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Mathematical model for Zika virus dynamics with sexual transmission route

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ABSTRACT

Zika virus is a flavivirus transmitted to humans primarily through the bite of infected *Aedes* mosquitoes. In addition to vector-borne spread, however, the virus can also be transmitted through sexual contact. In this paper, we formulate and analyze a new system of ordinary differential equations which incorporates both vector and sexual transmission routes. Theoretical analysis of this model when there is no disease induced mortality shows that the disease-free equilibrium is locally and globally asymptotically stable whenever the associated reproduction number is less than unity and unstable otherwise. However, when we extend this same model to include Zika induced mortality, which have been documented in Latin America, we find that the model exhibits a backward bifurcation. Specifically, a stable disease-free equilibrium co-exists with a stable endemic equilibrium when the associated reproduction number is less than unity. To further explore model predictions, we use numerical simulations to assess the importance of sexual transmission to disease dynamics. This analysis shows that risky behavior involving multiple sexual partners, particularly among male populations, substantially increases the number of infected individuals in the population, contributing significantly to the disease burden in the community.

1. Introduction

Historically confined to Africa and Southeast Asia (Olson and Ksiazek, 1981; Dick et al., 1952; Haddow et al., 2012), the recent introduction of Zika virus (ZIKV) into Latin America (Zanluca et al., 2015) has resulted in alarming progression (Traynor, 2016) of this disease across much of the New World. Indeed, as of May 26, 2016, only two countries in South America – Chile and Uruguay – had not yet reported autochthonous spread of Zika (Centers for Disease Control and Prevention, 2016a). Unfortunately, the emergence of Zika under these new conditions has brought with it new discoveries of troubling viral outcomes, including Guillan Barre syndrome (Oehler et al., 2014; Cao-Lormeau et al., 2016) and microcephaly (Mlakar et al., 2016; Oliveira Melo et al., 2016) in adults and newborns respectively. With the novel realization that Zika can cause severe complications, a disease once described as a 'mild form of dengue' has come to the forefront of public health discussions worldwide (Samarasekera and Triunfol, 2016).

Like all other arboviruses, Zika is predominantly transmitted by mosquitoes – in this case *Aedes* species (Haddow et al., 1964; Marcondes and Ximenes, 2016) such as the yellow fever mosquito, *Aedes aegypti* (Marchette et al., 1969). However, unlike other arboviruses, ZIKV also exhibits a second mode of transmission through sexual contact (Foy et al., 2011; D'Ortenzio et al., 2016; McCarthy, 2016; Hills et al., 2016; Musso et al., 2015; Venturi et al., 2016). This has not been previously documented for other arboviruses. Interestingly, the potential for sexual transmission of ZIKV was first discovered, largely by accident, by a microbiologist returning from studying mosquito-borne diseases in Senegal in 2008 (Foy et al., 2011). Unfortunately, however, due to funding constraints, and the relatively minor importance of Zika at the time, little effort was invested into further examining this unusual mechanism for arboviral transmission.

With the ongoing Zika outbreak in the Americas, however, new emphasis has been placed on the study of ZIKV biology, including its various modes of transmission. Interestingly, recent epidemiological studies have demonstrated that, rather than an anomaly, Foy et al.'s early observations of sexual transmission of Zika (Foy et al., 2011; D'Ortenzio et al., 2016; McCarthy, 2016; Hills et al., 2016; Musso et al., 2015; Venturi et al., 2016) represent a relatively common mode of spread of this disease (D'Ortenzio et al., 2016; McCarthy, 2016; Venturi et al., 2016). Simultaneously, several additional avenues of investigation have provided further support for the role of sexual transmission. First, ongoing surveillance

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indicates that the Zika virus can remain in male semen for at least 62 days (Mansuy et al., 2016; Atkinson et al., 2016). Second, an analysis of differences in ZIKV incidence rate among men and women in Rio de Janiero, Brazil suggests a high rate of male-to-female transmission of this disease (Coelho et al., 2016).

With ever increasing evidence that sexual transmission of ZIKV may be important, novel questions are raised regarding the roles and significance of sexual versus vector transmission and how these different modes of spread jointly contribute to disease epidemiology. Historically, one method for addressing disease dynamics of novel outbreaks has been through mathematical modeling. Although modeling of both arboviruses and sexually transmitted diseases have long histories in epidemiological literature, the combination – namely an arbovirus that is also transmitted through sexual contact – is novel. In this paper, we take a first step towards exploring the dynamics of Zika as it depends on both vector and sexual transmission. Specifically, in Section 2 we formulate the ZIKV model with the two different modes of transmission. Then, in Section 3 we investigate the theoretical properties of the model. Finally, in Section 4 we carry out numerical exploration of the model, with discussion and conclusions stated in Section 5.

