mu_m^2 D_1^2 D_2 D_3^2 D_4^2 D_5 (D_2 - \beta_Z \Lambda_h) (1 - R_{0Z}^{hm}). \end{aligned}$$

The solution to $f(\lambda_Z^{**})$ in (24) are $\lambda_Z^{**} = 0$ and $Q_1 \lambda_Z^{**2} + Q_2 \lambda_Z^{**} + Q_3 = 0$. Here, $\lambda_Z^{**} = 0$ represents the ZIKV only disease-free equilibrium point, and its stability has been previously examined. On the other hand, $Q_1 \lambda_Z^{**2} + Q_2 \lambda_Z^{**} + Q_3 = 0$ represents to the ZIKV endemic equilibrium. The nature of the polynomial $f(\lambda_Z^{**})$ in (24) is suggestive of the occurrence of backward bifurcation, often seen when both a stable disease-free equilibrium point (ZDFE) and a stable endemic equilibrium co-exist, provided that the basic reproduction number of the ZIKV only sub-model is below one (see for instance [33,38,43,45]). Biologically, the

backward bifurcation feature of the ZIKV only sub-model (15) makes effective control of ZIKV infection within the population difficult when the basic reproduction number is less than one. In backward bifurcation, multiple endemic equilibrium must exist. Hence, there are three cases which we have to consider of $Q_1 \lambda_Z^{**2} + Q_2 \lambda_Z^{**} + Q_3 = 0$ depending on the sign of Q_2 and Q_3 since Q_1 is always positive. The cases are;

1. If $Q_2 < 0$ and $Q_3 = 0$ or $Q_2^2 - 4Q_1Q_3 = 0$, then $f(\lambda_Z^{**})$ has a unique endemic equilibrium point (i.e. one positive root), and there is no possibility of backward bifurcation.
2. If $Q_2 < 0$, $Q_3 > 0$ and $Q_2^2 - 4Q_1Q_3 > 0$, then $f(\lambda_Z^{**})$ has two endemic equilibria (i.e. two positive roots), and therefore there is possibility of the occurrence of backward bifurcation.
3. Otherwise, there is none.

However, it is pertinent to note that $Q_3 > 0$ if $R_{0Z}^{hm} < 1$, and $Q_3 < 0$ if $R_{0Z}^{hm} > 1$. Therefore, the above examination leads to the following theorem.

Theorem 6. The ZIKV only sub-model (15) has;

1. Precisely one unique endemic equilibrium if $Q_3 < 0$ (i.e. $R_{0Z}^{hm} > 1$)
2. Precisely one unique endemic equilibrium if $Q_2 < 0$, and $Q_3 = 0$ or $Q_2^2 - 4Q_1Q_3 = 0$.
3. Precisely two endemic equilibria if $Q_3 > 0$ (i.e. $R_{0Z}^{hm} < 1$), $Q_2 < 0$ and $Q_2^2 - 4Q_1Q_3 > 0$.
4. No endemic equilibrium otherwise.

From case 3, the ZIKV only sub-model exhibit a backward bifurcation which occurs when multiple endemic equilibrium exists if and only if $R_{0Z}^{hm} < 1$.

3.2.5. The possibility of the existence of a backward bifurcation

We shall explore the possibility the existence of a backward bifurcation using the Center Manifold Theorem, as discussed by Castillo-Chavez and Song in [45].

Theorem 7. The ZIKV only sub-model (15) exhibits backward bifurcation at $R_{0Z}^{hm} = 1$, whenever $a > 0$

Proof. To apply the Center Manifold Theorem, we will carry out some modifications to the ZIKV only sub-model variables. Let $S_h = y_1$, $E_Z = y_2$, $I_Z = y_3$, $T_Z = y_4$, $R_Z = y_5$, $S_m = y_6$, $E_m = y_7$, $I_m = y_8$. Using the vector notation $y = (y_1, y_2, y_3, \dots, y_8)^T$ and $\frac{dy}{dt} = F(y)$, with $F = (f_1, f_2, f_3, \dots, f_8)^T$. Therefore, the ZIKV only sub-model (15) becomes

$$\begin{aligned} \frac{dy_1}{dt} &\equiv f_1 = (1 - \beta_Z y_3) \Lambda_h - \frac{(\alpha_Z y_3 + \alpha_{mZ} \omega y_8) y_1}{y_1 + y_2 + y_3 + y_4 + y_5} - \mu_h y_1 + \kappa_Z y_5 \\ \frac{dy_2}{dt} &\equiv f_2 = \frac{(\alpha_Z y_3 + \alpha_{mZ} \omega y_8) y_1}{y_1 + y_2 + y_3 + y_4 + y_5} - (\psi_Z + \mu_h) y_2 \\ \frac{dy_3}{dt} &\equiv f_3 = \psi_Z y_2 + \beta_Z \Lambda_h y_3 - (\gamma_Z + \delta_Z + \mu_h) y_3 \\ \frac{dy_4}{dt} &\equiv f_4 = \gamma_Z y_3 - (\tau_Z + \phi_Z \delta_Z + \mu_h) y_4 \\ \frac{dy_5}{dt} &\equiv f_5 = \tau_Z y_4 - (\kappa_Z + \mu_h) y_5 \\ \frac{dy_6}{dt} &\equiv f_6 = \Lambda_m - \frac{\alpha_m \omega y_3 y_6}{y_1 + y_2 + y_3 + y_4 + y_5} - \mu_m y_6 \\ \frac{dy_7}{dt} &\equiv f_7 = \frac{\alpha_m \omega y_3 y_6}{y_1 + y_2 + y_3 + y_4 + y_5} - (\psi_m + \mu_m) y_7 \\ \frac{dy_8}{dt} &\equiv f_8 = \psi_m y_7 - \mu_m y_8. \end{aligned} \tag{25}$$

We considered the transmission probability of ZIKV from infected mosquitoes to susceptible individuals (α_{mZ}) as the bifurcation parameter. Solving for $\alpha_{mZ} = \alpha_{mZ}^*$ from $R_{0Z}^{hm} = 1$, we have

$$\alpha_{mZ}^* = \frac{\Lambda_h \mu_m^2 D_5 (D_1 D_2 - (\alpha_Z \psi_Z + \beta_Z \Lambda_h D_1))}{\alpha_m \omega^2 \Lambda_m \mu_h \psi_m \psi_Z}$$

Evaluating the Jacobian of the transformed system (25) at ZDFE (ℓ_0^Z) with $\alpha_{mZ} = \alpha_{mZ}^*$, we have

$$J(\ell_0^Z) \Big|_{\alpha_{mZ}=\alpha_{mZ}^*} = \begin{bmatrix} -\mu_h & 0 & -(\beta_Z \Lambda_h + \alpha_Z) & 0 & \kappa_Z & 0 & 0 & -\alpha_{mZ}^* \omega \\ 0 & -D_1 & \alpha_Z & 0 & 0 & 0 & 0 & \alpha_{mZ}^* \omega \\ 0 & \psi_Z & \beta_H \Lambda_h - D_2 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \gamma_Z & -D_3 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -\tau_Z & -D_4 & 0 & 0 & 0 \\ 0 & 0 & -\frac{\alpha_m \omega \Lambda_m \mu_h}{\Lambda_h \mu_m} & 0 & 0 & -\mu_m & 0 & 0 \\ 0 & 0 & \frac{\alpha_m \omega \Lambda_m \mu_h}{\Lambda_h \mu_m} & 0 & 0 & 0 & -D_5 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \psi_m & -\mu_m \end{bmatrix}$$

where

$$D_1 = \psi_Z + \mu_h, D_2 = \gamma_Z + \delta_Z + \mu_h, D_3 = \tau_Z + \phi_Z \delta_Z + \mu_h, D_4 = \kappa_Z + \mu_h, \text{ and } D_5 = \psi_m + \mu_m.$$

The Jacobian matrix $J(\ell_0^Z) \Big|_{\alpha_{mZ}=\alpha_{mZ}^*}$ has a simple zero eigenvalue (a center) and all other eigenvalues having negative real part (hence, the center manifold theorem can be applied [38,45]) The right eigenvector, $w = (w_1, w_2, w_3, w_4, w_5, w_6, w_7, w_8)^T$, associated with the simple zero eigenvalue can be obtained from $J(\ell_0^Z) \Big|_{\alpha_{mZ}=\alpha_{mZ}^*} w = 0$, given by

$$\begin{aligned} -\mu_h w_1 - (\beta_Z \Lambda_h + \alpha_Z) w_3 + \kappa_Z w_5 - \alpha_{mZ}^* \omega w_8 &= 0 \\ -D_1 w_2 + \alpha_Z w_3 + \alpha_{mZ}^* \omega w_8 &= 0 \\ \psi_Z w_2 + (\beta_Z \Lambda_h - D_2) w_3 &= 0 \\ \gamma_Z w_3 - D_3 w_4 &= 0 \\ \tau_Z w_4 - D_4 w_5 &= 0 \\ -\frac{\alpha_m \omega \Lambda_m \mu_h}{\Lambda_h \mu_m} w_3 - \mu_m w_6 &= 0 \\ \frac{\alpha_m \omega \Lambda_m \mu_h}{\Lambda_h \mu_m} w_3 - D_5 w_7 &= 0 \\ \psi_m w_7 - \mu_m w_8 &= 0. \end{aligned} \tag{26}$$

From Eq. (26), we obtained

$$\begin{aligned} w_1 &= \frac{(\kappa_Z \gamma_Z \tau_Z \Lambda_h \mu_m^2 D_5 - \alpha_Z \Lambda_h \mu_m^2 D_3 D_4 D_5 - \alpha_{mZ}^* \alpha_m \omega^2 \Lambda_m \mu_h \psi_m D_3 D_4)}{\Lambda_h \mu_h \mu_m^2 D_3 D_4 D_5} \\ &\times w_3, w_2 = \frac{(D_2 - \beta_Z \Lambda_h)}{\psi_Z} w_3, \\ w_3 &= w_3 > 0, w_4 = \frac{\gamma_Z}{D_3} w_3, w_5 = \frac{\gamma_Z \tau_Z}{D_3 D_4} w_3, w_6 = -\frac{\alpha_m \omega \Lambda_m \mu_h}{\Lambda_h \mu_m^2} w_3, \\ w_7 &= \frac{\alpha_m \omega \Lambda_m \mu_h}{\Lambda_h \mu_m D_5} w_3, \\ w_8 &= \frac{\alpha_m \omega \Lambda_m \mu_h \psi_m}{\Lambda_h \mu_m^2 D_5} w_3 \end{aligned}$$

Similarly, the left eigenvector, $v = (v_1, v_2, v_3, v_4, v_5, v_6, v_7, v_8)$, satisfying $v \cdot w = 1$, associated with the simple zero eigenvalue can be obtained

from $vJ(\ell_0^Z) \Big|_{\alpha_{mZ}=\alpha_{mZ}^*} = 0$, given by

$$\begin{aligned} -\mu_h v_1 &= 0 \\ -(\beta_Z \Lambda_h + \alpha_Z) v_1 + \alpha_Z v_2 + (\beta_Z \Lambda_h - D_2) v_3 + \gamma_Z v_4 \\ &- \frac{\alpha_m \omega \Lambda_m \mu_h}{\Lambda_h \mu_m} v_6 + \frac{\alpha_m \omega \Lambda_m \mu_h}{\Lambda_h \mu_m} v_7 = 0 \\ -D_3 v_4 + \tau_Z v_5 &= 0 \\ \kappa_Z v_1 - D_4 v_5 &= 0 \\ -\mu_m v_6 &= 0 \\ -D_5 v_7 + \psi_m v_8 &= 0 \\ -\alpha_{mZ}^* \omega v_1 + \alpha_{mZ}^* \omega v_2 - \mu_m v_8 &= 0. \end{aligned} \tag{27}$$

From Eq. (27), we obtained

$$v_1 = v_4 = v_5 = v_6 = 0, v_3 = \frac{D_1}{\psi_Z} v_2, v_7 = \frac{\alpha_{mZ}^* \omega \psi_m}{\mu_m D_5} v_2, v_8 = \frac{\alpha_{mZ}^* \omega}{\mu_m} v_2.$$

Since $v_1 = v_4 = v_5 = v_6 = 0$ for $k = 1, 2, 3, \dots, 8$, the only non-zero partial derivatives of $f_1, f_2, f_3, \dots, f_8$ evaluated at ZDFE (ℓ_0^H) are

$$\begin{aligned} \frac{\partial^2 f_2}{\partial y_2 \partial y_3} &= \frac{\partial^2 f_2}{\partial y_3 \partial y_2} = \frac{\partial^2 f_2}{\partial y_3 \partial y_4} = \frac{\partial^2 f_2}{\partial y_4 \partial y_3} = \frac{\partial^2 f_2}{\partial y_3 \partial y_5} = \frac{\partial^2 f_2}{\partial y_5 \partial y_3} = -\frac{\alpha_Z \mu_h}{\Lambda_h}, \\ \frac{\partial^2 f_2}{\partial y_2 \partial y_8} &= \frac{\partial^2 f_2}{\partial y_8 \partial y_2} = \frac{\partial^2 f_2}{\partial y_3 \partial y_8} = \frac{\partial^2 f_2}{\partial y_8 \partial y_3} = \frac{\partial^2 f_2}{\partial y_4 \partial y_8} = \frac{\partial^2 f_2}{\partial y_8 \partial y_4} \\ &= \frac{\partial^2 f_2}{\partial y_5 \partial y_8} = \frac{\partial^2 f_2}{\partial y_8 \partial y_5} = -\frac{\alpha_{mZ}^* \omega \mu_h}{\Lambda_h}, \\ \frac{\partial^2 f_7}{\partial y_1 \partial y_3} &= \frac{\partial^2 f_7}{\partial y_3 \partial y_1} = \frac{\partial^2 f_7}{\partial y_2 \partial y_3} = \frac{\partial^2 f_7}{\partial y_3 \partial y_2} = \frac{\partial^2 f_7}{\partial y_3 \partial y_4} = \frac{\partial^2 f_7}{\partial y_4 \partial y_3} \\ &= \frac{\partial^2 f_7}{\partial y_3 \partial y_5} = \frac{\partial^2 f_7}{\partial y_5 \partial y_3} = -\frac{\alpha_m \omega \Lambda_m \mu_h^2}{\Lambda_h^2 \mu_m}, \\ \frac{\partial^2 f_7}{\partial y_3 \partial y_6} &= \frac{\partial^2 f_7}{\partial y_6 \partial y_3} = \frac{\alpha_m \omega \mu_h}{\Lambda_h}, \frac{\partial^2 f_7}{\partial y_3^2} = -\frac{2\alpha_m \omega \Lambda_m \mu_h^2}{\Lambda_h^2 \mu_m}, \frac{\partial^2 f_2}{\partial y_3^2} = -\frac{2\alpha_Z \mu_h}{\Lambda_h}, \\ \frac{\partial^2 f_2}{\partial y_8 \partial \alpha_{mZ}^*} &= \omega. \end{aligned} \tag{28}$$

The direction of the bifurcation at $R_{0Z}^{hm} = 1$ is determined by the signs of the bifurcation coefficients a and b , which can be obtained using the partial derivatives in (28). Thus, the bifurcation coefficients a and b , is given by (see Eqs. (29) and (30) which are given in Box 1) Since the bifurcation coefficient b is positive, it follows from theorem 4.1 in [45] that the ZIKV only sub-model exhibits a backward bifurcation at $R_{0Z}^{hm} = 1$ whenever the bifurcation coefficient a is positive. \square

Fig. 2 depicts the bifurcation diagram of Zika virus, the parameter values used are $\Lambda_h = 12.5$ and other parameter values in Table 2.

