Mathematical Analysis of a Chlamydia model with Nonlinear Incidence and Recovery Rates

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Abstract.

Chlamydia, one of the commonest sexually transmitted infections (STIs), remain a public health concern in both underdeveloped and developed countries of the world. Chlamydia has caused worrying public health consequences hence much research work is needed to check the spread of the disease in the population. In this paper, a mathematical model for Chlamydia is developed and analyzed with nonlinear incidence and recovery rates. Qualitative analysis of the model shows that the disease-free equilibrium is locally asymptotically stable using the method of linearization. Further, using the comparison theorem method, the disease-free equilibrium is found to be globally asymptotically stable whenever the associated reproduction number is less than unity. Furthermore, mathematical analysis of the reproduction number shows that the intervention levels and the maximum per capita recovery rate due to effective treatment has a significant impact in reducing the burden of Chlamydia in the population. Numerical results show a relationship between the transmission rate, intervention levels, maximum per capita recovery rate and the reproduction number. Sensitivity analysis was conducted on the parameters connected to the reproduction number, R_c and results reveal that the top parameters that significantly drive the dynamics of Chlamydia in the population are the transmission rate, intervention levels and the maximum per capita recovery rate. These parameters need to be checked by healthcare policy makers if the disease must be controlled in the population.

Keywords: Chlamydia, sensitivity analysis, mathematical analysis, nonlinear incidence and recovery rates.

1. INTRODUCTION

Chlamydia, one of the commonest sexually transmitted infections (STIs) is largely transmitted through vaginal, oral and anal sex. It is a preventable and curable STIs caused by the bacterium *Chlamydia trachomatis* (Centers for Disease Control and Prevention (CDC), 2023, World Health Organization (WHO), 2023, Cleveland Clinic, 2023). In 2020, an estimated 128.5 million new infections associated with Chlamydia was reported worldwide amongst adults between 15 to 49 years of age and their prevalence globally was estimated to be 4.0 percent for women and 2.5 percent for men (WHO, 2023). Further, reports from Statista show that in 2020 about 25.5 million people in Africa had Chlamydia. The prevalence rate was higher amongst females with about 14.7 million people infected while 10.8 million males were infected with the disease (Statista, 2023).

In Chlamydia infection, about 80 percent of infected people have no symptoms (WHO, 2023). If symptoms occur, they may not appear for about three weeks after having sex with someone who is infected with Chlamydia. In women, common symptoms include: a change in vaginal discharge, bleeding between menstrual period or after sex, itching or burning in and around the vagina, pain or discomfort in the lower abdomen, burning sensation when urinating while in men, common symptoms include: burning sensation when urinating, discharge from the penis and pain or discomfort in the testicles. Also, anal infection in women and men can equally cause pain, discharge and bleeding (CDC, 2023, WHO, 2023, Cleveland Clinic, 2023).

This bilinear incidence rate does not consider the influence of intervention levels. Also, most mathematical models often use a parameter to represent the rate of recovery after a successful treatment regime, see for example, Iboi and Okuonghae (2016) and Ashezua *et al*. (2023). This parameter cannot be interpreted to mean minimum and maximum per capita recovery rates.

Several authors have developed and analyzed mathematical models on the transmission dynamics of Chlamydia trachomatis without considering the type of nonlinear Monod type incidence and recovery rates as used in the work of Alshammari and Khan, (2021), see for example, Martin *et al.,* (1996), Mirjam *et al*. (1996), Wilson (2006), Sharomi and Gumel (2011) and Samanta and Sharma (2014). In this study, the use of the nonlinear Monod type incidence and recovery rates as used by Alshammari and Khan (2021) is adopted. The principal aim of using this type of nonlinear incidence and recovery rates is mainly to determine mathematically the impact of the intervention levels (d) and the maximum recovery rate (c_1) which are embedded in them.

The present study complements the aforementioned research works, particularly the one by Ashezua *et al.* (2023) by developing and analyzing an equivalent mathematical model for Chlamydia trachomatis transmission dynamics by including nonlinear incidence and recovery rates as used by Alshammari and Khan (2021).

