On the Co-infection of Malaria and Schistosomiasis

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Abstract Mathematical models for co-infection of diseases (that is, the simultaneous infection of an individual by multiple diseases) are sorely lacking in the literature. Here we present a mathematical model for the co-infection of malaria and schistosomiasis. We derive reproduction numbers for malaria and schistosomiasis independently, then combine these to determine the effects of disease interactions. Sensitivity indices show that malaria infection may be associated with an increased rate of schistosomiasis infection. However, schistosomiasis infection is not associated with an increased rate of malaria infection. Therefore, whenever there is co-infection of malaria and schistosomiasis in the community, our model suggests that control measures for each disease should be administered concurrently for effective control.

1 Introduction

Malaria and schistosomiasis often overlap in tropical and subtropical countries, imposing tremendous disease burdens [4, 8, 14]. The substantial epidemiological overlap of these two parasitic infections invariably results in frequent co-infections [7, 18]. The challenges facing the development of a highly effective malaria vaccine have generated interest in understanding the interactions between malaria and co-endemic helminth infections, such as those caused by Schistosoma, that could impair vaccine efficacy by modulating host-immune responses to *Plasmodium* infection and treatment [13, 14]. Both malaria and schistosomiasis are endemic to most African nations. However, the extent to which schistosomiasis modifies the rate of febrile malaria remains unclear.

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Mathematical modelling has been an important tool in understanding the dynamics of disease transmission and also in the decision-making processes regarding intervention mechanisms for disease control. For example, Ross [12] 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. Another classical result is due to Anderson and May [1], who derived a malaria model with the assumption that acquired immunity in malaria is independent of exposure duration.

There is an urgent need for co-infection models for infectious diseases, particularly those that mix neglected tropical diseases with "the big three" (HIV, TB and malaria) [8]. Recently, the authors in [10] proposed a model for schistosomiasis and HIV/AIDS co-dynamics, while the co-infection dynamics of malaria and cholera were studied in [11]. However, few studies have been carried out on the co-infection of schistosomiasis. To the best of our knowledge, no work has been done to investigate the malaria–schistosomiasis co-infection dynamics.

In this paper, we formulate and analyse an SIR (susceptible, infected and recovered) model for malaria–schistosomiasis co-infection, in order to understand the effect that controlling for one disease may have on the other.

2 Model Formulation

Our model subdivides the total human population, denoted by N_h, into subpopulations of susceptible humans S_h, individuals infected only with malaria I_m, individuals infected with only schistosomiasis I_{sc}, individuals infected with both malaria and schistosomiasis C_{ms}, individuals who have recovered from malaria R_m and individuals who have recovered from schistosomiasis R_s. The total mosquito vector population, denoted by N_v, is subdivided into susceptible mosquitoes S_v and mosquitoes infected with malaria I_v. Similarly, the total snail vector population, denoted by N_{sv}, is subdivided into susceptible snails S_{sv} and snails infected with schistosomiasis I_{sv}. Thus $N_h = S_h + I_m + I_s + C_{ms} + R_s + R_m$, $N_v = S_v + I_v$ and $N_{sv} = S_{sv} + I_{sv}$.

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

$$
\begin{aligned}
S_h' &= \Lambda_h + \varepsilon R_s + \alpha R_m - \beta_1 S_h - \lambda_1 S_h - \mu_h S_h \\
I_m' &= \beta_1 S_h - \lambda_1 I_m - (\psi + \mu_h + \phi) I_m \\
I_{sc}' &= \lambda_1 S_h - \beta_1 I_{sc} - (\omega + \mu_h + \eta) I_{sc} \\
C_{ms}' &= \beta_1 I_{sc} + \lambda_1 I_m - (\delta + \mu_h + \eta + \phi) C_{ms} \\
R_m' &= \psi I_m - (\alpha + \mu_h) R_m + \tau \delta C_{ms} \\
R_s' &= \omega I_{sc} - (\varepsilon + \mu_h) R_s + (1 - \tau) \delta C_{ms}
\end{aligned}
$$