3.3. HIV-ZIKV co-infection model

The disease-free equilibrium (ℓ_0^{HZ}) of the HIV-ZIKV co-infection model (1) is obtained by setting all the infected variables to zero and equating the right hand side of the HIV-ZIKV co-infection model (1) to zero, given by

$$\begin{aligned} \ell_0^{HZ} &= (S_h^*, E_Z^*, I_Z^*, T_Z^*, R_Z^*, E_H^*, I_H^*, A^*, T_H^*, E_{HZ}^*, H_1^*, H_2^*, H_3^*, I_{HZ}^*, \\ &I_{AZ}^*, T_{HZ}^*, S_m^*, E_m^*, I_m^*) \\ &= \left(\frac{\Lambda_h}{\mu_h}, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, \frac{\Lambda_m}{\mu_m}, 0, 0 \right) \end{aligned} \tag{31}$$

Like the cases of the HIV only and ZIKV only sub-models in Sections 3.1.2 and 3.2.2, It can be shown using the next generation operator method described in [41], that the basic reproduction number

$$\begin{aligned}
 a &= \sum_{k,i,j=1}^n v_k w_i w_j \frac{\partial^2 f_k}{\partial y_i \partial y_j} (\ell_0^Z) \\
 a &= - \frac{2v_2 w_3^2 \mu_h (\alpha_{mZ}^* \alpha_m \omega^2 \psi_m \Lambda_m \mu_h + \alpha_Z \Lambda_h \mu_m^2 D_5) (D_3 D_4 ((D_2 - \beta_Z \Lambda_h) + \psi_Z) + \gamma_Z \psi_Z (D_4 + \tau_Z))}{\Lambda_h^2 \mu_m^2 \psi_Z D_3 D_4 D_5} \\
 &\quad - \frac{2v_2 w_3^2 \alpha_{mZ}^* \alpha_m \omega^2 \psi_m \Lambda_m \mu_h^2 (D_3 D_4 (\mu_m (D_2 - \beta_Z \Lambda_h) + \psi_Z (\mu_m + \omega)) + \gamma_Z \psi_Z \mu_m (D_4 + \tau_Z))}{\Lambda_h^2 \mu_m^3 \psi_Z D_3 D_4 D_5} \\
 &\quad \frac{2v_2 w_3^2 \alpha_{mZ}^* \omega \psi_m (\kappa_Z \gamma_Z \tau_Z \Lambda_h \mu_m^2 D_5 - \alpha_Z \Lambda_h \mu_m^2 D_3 D_4 D_5 - \alpha_{mZ}^* \alpha_m \omega^2 \Lambda_m \mu_h \psi_m D_3 D_4)}{\Lambda_h \mu_h \mu_m^3 D_3 D_4 D_5^2},
 \end{aligned} \tag{29}$$

$$\begin{aligned}
 b &= \sum_{k,i=1}^n v_k w_i \frac{\partial^2 f_k}{\partial y_i \partial \alpha_{mZ}^*} (\ell_0^Z) \\
 b &= \frac{v_2 w_3 \alpha_m \omega^2 \psi_m \Lambda_m \mu_h}{\Lambda_h \mu_m^2 D_5} > 0.
 \end{aligned} \tag{30}$$

Box I.

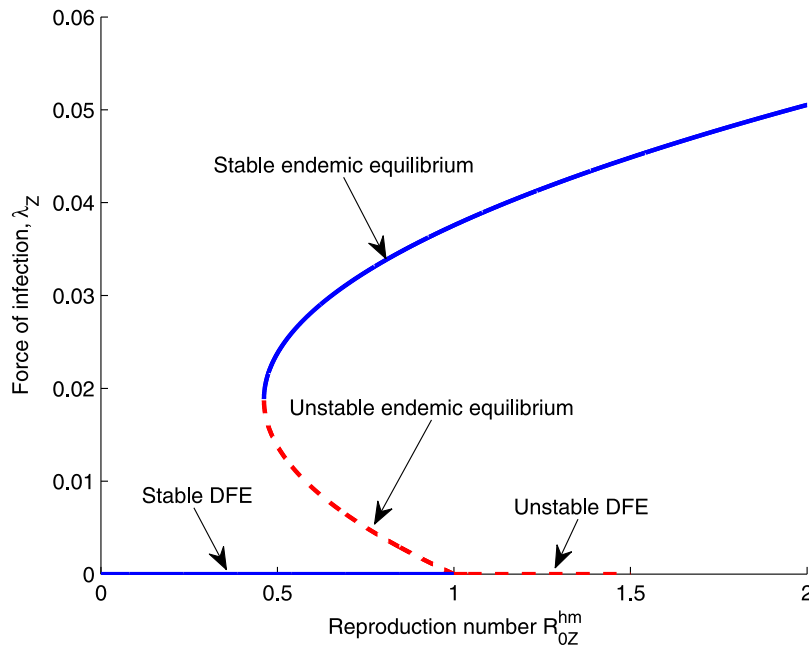


Fig. 2. Bifurcation diagram of the ZIKV only sub-model.

of the HIV-ZIKV co-infection model (1), denoted by R_{0HZ} , is given by

$$R_{0HZ} = \max \{ R_{0H}, R_{0Z}^{hm} \} \tag{32}$$

Theorem 8. The disease-free equilibrium point of the HIV-ZIKV model (1), is locally asymptotically stable if $R_{0HZ} < 1$, and unstable if $R_{0HZ} > 1$.

Proof. The proof is similar like the cases of HIV only and ZIKV only sub-models. □

Similarly, like in the case of the ZIKV-only sub-model, the full HIV-ZIKV co-infection model (1) also undergoes the phenomenon of backward bifurcation.

Theorem 9. The full HIV-ZIKV co-infection model (1) undergoes backward bifurcation at $R_{0HZ} = 1$, whenever $a > 0$.

The proof of Theorem 9 is in the Appendix.

3.4. Sensitivity analysis

In this section, we shall carry out the sensitivity analysis of the basic parameters that constitutes the basic reproduction number of HIV only sub-model and ZIKV only sub-model, in order to determine the significance of each parameter to the transmission of HIV and ZIKV. We shall employ the approach presented in [43]. Following the approach in [43], we use the normalized forward sensitivity index of a variable,

$$\begin{aligned}
 \mathcal{F}_{\alpha_m}^{R_{0Z}^{hm}} &= \frac{\alpha_m \alpha_{mZ} \omega^2 \Lambda_m \mu_h \psi_m \psi_Z}{(\alpha_Z \psi_Z + \beta_Z \Lambda_h (\psi_Z + \mu_h)) (\psi_m + \mu_m) \Lambda_h \mu_m^2 + \alpha_m \alpha_{mZ} \omega^2 \Lambda_m \mu_h \psi_m \psi_Z} = 0.997, \\
 \mathcal{F}_{\alpha_{mZ}}^{R_{0Z}^{hm}} &= \frac{\alpha_m \alpha_{mZ} \omega^2 \Lambda_m \mu_h \psi_m \psi_Z}{(\alpha_Z \psi_Z + \beta_Z \Lambda_h (\psi_Z + \mu_h)) (\psi_m + \mu_m) \Lambda_h \mu_m^2 + \alpha_m \alpha_{mZ} \omega^2 \Lambda_m \mu_h \psi_m \psi_Z} = 0.997, \\
 \mathcal{F}_{\omega}^{R_{0Z}^{hm}} &= \frac{2 \alpha_m \alpha_{mZ} \omega^2 \Lambda_m \mu_h \psi_m \psi_Z}{(\alpha_Z \psi_Z + \beta_Z \Lambda_h (\psi_Z + \mu_h)) (\psi_m + \mu_m) \Lambda_h \mu_m^2 + \alpha_m \alpha_{mZ} \omega^2 \Lambda_m \mu_h \psi_m \psi_Z} = 1.995, \\
 \mathcal{F}_{\beta_Z}^{R_{0Z}^{hm}} &= \frac{\beta_Z \Lambda_h^2 \mu_m^2 (\psi_Z + \mu_h) (\psi_m + \mu_m)}{(\alpha_Z \psi_Z + \beta_Z \Lambda_h (\psi_Z + \mu_h)) (\psi_m + \mu_m) \Lambda_h \mu_m^2 + \alpha_m \alpha_{mZ} \omega^2 \Lambda_m \mu_h \psi_m \psi_Z} = 0.000018, \\
 \mathcal{F}_{\Lambda_h}^{R_{0Z}^{hm}} &= \frac{\beta_Z \Lambda_h^2 \mu_m^2 (\psi_Z + \mu_h) (\gamma_Z + \delta_Z + \mu_h) (\psi_m + \mu_m) - \alpha_m \alpha_{mZ} \omega^2 \Lambda_m \mu_h \psi_m \psi_Z}{(\alpha_Z \psi_Z + \beta_Z \Lambda_h (\psi_Z + \mu_h)) (\psi_m + \mu_m) \Lambda_h \mu_m^2 + \alpha_m \alpha_{mZ} \omega^2 \Lambda_m \mu_h \psi_m \psi_Z} = -0.997, \\
 \mathcal{F}_{\Lambda_m}^{R_{0Z}^{hm}} &= \frac{\alpha_m \alpha_{mZ} \omega^2 \Lambda_m \mu_h \psi_m \psi_Z}{(\alpha_Z \psi_Z + \beta_Z \Lambda_h (\psi_Z + \mu_h)) (\psi_m + \mu_m) \Lambda_h \mu_m^2 + \alpha_m \alpha_{mZ} \omega^2 \Lambda_m \mu_h \psi_m \psi_Z} = 0.997, \\
 \mathcal{F}_{\psi_Z}^{R_{0Z}^{hm}} &= \frac{\alpha_Z \psi_Z \Lambda_h \mu_h \mu_m^2 (\psi_m + \mu_m) + \alpha_m \alpha_{mZ} \omega^2 \Lambda_m \mu_h^2 \psi_m \psi_Z}{(\psi_Z + \mu_h) ((\alpha_Z \psi_Z + \beta_Z \Lambda_h (\psi_Z + \mu_h)) (\psi_m + \mu_m) \Lambda_h \mu_m^2 + \alpha_m \alpha_{mZ} \omega^2 \Lambda_m \mu_h \psi_m \psi_Z)} = 0.0123, \\
 \mathcal{F}_{\psi_m}^{R_{0Z}^{hm}} &= \frac{\alpha_m \alpha_{mZ} \omega^2 \Lambda_m \mu_h \mu_m \psi_m \psi_Z}{(\psi_m + \mu_m) ((\alpha_Z \psi_Z + \beta_Z \Lambda_h (\psi_Z + \mu_h)) (\psi_m + \mu_m) \Lambda_h \mu_m^2 + \alpha_m \alpha_{mZ} \omega^2 \Lambda_m \mu_h \psi_m \psi_Z)} = 0.143, \\
 \mathcal{F}_{\gamma_Z}^{R_{0Z}^{hm}} &= -\frac{\gamma_Z}{(\gamma_Z + \delta_Z + \mu_h)} = -0.464, \mathcal{F}_{\delta_Z}^{R_{0Z}^{hm}} = -\frac{\delta_Z}{(\gamma_Z + \delta_Z + \mu_h)} = -0.418, \\
 \mathcal{F}_{\mu_m}^{R_{0Z}^{hm}} &= -\frac{(2 \alpha_m \alpha_{mZ} \omega^2 \Lambda_m \mu_h \psi_m^2 \psi_Z + 3 \alpha_m \alpha_{mZ} \omega^2 \Lambda_m \mu_h \mu_m \psi_m \psi_Z)}{(\psi_m + \mu_m) ((\alpha_Z \psi_Z + \beta_Z \Lambda_h (\psi_Z + \mu_h)) (\psi_m + \mu_m) \Lambda_h \mu_m^2 + \alpha_m \alpha_{mZ} \omega^2 \Lambda_m \mu_h \psi_m \psi_Z)} = -2.137, \\
 \mathcal{F}_{\mu_m}^{R_{0Z}^{hm}} &= \frac{\alpha_m \alpha_{mZ} \omega^2 \Lambda_m \psi_m \psi_Z ((\psi_Z + \mu_h) (\gamma_Z + \delta_Z + \mu_h) - \mu_h ((\psi_Z + \mu_h) + (\gamma_Z + \delta_Z + \mu_h)))}{\Lambda_h \mu_m^2 (\psi_Z + \mu_h)^2 (\gamma_Z + \delta_Z + \mu_h)^2 (\psi_m + \mu_m)} \\
 &\quad - \frac{(\alpha_Z \psi_Z ((\psi_Z + \mu_h) + (\gamma_Z + \delta_Z + \mu_h)) + \beta_Z \Lambda_h (\psi_Z + \mu_h)^2)}{(\psi_Z + \mu_h)^2 (\gamma_Z + \delta_Z + \mu_h)^2} = 0.867.
 \end{aligned}$$

Box II.

'u', that depends differentially on the parameter, 'x', defined as

$$\mathcal{F}_x^u = \frac{\partial u}{\partial x} \times \frac{x}{u}. \tag{33}$$

Hence, the sensitivity index of the basic reproduction number of the HIV only sub-model (5) and ZIKV only sub-model (15) with respect to the parameter 'x', are given by

$$\mathcal{F}_x^{R_{0H}} = \frac{\partial R_{0H}}{\partial x} \times \frac{x}{R_{0H}}, \text{ and } \mathcal{F}_x^{R_{0Z}^{hm}} = \frac{\partial R_{0Z}^{hm}}{\partial x} \times \frac{x}{R_{0Z}^{hm}}. \tag{34}$$

Firstly, we compute the sensitivity indices of the basic parameters of the ZIKV only sub-model.

$$\begin{aligned}
 \mathcal{F}_{\alpha_Z}^{R_{0Z}^{hm}} &= \frac{\psi_Z}{(\psi_Z + \mu_h) (\gamma_Z + \delta_Z + \mu_h)} \\
 &\quad \times \frac{\alpha_Z \Lambda_h \mu_m^2 (\psi_Z + \mu_h) (\gamma_Z + \delta_Z + \mu_h) (\psi_m + \mu_m)}{(\alpha_Z \psi_Z + \beta_Z \Lambda_h (\psi_Z + \mu_h)) (\psi_m + \mu_m) \Lambda_h \mu_m^2 + \alpha_m \alpha_{mZ} \omega^2 \Lambda_m \mu_h \psi_m \psi_Z}.
 \end{aligned}$$

We have that,

$$\begin{aligned}
 \mathcal{F}_{\alpha_Z}^{R_{0Z}^{hm}} &= \frac{\alpha_Z \Lambda_h \mu_m^2 (\psi_m + \mu_m)}{(\alpha_Z \psi_Z + \beta_Z \Lambda_h (\psi_Z + \mu_h)) (\psi_m + \mu_m) \Lambda_h \mu_m^2 + \alpha_m \alpha_{mZ} \omega^2 \Lambda_m \mu_h \psi_m \psi_Z} \\
 &= 0.0027.
 \end{aligned}$$

Similarly, (see Box II).

