Infectious Disease Modelling 2 (2017) 455–474

Contents lists available at ScienceDirect

Infectious Disease Modelling

journal homepage: www.keaipublishing.com/idm

Mathematical analysis of a model for zoonotic visceral leishmaniasis

Nafiu Hussaini [a], Kamaldeen Okuneye [b], Abba B. Gumel [b, *]

[a] Department of Mathematical Sciences, Bayero University Kano, P.M.B. 3011, Kano, Nigeria
[b] School of Mathematical and Statistical Sciences, Arizona State University, Tempe, AZ 85287, USA

A R T I C L E I N F O

Article history:
Received 12 November 2017
Accepted 6 December 2017
Available online 13 December 2017

Keywords:
Leishmania infantum
Zoonotic visceral leishmaniasis (ZVL)
Reproduction number
Stability
Backward bifurcation

A B S T R A C T

Zoonotic visceral leishmaniasis (ZVL), caused by the protozoan parasite *Leishmania infantum* and transmitted to humans and reservoir hosts by female sandflies, is endemic in many parts of the world (notably in Africa, Asia and the Mediterranean). This study presents a new mathematical model for assessing the transmission dynamics of ZVL in human and non-human animal reservoir populations. The model undergoes the usual phenomenon of backward bifurcation exhibited by similar vector-borne disease transmission models. In the absence of such phenomenon (which is shown to arise due to the disease-induced mortality in the host populations), the nontrivial disease-free equilibrium of the model is shown to be globally-asymptotically stable when the associated reproduction number of the model is less than unity. Using case and demographic data relevant to ZVL dynamics in Aracatuba municipality of Brazil, it is shown, for the default case when systemic insecticide-based drugs are not used to treat infected reservoir hosts, that the associated reproduction number of the model ($\mathscr{R}_0$) ranges from 0.3 to 1.4, with a mean of $\mathscr{R}_0 = 0.85$. Furthermore, when the effect of such drug treatment is explicitly incorporated in the model (i.e., accounting for the additional larval and sandfly mortality, following feeding on the treated reservoirs), the range of $\mathscr{R}_0$ decreases to $\mathscr{R}_0 \in [0.1,\ 0.6]$, with a mean of $\mathscr{R}_0 = 0.35$ (this significantly increases the prospect of the effective control or elimination of the disease). Thus, ZVL transmission models (in communities where such treatment strategy is implemented) that do not explicitly incorporate the effect of such treatment may be over-estimating the disease burden (as measured in terms of $\mathscr{R}_0$) in the community. It is shown that $\mathscr{R}_0$ is more sensitive to increases in sandfly lifespan than that of the animal reservoir (so, a strategy that focuses on reducing sandflies, rather than the animal reservoir (e.g., *via* culling), may be more effective in reducing ZVL burden in the community). Further sensitivity analysis of the model ranks the sandfly removal rate (by natural death or by feeding from insecticide-treated reservoir hosts), the biting rate of sandflies on the reservoir hosts and the progression rate of exposed reservoirs to active ZVL as the three parameters with the most effect on the disease dynamics or burden (as measured in terms of the reproduction number $\mathscr{R}_0$). Hence, this study identifies the key parameters that play a key role on the disease dynamics, and thereby contributing in the design of effective control strategies (that target the identified parameters).

* Corresponding author.
E-mail address: agumel@asu.edu (A.B. Gumel).
Peer review under responsibility of KeAi Communications Co., Ltd.

https://doi.org/10.1016/j.idm.2017.12.002

1. Introduction

The protozoan *Leishmania infantum* (syn., *L. chagasi*) is the causative agent of zoonotic visceral leishmaniasis (ZVL) in humans and canine leishmaniasis (CanL) in dogs (Hartemink et al., 2011; Podaliri Vulpiani, Iannetti, Paganico, Iannino, & Ferri, 2011; Ribas, Zaher, Shimozako, & Massad, 2013). The protozoan parasite is transmitted from infected animal hosts (domestic dogs serve as principal reservoirs) to susceptible female sandflies (*Diptera: Phlebotomine*) and then to susceptible humans (who are regarded as dead-end hosts of the disease) (Elnaiem et al., 2001; Hoogstraal & Heyneman, 1969; Hussaini, Lubuma, Barley, & Gumel, 2016; Kirk, 1939; Podaliri Vulpiani et al., 2011; Ribas et al., 2013). ZVL, which is endemic in Africa, Europe (particularly the Mediterranean region) and Asia (particularly the Indian subcontinent) (European Centre for Disease Prevention and Control, ; Podaliri Vulpiani et al., 2011), is an acute and life-threatening emerging disease with estimated yearly incidence in the range 200 000 to 400 000 (Leta, Dao, Mesele, & Alemayehu, 2014; World Health Organization). Furthermore, increase in risk factors associated with climate change and other environmental challenges makes ZVL to be a growing major public health concern (Hartemink et al., 2011).

