Mathematical Biosciences 252 (2014) 14–26

Contents lists available at ScienceDirect

Mathematical Biosciences

journal homepage: www.elsevier.com/locate/mbs

Insecticide-resistant mosquitoes and malaria control

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ARTICLE INFO

Article history:
Received 1 July 2013
Received in revised form 3 March 2014
Accepted 3 March 2014
Available online 19 March 2014

Keywords:
Mutation
Fixed point
Bifurcation
Insecticide-resistance
Threshold

ABSTRACT

The emergence of insecticide-resistant mosquitoes strongly challenges the fight against mosquito-borne diseases, in particular malaria. In this paper, we formulate a system of nonlinear difference equations for malaria transmission cycle. Our model incorporates compartments for insecticide-resistant mosquitoes, where mutation is the only evolutionary force involved in the occurrence of resistant allele in the mosquito population. By deriving an epidemiological threshold, the global stability of the disease and the resistance-free fixed point is established for reduced recruitment rates of resistant mosquitoes. Furthermore, by employing numerical techniques, we showed that the mosquito–human transmission cycle of malaria and its prevalence could be impacted by mutation rate, the personal protection of hosts and the density of mosquitoes. Our results highlight that given a large mosquito population, the presence of even a small number of resistant mosquitoes to an insecticide could make the insecticide ineffective for malaria control. This suggests the need for effective insecticide management strategy, alternate mosquito control approaches, educating the public about personal protection and reduction of mosquito population in a given environment.

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1. Introduction

Mosquito-borne diseases such as malaria, dengue fever and West Nile Virus (WNV) are transmitted among humans through infected vectors. Most of these diseases, which thrive in tropical and subtropical areas of the world, are responsible for high level of morbidity and mortality. They also have significant impact on the socio-economic development of many developing countries [11,25,29].

While chemical insecticides against adult mosquitoes are among the primary part of sustainable intervention strategies to mitigate malaria [36], the emergence of insecticide-resistant mosquitoes is becoming prevalent and it threatens the efficacy of these chemicals which could potentially compromise control efforts [10,25,29]. A slight level of pesticide resistance causes a challenge to malaria control when mosquito population rises. These combination of abundant mosquito population and emergence of pesticide resistance is among the most pressing problems that must be addressed by any effort to control mosquito-borne diseases. Insecticide resistance could emerge due to excessive spray of chemicals, interaction with environmental factors and sometimes due to misuse (failure to follow manufacturer's instruction) pesticides. Furthermore, recent observations suggest that insecticide resistance is mainly a result of indoor residual spraying (IRS) which could indicate the surge of resistance to pyrethroids, the widely used chemical in insecticide-treated bed nets (ITNs) for malaria control [21]. Based on the WHO susceptibility tests, DDT and Pyrethroids resistance have been reported in malaria vector mosquitoes recently [13,29]. Emergence of insecticide resistance is a wide spread problem and is blamed for failure to eradicate mosquito-borne diseases, in particular malaria [6,23,29]. While the intensity is high in developing countries, surveillance indicates that developed countries are not immune to the problem. The number of cases of insecticide resistance of Aedes aegypti (mosquito genus transmitting dengue and yellow fever) populations to organophosphate insecticide tempos is increasing in Asia, Caribbean and South America [40]. Insecticide resistance increases the likelihood of disease spread by mosquitoes, because it allows mosquitoes to live longer withstanding insecticide. It is clear that insecticide resistance is a complex problem and understanding its effects on the spread of disease requires designing resistance management strategies [14,32,35,36,39], as well as more analytical and computational studies.

Mathematical models have been useful tools in looking into the dynamics of several mosquito-borne diseases and the outcomes of mosquito control managements in the fight against these diseases

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http://dx.doi.org/10.1016/j.mbs.2014.03.007
0025-5564/Published by Elsevier Inc.

[3–5,11,12,19,22,27,30,33]. In particular, discrete-time models are appropriate for vector-borne diseases where data and results are counted on time intervals such as days, weeks or months. A few discrete models are applied to studies of vector-borne diseases without incorporating insecticide resistance [3,7,12,22,25]. The emergence of insecticide-resistant mosquitoes have been the focus of better intervention strategies in mosquito controls. In this regard, mathematical models play notable roles in suggesting insecticide improvement to reduce evolution of resistance such as adding synergies to bed nets [2], investigating alternative approaches other than insecticide spray such as introduction of larvivorous fish [27], genetic altering of disease transmitting mosquitoes [25], employing fungal biopesticides [28].

Regardless of the emergence of insecticide-resistant mosquitoes, insecticides are used to a large extent in malaria control, because they are affordable and best, at least among existing methods so far. Besides to this, there are limited variety of chemicals to be used for IRS and ITNs (see [35] and references therein). With this in mind, it is important to have insight into resistance management strategies and relevant facts. First, the size of mosquito population which could cause a threat to the fight against malaria even in the presence of a small number of insecticide-resistant mosquitoes. Second, the long term effects of higher mutation rate on the disease dynamics. Third, the effects of strengthening personal protection and interacted vector management strategies on controlling malaria prevalence. Our aim is to investigate these three phenomena and address their combined effects and highlight the importance of proactive approach to control insecticide resistance.