In similar reasoning, we obtained the sensitivity indices of the basic parameters of the HIV only sub-model, given by

$$\mathcal{F}_{\alpha_H}^{R_{0H}} = 0.9886, \mathcal{F}_{\beta_H}^{R_{0H}} = 0.0082, \mathcal{F}_{\psi_H}^{R_{0H}} = 0.0193, \mathcal{F}_{\Lambda_h}^{R_{0H}} = 0.0082,$$

$$\mathcal{F}_{q_1}^{R_{0H}} = -0.548, \mathcal{F}_{q_2}^{R_{0H}} = -0.029, \mathcal{F}_{\rho_1}^{R_{0H}} = -0.124, \mathcal{F}_{\eta_1}^{R_{0H}} = 0.0311,$$

$$\mathcal{F}_{\eta_2}^{R_{0H}} = 0.273, \mathcal{F}_{\phi_H}^{R_{0H}} = -0.0003, \mathcal{F}_{\delta_H}^{R_{0H}} = -0.0018, \mathcal{F}_{\mu_h}^{R_{0H}} = -0.318.$$

3.4.1. Interpretation of the sensitivity indices

The bar chart of the sensitivity indices of the basic reproduction number of the two diseases are depicted in Figs. 3 and 4 respectively. Those parameters with positive indices for HIV only sub-model and ZIKV only sub-model have significant impact on accelerating the spread of diseases, if their values are increasing (while other parameters remain constant). Thus, if their values increases the basic reproduction number increases as well. Conversely, when parameters with negative indices rise in value, they play a role in alleviating disease burdens, leading to a decrease in the basic reproduction numbers.

3.5. The impact of HIV on ZIKV infection

In this section, we shall investigate the impact of HIV infection on the transmission of ZIKV using the approach described in [46]. Following the approach in [46], we first expressed the basic reproduction number of ZIKV (R_{0Z}^{hm}) in terms of the basic reproduction number of HIV (R_{0H}). To do this, we expressed the parameter Λ_h (as it is common for both ZIKV and HIV equilibrium points) in Eq. (7) in terms of R_{0H} , we have

$$R_{0H} = \frac{\alpha_H \psi_H (B_3 B_4 + \eta_1 \rho_1 B_4 + \eta_2 (q_1 B_3 + q_2 \rho_1))}{B_1 B_2 B_3 B_4} + \frac{\beta_H \Lambda_h}{B_2}$$

where

$$B_1 = \psi_H + \mu_h, B_2 = \rho_1 + q_1 + \mu_h, B_3 = q_2 + \delta_H + \mu_h, B_4 = \phi_H \delta_H + \mu_h.$$

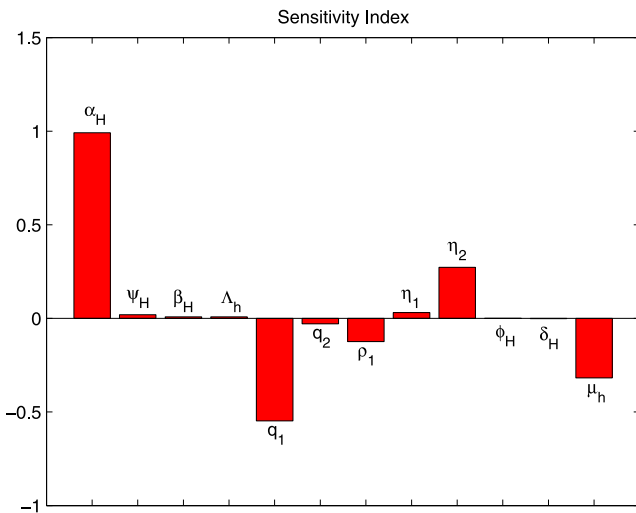


Fig. 3. Sensitivity index of the basic reproduction number of the HIV only sub-model.

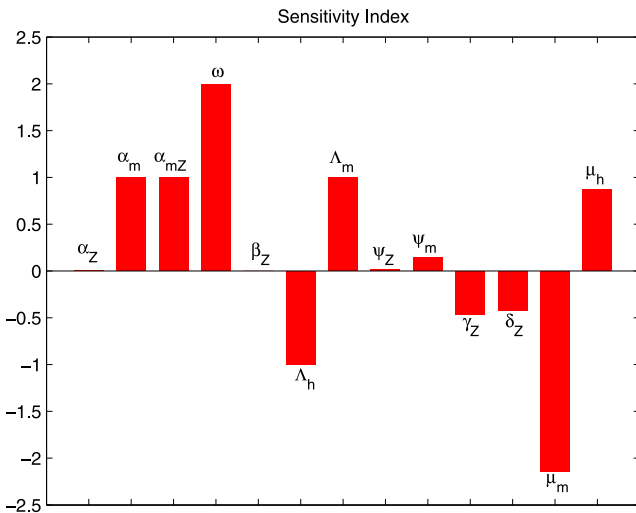


Fig. 4. Sensitivity index of the basic reproduction number of the ZIKV only sub-model.

Solving for Λ_h , we obtained

$$\Lambda_h = \frac{B_1 B_2 B_3 B_4 R_{0H} - \alpha_H \psi_H (B_3 B_4 + \eta_1 \rho_1 B_4 + \eta_2 (q_1 B_3 + q_2 \rho_1))}{\beta_H B_1 B_3 B_4} \quad (35)$$

Substituting the expression of Λ_h into R_{0Z}^{hm} in Eq. (19), we obtained R_{0Z}^{hm} in terms of R_{0H} , given as

$$R_{0Z}^{hm} = \frac{\alpha_Z \psi_Z}{D_1 D_2} + \frac{\beta_Z (B_1 B_2 B_3 B_4 R_{0H} - \alpha_H \psi_H (B_3 B_4 + \eta_1 \rho_1 B_4 + \eta_2 (q_1 B_3 + q_2 \rho_1)))}{\beta_H B_1 B_3 B_4 D_2} + \frac{\alpha_m \alpha_{mZ} \omega^2 \Lambda_m \mu_h \psi_m \psi_Z \beta_H B_1 B_3 B_4}{\mu_m^2 D_1 D_2 D_5 (B_1 B_2 B_3 B_4 R_{0H} - \alpha_H \psi_H (B_3 B_4 + \eta_1 \rho_1 B_4 + \eta_2 (q_1 B_3 + q_2 \rho_1)))} \quad (36)$$

where

$$D_1 = \psi_Z + \mu_h, D_2 = \gamma_Z + \delta_Z + \mu_h, D_3 = \tau_Z + \phi_Z \delta_Z + \mu_h,$$

$$D_4 = \kappa_Z + \mu_h, D_5 = \psi_m + \mu_m.$$

The partial derivatives of R_{0Z}^{hm} with respect to R_{0H} is given by

$$\frac{\partial R_{0Z}^{hm}}{\partial R_{0H}} \equiv \Theta_Z^H = \frac{\beta_Z B_2}{\beta_H D_2}$$

Table 2
Parameter values for model (1).

Parameter	Value	Source
Λ_h	0.0014	[47]
Λ_m	100	[38]
β_Z	0.012	Fitted
β_H	0.4	[48]
β_{HZ}	0.2	Assumed
f	0.5	Assumed
q_1	0.25	[28,49]
q_2	0.6	[50]
θ	0.2	Assumed
ψ_Z	0.6438	Fitted
ψ_H	0.4	Assumed
ψ_{HZ}	0.2	Assumed
ψ_m	$\frac{1}{3.5}$	[34]
γ_Z	0.0314	Fitted
α_Z	0.025	Fitted
α_{mZ}	0.0441	Fitted
α_m	0.04791	Fitted
α_H	0.3425	[30]
μ_h	0.008	[47]
μ_m	$\frac{1}{21}$	[34]
ω	0.45	[33]
ϵ_1	0.15	Assumed
τ_Z	0.0821134337	Fitted
η_1	0.4	Assumed
η_2	0.01	[51]
η_3	0.2	Assumed
η_4	0.005	Assumed
ρ_1	0.07	[28]
ν	0.03	Assumed
ϑ	0.2	Assumed
ρ_2	0.1	Assumed
δ_H	0.01	[48]
δ_Z	0.028348	Fitted
ξ_1	0.23	Assumed
ξ_2	0.31	Assumed
γ_{HZ}	0.3	Assumed
γ_{AZ}	0.5	Assumed
ϕ_Z	0.0065	Fitted
ϕ_H	0.001	Assumed
ϕ_{HZ}	0.0075	Assumed
ϕ_{AZ}	0.0088	Assumed
ϵ_2	0.22	Assumed
κ_Z	0.23	Fitted
ϵ_3	0.28	Assumed
δ_{HZ}	0.009	Assumed
δ_{AZ}	0.016	Assumed

$$= \frac{\alpha_m \alpha_{mZ} \omega^2 \Lambda_m \mu_h \psi_m \psi_Z \beta_H B_1^2 B_2^2 B_3^2 B_4^2}{\mu_m^2 D_1 D_2 D_5 (B_1 B_2 B_3 B_4 R_{0H} - \alpha_H \psi_H (B_3 B_4 + \eta_1 \rho_1 B_4 + \eta_2 (q_1 B_3 + q_2 \rho_1)))^2} \quad (37)$$

Thus, it is observed that the partial derivative R_{0Z}^{hm} with respect to R_{0H} is positive. Therefore, the result imply that a rise in HIV infection within the population will enhance the transmission of ZIKV positively.

4. Numerical simulations

In this section, we shall carry out the numerical simulations of the HIV-ZIKV co-infection model (1) using MATLAB with the parameter values in Table 2, in order to illustrate some of the analytic results obtained in the study.

We validate our ZIKV only sub-model by fitting the ZIKV only sub-model to the weekly confirmed cases of Zika virus in Brazil, in the year 2018. The Zika virus weekly data is obtained from the Pan American Health Organization (PAHO) [52], which is presented in Table 3. The model data fitting was carried out using the fmincon algorithm in MATLAB. The total human population in Brazil is estimated to be 210,166,592 [53] and the initial conditions of the state variables used for the model data fitting are $S_h(0) = 210134730$, $E_Z(0) = 30000$, $I_Z(0) = 1500$, $T_Z(0) = 360$, $R_Z(0) = 0$, $S_m(0) = 5000$, $E_m(0) = 1500$,

Table 3
PAHO data for the weekly confirmed cases of ZIKV in Brazil, 2018.

Week	Confirmed cases	Week	Confirmed cases	Week	Confirmed cases	Week	Confirmed cases
1	360	14	676	27	367	40	218
2	419	15	650	28	327	41	211
3	493	16	613	29	386	42	219
4	431	17	468	30	338	43	193
5	503	18	534	31	290	44	228
6	459	19	518	32	281	45	194
7	463	20	475	33	290	46	213
8	423	21	439	34	285	47	199
9	558	22	395	35	219	48	237
10	631	23	361	36	209	49	186
11	687	24	365	37	211	50	188
12	760	25	312	38	173	51	138
13	579	26	313	39	192	52	43

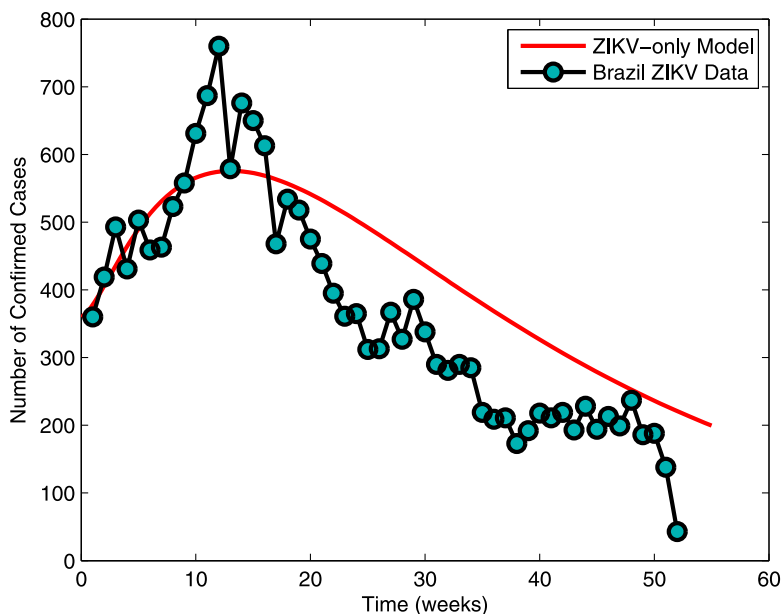


Fig. 5. Data-fitting of the ZIKV only sub-model.

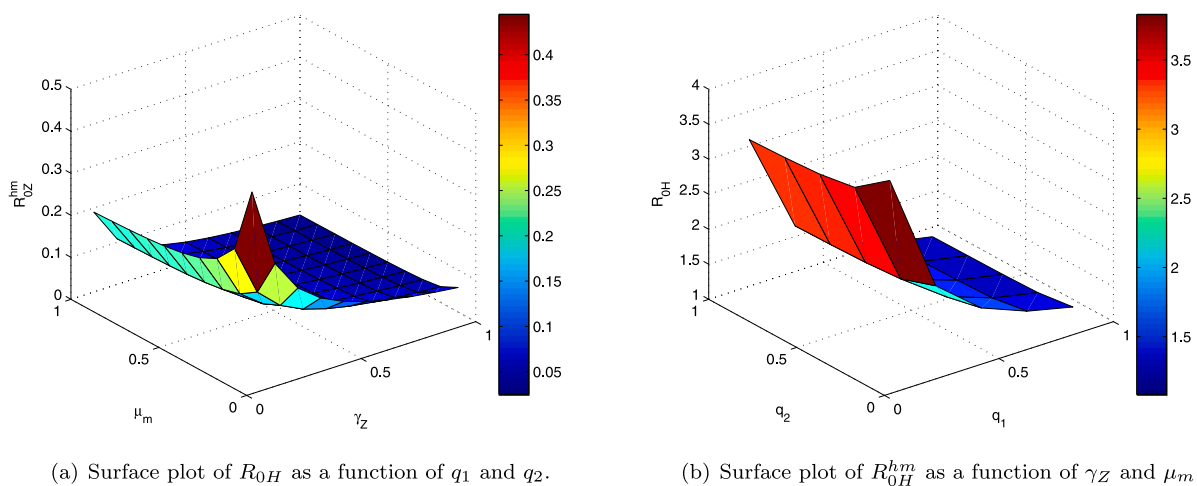


Fig. 6. Surface plots of the Basic reproduction numbers.

and $I_m(0) = 700$. It is important to note that a large proportion of ZIKV infected individuals are asymptomatic and as such, the confirmed cases are the those reported and receiving treatment. The data-fitting of ZIKV

only sub-model to the Number of confirmed cases of ZIKV in Brazil is depicted in Fig. 5.