$$\begin{aligned} S_v' &= \Lambda_v - \beta_2 S_v - \mu_v S_v \\ I_v' &= \beta_2 S_v - \mu_v I_v \\ S_{sv}' &= \Lambda_s - \lambda_2 S_{sv} - \mu_{sv} S_{sv} \\ I_{sv}' &= \lambda_2 S_{sv} - \mu_{sv} I_{sv}, \end{aligned} \tag{1}$$

with the transmission rates given by

$$\beta_1 = \frac{\beta_h I_v}{N_h}, \quad \lambda_1 = \frac{\lambda I_{sv}}{N_h}, \quad \beta_2 = \frac{\beta_v (I_m + C_{ms})}{N_h}, \quad \lambda_2 = \frac{\lambda_s (I_{sc} + C_{ms})}{N_h}.$$

Birth rates for humans, mosquitoes and snails are, respectively, Λ_h, Λ_v and Λ_{sv}, while the corresponding mortality rates are μ_h, μ_v and μ_{sv}. Here η is the schistosomiasis-related death rate and ϕ is the malaria-related death rate. The immunity-waning rates for malaria and schistosomiasis are α and ε respectively, while the recovery rates from malaria, schistosomiasis and co-infection are ψ, ω and δ respectively. The term $\tau\delta$ accounts for the portion of co-infected individuals who recover from malaria, while $(1 - \tau)\delta$ accounts for co-infected individuals who recover from schistosomiasis; thus τ (satisfying $0 \leq \tau \leq 1$) represents the likelihood of individuals to recover from malaria first. Note that all parameters might in practice vary with time; however, we shall take variations in our critical parameters into account with a sensitivity analysis.

3 Analysis of Malaria–Schistosomiasis Co-infection Model

The malaria–schistosomiasis model (1) has a disease-free equilibrium, given by

$$\mathscr{E}_0 = (S_h^*, I_m^*, I_{sc}^*, C_{ms}^*, R_m^*, R_s^*, S_v^*, I_v^*, S_{sv}^*, I_{sv}^*) = \left(\frac{\Lambda_h}{\mu_h}, 0, 0, 0, 0, 0, \frac{\Lambda_v}{\mu_v}, 0, \frac{\Lambda_s}{\mu_{sv}}, 0 \right).$$

The linear stability of $\mathscr{E}_0$ can be established using the next-generation method [17] on the system (1). It follows that the reproduction number of the malaria–schistosomiasis model (1), denoted by $\mathscr{R}_{msc}$, is given by

$$\mathscr{R}_{msc} = \max\{\mathscr{R}_{sc}, \mathscr{R}_{0m}\},$$

where

$$\mathscr{R}_{0m} = \sqrt{\frac{\Lambda_v \beta_h \beta_v \mu_h}{\Lambda_h \mu_v^2 (\psi + \phi + \mu_h)}}$$

$$\mathscr{R}_{sc} = \sqrt{\frac{\lambda \lambda_s \Lambda_s \mu_h}{\Lambda_h (m + \omega + \mu_h) \mu_{sv}^2}}.$$

Note that the reproduction number produced by the next-generation method produces a threshold quantity and not necessarily the average number of secondary infections [9]. We thus have the following theorem.

Theorem 1 *The disease-free equilibrium $\mathscr{E}_0$ is locally asymptotically stable whenever $\mathscr{R}_{msc} < 1$ and unstable otherwise.*

3.1 Impact of Disease Interactions

To analyse the effects of schistosomiasis on malaria and vice versa, we begin by expressing $\mathscr{R}_{sc}$ in terms of $\mathscr{R}_{0m}$. We solve for μ_h to get

$$\mu_h = \frac{D_1 \mathscr{R}_{0m}^2}{D_2 - D_3 \mathscr{R}_{0m}^2} ,$$

where

$$D_1 = \Lambda_h \mu_v^2 (\psi + \phi) , \qquad D_2 = \Lambda_v \beta_h \beta_v , \qquad D_3 = \Lambda_h \mu_v^2 .$$