2. Model formulation

We use a compartmental modeling framework to explore Zika virus transmission dynamics when, in addition to vector-borne spread, there is an additional sexual transmission route. Specifically, we divide the human population into female and male subpopulations. We then further divide these subgroups into susceptible (S_i), exposed (E_i), infected (I_i) and recovered (R_i) classes, where $i = F, M$ for females and males respectively. Hence, the equation for the total number of females is: $N_F = S_F + E_F + I_F + R_F$, while the equation for the total number of males is: $N_M = S_M + E_M + I_M + R_M$. The total human population is then given by $N_H = N_F + N_M$.

The total mosquito population, denoted (N_V), is likewise subdivided into susceptible mosquitoes (S_V), exposed mosquitoes (E_V) and infectious mosquitoes (I_V), hence: $N_V = S_V + E_V + I_V$.

Let Π_H be the recruitment rate of susceptible individuals into the human population and assume that half of these are females. In this case, the rate at which females are born is given by $\Pi_F = \Pi_H/2$. At the same time, the female population is reduced as a result of natural death at a rate (μ_F). The total number of humans and mosquitoes in the community determines the average number of mosquito bites a human will receive. Here, we assume that the mosquito biting rate, b_V, is constant, and represents the maximal rate allowed by the gonotrophic cycle (Wonham et al., 2006). Let b_H be the rate at which bites are received by a single human. For the number of bites to be conserved, the total number of bites by mosquitoes must be equal to the total number of bites received by humans. Hence,

$$b_V N_V = b_H(N_H, N_V) N_H$$

so that,

$$N_V = \frac{b_H(N_H, N_V) N_H}{b_V} \tag{2.1}$$

Let $b_H\beta_V$ be the effective contact rate between a susceptible human and infectious mosquitoes, where β_V is the transmission probability per contact from an infectious mosquito to a susceptible human. Also, let $b_V\beta_V$ be the effective contact rate between a susceptible mosquito and infectious human, where β_V is the transmission probability per contact from an infectious human to a susceptible mosquito. In this case, susceptible females acquire infection, following effective contact with an infectious mosquito, at a rate λ_{F1}, given by,

$$\lambda_H(I_V, N_H) = \frac{b_H(N_F, N_V)\beta_H I_V}{N_V}. \tag{2.2}$$

Substituting (2.1) in (2.2) we obtain,

$$\lambda_H(I_V, N_H) = \frac{b_V \beta_H I_V}{N_H}.$$

It can also be shown that the rate at which mosquitoes acquire infection from infectious humans is given by

$$\lambda_V(I_F, I_M, N_H) = \frac{b_V \beta_V (I_F + I_M)}{N_H}.$$

The parameter β_V is the probability that a bite from a susceptible mosquito to a human will lead to infection of the mosquito.

For sexual transmission, we assume that the infection rate of susceptible females by infected males (λ_{FM}) is given as:

$$\lambda_{FM}(I_M, N_M) = \frac{C_F \beta_M I_M}{N_M} \tag{2.3}$$

where the parameter β_M is the probability that a sexual contact with an infectious male will lead to infection of the susceptible female and the parameter C_F is the contact rate between males and females. It is assumed that the contact rate is constant. Thus, for the number of contact to be conserved, the total number of contacts by males (C_{M_1}) must be equal to the total number of contacts by females (C_F),

$$C_{M_1} N_M = C_F N_F$$

so that,

$$N_M = \frac{C_F N_F}{C_{M_1}} \tag{2.4}$$

Using Eq. (2.4) in Eq. (2.3) we obtain,

$$\lambda_{FM}(I_M, N_F) = \frac{C_{M_1} \beta_M I_M}{N_F}.$$

We do not consider sexual transmission between female partners, since this is extremely rare in other sexually transmitted diseases, and thus is not expected to occur for Zika either (Petersen et al., 1992).

Hence, susceptible females become infected following effective contact with infected mosquitoes at a rate $\lambda_{F1}(I_V, N_H)$ and from sexual contact with infected males at a rate $\lambda_{FM}(I_M, N_F)$ after which they move to the exposed class. This gives

$$\frac{dS_F}{dt} = \Pi_F - \frac{b_V \beta_H I_V S_F}{N_H} - \frac{C_{M_1} \beta_M I_M S_F}{N_F} - \mu_F S_F.$$

Exposed females move to the infectious class due to disease progression at a rate σ_F. The population of exposed females is decreased due to natural death at a rate μ_F. Thus, the equation for the exposed class is represented by

$$\frac{dE_F}{dt} = \frac{b_V \beta_H I_V S_F}{N_H} + \frac{C_{M_1} \beta_M I_M S_F}{N_F} - (\sigma_F + \mu_F) E_F.$$

Likewise, the infected class population is decreased as a result of recovery at a rate γ_F and natural death at a rate μ_F. Hence, we have