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A co-infection model of malaria and cholera diseases with optimal control

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ABSTRACT

In this paper we formulate a mathematical model for malaria--cholera co-infection in order to investigate their synergistic relationship in the presence of treatments. We first analyze the single infection steady states, calculate the basic reproduction number and then investigate the existence and stability of equilibria. We then analyze the co-infection model, which is found to exhibit backward bifurcation. The impact of malaria and its treatment on the dynamics of cholera is further investigated. Secondly, we incorporate time dependent controls, using Pontryagin's Maximum Principle to derive necessary conditions for the optimal control of the disease. We found that malaria infection may be associated with an increased risk of cholera but however, cholera infection is not associated with an increased risk for malaria. Therefore, to effectively control malaria, the malaria intervention strategies by policy makers must at the same time also include cholera control.

1. Introduction

Q2 Malaria is a preventable and curable vector borne disease. The strategy for reducing malaria transmission is to protect individuals from mosquito bites by the distribution of inexpensive mosquito nets and insect repellents or by mosquito control measures such as indoor spraying of insecticides and draining of stagnant water where mosquitoes breed [27]. The recent flooding across Africa and Asia continents posed a serious challenge to good environmental sanitation and availability of clean water thereby providing breeding condition for malaria and cholera to strive [2].

The study of the epidemiology of cholera was heralded by John Snow and this began the modern epidemiology research [13]. The link between contaminated drinking water and cholera was long established. Cholera is a severe bacterial infection that produces profuse watery diarrhea and vomiting and can lead to severe dehydration and electrolyte imbalance and finally death if this is not corrected. Cholera is transmitted through ingestion of water contaminated (usually from feces or effluent) with the bacterium *Vibrio cholerae*. Human colonization of cholera creates a hyper infectious state that is maintained after dissemination and this contributes to epidemic disease. Prevention of cholera is achieved by good sanitation and water treatment [33].

Mathematical modeling has been an important tool in understanding the dynamics of disease transmission and also in decision making processes regarding intervention mechanisms for disease control. For example, Ross [32] developed the first mathematical models of malaria transmission. His focus was on mosquito control and he showed that for the disease to be eliminated the mosquito population should be brought below a certain threshold. Other studies include Koella and Anita [16] who included a latent class for mosquitoes. They considered different strategies to reduce the spread of resistance and studied the sensitivity of their results to the parameters. Anderson and May [5] derived a malaria model with the assumption that acquired immunity in malaria is independent of exposure duration. Different control measures and the role of transmission rate on the disease prevalence were further examined. Nikolaos et al. [26] proposed a detailed analysis of a dynamical model to describe pathogenesis of HIV infection. Christopher and Jorge [8] derived a simple two-dimensional SIS (susceptible--infected--susceptible) model with vaccination and multiple endemic states. Guihua and Zhen [11] studied the global dynamics of an SEIR (susceptible--exposed--infected--recovered) epidemic model in which latent and immune states were infective.

However, a few studies have been carried out on the formulation and application of optimal control theory to cholera models. To the best of our knowledge no work has been done to investigate the malaria--cholera co-infection dynamics or the application of optimal control methods. Only recently, the authors in [20] proposed and examined a deterministic model for the co-infection of HIV and malaria in a community. Also, the authors in [19] examined a deterministic model for the co-infection of tuberculosis and malaria, while in [23] the authors proposed a model for schistosomiasis and HIV/AIDS co-dynamics. The authors in [25] formulated a mathematical model

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for cholera to include essential components such as hyper-infectious, short-lived bacterial state, a separate class for mild human infections and waning disease immunity. Also in [33], the authors presented a model for cholera epidemics which comprises seasonality, loss of host immunity and control mechanisms acting to reduce cholera transmission. A mathematical model of cholera transmission was examined in [24] to study the impact of public health educational campaigns, vaccination and treatment as control strategies in curtailing the disease. The authors in [36] carried out global stability analysis for deterministic cholera epidemic models. In [34], a general compartmental model for cholera was formulated that incorporates two pathways of transmission. A simple mathematical model was presented in [23] to assess whether HIV infection is associated with an increased risk for cholera or not. Authors in [35] studied a mathematical model for cholera that incorporates hyper infectivity and temporary immunity using distributed delays.

In this paper, we formulate an SIR (susceptible, infected and recovered) model for malaria--cholera co infection with the optimal control problem. Our model include five different control strategies, namely malaria prevention (treated bednets), cholera prevention (sanitations and proper hygiene), malaria treatment, cholera treatment and combined therapy for malaria--cholera infection as time dependent control strategies, in order to determine the optimal strategy for the control of the diseases.

The paper is organized as follows: Section 2 is devoted to the model description and the underlying assumptions. In Section 3, we analyze the cholera only model. Section 4 is devoted to the analysis of the malaria only model while in Section 5 the co-infection model is analyzed. In Section 6 we use Pontryagin's Maximum Principle to investigate analysis of control strategies and to determine the necessary conditions for the optimal control of the disease. In Sections 7 and 8 we discuss the numerical methods used and the numerical results respectively. Our conclusion is presented in Section 9.

2. Model formulation

The model sub-divides the total human population, denoted by N_h, into sub-populations of susceptible humans S_h, individuals infected with malaria only I_m, individuals infected with cholera only I_c, individuals infected with both malaria and cholera G_{mc}, individuals who recovered from malaria only R_m, individuals who recovered from cholera only R_c, individuals who recovered from both malaria and cholera R_{mc}. So that $N_h = S_h + I_m + I_c + G_{mc} + R_m + R_c + R_{mc}$.