Substituting into the expression for $\mathscr{R}_{sc}$, we obtain

$$\mathscr{R}_{sc} = \sqrt{\frac{\lambda \lambda_s \Lambda_s D_1 \mathscr{R}_{0m}^2}{[(\eta + \omega) D_2 + (D_1 - (\eta + \omega) D_3) \mathscr{R}_{0m}^2] \Lambda_h \mu_{sv}^2}} . \tag{2}$$

Differentiating $\mathscr{R}_{sc}$ with respect to $\mathscr{R}_{0m}$ leads to

$$\frac{\partial \mathscr{R}_{sc}}{\partial \mathscr{R}_{0m}} = \frac{(\eta + \omega) D_2 \sqrt{\frac{\lambda \lambda_s \Lambda_s D_1 \mathscr{R}_{0m}^2}{[(\eta+\omega) D_2 + (D_1 - (\eta+\omega) D_3) \mathscr{R}_{0m}^2] \Lambda_h \mu_{sv}^2}}}{[(\eta + \omega) D_2 \mathscr{R}_{0m} + (D_1 - (\eta + \omega) D_3) \mathscr{R}_{0m}^3]} . \tag{3}$$

Similarly, expressing μ_h in terms of $\mathscr{R}_{sc}$, we get

$$\mu_h = \frac{D_4 \mathscr{R}_{sc}^2}{D_5 - D_6 \mathscr{R}_{sc}^2} , \tag{4}$$

where

$$D_4 = \Lambda_h \mu_{sv}^2 (\eta + \omega) , \qquad D_5 = \lambda \lambda_s \Lambda_s , \qquad D_6 = \Lambda_h \mu_{sv}^2 .$$

Substituting into the expression for $\mathscr{R}_{0m}$, we obtain

$$\mathscr{R}_{0m} = \sqrt{\frac{D_4\beta_h\beta_v\Lambda_v\mathscr{R}_{sc}^2}{[(\phi+\psi)D_5 + (D_4-(\phi+\psi)D_6)\mathscr{R}_{sc}^2]\Lambda_h\mu_{sv}^2}}\,. \tag{5}$$

3.2 Sensitivity Indices of R_{sc} when Expressed in Terms of R_{0m}

We next derive the sensitivity of R_{sc} in (2) (i.e., when expressed in terms of R_{0m}) to each of the 13 different parameters. However, the expression for the sensitivity indices for some of the parameters are complex, so we evaluate the sensitivity indices of these parameters at the baseline parameter values as given in Table 1. Since the effect of immunity in the control of re-infection is not entirely known [6], we have assumed the schistosomiasis immunity waning rate. Due to a lack of data in the literature, assumptions were made for the recovery rate of co-infected individuals, δ, recovery rate of schistosomiasis-infected individuals, ω, and the rate of recovery from malaria for co-infected individuals, τ.

Table 1 Parameters in the co-infection model

Parameter	Description	value	Ref
ϕ	Malaria-induced death	0.05–0.1 day^{-1}	[16]
β_h	Malaria transmissibility to humans	0.034 day^{-1}	[2]
β_v	Malaria transmissibility to mosquitoes	0.09 day^{-1}	[2]
λ	Schistosomiasis transmissibility to humans	0.406 day^{-1}	[15]
λ_s	Schistosomiasis transmissibility to snails	0.615 day^{-1}	[3]
μ_h	Natural death rate in humans	0.00004 day^{-1}	[2]
μ_v	Natural death rate in mosquitoes	1/15–0.143 day^{-1}	[2]
μ_{sv}	Natural death rate in snails	0.000569 day^{-1}	[3, 15]
α	Malaria immunity waning rate	1/(60*365) day^{-1}	[2]
ε	Schistosomiasis immunity waning rate	0.013 day^{-1}	Assumed
Λ_h	Human birth rate	800 people/day	[3]
Λ_v	Mosquitoes birth rate	1000 mosquitoes/day	[2]
Λ_s	Snail birth rate	100 snails/day	[5]
δ	Recovery rate of co-infected individual	0.35 day^{-1}	Assumed
ω	Recovery rate of schistosomiasis-infected individual	0.0181 day^{-1}	Assumed
ψ	Recovery rate of malaria-infected individual	1/(2*365) day^{-1}	[2]
τ	Co-infected proportion who recover from malaria only	0.1	Assumed
η	Schistosomiasis-induced death	0.0039 day^{-1}	[3]