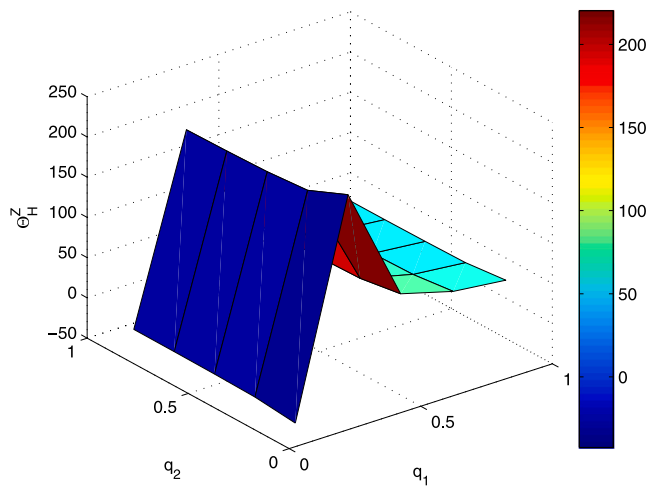


Fig. 7. Surface plot of the impact HIV treatment rates (q_1 and q_2) on ZIKV infection.

Table 4
Values of R_{0Z}^{hm} while varying γ_Z in the disease free equilibrium.

γ_Z	R_{0Z}^{hm}
0.1	0.3488
0.3	0.1414
0.5	0.0887
0.7	0.0646
0.9	0.0508

Table 5
Values of R_{0H} while varying q_1 in the disease free equilibrium.

q_1	R_{0H}
0.1	0.7227
0.3	0.4051
0.5	0.3073
0.7	0.2597
0.9	0.2317

Table 6
Values of R_{0H} while varying q_2 in the disease free equilibrium.

q_2	R_{0H}
0.1	0.5023
0.3	0.4602
0.5	0.4506
0.7	0.4464
0.9	0.4440

Table 7
Values of R_{0Z}^{hm} while varying γ_Z in the endemic equilibrium.

γ_Z	R_{0Z}^{hm}
0.1	67.1294
0.3	27.2128
0.5	17.0653
0.7	12.4302
0.9	9.7752

Table 8
Values of R_{0H} while varying q_1 in the endemic equilibrium.

q_1	R_{0H}
0.35	2.8914
0.45	2.5292
0.55	2.2824
0.65	2.1034

Results and discussion

Fig. 6a is the surface plot of the HIV basic reproduction number (R_{0HZ}) as a function of the treatment rate of HIV-only infected

Table 9
Values of R_{0H} while varying q_2 in the endemic equilibriums.

q_2	R_{0H}
0.1	3.9076
0.3	3.5708
0.5	3.4941
0.7	3.4601
0.9	3.4409

individuals with no clinical symptoms of AIDS (q_1) and treatment rate of HIV-only infected individuals showing clinical symptoms of AIDS (q_2), it is observed that as the treatment rates q_1 and q_2 increases, the value of the HIV reproduction number (R_{0H}) decreases. More importantly, from the observation of Fig. 6a, the treatment rate of HIV-only infected individuals with no clinical symptoms of AIDS (q_1) has a much more effect of reducing the value of the HIV reproduction number (R_{0H}) compared to the treatment rate of the HIV-only infected individuals with clinical symptoms of AIDS (q_2), which is in line with the sensitivity analysis in Section 3.4. If we can step up treatment rate of HIV-only infected individuals with no clinical symptoms of AIDS to about 70%, then the HIV basic reproduction number will reduce significantly. Fig. 6b depicts the surface plot of ZIKV basic reproduction number (R_{0Z}^{hm}) as a function of the treatment rate of ZIKV-only infected individuals (γ_Z) and the death rate of the vector (mosquito) (μ_m), it is observed that as the values of the treatment rate ZIKV-only infected individuals (γ_Z) and the vector death rate (μ_m) reduces the value of the ZIKV basic reproduction number (R_{0Z}^{hm}) increases, and as their values increases the ZIKV basic reproduction number decreases. Fig. 7 depicts the surface plots of the impact of the treatment rate of HIV-only infected individuals with no clinical symptoms of AIDS (q_1) and treatment rate of HIV-only infected individuals showing clinical symptoms of AIDS (q_2) on ZIKV infection. It is observed that when both HIV treatment rates (q_1 and q_2) are low, HIV infection increases, which leads to an increase in ZIKV infection. This is in line with Section 3.5. Fig. 8 depicts the simulations of the cumulative number of new cases of HIV and ZIKV using parameter values in Table 2. Fig. 8a illustrates the effect of the treatment rate of HIV-only infected individuals with no clinical symptoms of AIDS (q_1) on the cumulative number of new cases of HIV. It is observed that as the treatment rates (q_1) increases, the cumulative number of new cases of HIV decreases. Similar result was observed in Fig. 8b, it was observed that as the treatment rate of ZIKV-only infected individuals (γ_Z) increases, the cumulative number of new cases ZIKV reduces. Fig. 8c shows the effect of the mosquito-biting rate (ω) on the cumulative new cases of ZIKV, it is observed that there is increase in the cumulative new cases of ZIKV as the value of the mosquito-biting rate (ω) increases. Fig. 9 is the simulation of the population of HIV-only infected individuals (I_H), ZIKV-only infected individuals (I_Z), HIV-only infected individuals showing clinical symptoms of AIDS (A), HIV-only infected individuals (I_H), Co-infected individuals (I_{HZ}), Co-infected individuals (I_{AZ}), using parameter values in Table 2 with $\alpha_H = 0.1$, $\alpha_{mZ} = 0.003$, $\omega = 0.1$, and $\psi_Z = 0.0438$ (so that $R_{0H} = 0.4482$, $R_{0Z}^{hm} = 0.7020$, and $R_{0HZ} = 0.7020$). Fig. 9 illustrates the convergence to the local stability of the disease-free equilibrium in line with Theorems 2, 5 and 8.

Fig. 10 is the simulations of the cumulative new cases of HIV and ZIKV when the basic reproduction number of the co-infection is less than one ($R_{0HZ} = 0.7020$). Fig. 10a and c illustrates the effect of the HIV treatment rates q_1 and q_2 on the cumulative new cases of HIV infection, it is observed that as the treatment rates increases, the cumulative new cases of HIV reduces tremendously. Similar result was observed in the cumulative new cases of ZIKV infection in Fig. 10b, when the treatment rate (γ_Z) was varied. Fig. 11 is the simulation of the population of HIV-only infected individuals (I_H), ZIKV-only infected individuals (I_Z), HIV-only infected individuals showing clinical symptoms of AIDS (A), HIV-only infected individuals (I_H), Co-infected individuals (I_{HZ}),

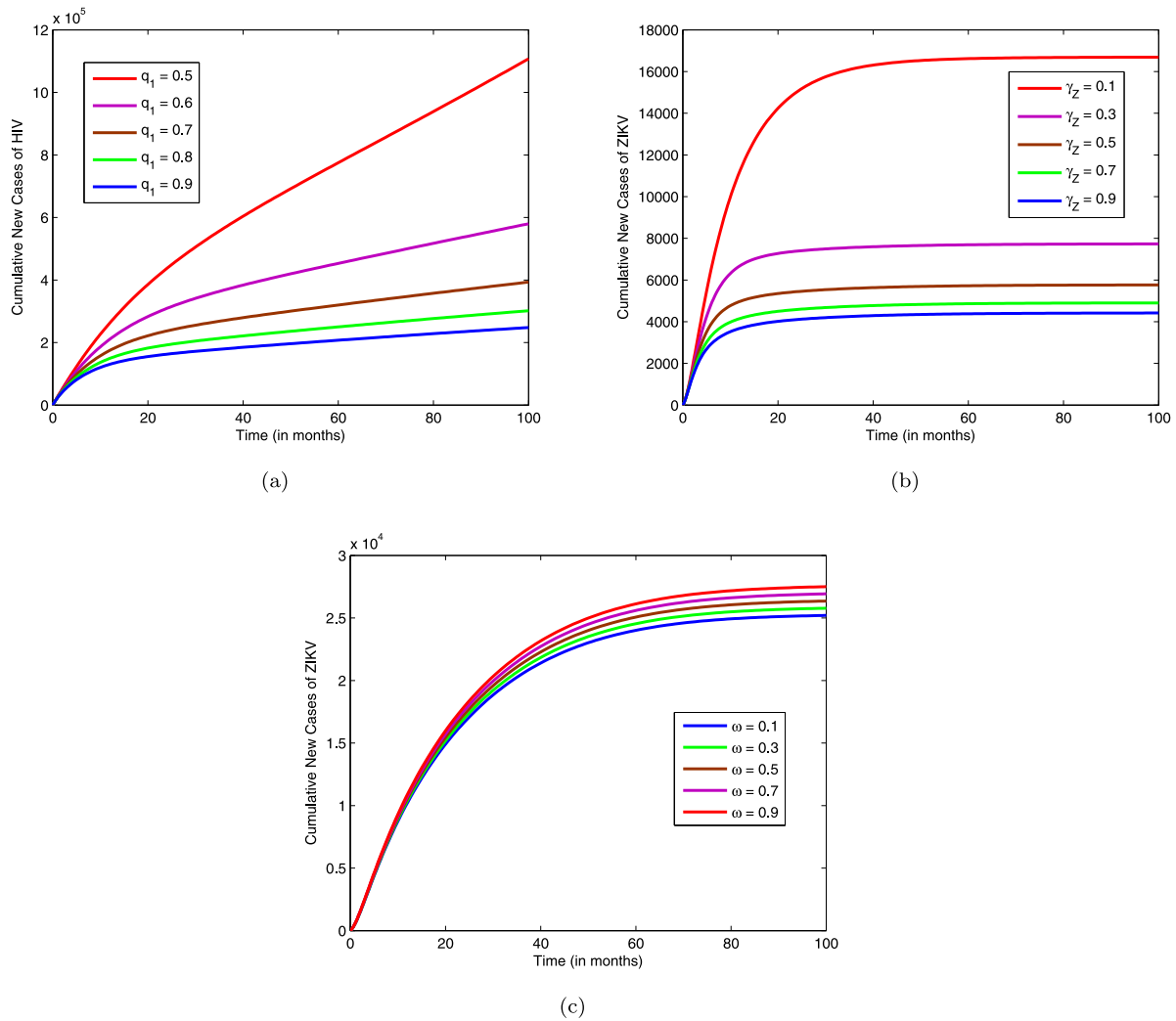


Fig. 8. Simulations of full model (1) showing the plots for (a) The effect of q_1 on the cumulative new cases of HIV (b) The effect of γ_Z on the cumulative new cases of ZIKV (c) The effect of ω on the cumulative new cases of ZIKV.

Co-infected individuals (I_{AZ}), using parameter values in Table 2 with $\alpha_H = 0.8$ and $\beta_H = 0.6$ (so that $R_{0H} = 3.4743$, $R_{0Z}^{hm} = 135.1030$, and $R_{0HZ} = 135.1030$). Fig. 11 illustrates the convergence to the endemic equilibrium while varying the treatment rate of the respective infected compartments. It is observed an increase in the treatment rates reduces the number of infected individuals of both diseases. Fig. 12 depicts the simulations of the HIV-only infected compartment, using parameter values in Table 2 with to illustrate the endemic equilibrium of the HIV only sub-model in line with Theorem 4. It was observed that when the treatment rates (q_1 and q_2) are above 0.5, the number of the HIV infected individuals decrease. Fig. 13 is the simulation of the effects of the vertical transmission rate (β_H and β_Z) on the full HIV-ZIKV co-infection model. In Fig. 13a and d, it is observed that the HIV vertical transmission rate (β_H) has a direct relationship with the cumulative new cases of HIV and the HIV-only infected individuals $I_H(t)$, it is shown that as the value of β_H increases the number of new cases of HIV increases as well as the number of HIV-only infected individuals. Similar results is observed for the ZIKV vertical transmission rate (β_Z) in Fig. 13b and c. Fig. 14 depicts the simulations of the effect of HIV treatment rate (q_1) on the co-infected compartments, it is observed that as the HIV treatment rate increases the number of co-infected individuals reduces within the period of 40 months. Thus, this indicates that an increase in HIV treatment rate reduces the burden of the co-infection with Zika virus. Fig. 15a, b, and c depicts the simulation of the effect of the modification parameter that accounts for decrease in sexual activity by individuals with ZIKV symptoms (due to

ill health) (θ) on the co-infected compartments I_{HZ} , I_{AZ} , and T_{HZ} , as the rate reduces the number of co-infected individuals increases, this shows that the increasing the value of θ decreases the number of co-infection.