An adult female sandfly lays about 40 – 70 eggs during a single gonotrophic cycle (these eggs are typically laid in damp dark places in the cattle sheds, animal burrows, tree roots and in soil rich in organic matter) (European Centre for Disease Prevention and Control, ; Sand fly life cycle,). The eggs laid in these micro-habitats hatch into larvae in 4 – 20 days (European Centre for Disease Prevention and Control,). Larvae develop into four instar stages (each one larger than the one before; the newly hatched first instar larvae have two rear bristles, while all later larval developments have four rear bristles) (European Centre for Disease Prevention and Control,). Larvae are mainly scavengers found in moist areas, such as animal burrows, feeding on organic matter (e.g., fungi, decaying leaves and animal faeces) (European Centre for Disease Prevention and Control, ; Sand fly life cycle,). During the fourth molt, the larva matures into a pupa (the whole process of maturation from larvae to pupae takes about 20 – 30 days depending on species, temperature and nutrient availability) (European Centre for Disease Prevention and Control,). Pupae then develop into adult sandflies in about 6 – 13 days (European Centre for Disease Prevention and Control, ; Sand fly life cycle,). Thus, the duration of the whole cycle, from egg laying to an adult sandfly, varies between 30 and 63 days depending on species, temperature and nutrient availability (European Centre for Disease Prevention and Control,). Adult sandflies usually mate within a few days after emerging from the pupal stage, after which the female sandfly moves to quest for blood meal required to produce eggs (European Centre for Disease Prevention and Control,). The feeding activity of the female adult sandfly is influenced by temperature, humidity and air movement (European Centre for Disease Prevention and Control, ; Sand fly life cycle,). Sandflies, which are active and feed during the early morning and evening hours when temperature falls and humidity rises, have an average lifespan of about 14 days (European Centre for Disease Prevention and Control, ; Sand fly life cycle,). A schematic description of the life-cycle of the sandfly is depicted in Fig. 1. Although there is a vaccine against ZVL in animal populations (CaniLeish) (CaniLeish, 2017; Vetlife), no such vaccine currently exists for use in humans (although a number of candidate vaccines are at various stages of development and clinical trials) (Gillespie et al., 2016; Kumar & Engwerda, 2014; Mcallister, 2014) (it is however, known that an effective vaccine against leishmaniasis will prompt long-lasting immunity in humans (Bertholet et al., 2009; Gillespie et al., 2016; Mcallister, 2014; Nagill & Kaur, 2011)). Furthermore, although ZVL is curable using drugs such as *miltefosine*, *paromomycin* and *liposomal amphotericin B* (Chappuis et al., 2007), basic anti-ZVL preventive measures (such as personal protection against sandfly bites and sandfly-reduction strategies focused on spraying anti-sandfly insecticides in human and animal reservoir habitats) remain perhaps the most effective method for combating ZVL spread in humans (World Health Organization). Treatment of animal reservoir (with systemic insecticide-based drugs, such as *fipronil*) are implemented in places like Bihar, India (Poché, Grant, & Wang, 2016). An additional benefit of the treatment strategy is that it reduces the

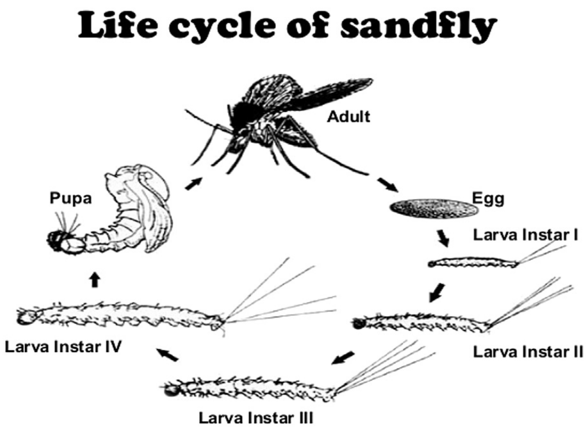

Fig. 1. Schematic diagram of the life-cycle of the sandfly (Sharma,).