Table 2 Sensitivity indices of R_{sc} expressed in terms of R_{0m}

	Parameter	Description	Sensitivity index if $R_{0m} < 1$	Sensitivity index if $R_{0m} > 1$
1	μ_{sv}	Snail mortality	−1	−1
2	μ_v	Mosquito mortality	0.56	0.07
3	λ_s	Schistosomiasis transmissibility to snails	0.5	0.5
4	Λ_s	Snail birth rate	0.5	0.5
5	β_h	Malaria transmissibility to humans	−0.28	−0.03
6	β_v	Malaria transmissibility to mosquitoes	−0.28	−0.03
7	Λ_v	Mosquito birth rate	−0.28	−0.03
8	Λ_h	Human birth rate	−0.22	−0.47
9	ϕ	Malaria-induced death	0.12	−0.31
10	ω	Recovery from schistosomiasis	−0.10	0.26
11	m	Schistosomiasis-induced death	−0.02	0.05
12	ψ	Recovery from malaria rate	0.003	−0.0084

The sensitivity index of R_{sc} with respect to λ, for example, is

$$\Upsilon_{\lambda}^{R_{sc}} \equiv \frac{\partial R_{sc}}{\partial \lambda} \times \frac{\lambda}{R_{sc}} = 0.5 \, . \tag{6}$$

The detailed sensitivity indices of R_{sc} resulting from the evaluation of the other parameters of the model are shown in Table 2.

Table 2 shows the parameters, arranged from the most sensitive to the least. For $R_{0m} < 1$, the most sensitive parameters are the snail mortality rate, the mosquito mortality rate, the transmissibility of schistosomiasis to snails and the snail birth rate (μ_{sv}, μ_v, λ_s and Λ_s, respectively). Since $\Upsilon_{\mu_{sv}}^{R_{sc}} = -1$, increasing (or decreasing) the snail mortality rate μ_{sv} by 10 % decreases (or increases) R_{sc} by 10 %; similarly, increasing (or decreasing) the mosquito mortality rate, μ_v, by 10 % increases (or decreases) R_{sc} by 5.6 %. In the same way, increasing (or decreasing) the transmissibility of schistosomiasis to snails, λ_s, increases (or decreases) R_{sc} by 5 %. As the malaria parameters β_h, β_v and Λ_v increase/decrease by 10 %, the reproduction number of schistosomiasis, R_{sc}, decreases by 2.8 % in all three cases.

For $R_{0m} > 1$, the most sensitive parameters are the snail mortality rate, the rate of a snail getting infected with schistosomiasis, the snail birth rate, the human birth rate, malaria-induced death and recovery from schistosomiasis (μ_{sv}, λ_s, Λ_s, Λ_h, ϕ, ω, respectively). Since $\Upsilon_{\lambda_s}^{R_{sc}} = 0.5$, increasing (or decreasing) by 10 % increases (or decreases) R_{sc} by 5 %; similarly, increasing (or decreasing) the recovery rate, ω, by 10 % increases (or decreases) R_{sc} by 2.6 %. Also, as the malaria parameters β_h, β_v and Λ_v increase/decrease by 10 %, the reproduction number of schistosomiasis, R_{sc}, decreases by only 0.3 % in all three cases.