5. Conclusion

This paper establishes and rigorously examines a deterministic mathematical model that comprehensively accounts for both the vertical and horizontal transmission dynamics of HIV and ZIKV co-infection. The investigation delves into the sexual and vector-based pathways involved in ZIKV horizontal transmission. Initially, qualitative analysis were conducted on two sub-models: the HIV only and the ZIKV only sub-models. The basic reproduction numbers for these sub-models were determined, followed by an evaluation of their disease-free equilibrium's local stability. The study reveals that the HIV only sub-model maintains a globally stable disease-free equilibrium if the HIV reproduction number is below one. However, in contrast, the ZIKV only sub-model exhibits a phenomenon of backward bifurcation when its associated reproduction number is less than unity, distinguishing it from the HIV only sub-model. The investigation further employs the center manifold theory to demonstrate that the full HIV-ZIKV co-infection model also experiences backward bifurcation. Additionally, a sensitivity analysis was performed on the basic reproduction numbers of the HIV and ZIKV sub-models to evaluate the significance of each

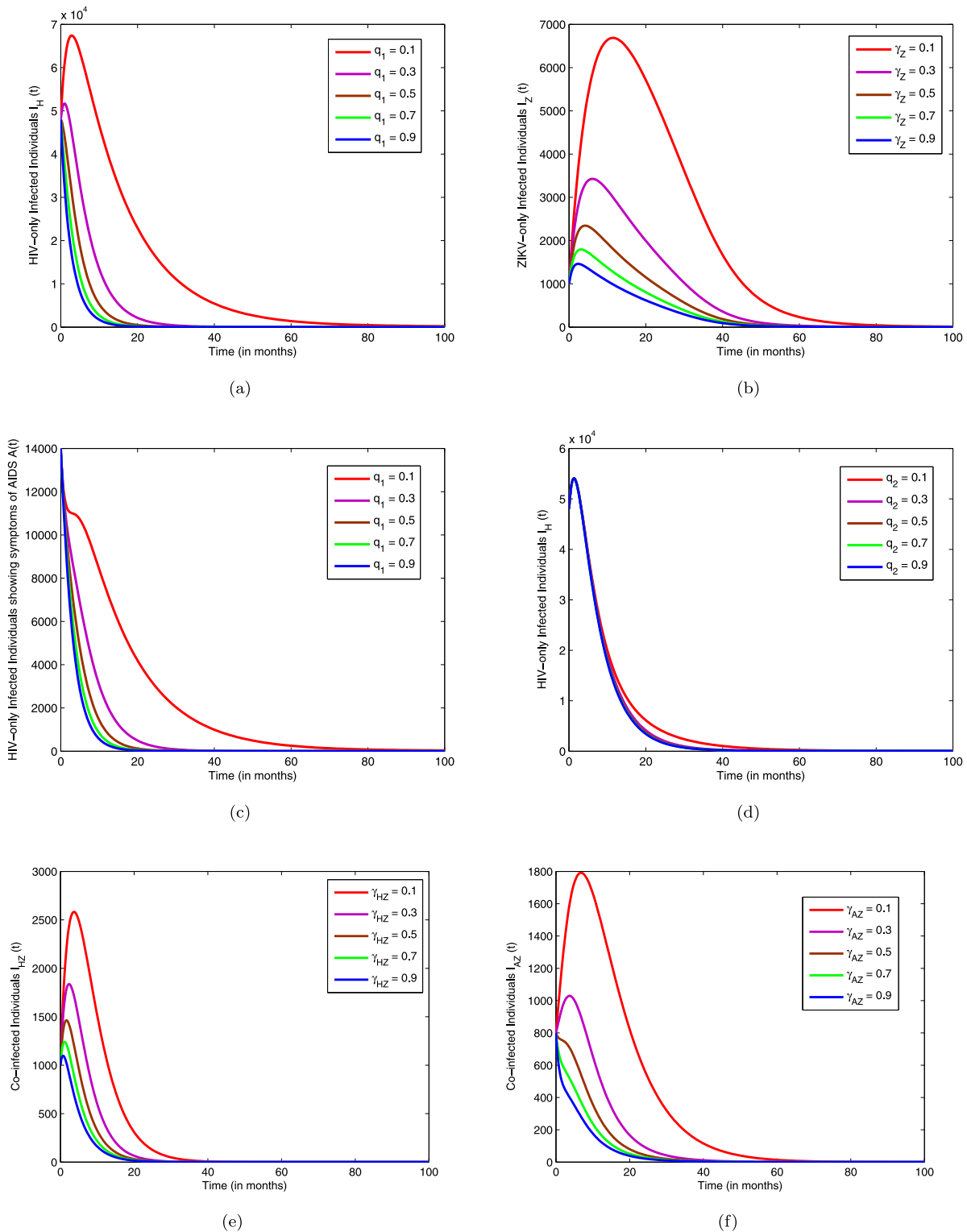


Fig. 9. Simulations of the full model (1) showing the plots for (a) HIV-only infected individuals (I_H) (b) ZIKV-only infected individuals (I_Z) (c) HIV-only infected individuals showing clinical symptoms of AIDS (A) (d) HIV-only infected individuals (I_H) (e) Co-infected individuals (I_{HZ}) (f) Co-infected individuals (I_{AZ}), for the case when $R_{0HZ} < 1$ while varying the treatment rates. Parameter values used are as in Table 2 with $\alpha_H = 0.1$, $\alpha_{mZ} = 0.003$, $\omega = 0.1$, and $\psi_Z = 0.0438$ (so that $R_{0H} = 0.4428$, $R_{0Z}^{hm} = 0.7020$, and $R_{0HZ} = 0.7020$). The values of the reproduction numbers when the treatment rates are varied can be found in Tables 4-6.

parameter in influencing the transmission of both HIV and ZIKV infections. We then corroborated our theoretical analysis by numerically simulating the full HIV-ZIKV co-infection model. The key findings of this study are:

1. The HIV only sub-model disease-free equilibrium is globally asymptotically stable when the HIV only basic reproduction number is less than one.

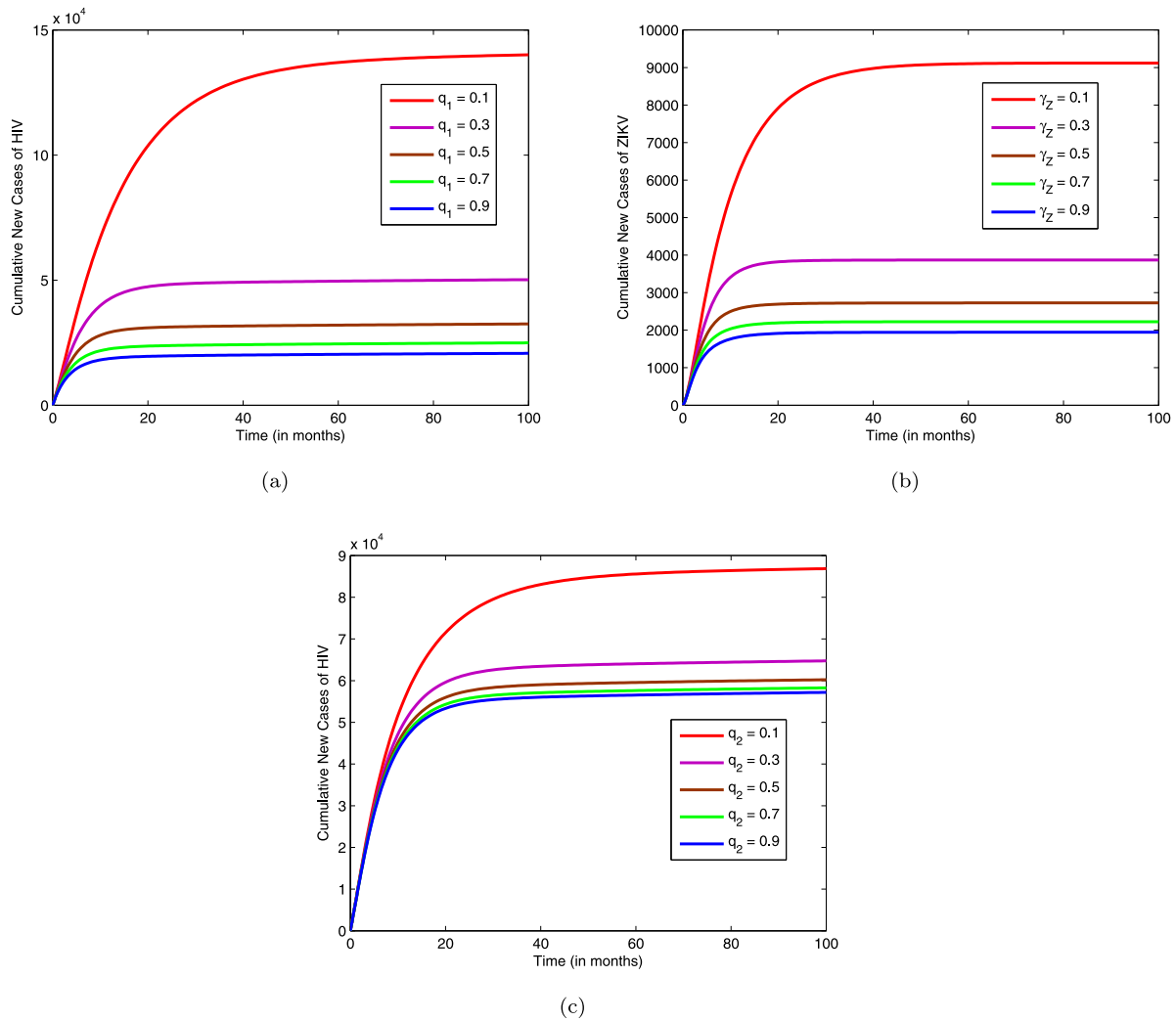


Fig. 10. Simulation of the full model (1) showing the plots for (a) The effect of q_1 on the cumulative new cases of HIV (b) The effect of γ_Z on the cumulative new cases of ZIKV (c) The effect of q_2 on the cumulative new cases of HIV, for the case when $R_{0HZ} = 0.7020 < 1$.

2. The ZIKV only sub-model undergoes the phenomenon of backward bifurcation when the ZIKV associated reproduction number is less than unity. Consequently, the bifurcation property complicates the effective control of ZIKV infection in the population when the reproduction number is less than unity.
3. It is shown using the center manifolds theory that the full HIV-ZIKV model exhibits the occurrence of backward bifurcation.
4. The sensitivity analysis of the HIV only and ZIKV only sub-models basic reproduction numbers indicates that the top rank parameters that greatly influenced the HIV and Zika transmission are mosquito-biting rate (ω), HIV transmission rate (α_H), modification parameters (η_1 and η_2), ZIKV transmission rates ($\alpha_m, \alpha_{mZ}, \alpha_Z$), and mosquito recruitment rate (Λ_m).
5. The rise in HIV infection within the population will enhance the transmission of ZIKV positively.
6. HIV and ZIKV co-exist when their basic reproduction number surpasses one.
7. Increasing the treatment rate significantly reduces the burden of the co-infection with Zika virus.

The study can be extended in numerous ways

1. By reformulating the model and incorporating time dependent optimal control measures such as usage of bed nets, compliance

to the usage of condom etc, in a view to procuring optimal strategies that can help mitigate the spread of the two diseases and their co-infection. Thus, the cost-effectiveness analysis of the control strategies can as well be investigated.

2. he model can be reformulated as Caputo based and Atangana-Baleanu based fractional order model and solved numerically.
3. Introducing age structured model, to gain more insight into the dynamics of HIV and Zika virus co-infection in various age groups.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix. Proof of Theorem 9

Proof. The proof is also base on using the center manifold theory on the full HIV-ZIKV co-infection model (1). Similarly, we will carry out some modifications to the model variables for conveniences. Let $S_h = y_1, E_Z = y_2, I_Z = y_3, T_Z = y_4, R_Z = y_5, E_H = y_6, I_H = y_7, A = y_8, T_H = y_9, E_{HZ} = y_{10}, H_1 = y_{11}, H_2 = y_{12}, H_3 = y_{13},$

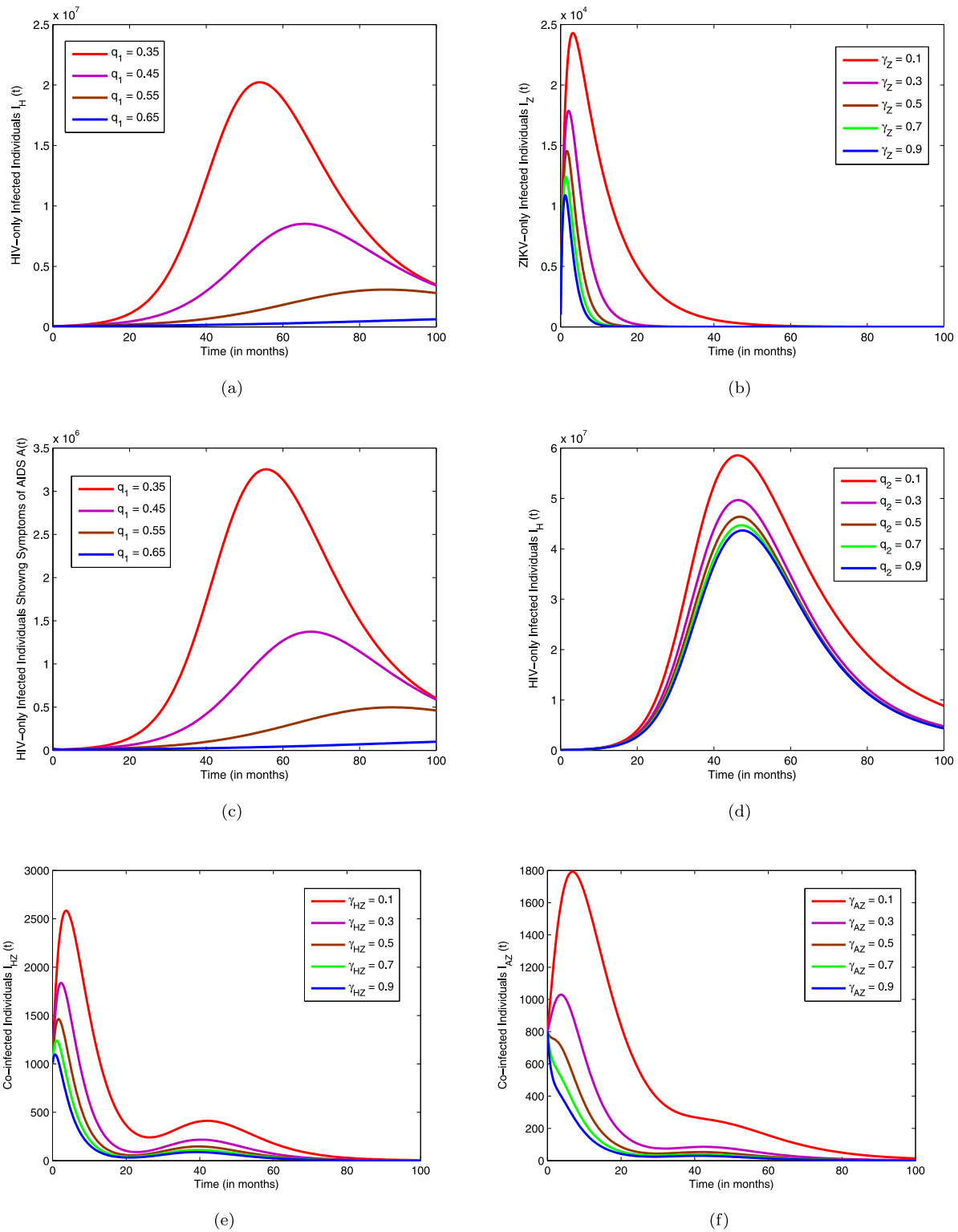


Fig. 11. Simulations of the full model (1) showing the plots for (a) HIV-only infected individuals (I_H) (b) ZIKV-only infected individuals (I_Z) (c) HIV-only infected individuals showing clinical symptoms of AIDS (A) (d) HIV-only infected individuals (I_H) (e) Co-infected individuals (I_{HZ}) (f) Co-infected individuals (I_{AZ}), for the case when $R_{0HZ} > 1$ while varying the treatment rates. Parameter values used are as in Table 2 with $\alpha_H = 0.8$ and $\beta_H = 0.6$ (so that $R_{0H} = 3.4743$, $R_{0Z}^{lim} = 135.1030$, and $R_{0HZ} = 135.1030$). The values of the reproduction numbers when the treatment rates are varied can be found in Table 7, Tables 8 and 9.