The rest of the paper is organized as follows. The model is developed in Section 2 and analyzed in Section 3. Sensitivity analysis is presented in Sections 4 while the concluding remarks in Section 5

2. MODEL FORMULATION

The total sexually active population at time t, denoted by $N(t)$ is divided into the mutually exclusive compartments of the susceptible individuals $(S(t))$, exposed individuals $(E(t))$, asymptomatic individuals $(I_a(t))$, symptomatic individuals $(I_s(t))$ and recovered individuals $(R(t))$. Let Λ represent the recruitment rate of newborns and sexually active individuals (assumed susceptible) into the population. Further, it is assumed that β_1 is the rate of transmission of chlamydia infection from infectives in the asymptomatic stage to the susceptible and β_2 is the rate of transmission of chlamydia infection from infectives in the symptomatic stage to the susceptibles. The parameter μ is the natural death rate associated to all the epidemiological

classes. Let $\rho\eta$ be the proportion of exposed individuals who are asymptomatic while $(1-\rho)\eta$ is the proportion of exposed individuals who are symptomatic. Let η be the progression rate of individuals in the exposed class to the asymptomatic and symptomatic stages of infection, respectively.

The term κm accounts for the rate at which individuals in class I_a recover naturally and progress to class R while the term $(1-\kappa)m$ is the proportion of individuals in class I_a who progress to class I_s. Individuals in class I_s recover at a rate $c(\alpha, I_s)$ as represented by equation (3). In equation (3), the parameters c_0 and c_1 $(0 < c_0 < c_1)$ represent the minimum and maximum per capita recovery rates due to sufficiency of the health care resources and the number of infected sub-population. The parameter α represents the impact of the number of hospital beds on the transmission dynamics of Chlamydia trachomatis. Also, recovered individuals become susceptible to Chlamydia infection again at a rate ψ.

Putting together these definitions and assumptions, it follows that the model for the transmission dynamics of chlamydia trachomatis in a sexually active population is given by the following system of non-linear ordinary differential equations (the schematic diagram of model (1) is shown in Figure 1, and the state variables and parameters of the model are presented in Table 1):

$$\begin{aligned}
\frac{dtS(t)}{dt} &= \Lambda - \lambda S - \mu S + \psi R,\\
\frac{dE(t)}{dt} &= \lambda S - [\rho\eta + (1-\rho)\eta + \mu]E,\\
\frac{dI_a}{dt} &= \rho\eta E - [\kappa m + (1-\kappa)m + \mu]I_a,\\
\frac{dI_s(t)}{dt} &= (1-\rho)\eta E + (1-k)mI_a - c(a, I_s)I_s - \mu I_s,\\
\frac{dR(t)}{dt} &= c(a, I_s)I_s + kmI_a - (\mu + \psi)R.
\end{aligned} \tag{1}$$

