Infectious Disease Modelling 2 (2017) 244–267

Contents lists available at ScienceDirect

Infectious Disease Modelling

journal homepage: www.keaipublishing.com/idm

Mathematical model of Zika virus with vertical transmission

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ARTICLE INFO

Article history:
Received 28 December 2016
Received in revised form 19 May 2017
Accepted 20 May 2017
Available online 23 May 2017

Keywords:
Zika virus
Vertical transmission
Microcephaly
Stability
Control

ABSTRACT

Zika is a flavivirus transmitted to humans through either the bites of infected *Aedes* mosquitoes or sexual transmission. Zika has been linked to congenital anomalies such as microcephaly. In this paper, we analyze a new system of ordinary differential equations which incorporates human vertical transmission of Zika virus, the birth of babies with microcephaly and asymptomatically infected individuals. The Zika model is locally and globally asymptotically stable when the *basic reproduction number* is less than unity. Our model shows that asymptomatic individuals amplify the disease burden in the community, and the most important parameters for ZIKV spread are the death rate of mosquitoes, the mosquito biting rate, the mosquito recruitment rate, and the transmission *per* contact to mosquitoes and to adult humans. Scenario exploration indicates that personal-protection is a more effective control strategy than mosquito-reduction strategy. It also shows that delaying conception reduces the number of microcephaly cases, although this does little to prevent Zika transmission in the broader community. However, by coupling aggressive vector control and personal protection use, it is possible to reduce both microcephaly and Zika transmission. 2000 Mathematics Subject Classifications: 92B05, 93A30, 93C15.

1. Introduction

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

In December 2015, the European Centre for Disease Prevention and Control issued a comprehensive update on the possible association between ZIKV, congenital microcephaly and Guillain-Barre (European Centre for Disease Prevention and Control,

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Peer review under responsibility of KeAi Communications Co., Ltd.

http://dx.doi.org/10.1016/j.idm.2017.05.003

2015). Most evidence, however, is correlative. In Brazil, for example, 2782 cases of microcephaly were reported in the year following ZIKV introduction, as compared with 147 cases and 167 cases in the two years prior to ZIKV arrival (Romero, 2015). Retrospective analysis of data from French Polynesia similarly uncovered an unusual number of babies born with neural defects during the height of the ZIKV outbreak (Vogel, 2016). Over this same period, French Polynesia also saw a spike in Guillain-Barre syndrome (FauciMorens, 2016; Oehler et al., 2014), as well as increases in a range of other neurologic conditions including meningitis, meningoencephalitis, and myelitis (Talan, 2016). More recently, a series of Latin American countries, including Brazil, Colombia, and Venezuela have observed similar upticks in the incidence of Guillain-Barre (World Health Organization, 2016a, World Health Organization, 2016b), consistent with the proposed relationship between this disorder and ZIKV infection.

In addition to correlative support, several clinical and lab-based findings hint at potential mechanisms to explain the link between ZIKV and neural complications (Mlakar et al., 2016). In 1952, for example, Dick et al (Dick, Kitchen, & Haddow, 1952). demonstrated ZIKV tropism to the brain in intraperitoneally infected mice. Expanding on this finding, Bell, and colleagues (Bell, Field, & Narang, 1971) later showed that both neurons and glia could be infected by ZIKV. More recently, a number of studies, have demonstrated evidence of intrauterine infection with ZIKV (Oliveira Melo et al., 2016), including infection of the fetal brain (Martines, 2015; Rubin, Greene, & Baden, 2016). This latter finding, in particular, provides a direct path from maternal ZIKV infection to microcephaly – a rare neurological condition in which an infant's brain develops abnormally in the womb or does not grow as it should after birth (Mayo Foundation for Medical Education and Research, 2016). Ultimately, microcephaly results in an infant's head size being significantly smaller than the heads of other children of the same age and sex (Mayo Foundation for Medical Education and Research, 2016). Although microcephaly can range from mild to severe, cases currently associated with the ZIKV outbreak in Brazil are notable for the level of damage observed in the brains of affected infants (da Silva et al., 1953; Talan, 2016). Furthermore, congenital Zika usually come with a wide spectrum of clinical features (da Silva et al., 1953).

In this paper, we develop and analyze a mathematical model for ZIKV. Our focus is multi-fold. First, we consider overall ZIKV transmission in the adult population. Second, we consider ZIKV transmission to infants, either directly by mosquitoes or else prior to birth through vertical transmission from the mother. Infant ZIKV cases may be particularly severe because central nervous system (CNS) infections in young children can cause long-term damage to the developing brain (Bundy, 2014, p. 221). Finally, we consider microcephaly rates, which we assume occur as a result of vertical transmission of ZIKV to the fetus during the early stages of pregnancy. The paper is organized as follows. The model is formulated in Section 2 and we investigate the theoretical properties of the Zika model with mother-to-child vertical transmission in Section 3. In Section 4, we assess the impact of the asymptomatic classes and identify key parameters with the most impact on disease burden in Section 5. We conduct numerical exploration of three control strategies in Section 6. The study results are discussed in Section 7.

2. Model formulation

We model the transmission dynamics of ZIKV using a compartmental framework. We consider two human populations consisting of adults and newly born babies as well as the vector population. The population of newly born babies consists of

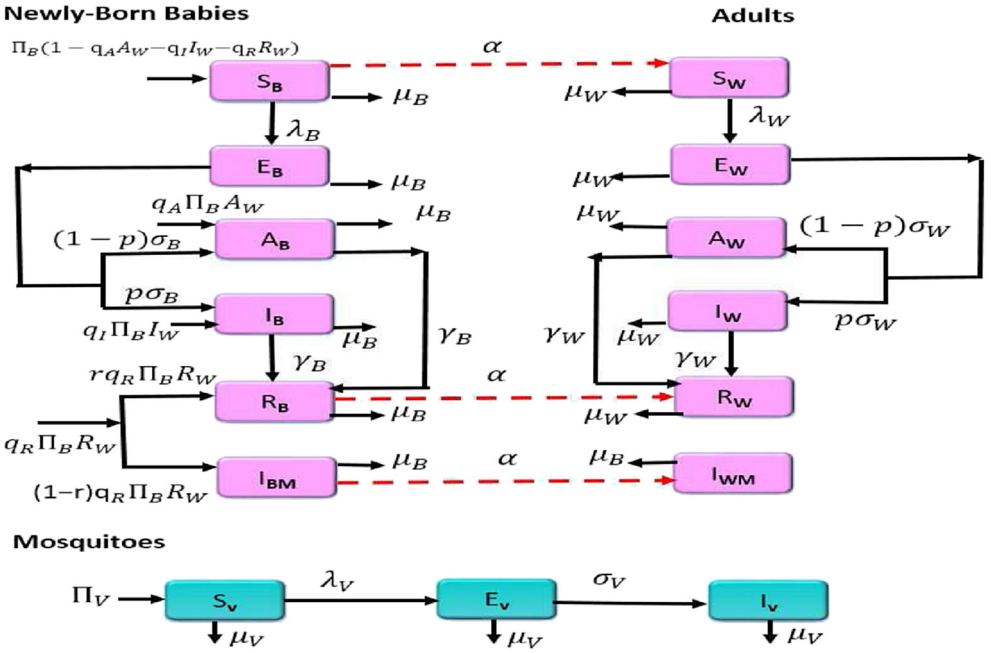

Fig. 1. Flow diagram of the Zika transmission model.