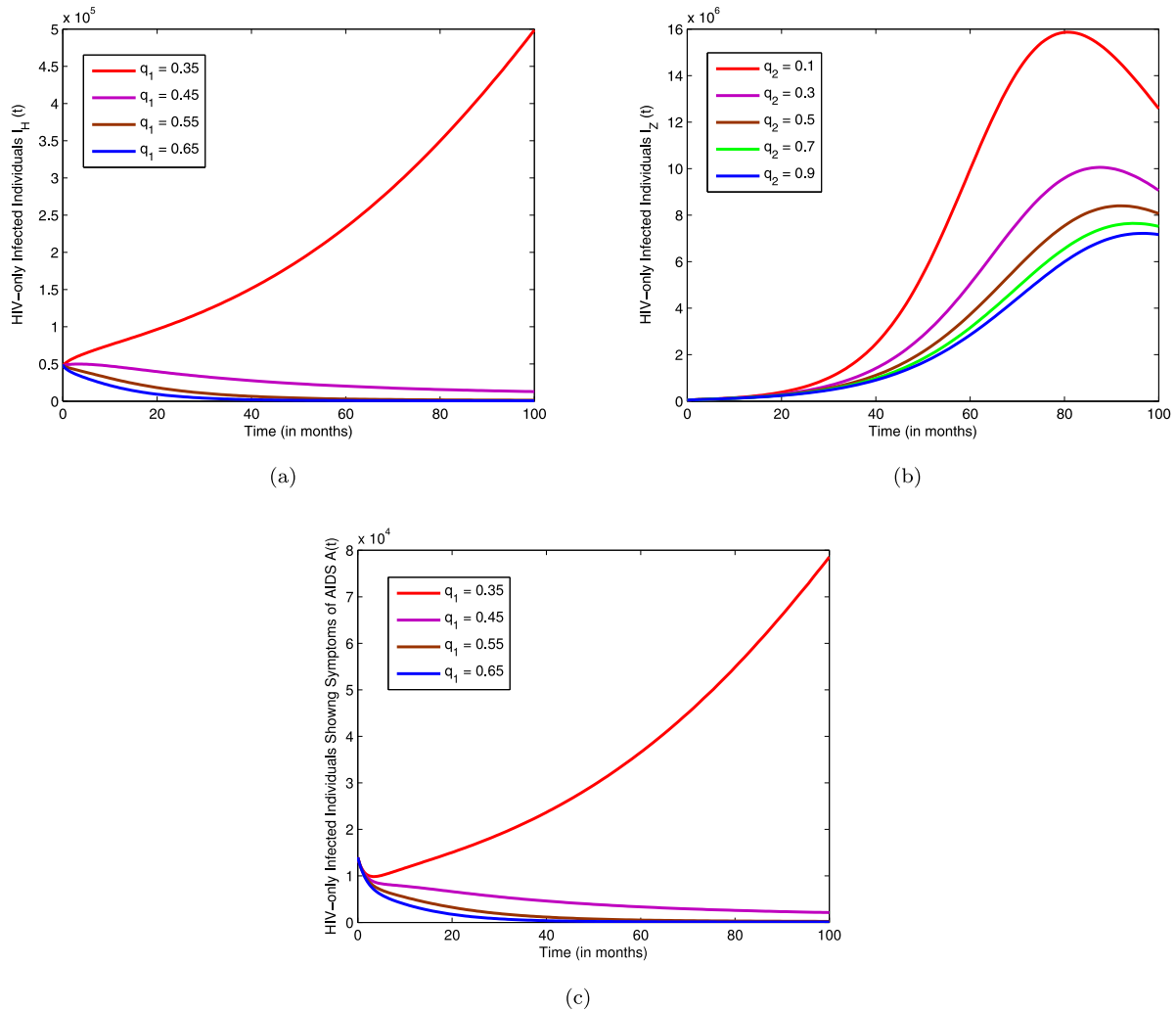


Fig. 12. Simulations of the HIV only infected compartments for the cases when $R_{0H} = 1.4936 > 1$.

$I_{HZ} = y_{14}$, $I_{AZ} = y_{15}$, $T_{HZ} = y_{16}$, $S_m = y_{17}$, $E_m = y_{18}$, $I_m = y_{19}$. So that $N_h = \sum_{i=1}^{16} y_i$. Using the vector notation $y = (y_1, y_2, y_3, \dots, y_{19})^T$ and $\frac{dy}{dt} = F(y)$, with $F = (f_1, f_2, f_3, \dots, f_{19})^T$. Therefore, the full HIV-ZIKV co-infection model system (1) becomes

$$\frac{dy_1}{dt} \equiv f_1 = (1 - \beta_Z y_3 - \beta_H y_7 - \beta_{HZ} y_{14}) \Lambda_h - (\lambda_Z + \lambda_H + \mu_h) y_1 + \kappa_Z y_5$$

$$\frac{dy_2}{dt} \equiv f_2 = \lambda_Z y_1 - \lambda_H y_2 - (\psi_Z + \mu_h) y_2$$

$$\frac{dy_3}{dt} \equiv f_3 = \psi_Z y_2 + \beta_Z \Lambda_h y_3 - \theta \lambda_H y_3 - (\gamma_Z + \delta_Z + \mu_h) y_3$$

$$\frac{dy_4}{dt} \equiv f_4 = \gamma_Z y_3 - (\tau_Z + \phi_Z \delta_Z + \mu_h) y_4$$

$$\frac{dy_5}{dt} \equiv f_5 = \tau_Z y_4 + \upsilon y_{16} - (\kappa_Z + \mu_h) y_5$$

$$\frac{dy_6}{dt} \equiv f_6 = \lambda_H y_1 - \lambda_Z y_6 - (\psi_H + \mu_h) y_6$$

$$\frac{dy_7}{dt} \equiv f_7 = \psi_H y_6 + \beta_H \Lambda_h y_7 - \epsilon_1 \lambda_Z y_7 - (\rho_1 + q_1 + \mu_h) y_7$$

$$\frac{dy_8}{dt} \equiv f_8 = \rho_1 y_7 - \epsilon_2 \lambda_Z y_8 - (q_2 + \delta_H + \mu_h) y_8$$

$$\frac{dy_9}{dt} \equiv f_9 = q_1 y_7 + q_2 y_8 - \epsilon_3 \lambda_Z y_9 - (\phi_H \delta_H + \mu_h) y_9$$

$$\frac{dy_{10}}{dt} \equiv f_{10} = \lambda_H y_2 + \lambda_Z y_6 - (\psi_{HZ} + \mu_h) y_{10}$$

$$\frac{dy_{11}}{dt} \equiv f_{11} = \theta \lambda_H y_3 - (\vartheta + \delta_Z + \mu_h) y_{11}$$

$$\frac{dy_{12}}{dt} \equiv f_{12} = \epsilon_1 \lambda_Z y_7 + f \epsilon_3 \lambda_Z y_9 - (\xi_1 + \mu_h) y_{12}$$

$$\frac{dy_{13}}{dt} \equiv f_{13} = \epsilon_2 \lambda_Z y_8 + (1 - f) \epsilon_3 \lambda_Z y_9 - (\xi_2 + \delta_H + \mu_h) y_{13}$$

$$\frac{dy_{14}}{dt} \equiv f_{14} = \psi_{HZ} y_{10} + \vartheta y_{11} + \xi_1 y_{12} + \beta_{HZ} \Lambda_h y_{14} - (\gamma_{HZ} + \rho_2 + \delta_{HZ} + \mu_h) y_{14}$$

$$\frac{dy_{15}}{dt} \equiv f_{15} = \xi_2 y_{13} + \rho_2 y_{14} - (\gamma_{AZ} + \delta_{AZ} + \mu_h) y_{15}$$

$$\frac{dy_{16}}{dt} \equiv f_{16} = \gamma_{HZ} y_{14} + \gamma_{AZ} y_{15} - (\upsilon + \phi_{HZ} \delta_{HZ} + \phi_{AZ} \delta_{AZ} + \mu_h) y_{16}$$

$$\frac{dy_{17}}{dt} \equiv f_{17} = \Lambda_m - \lambda_m y_{17} - \mu_m y_{17}$$

$$\frac{dy_{18}}{dt} \equiv f_{18} = \lambda_m y_{17} - (\psi_m + \mu_m) y_{18}$$

$$\frac{dy_{19}}{dt} \equiv f_{19} = \psi_m y_{18} - \mu_m y_{19}$$

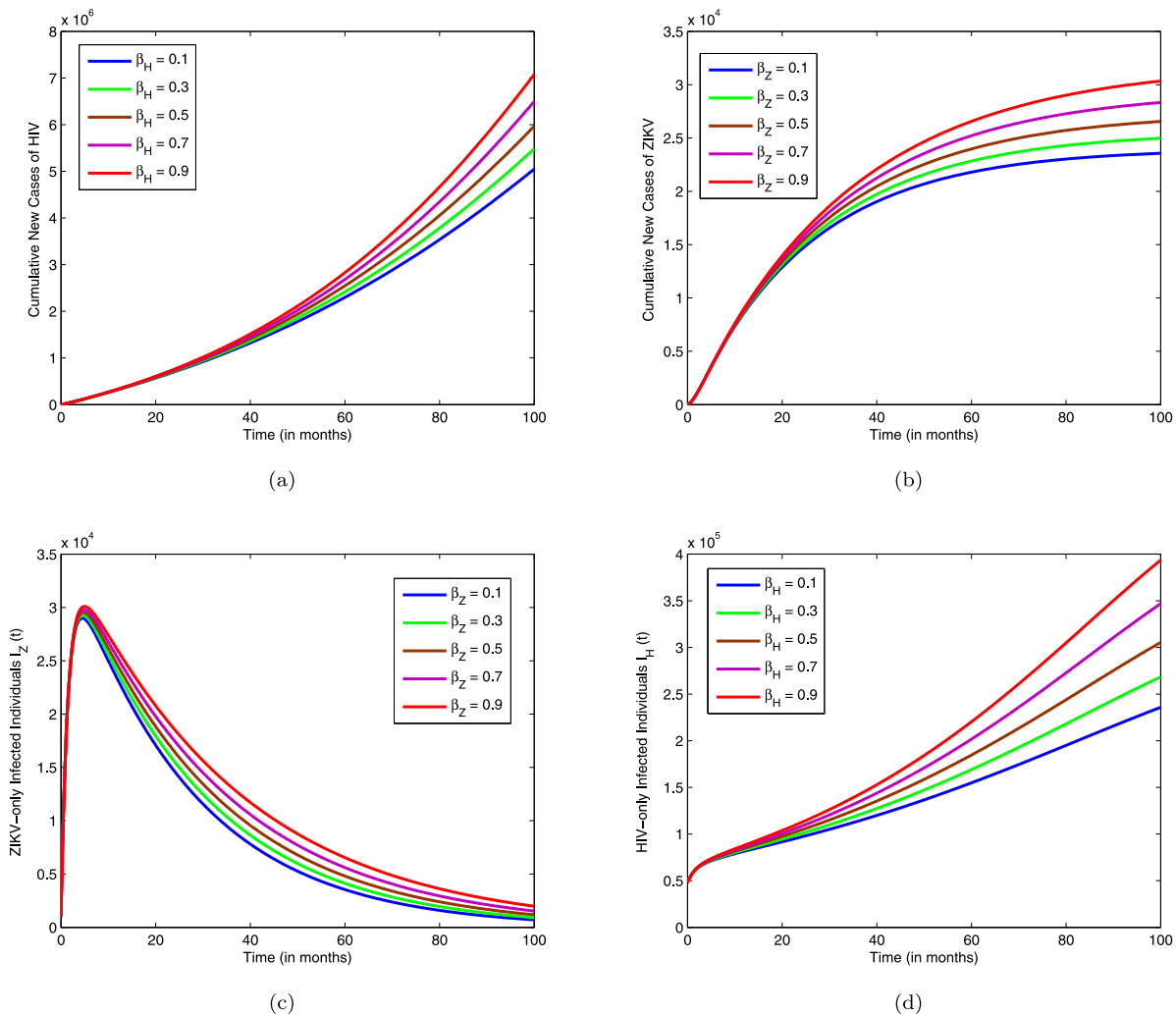


Fig. 13. Simulations of the full model (1) showing the effect of the vertical transmission on (a) Cumulative new cases of HIV (b) Cumulative new cases of ZIKV (c) ZIKV-only infected individuals (I_Z) (d) HIV-only infected individuals (I_H).

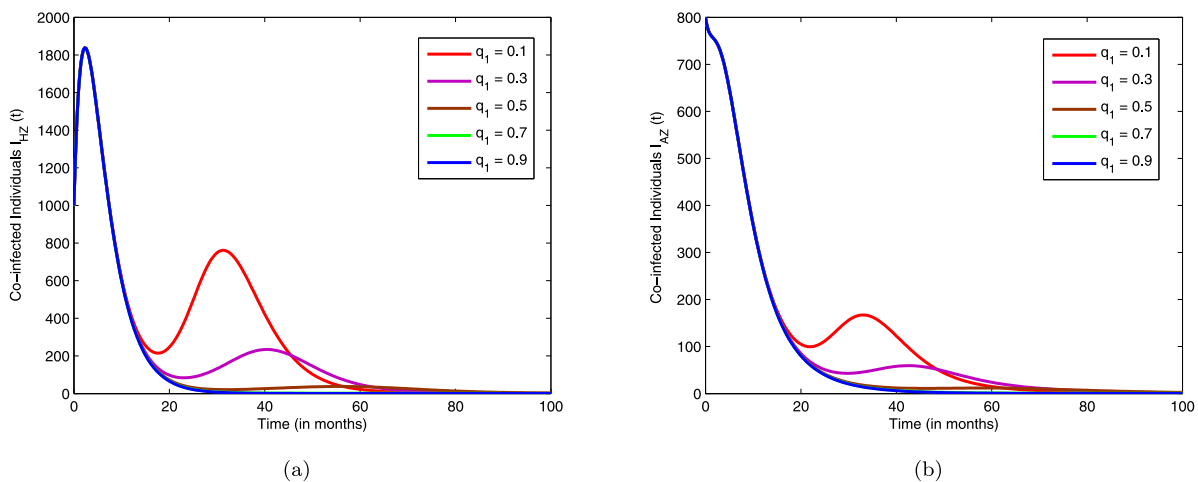


Fig. 14. Simulations of the full model (1) showing the effect of the HIV treatment rate on (a) Co-infected individuals (I_{HZ}) (b) Co-infected individuals (I_{AZ}). Using $\alpha_H = 0.8$, other parameters are as in Table 2.