where,

$$\lambda = \frac{(\beta_1 I_a + \beta_2 I_s)}{d + (I_a + I_a)} \tag{2}$$

and

$$c(a, I_s) = \left[c_0 + \frac{(c_1 - c_0)\alpha}{(a + I_s)}\right] \tag{3}$$

The total population size is given by

$$N = S + E + I_a + I_s + R. \tag{4}$$

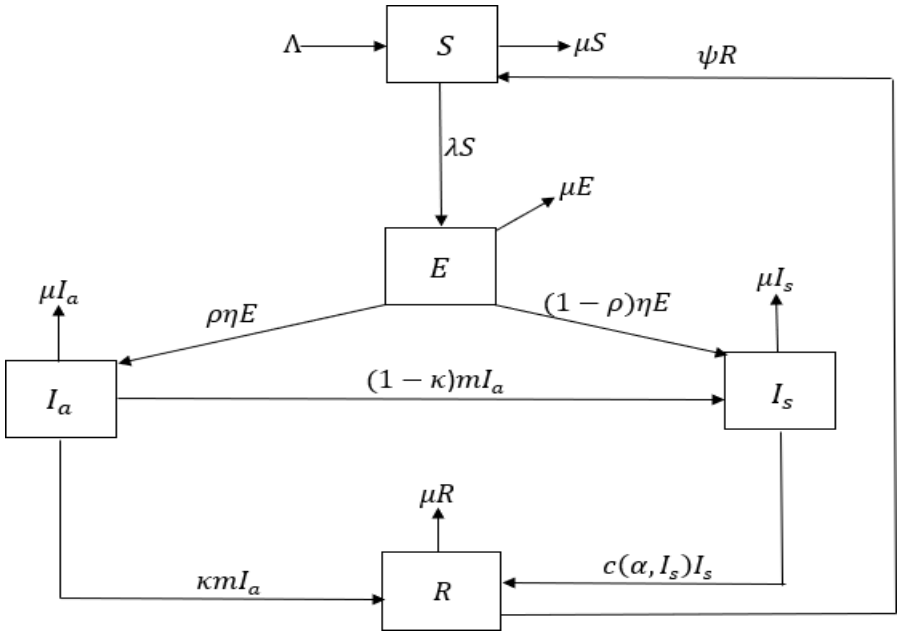

Figure 1: Schematic diagram for model (1)

2.1 Basic properties

For model (1) to be epidemiologically meaningful, it is vital to show that all its state variables are non-negative for all time, *t*. In order words, the solutions of model (1) with positive initial data will remain positive for all $t \geq 0$.

Table 2.1: Interpretation of state variables/parameters in the chlamydia model (1).

Variables/parameters	Interpretation
S	Susceptible individuals
E	Exposed individuals
I_a	Asymptomatic individuals
I_s	Symptomatic individuals
R	Recovered individuals
Λ	Recruitment rate
β_1	The transmission rate from I_a to S
β_2	The transmission rate from I_s to S
μ	Natural death rate
$\rho\eta$	Proportion of exposed individuals who are asymptomatic
$(1-\rho)\eta$	Proportion of exposed individuals who are symptomatic
ψ	The rate at which recovered individuals become susceptible
η, m	Progression rates
km	Accounts for the proportion of the asymptomatic individuals who

	recover and moved to R
$(1 - km)$	Accounts for the proportion of the asymptomatic individuals who progress to the $I_s$stage of infection
λ	Force of infection
d	Intervention levels
α	Impact of the number of hospital beds on the transmission of chlamydia
$c_o(c_1)$	Minimum and maximum per capita recovery rates

2.1.1 Positivity and boundedness of solution.

Since the model (1) monitors the human population, the state variables and parameters of the model are non-negative. Consider the biologically feasible region.

$$\Phi = \{(S, E, I\ , I\ , R)\} \in \mathbb{R}_+^5 : N \leq \frac{\Lambda}{\mu} \tag{5}$$

It can be shown that the set Φ is a positively invariant set and a global attractor of this system. This implies that, any phase trajectory initiated anywhere in the non-negative region $R^5$of the phase space will eventually enter the region Φ and remains in Φ thereafter.

Lemma 2.1. *The region Φ is positively invariant for model (1).*

Proof. The rate of change of the total population with time is given by

$$\frac{dN}{dt} = \Lambda - \mu N. \tag{6}$$

Since the right-hand side of (5) is bounded by $\Lambda - \mu N$, we can show using a standard comparison theorem (Lakshmikantham *et al*. 1989) that

$$N\ (t) \leq\ N\ (0) exp^{-\mu t} + \frac{\Lambda}{\mu}(1 - exp^{-\mu t}) \tag{7}$$

In particular, if $N(0) \leq \frac{\Lambda}{\mu}$ then $N\ (t)\ \leq \frac{\Lambda}{\mu}$. Therefore, Φ is positively invariant.

3 Mathematical analysis

3.1 Asymptotic stability of disease-free equilibrium (DFE)

The DFE of the model (1) is given by $E_1 = (\mathrm{S}^*, \mathrm{E}^*, \mathrm{I}_\mathrm{a}^*, \mathrm{I}_\mathrm{s}^*, \mathrm{R}^*) = \left(\frac{\Lambda}{\mu}, 0,0,0,0\right)$

The reproduction number of model (1) will be obtained using the next generation operator method. The notations as used in (van den Driessche and Watmough, 2002) is adopted, the non-negative

matrix, F, of new infection terms and the M -matrix, V, of transition terms associated with model (1) are

$$F = \begin{pmatrix} 0 & \frac{\beta_1 \Lambda}{\mu d} & \frac{\beta_2 \Lambda}{\mu d} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \text{ and } V = \begin{pmatrix} k_1 & 0 & 0 \\ -\rho\eta & k_2 & 0 \\ -k_3 & -k_4 & (c_1 + \mu) \end{pmatrix}$$

where,

$$k_1 = [\rho\eta + (1-\rho)\eta + \mu], k_2 = [\kappa m + (1-\kappa)m + \mu], k_3 = (1-\rho)m \\ k_4 = (1-\kappa)m\,. \tag{8}$$