Table 3 Sensitivity indices of R_{0m} expressed in terms of R_{sc}

	Parameter	Description	Sensitivity index if $R_{sc} < 1$	Sensitivity index if $R_{sc} > 1$
1	β_v	Malaria transmissibility to mosquitoes	0.5	0.5
2	Λ_v	Mosquito birth rate	0.5	0.5
3	λ	Schistosomiasis transmissibility to humans	−0.5	−0.5
4	λ_s	Schistosomiasis transmissibility to snails	−0.5	−0.5
5	Λ_s	Snail birth rate	−0.5	−0.5
6	ϕ	Malaria-induced death	−0.49	−0.49
7	ω	Recovery from schistosomiasis	0.41	0.41
8	m	Schistosomiasis-induced death	0.09	0.09
9	ψ	Recovery from malaria	−0.01	−0.01
10	μ_{sv}	Snail mortality	0.0000002	0.000007
11	Λ_h	Human birth rate	0.0000001	0.000004

It is clear that R_{sc} is sensitive to changes in R_{0m}. That is, the sensitivity of R_{sc} to parameter variations depends on R_{0m}; whenever, $R_{0m} < 1$, R_{sc} is less sensitive to the malaria parameters.

3.3 Sensitivity Indices of R_{0m} when Expressed in Terms of R_{sc}

Similar to the previous subsection, we derive the sensitivity of R_{0m} in (5) (i.e. when expressed in terms of R_{sc}) to each of the different parameters. The sensitivity index of R_{0m} with respect to β_h, for example, is

$$\Upsilon_{\beta_h}^{R_{0m}} \equiv \frac{\partial R_{0m}}{\partial \beta_h} \times \frac{\beta_h}{R_{0m}} = 0.5\,. \tag{7}$$

The detailed sensitivity indices of R_{0m} resulting from the evaluation to the other parameters of the model are shown in Table 3. It is clearly seen from Table 3 that the malaria reproduction number, R_{0m}, is not sensitive to any variation in the schistosomiasis reproduction number R_{sc}.

4 Numerical Simulations

Table 1 lists the parameter descriptions and values used in the numerical simulation of the co-infection model.

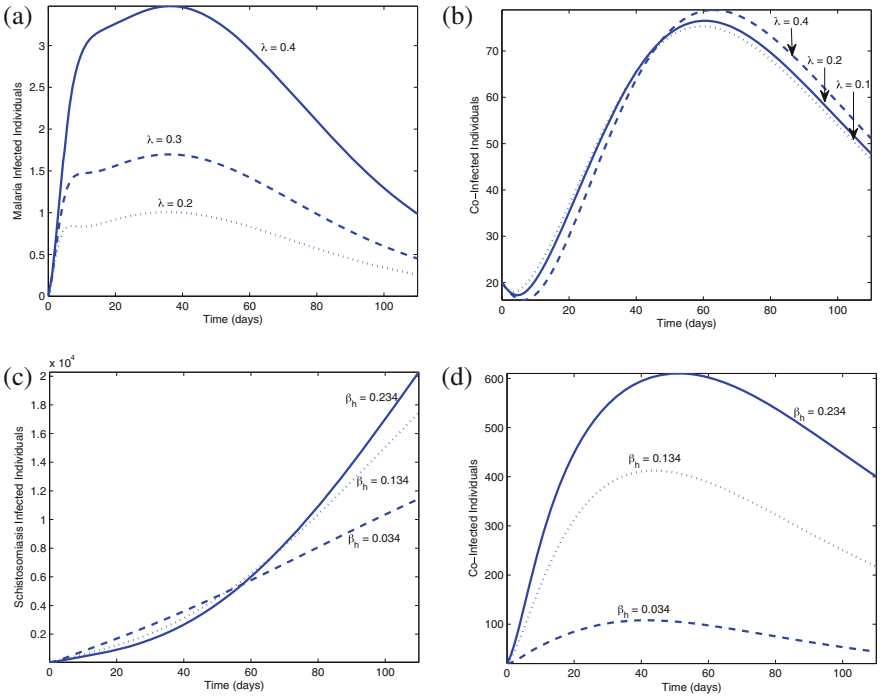

Fig. 1 Simulations of the malaria–schistosomiasis model showing the effect of varying transmission rates