This paper is organized as follows. In Section 2, we formulate the basic discrete model which extends the Blayneh and Jang [3] model by incorporating insecticide-resistance in the mosquito population. Considering a geometric reproduction rate for mosquitoes, analytical and numerical results are presented in Sections 3.1 and 3.2. In Section 3.2, we present conditions for the existence of disease-free and endemic fixed points, both with and without insecticide-resistance. Also, numerical examples are given in the same section. In Section 4, a nonlinear mosquito reproduction function (Ricker type) is introduced and emergence of cycles, period doubling bifurcations, as well as chaotic behaviors of the disease and the resistance level are studied numerically. Further numerical simulations are carried out to get more insight about the difficulty of disease control for higher mutation rate. Other numerical results show that even if the number of insecticide-resistant mosquitoes is small, increased mosquito population could make disease elimination difficult. The effects of controlling host-mosquito contact and the impact of reducing mosquito density on the disease dynamics are additional results. The key results are discussed and concluding remarks are given in Section 5.

2. Deterministic model

We formulate a time-discrete compartmental model for vector-host transmission cycle of malaria. We assume that only one type of insecticide is sprayed in a community and that a proportion of the mosquito population in the community could develop resistance to the insecticide through mutation at a rate of $\mu > 0$. When $\mu = 0$, mosquitoes in the community do not develop resistance to the insecticide. Furthermore, we assume that mutation is the only evolutionary force involved in the occurrence of resistant allele in the mosquito population.

Each of the mosquito groups classified as insecticide sensitive and resistant is further divided into susceptible and infectious compartments. In perspective, at generation t, $(u_r)_t$ is the size of uninfected, and $(v_r)_t$ is the size of infectious mosquitoes, both are insecticide-resistant. Whereas, $(u_s)_t$ and $(v_s)_t$ are the number of susceptible and infectious mosquitoes, respectively and both are sensitive to insecticide. Mosquitoes could transmit a disease to hosts regardless of their status as resistant or as susceptible to insecticide used in mosquito control. We assume that resistance is inherited (vertically transmitted). Consequently, the recruitment rate of adult mosquitoes produced by insecticide-resistant female mosquitoes is modeled by

$$F((u_r)_t + (v_r)_t).$$

We will consider specific functions for F in Section (3.1). On the other hand, the recruitment rate of mosquitoes which are sensitive to insecticide is

$$H((u_s)_t + (v_s)_t).$$

The reproduction function of humans is defined by $B(N_t)$, where $N_t = s_t + i_t$ is the total human population size, s_t, is the size of humans and i_t is the size of infectious humans. A fraction μ of the insecticide-sensitive mosquitoes develops resistance and moves to the resistant class. The probability of disease transmission from infectious hosts to susceptible mosquitoes is defined by $1 - Q\left(\frac{i_t}{N_t}\right)$. Accordingly, the number of insecticide-sensitive mosquitoes which are susceptible to the disease at generation t is

$$\alpha_1(1-\mu)Q\left(\frac{i_t}{N_t}\right)(u_s)_t,$$

where α_1 is the survival rate of insecticide-sensitive mosquitoes per day. Likewise,

$$\alpha_1(1-\mu)\left(1 - Q\left(\frac{i_t}{N_t}\right)\right)(u_s)_t$$

is the number of insecticide sensitive mosquitoes which become infectious through contact with infectious hosts. Therefore, the next generation of infectious, but insecticide-sensitive mosquitoes is

$$(v_s)_{t+1} = \alpha_1(1-\mu)\left(1 - Q\left(\frac{i_t}{N_t}\right)\right)(u_s)_t + \alpha_1(1-\mu)(v_s)_t.$$

The next generation of mosquitoes which are insecticide-resistant and infectious is the class $(v_r)_{t+1}$. Contributions to this class come from (i) insecticide-resistant mosquitoes which become infectious through contact with infectious hosts, which is

$$\alpha_2\left(1 - Q\left(\frac{i_t}{N_t}\right)\right)(u_r)_t,$$

where α_2 is the survival rate of insecticide mosquitoes per day, (ii) insecticide-sensitive mosquitoes which become infectious and a fraction of which develops resistant mutation, which is

$$\alpha_2\mu\left(1 - Q\left(\frac{i_t}{N_t}\right)\right)(u_s)_t,$$

(iii) mosquitoes which develop insecticide-resistance $\alpha_2\mu(v_s)_t$ and (iv) a group which is already surviving as insecticide-resistant $\alpha_2(v_r)_t$. Adding all of these terms, the next generation of infectious and insecticide-resistant mosquitoes is

$$(v_r)_{t+1} = \alpha_2\left(1 - Q\left(\frac{i_t}{N_t}\right)\right)(u_r)_t + \alpha_2\mu\left(1 - Q\left(\frac{i_t}{N_t}\right)\right)(u_s)_t + \alpha_2\mu(v_s)_t + \alpha_2(v_r)_t.$$

The probability that a susceptible host individual gets infection as a result of contact with infectious mosquito (sensitive or insecticide-resistant) is

$$1 - P\left(\frac{(v_s)_t + (v_r)_t}{Z_t}\right),$$