It follows that the reproduction number of the model (1), denoted by R_c, is given by

$$R_c = \rho(FV^{-1}) = \frac{\beta_1 \Lambda \rho \eta}{\mu d k_1 k_2} + \frac{\beta_2 \Lambda \rho \eta k_4 + k_2 k_3}{\mu d k_1 k_2 (c_1 + \mu)} \tag{9}$$

With $R_c^1 = \frac{\beta_1 \Lambda \rho \eta}{\mu d k_1 k_2}, R_c^2 = \frac{\beta_2 \Lambda \rho \eta k_4 + k_2 k_3}{\mu d k_1 k_2 (c_1 + \mu)}$ *and* $R_c^3 = \frac{\beta_2 \Lambda k_3}{\mu d k_1 (c_1 + \mu)}$, *where* $\rho(FV^{-1})$, *where* $\rho(FV^{-1})$ is the spectral radius of the matrix(FV^{-1}).

The local stability of E_1 is obtained using the Heffernan *et al.* (2005) method as used in the work of Akinwande *et al.* (2022). It is proved in the following theorem.

Theorem 3.1. *The disease-free equilibrium, E_1 of the system (1) is locally asymptotically stable if $R_c < 1$ and unstable if $R_c > 1$.*

Proof. The stability of E_1 is proved from the roots of the characteristics polynomial which states that the equilibrium is stable if the roots of the characteristics polynomial are all real and negative. Thus, the Jacobian matrix of the system (1) at E_1 is given by

$$J = \begin{pmatrix} \mu & 0 & -\frac{\beta_1 \Lambda}{\mu d} & -\frac{\Lambda \beta_2}{\mu d} & \psi \\ 0 & -k_1 & \frac{\Lambda \beta_1}{\mu d} & \frac{\Lambda \beta_2}{\mu d} & 0 \\ 0 & \rho\eta & -k_2 & 0 & 0 \\ 0 & k_3 & k_4 & -c_1 & 0 \\ 0 & 0 & km & c_1 & -k_5 \end{pmatrix}$$

where,

$$k_1 = [\rho\eta + (1-\rho)\eta + \mu], k_2 = [\kappa m + (1-\kappa)m + \mu], \\ k_3 = (1-\rho)m, k_4 = (1-\kappa)m, k_5 = (\mu + \psi). \tag{10}$$

The characteristics polynomial is given by

$$(-\mu - \lambda)(k_5 + \lambda)[M_3\lambda^3 + M_2\lambda^2 + M_1\lambda + M_0] = 0, \tag{11}$$

with,

$$\begin{aligned} M_3 &= \mu d, \\ M_2 &= \mu d(c_1 + k_1 + k_2), \\ M_1 &= \mu d[k_2(c_1 + k_1) + c_1 k_1[1 - c_1 k_2 R_c^1 - c_1(c_1 + \mu)]R_c^3], \\ M_0 &= \mu d c_1 k_1 k_2[1 - R_c^1 - c_1(c_1 + \mu)(R_c^2 + R_c^3)]. \end{aligned} \tag{12}$$

It is observed from (11) that $\lambda_1 = -\mu \; and \; \lambda_2 = -k_5$. Now, according to Heffernan *et al*. (2005), if M_3, M_2, M_1, M_0 are all positive, then the roots of equation (11) have negative real parts whenever $R_C < 1$. Therefore, the disease-free equilibrium, E_1 is locally asymptotically stable since $M_i > 0, i = 0,1,2,3$ when $R_C < 1$. However, if $R_C > 1, M_0 < 0$. The implication is that positive real parts exist and hence E_1 is unstable if $R_c > 1$.

To establish the global stability of the Chlamydia-free equilibrium, the following results is proved.

Theorem 3.2. *The DFE of model (1) is globally asymptotically stable in* Φ *whenever* $R_C \leq 1$.