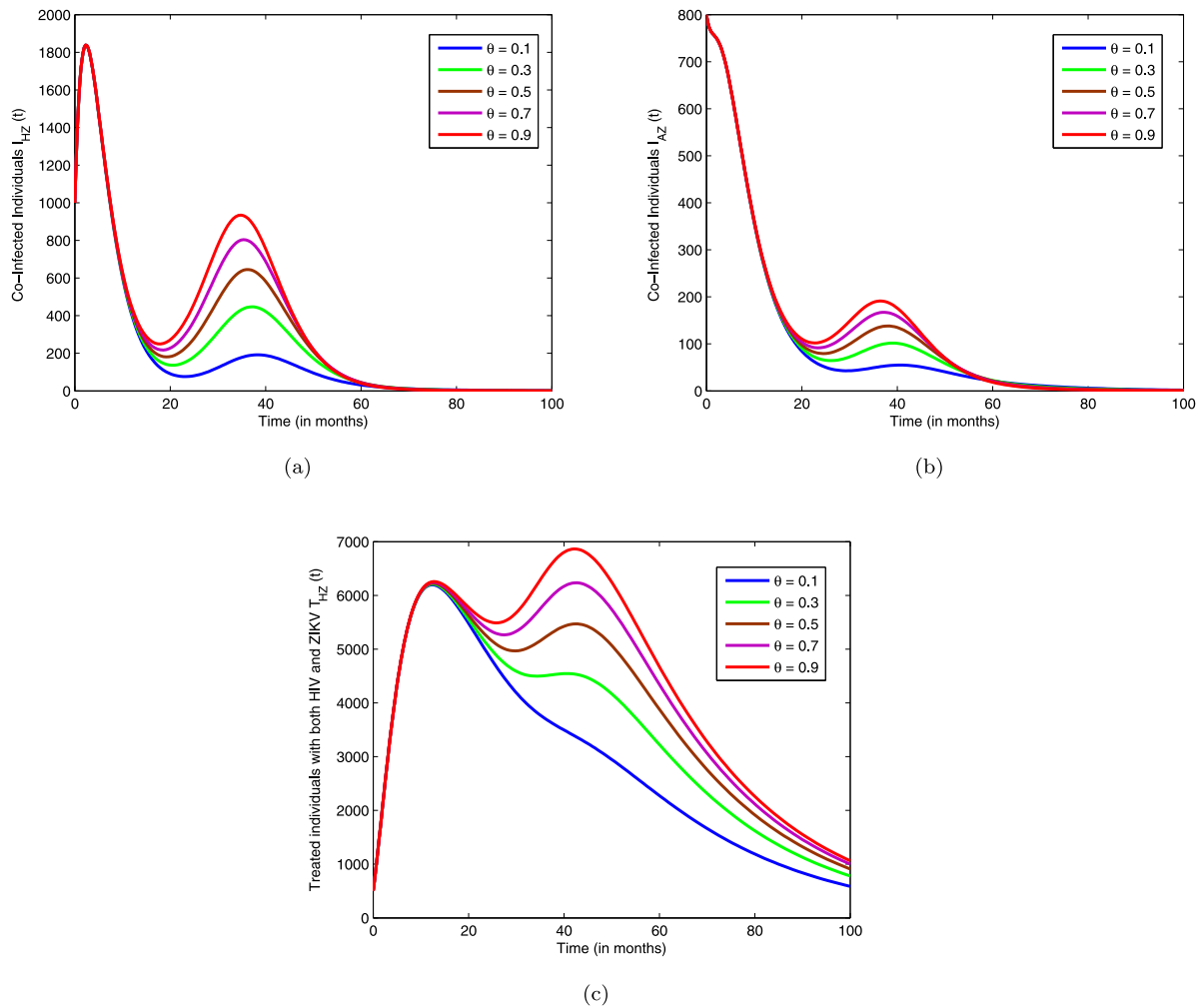


Fig. 15. Simulations of the full model (1) showing the effect of θ on (a) Co-infected individuals (I_{HZ}) (b) Co-infected individuals (I_{AZ}) (c) Treated individuals for both HIV and ZIKV (T_{HZ}). Using $\alpha_H = 0.8$, other parameters are as in Table 2.

where

$$\lambda_Z = \frac{\alpha_Z (y_3 + y_{11} + y_{14} + y_{15}) + \alpha_{mZ} \omega y_{19}}{\sum_{i=1}^{16} y_i},$$

$$\lambda_m = \frac{\alpha_m \omega (y_3 + y_{11} + y_{14} + y_{15})}{\sum_{i=1}^{16} y_i}, \text{ and}$$

$$\lambda_H = \frac{\alpha_H (y_7 + \eta_1 (y_8 + y_{13}) + \eta_2 y_9 + y_{12} + y_{14} + \eta_3 y_{15} + \eta_4 y_{16})}{\sum_{i=1}^{16} y_i}.$$

Here, we considered the transmission probability of HIV from infected individuals to susceptible individuals (α_H) as the bifurcation parameter. Solving for $\alpha_H = \alpha_H^*$ from $R_{0HZ} = 1$ (i.e. $R_{0Z}^{hm} < R_{0H} = 1$), we obtained

$$\alpha_H^* = \frac{B_1 B_2 B_3 B_4 - \beta_H \Lambda_h B_1 B_3 B_4}{\psi_H (B_3 B_4 + \eta_1 \rho_1 B_4 + \eta_2 (q_1 B_3 + q_2 \rho_1))}$$

Computing the eigenvalues of the associated Jacobian of the transformed system (38) at the disease-free equilibrium (denoted by $J(\ell_0^{HZ})$), it can be shown that the Jacobian matrix $J(\ell_0^{HZ})$ evaluated at $\alpha_H = \alpha_H^*$, denoted by $J(\ell_0^{HZ})|_{\alpha_H = \alpha_H^*}$, has a right eigenvector given by

$$w = (w_1, w_2, w_3, w_4, w_5, w_6, w_7, w_8, w_9, w_{10}, w_{11}, w_{12}, w_{13}, w_{14}, w_{15}, w_{16}, w_{17}, w_{18}, w_{19})^T$$

(38) where,

$$w_1 = \frac{1}{\mu_h} \times \left(\frac{(\Lambda_h \mu_m^2 G_{16} (\kappa_5 \tau_Z \gamma_Z - G_3 G_4 (\beta_Z \Lambda_h + \alpha_Z)) - \alpha_{mZ} \omega^2 \Lambda_m \mu_h \psi_m G_3 G_4) w_3}{\Lambda_h \mu_m^2 G_3 G_4 G_{16}} - \frac{(G_8 ((\beta_H \Lambda_h - \alpha_H) G_7 + \alpha_H \eta_1 \rho_1) + \alpha_H \eta_2 (G_7 q_1 + \rho_1 q_2)) w_7}{G_7 G_8} \right),$$

$$w_2 = -\frac{(\beta_Z \Lambda_h - G_2)}{\psi_Z} w_3,$$

$$w_3 = w_3 > 0, w_4 = \frac{\gamma_Z}{G_3} w_3, w_5 = \frac{\tau_Z \gamma_Z}{G_3 G_4} w_3, w_6 = -\frac{(\beta_H \Lambda_h - G_6)}{\psi_H} w_7,$$

$$w_7 = w_7 > 0, w_8 = \frac{\rho_1}{G_7} w_7,$$

$$w_9 = \frac{G_7 q_1 + \rho_1 q_2}{G_7 G_8} w_7, w_{10} = 0, w_{11} = 0, w_{12} = 0, w_{13} = 0, w_{14} = 0, w_{15} = 0, w_{16} = 0,$$

$$w_{17} = -\frac{\alpha_m \omega \Lambda_m \mu_h}{\Lambda_h \mu_m^2} w_3, w_{18} = \frac{\alpha_m \omega \Lambda_m \mu_h}{\Lambda_h \mu_m G_{16}} w_3, w_{19} = \frac{\alpha_m \omega \Lambda_m \mu_h \psi_m}{\Lambda_h \mu_m^2 G_{16}} w_3.$$

With

$$G_1 = \psi_Z + \mu_h, G_2 = \gamma_Z + \delta_Z + \mu_h, G_3 = \tau_Z + \phi_Z \delta_Z + \mu_h, G_4 = \kappa_Z + \mu_h, G_5 = \psi_H + \mu_h, G_6 = \rho_1 + q_1 + \mu_h, G_7 = q_2 + \delta_H + \mu_h, G_8 = \phi_H \delta_H + \mu_h, G_9 = \psi_{HZ} + \mu_h, G_{10} = \vartheta + \delta_Z + \mu_h, G_{11} = \xi_1 + \mu_h, G_{12} = \xi_2 + \delta_H + \mu_h, G_{13} = \gamma_{HZ} + \rho_2 + \delta_{HZ} + \mu_h, G_{14} = \gamma_{AZ} + \delta_{AZ} + \mu_h, G_{15} = v + \phi_{HZ} \delta_{HZ} + \phi_{AZ} \delta_{AZ} + \mu_h, \text{ and } G_{16} = \psi_m + \mu_m.$$

$$\begin{aligned}
 a = & - \frac{2v_2w_3^2(\alpha_Z\Lambda_h\mu_h\mu_m^2G_{16} + \alpha_m\alpha_{mZ}\omega^2\Lambda_m\mu_h^2\psi_m)(\gamma_Z\psi_Z(G_4 + \tau_Z) - (\beta_Z\Lambda_h - G_2)G_3G_4)}{\Lambda_h^2\mu_m^2\psi_ZG_3G_4G_{16}} \\
 & - \frac{2v_2w_3w_7(\alpha_Z\Lambda_h\mu_h\mu_m^2G_{16} + \alpha_m\alpha_{mZ}\omega^2\Lambda_m\mu_h^2\psi_m)(\psi_H(G_8(G_7 + \rho_1) + (G_7q_1 + \rho_1q_2)) - (\beta_H\Lambda_h - G_6)G_7G_8)}{\Lambda_h^2\mu_m^2\psi_HG_7G_8G_{16}} \\
 & - \frac{2v_2w_3^2\alpha_m\alpha_{mZ}\omega^2\Lambda_m\mu_h\psi_m(\Lambda_h\mu_m^2G_{16}(\kappa_5\tau_Z\gamma_Z - G_3G_4(\beta_Z\Lambda_h + \alpha_Z)) - \alpha_{mZ}\alpha_m\omega^2\Lambda_m\mu_h\psi_mG_3G_4)}{\Lambda_h^3\mu_m^4G_3G_4G_{16}} + \\
 & \frac{2v_2w_3w_7\alpha_m\alpha_{mZ}\omega^2\Lambda_m\mu_h\psi_m(G_8((\beta_H\Lambda_h - \alpha_H)G_7 + \alpha_H\eta_1\rho_1) + \alpha_H\eta_2(G_7q_1 + \rho_1q_2))}{\Lambda_h^2\mu_m^2G_7G_8G_{16}} \\
 & - \frac{2v_2w_3^2\alpha_Z\mu_h(\Lambda_h\mu_m^2G_{16} + \alpha_m\alpha_Z\omega\Lambda_m\mu_h^2\psi_m)}{\Lambda_h^2\mu_m^2G_{16}} - \frac{2v_2w_3^2\alpha_m\alpha_{mZ}\omega^2\Lambda_m\mu_h^2\psi_m(\alpha_m\omega + \mu_m)}{\Lambda_h^2\mu_m^3G_{16}} \\
 & \frac{2v_2w_3^2\alpha_m\alpha_{mZ}\omega^2\Lambda_m\mu_h^2\psi_m(\mu_m\gamma_Z\psi_Z(G_4 + \tau_Z) - (\beta_Z\Lambda_h - G_2)\mu_mG_3G_4)}{\Lambda_h^2\mu_m^3\psi_ZG_3G_4G_{16}} \\
 & - \frac{2v_2w_3w_7\alpha_m\alpha_{mZ}\omega^2\Lambda_m\mu_h^2\psi_m(\psi_H(G_8(G_7 + \rho_1) + (G_7q_1 + \rho_1q_2)) - (\beta_H\Lambda_h - G_6)G_7G_8)}{\Lambda_h^2\mu_m^2\psi_HG_7G_8G_{16}} + \\
 & \frac{2v_6w_3w_7\alpha_H^*\mu_h(\psi_Z(G_3G_4 + \gamma_ZG_4 + \gamma_Z\tau_Z) - (\beta_Z\Lambda_h - G_2)G_3G_4)(G_7G_8 + \eta_2(G_7q_1 + \rho_1q_2) + \eta_1\rho_1G_8)}{\Lambda_h\psi_ZG_3G_4G_7G_8} \\
 & \frac{2v_6w_7\alpha_H^*\mu_h(\beta_H\Lambda_h - G_6)(G_7G_8 + \eta_2(G_7q_1 + \rho_1q_2) + \eta_1\rho_1G_8)}{\Lambda_h\psi_HG_7G_8} - \frac{2v_6w_7^2\alpha_H^*\mu_h\eta_2(G_7q_1 + \rho_1q_2)^2}{\Lambda_hG_7^2G_8^2} \\
 & \frac{2v_6w_7^2\alpha_H^*\mu_h(G_7^2G_8 + \eta_1\rho_1^2G_8 + (1 + \eta_2)(G_7q_1 + \rho_1q_2)G_7)}{\Lambda_hG_7^2G_8} \\
 & \frac{2v_6w_7^2\alpha_H^*\mu_h\rho_1(G_7G_8(1 + \eta_1) + (\eta_1 + \eta_2)(G_7q_1 + \rho_1q_2))}{\Lambda_hG_7^2G_8},
 \end{aligned}$$

Box III.