The total vector population, denoted by N_v, is sub-divided into susceptible mosquitoes S_v, mosquitoes infected with malaria I_v. Thus, $N_v = S_v + I_v$.

The model is given by the following system of ordinary differential equations:

$$\begin{cases} \frac{d}{dt}S_h = \Lambda_h + \kappa R_m + \omega R_c + \psi R_{mc} - \beta_h I_v S_h - \lambda S_h - \mu_h S_h \\ \frac{d}{dt}I_m = \beta_h I_v S_h - \lambda I_m - (\alpha + \mu_h + \phi) I_m \\ \frac{d}{dt}I_c = \lambda S_h - \beta_h I_v I_c - (\delta + \mu_h + m) I_c \\ \frac{d}{dt}G_{mc} = \beta_h I_v I_c + \lambda I_m - (\sigma + \mu_h + \eta + q) G_{mc} \\ \frac{d}{dt}R_m = \alpha I_m - (\kappa + \mu_h) R_m + \epsilon(1-\sigma) G_{mc} \\ \frac{d}{dt}R_c = \delta I_c - (\omega + \mu_h) R_c + (1-\epsilon)(1-\sigma) G_{mc} \\ \frac{d}{dt}R_{mc} = \sigma G_{mc} - (\psi + \mu_h) R_{mc} \\ \frac{d}{dt}B_c = \rho(I_c + \theta G_{mc}) - \mu_b B_c \\ \frac{d}{dt}S_v = \Lambda_v - \beta_v (I_m + G_{mc}) S_v - \mu_v S_v \\ \frac{d}{dt}I_v = \beta_v S_v (I_m + G_{mc}) - \mu_v I_v \end{cases} \tag{1}$$

Here,

$$\lambda = \frac{B_c \nu}{K + B_c}, \tag{2}$$

where B_c is the bacteria population, the ingestion rate is ν and K is the bacteria concentration. Also, m, η are cholera related death rates respectively, and ϕ, q are malaria related death rates respectively, while ρ is the average contribution of each cholera infected individual to the aquatic population of *V. cholerae*. The immunity waning rates are κ, ω, ψ respectively and α, δ, σ respectively are the recovery rates. The term $\epsilon(1-\sigma)$ are the dually infected individuals who recovered from malaria only. And $(1-\epsilon)(1-\sigma)$ are the dually infected individuals who recovered from cholera only. That is, $\sigma + \epsilon(1-\sigma) + (1-\epsilon)(1-\sigma) = 1$. While μ_h and μ_v are respectively the humans and mosquitoes mortality rates and θ is the modification parameter.

Our assumptions in the model are as follows:

- Mosquitoes do not suffer mosquito-induced death.
- Individuals infected with both malaria and cholera can only infect mosquitoes with malaria parasites.

3. Cholera only model

Here, we consider the cholera only model.

$$\begin{cases} \frac{d}{dt}S_h = \Lambda_h + \omega R_c - \lambda S_h - \mu_h S_h \\ \frac{d}{dt}I_c = \lambda S_h - (\delta + \mu_h + m) I_c \\ \frac{d}{dt}R_c = \delta I_c - (\omega + \mu_h) R_c \\ \frac{d}{dt}B_c = \rho I_c - \mu_b B_c \end{cases} \tag{3}$$

3.1. Stability of the disease-free equilibrium (DFE)

The cholera only model (3) has a DFE, obtained by setting the right-hand sides of the equations in the model to zero, given by

$$\mathcal{E}_{0c} = (S_h^*, I_c^*, R_c^*, B_c^*) = \left(\frac{\Lambda_v}{\mu_h}, 0, 0, 0\right).$$

The linear stability of $\mathcal{E}_{0c}$ can be established using the next generation operator method in Driessche and Watmough [9] on the system (3). It follows that the reproduction number of the cholera only model (3), denoted by $\mathcal{R}_{0c}$, is given by

$$\mathcal{R}_{0c} = \frac{\nu \rho \Lambda_v}{\mu_b \mu_h K (m + \delta + \mu_h)}, \tag{4}$$

Further, using Theorem 2 in Driessche and Watmough [9], the following result is established. The DFE is locally asymptotically stable if $\mathcal{R}_{0c} < 1$ and unstable if $\mathcal{R}_{0c} > 1$.

3.1.1. Existence of endemic equilibrium

Lemma 1. *The cholera only model has a unique endemic equilibrium if and only if* $\mathcal{R}_{0c} > 1$.

Proof. Calculating the endemic equilibrium point, we obtain,

$$\begin{cases} S_h^* = \frac{\Lambda_h + \omega R_c^*}{\mu_h + \lambda^*} \\ I_c^* = \frac{\lambda^* S_h^*}{m + \delta + \mu_h} \\ R_c^* = \frac{\delta I_c^*}{\omega + \mu_h} \\ B_c^* = \frac{\rho I_c^*}{\mu_b} \end{cases} \tag{5}$$

Hence, the cholera force of infection (see (2)), λ^*, satisfies the following polynomial

$$P(\lambda^*) = A(\lambda^*)^2 + B(\lambda^*) = 0 \tag{6}$$