Figure 1a,b shows the effect of varying the schistosomiasis transmission parameter λ on the number of individuals infected with malaria, I_m, and the number of co-infected individuals, C_{ms}. This illustrates that effective control of schistosomiasis would enhance the control of malaria. Conversely, Fig. 1c,d shows the effect of varying the malaria transmission parameter β_h on the number of individuals infected with schistosomiasis, I_{sc}, and the number of co-infected individuals. This illustrates that effective control of malaria would enhance control of co-infection but have only minimal effect on schistosomiasis prevalence.

Figure 2 shows the effect of varying the death rate of mosquitoes μ_v (for example, through spraying) on the number of individuals infected with schistosomiasis and the number of co-infected individuals. As the mosquitoes are controlled, the number of individuals infected with malaria falls dramatically, as does the number of co-infected individuals, while the number of schistosomiasis-infected individuals only decreases slightly.

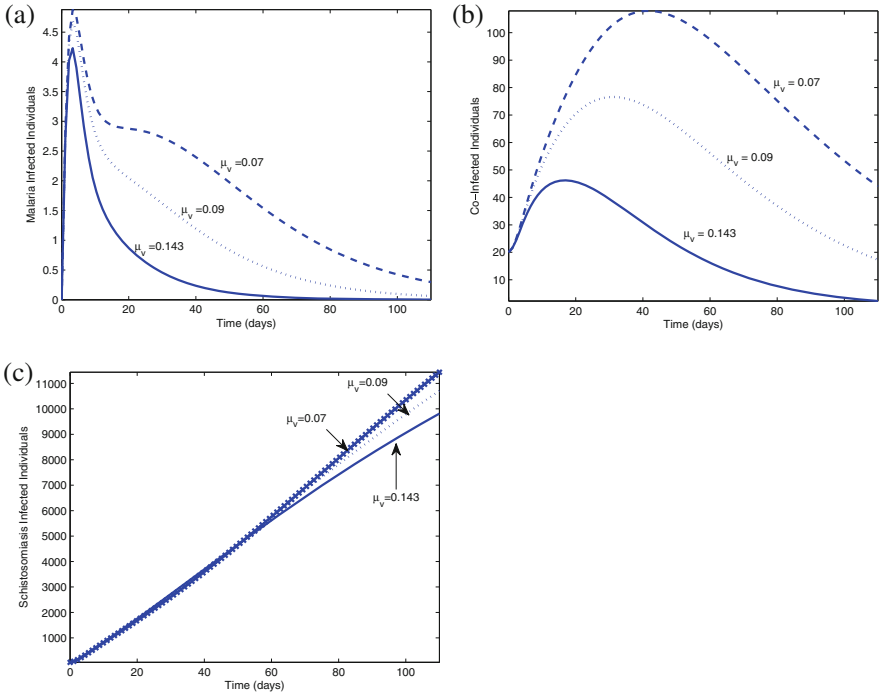

Fig. 2 Simulations of the malaria–schistosomiasis model showing the effect of varying the mosquito death rate

5 Concluding Remarks

In this paper, we formulated and analysed a deterministic model for the transmission of malaria–schistosomiasis co-infection. We derived basic reproduction numbers for each infection and determined the sensitivity of each reproduction number to all parameters. Our analysis shows that malaria infection may be associated with an increased rate of schistosomiasis infection. However, in our model, schistosomiasis infection is not associated with an increased rate of malaria infection. Therefore, whenever there is co-infection of malaria and schistosomiasis in the community, our model suggests that control measures for both diseases should be administered concurrently for effective control.

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