Furthermore, the matrix $J(\varphi_0^{HZ})|_{\alpha_H = \alpha_H^*}$ has a left eigenvector, given by

$$v = (v_1, v_2, v_3, v_4, v_5, v_6, v_7, v_8, v_9, v_{10}, v_{11}, v_{12}, v_{13}, v_{14}, v_{15}, v_{16}, v_{17}, v_{18}, v_{19})$$

where,

$$\begin{aligned}
 v_1 = v_4 = v_5 = v_{17} = 0, v_2 = v_2 > 0, v_3 = \frac{G_1}{\psi_Z}v_2, v_6 = v_6 > 0, \\
 v_7 = \frac{G_5}{\psi_{HZ}}v_6, v_8 = \frac{\alpha_H(G_8\eta_1 + q_2\eta_2)}{G_7G_8}v_6, \\
 v_9 = \frac{\alpha_H\eta_2}{G_8}v_6, v_{10} = \frac{\psi_{HZ}}{G_9}v_{14}, \\
 v_{11} = \frac{(\alpha_Z\Lambda_h\mu_m^2G_{16} + \alpha_{mZ}\alpha_m\omega^2\Lambda_m\mu_h\psi_m)v_2 + \Lambda_h\mu_m^2\theta G_{16}v_{14}}{\Lambda_h\mu_m^2G_{10}G_{16}}, \\
 v_{12} = \frac{\alpha_Hv_6 + \xi_1v_{14}}{G_{11}}, v_{13} = \frac{\alpha_H\eta_1v_6 + \xi_2v_{15}}{G_{12}}, v_{14} = v_{14} > 0, v_{15} = v_{15} > 0, \\
 v_{16} = \frac{\alpha_H\eta_4}{G_{15}}v_6, \\
 v_{18} = \frac{\alpha_{mZ}\omega\psi_m}{\mu_mG_{16}}v_2, v_{19} = \frac{\alpha_{mZ}\omega}{\mu_m}v_2.
 \end{aligned}$$

After some intensive computations, it can be shown that (see Box III) and

$$b = \frac{v_6w_7(G_7G_8 + \eta_1\rho_1G_8 + \eta_2(G_7q_1 + \rho_1q_2))}{G_7G_8} > 0. \tag{39}$$

Since the bifurcation coefficient b is positive, it follows that the HIV-ZIKV co-infection model (1) exhibits a backward bifurcation at $R_{0HZ} = 1$ whenever the bifurcation coefficient $a > 0$. \square

References

- [1] WHO, HIV/AIDS, 2012.
- [2] Overview of the Global AIDS Epidemic, 2006 Report on the Global AIDS Epidemic, Joint United Nations Programme on HIV/AIDS, ISBN: 9291734799, 2006.
- [3] WHO, Report on global hiv/aids, 2019.
- [4] A. Kapila, S. Chaudhary, R.B. Sharma, H. Vashist, S.S. Sisodia, A. Gupta, A review on: HIV AIDS, Indian J. Pharm. Biol. Res. 4 (03) (2016) 69-73, <http://dx.doi.org/10.30750/ijpbr.4.3.9>.
- [5] WHO, Fact sheet report on HIV/AIDS, 2022, <https://www.who.int/news-room/fact-sheets/detail/hiv-aids>.
- [6] R. Adelman, Mother to child HIV transmission in Africa, in: Policy Fact, 2001.
- [7] A.I. Abushouk, A. Negida, H. Ahmed, An updated review of Zika virus, J. Clin. Virol. Off. Publ. Pan. Am. Soc. Clin. Virol. 84 (2016) <http://dx.doi.org/10.1016/j.jcv.2016.09.012>, 53-43, PMID: 27721110.
- [8] F.N. Macnamara, Zika virus: a report on three cases of human infection during an epidemic of jaundice in Nigeria, Trans. R. Soc. Trop. Med. Hyg. 48 (1954) 139-143, PMID: 13157159.
- [9] O. Faye, O. Faye, D. Diallo, M. Diallo, M. Weidmann, A. Sall, Quantitative real-time pcr detection of zika virus and evaluation with field-caught mosquitoes, Virol. J. 10 (311) (2013) 1-8, <http://dx.doi.org/10.1186/1743-422X-10-311>.
- [10] B. Berkowitz, L. Karklis, S. Tan, D. Lu, P. Clark, What You Need To Know About the Zika Virus, The Washington Post, 2016, <https://www.washingtonpost.com/graphics/health/zika-virus/>.
- [11] N.R. Faria, R.D.S.D.S. Azevedo, M.U.G. Kraemer, et al., Zika virus in the americas: early epidemiological and genetic findings, Science 352 (6283) (2016) 345-349, <http://dx.doi.org/10.1126/science.aaf5036>.
- [12] R.P.M. Abrams, J. Solis, Therapeutic approaches for zika virus infection of the nervous system, Neurotherapeutics 14 (4) (2017) 1027-1048, <http://dx.doi.org/10.1007/s13311-017-0575-2>.
- [13] R. Basu, E. Tumban, Zika Virus on a Spreading Spree: what we now know that was unknown in the, Virol. J. 13 (1) (2016) 165, <http://dx.doi.org/10.1186/s12985-016-0623-2>.
- [14] M. Didier, E.J. Nilles, V.M. Cao-Lormeau, Rapid spread of emerging Zika virus in the Pacific area, Clin. Microbiol. Infect. 20 (10) (2014) 0595-0596.
- [15] N.K. Goswami, A.K. Srivastav, M. Ghosh, B. Shanmukha, J. Phys. : Conf. Ser. 1000 (2018) 012114, <http://dx.doi.org/10.1088/1742-6596/1000/1/012114>.

- [16] D. Musso, D.J. Gubler, Zika virus, *Clin. Microbiol. Rev.* 29 (2016) <http://dx.doi.org/10.1128/CMR.00072-15>, 487–443, PMID: 27029595.
- [17] V.M. Cao-Lormeau, A. Blake, S. Mons, S. Lastere, C. Roche, J. Vanhomwegen, et al., Guillain-Barre Syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study, *Lancet Lond Engl.* 387 (2016) 1531–1543, [http://dx.doi.org/10.1016/S0140-6736\(16\)00562-6](http://dx.doi.org/10.1016/S0140-6736(16)00562-6), PMID: 26948433.
- [18] C.A. Moore, J.E. Staples, W.B. Dobyns, A. Pessoa, C.V. Ventura, E.B. Fonseca, E.M. Ribeiro, L.O. Ventura, N.N. Neto, J.F. Arena, S.A. Rasmussen, Characterizing the pattern of anomalies in congenital zika syndrome for pediatric clinicians, *JAMA Pediatr.* 171 (2017) <http://dx.doi.org/10.1001/jamapediatrics.2016.3982>, 288–243, PMID: 27812690.
- [19] G.M. Blohm, J.A. Lednicky, M. MaÁrquez, S.K. White, J.C. Loeb, C.A. Pacheco, D.J. Nolan, T. Paisie, M. Salemi, A.J. Rodrigues-Morales, J.J. Glenn Morris, J.R.C. Pulliam, A.E. Paniz-Mondolfi, Evidence for mother-to-child transmission of Zika virus through breast milk, *Clin. Infect. Dis. Off. Publ. Infect. Dis. Soc. Am.* (2017) <http://dx.doi.org/10.1093/cid/cix968>, PMID: 29300859.
- [20] WHO Statement on the First Meeting of the International Health Regulations (2005) Emergency Committee on Zika Virus and Observed Increase in Neurological Disorder Sandneo Natalmal for Matians, World Health Organization (WHO), 2016, <http://www.who.int/mediacentre/news/statements/2016/1st-emergencycommittee-zika/en/>, Accessed on February 26 2016.
- [21] Zika Virus Infection, Pan American Health Organization (PAHO), 2016, http://www.paho.org/hq/index.php?option=com_content&view=article&id=11585&Itemid=41688&lang=en, Accessed on May 16 2016.
- [22] EstatôÁsticas, UNAIDS Brasil, 2017, [Internet] [cited 18 2017]. Available: <http://un aids.org.br/estatisticas/>.
- [23] C. Mitchell, PAHO WHO | Zika Cumulative Cases, Pan American Health Organization/World Health Organization, 2016.
- [24] G.A. Calvet, A.M.B. Filippis, M.C.L. Mendonca, P.C. Sequeira, A.M. Siqueira, V.G. Veloso, R.M. Nogueira, P. Brasil, First detection of autochthonous Zika virus transmission in a HIV-infected patient in Rio de Janeiro, Braz. *J. Clin. Virol. Off. Publ. Pan. Am. Soc. Clin. Virol.* 74 (2016) 1–43, <http://dx.doi.org/10.1016/j.jcv.2015.11.014>, PMID: 26615388.
- [25] E.C. João, M.I.F. Gouvea da Silveria, M.L.B. Teixeira, W. Mendes-Silva, J.S. Esteves, E.M. Santos, et al., Zika virus infection associated with congenital birth defects in a HIV-infected pregnant woman, *Pediatr. Infect. Dis. J.* 36 (2017) 500–543, <http://dx.doi.org/10.1097/INF.0000000000001482>, PMID: 28403053.
- [26] H.A. Rothan, M.R.M. Bidokhti, S.N. Byrareddy, Current concerns and perspectives on Zika virus co-infection with arboviruses and HIV, *J. Autoimmun.* (2018) <http://dx.doi.org/10.1016/j.jaut.2018.01.002>, PMID:29352633.
- [27] J. Mushanyu, A note on the impact of late diagnosis on hiv/aids dynamics: a mathematical modelling approach, *BMC Res. Notes* 13 (1) (2020) 1–8.
- [28] T.K. Ayele, E.F. Doungmo Goufo, S. Mugisha, Mathematical modeling of HIV/AIDS with optimal control: A case study in Ethiopia, *Res. Phys.* (ISSN: 2211-3797) 26 (2021) 104263, <http://dx.doi.org/10.1016/j.rinp.2021.104263>.
- [29] C.N. Podder, O. Sharomi, A.B. Gumel, E. Strawbridge, Mathematical analysis of a model for assessing the impact of antiretroviral therapy, voluntary testing and condom use in curtailing the spread of HIV, *Differ. Equ. Dyn. Syst.* 19 (4) (2011) 283–302, <http://dx.doi.org/10.1007/s12591-011-0090-6>, Epub 2011 may 5. PMID: 32218648; PMCID: PMC7090688.
- [30] A. Nwankwo, D. Okuonghae, Mathematical analysis of the transmission dynamics of HIV syphilis Co-infection in the presence of treatment for syphilis, *Bull. Math. Biol.* 80 (2018) 437–492.
- [31] E.J. Moore, S. Sirisubtawee, S. Koonprasert, A Caputo-Fraberzio fractional differential equation model for HIV/AIDS with treatment compartment, *Adv. Differ. Equ.* 2019 (2019) 200, <http://dx.doi.org/10.1186/s13662-019-2138-9>.
- [32] A. Omame, M. Abbas, A.-H. Abdel-Aty, Assessing the impact of SARS-CoV-2 infection on the dynamics of dengue and HIV via fractional derivatives, *Chaos Solitons Fractals* 162 (1) (2022) 112427, <http://dx.doi.org/10.1016/j.chaos.2022.112427>.
- [33] S.K. Biswas, U. Ghosh, S. Sarkar, Mathematical model of Zika virus dynamics with vector control and sensitivity analysis, *Infect. Dis. Modell.* 5 (2019) 23–41, <http://dx.doi.org/10.1016/j.idm.2019.12.001>.
- [34] F.B. Augusto, S. Bewick, W.F. Fagan, Mathematical model of Zika virus with vertical transmission, *Infect. Dis. Model.* 2 (2017) 244–267.
- [35] A. Ali, Q. Iqbal, J.K.K. Asamoah, S. Islam, Mathematical modeling for the transmission potentials of Zika virus with optimal control strategies, *Eur. Phys. J. Plus* 137 (2022) 146, <http://dx.doi.org/10.1140/epjp/s13360-022-02368-5>.
- [36] M.A. Ibrahim, A. Denes, A mathematical model for Zika virus infection and microcephaly risk considering sexual and vertical transmission, *Axioms* 12 (2023) 263, <http://dx.doi.org/10.3390/axioms12030263>.
- [37] A. Omame, M. Abbas, Backward bifurcation and optimal control in a co-infection model for SARS-CoV-2 and ZIKV, *Results Phys.* (2022) 105481, <http://dx.doi.org/10.1016/j.rinp.2022.105481>.
- [38] S.A. Jose, R. Raja, B.I. Omede, R.P. Agarwal, J. Alzabut, J. Cao, V.E. Balas, Mathematical modelling on co-infection: transmission dynamics of Zika virus and Dengue fever, *Nonlinear Dyn.* 111 (2023) 4879–4914, <http://dx.doi.org/10.1007/s11071-022-08063-5>.
- [39] S. Lakshmikantham, S. Leela, A.A. Martynuk, *Stability Analysis of Nonlinear Systems*, Marcel Dekker, Inc., New York, Basel, 1989.
- [40] H.W. Hethcote, The mathematics of infectious diseases, *SIAM Rev.* 42 (2000) 599–653.
- [41] D. Van-Driessche, J. Watmough, Reproduction numbers and subthreshold endemic equilibria for compartmental models of disease transmission, *Math. Biosci.* 180 (1) (2002) 29–48.
- [42] T.S. Hassan, E.M. Elabbasy, A.E. Matouk, R.A. Ramadan, A.T. Abdulrahman, I. Odinaev, Routh–Hurwitz stability and quasiperiodic attractors in a fractional-order model for awareness programs: Applications to COVID-19 pandemic, *Discrete Dyn. Nat. Soc.* (2022) <http://dx.doi.org/10.1155/2022/1939260>.
- [43] B.I. Omede, O.J. Peter, W. Atokolo, B. Bolaji, T.A. Ayoola, A mathematical analysis of a two strain tuberculosis model dynamics with exogeneous re-infection, *Healthc. Anal.* 4 (2023) 100266, <http://dx.doi.org/10.1016/j.health.2023.100266>.
- [44] J.P. Lasalle, *The Stability of Dynamical Systems*, in: *Regional Conference Series in Applied Mathematics*, SIAM, Philadelphia, 1976.
- [45] C. Castillo-Chavez, B. Song, Dynamical models of tuberculosis and their applications, *Math. Biosci. Eng.* 2 (2004) 361–404.
- [46] K.G. Mekonen, L.L. Obsu, Mathematical modeling and analysis for the co-infection of COVID-19 and tuberculosis, *Heliyon* 19 (2022) 8380–8410.
- [47] The world bank. <https://data.worldbank.org/indicator/SP.DYN.CBRT.IN?locations=BR>.
- [48] O. Sharomi, C.N. Podder, A.B. Gumel, Mathematical analysis of the transmission dynamics of HIV/TB coinfection in the presence of treatment, *Math. Biosci. Eng.* 5 (2008) 145–174.
- [49] <https://www.unaids.org>.
- [50] D. Omale, Mathematical modelling on the control of HIV/AIDS with campaign on vaccination and therapy, in: *ITM Web of Conferences*, Vol. 31, 2020, p. 03003.
- [51] S.M. Garba, A.B. Gumel, Mathematical recipe for HIV elimination in Nigeria, *J. Niger. Math. Soc.* 29 (2010) 51–112.
- [52] Pan American health organization (PAHO). www3.paho.org/data/index.php/en/mnu-topics/zika-bra-en/.
- [53] The world bank. <https://data.worldbank.org/indicator/SP.POP.TOTL?end+2018&locations=BR>.