Proof. Note here that the equations for the infected classes of the model (1) are written in the matrix-vector form as follows:

$$\frac{dY(t)}{dt} = \left[(F - V) - \left(1 - \frac{S}{N}\right)W\right]Y(t) \tag{13}$$

where $Y(t) = [E(t), I_a(t), I_s(t), R(t)]^T$ and the matrices F and V are given in Section 3. Furthermore,

$$W = \begin{pmatrix} 0 & \frac{\beta_1 \Lambda}{\mu d} & \frac{\beta_2 \Lambda}{\mu d} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

Since W is a nonnegative matrix and $S \leq N$ in Φ, it follows that

$$\frac{dY(t)}{dt} \leq [(F - V)]Y(t) \tag{14}$$

Using the fact that the eigenvalues of the matrix $F - V$ all have negative real parts (that is, $\rho(FV^{-1}) < 1$ if $(R_C < 1)$, it follows that the linearized differential inequality system (13) is stable whenever $R_C < 1$. Thus, by the comparison theorem (Lakshmikantham *et al*., (1989)),

$$\lim_{t \to \infty} E(t), \; I_a(t), \; I_s(t), R(t) = (0,0,0,0) \tag{15}$$

It can be shown by substituting the DFE (E_1) into (1) that, $S(t) \longrightarrow \frac{\Lambda}{\mu}$ as $t \longrightarrow \infty$. Hence,

$$\lim_{t \to \infty} S(t), E(t), I(t), I(t), R(t) = \left(\frac{\Lambda}{\mu}, 0,0,0,0\right) = E_1 \tag{16}$$

Thus, every solution to the equation of the model (1) and initial conditions Φ, approaches the DFE (E_1) as $t \to \infty$ whenever $R_C < 1$.

3.2 Analysis of the reproduction number, R_C

In this subsection, the threshold parameter, R_c is used to determine the impact of the maximum recovery rate (c_1), intervention levels (d) for the asymptomatic and symptomatic individuals on the control of Chlamydia infection in the population. It is obvious from (9) that

$$\lim_{t\longrightarrow\infty} R_c = 0,$$
$$\lim_{c_1\longrightarrow\infty} \frac{\beta_1\Lambda\rho\eta}{\mu d k_1 k_2} > 0, \tag{17}$$

Therefore, a Chlamydia control programme that results in high application of intervention levels and maximum per capita recovery rate due to sufficiency of healthcare resources can lead to an effective Chlamydia control in the population if the respective right-hand sides of (17) are less than one. From (17), it is observed that a near total elimination of Chlamydia appears achievable. In this situation, the strategy is to focus on an effective intervention plan(s) such as advising infected individuals (both asymptomatic and symptomatic) to religiously take their drugs, abstaining from unprotected sex while on treatment and susceptible individuals to properly use condoms if they must engage in any form of sexual activity. The aforementioned intervention plan(s) will certainly help in curtailing the spread of Chlamydia in the community.

Further, by computing the partial derivatives of R_C with respect to the intervention levels (d) and maximum per capita recovery rate (c_1) due to effective treatment clearly shows the impact of these parameters on the control of Chlamydia in the population. These yields

$$\frac{\partial R_c}{\partial \psi} = -\frac{\Lambda[\beta_1\rho\eta(c_1+\mu)+\beta_2(\rho\eta k_4 + k_2 k_3)]}{\mu d^2 k_1 k_2 (c_1+\mu)} < 0,$$
$$\frac{\partial R_c}{\partial c_1} = -\frac{\beta_2\Lambda(\rho\eta k_4 + k_2 k_3)}{\mu d k_1 k_2 (c_1+\mu)^2} < 0. \tag{18}$$

It is observed from (18) that the partial derivatives are less than zero. Thus, an effective application of the intervention strategies and maximum per capita recovery rate due to proper adherence to treatment plan will have a positive impact in reducing Chlamydia burden in the community.

4 Sensitivity Analysis

Sensitivity analysis is usually conducted on the parameters of the model connected to the reproduction number R_C using the parameter values in Table 4.1. The essence of this analysis is to determine the relative importance of each parameter in the model that contribute to the Chlamydia transmission. A method similar to the ones outlined in the work Ashezua *et al*. (2023) was utilized to obtain the sensitivity indices of all the parameters contained in the reproduction number using the formula in (19).

$$\Pi_q^{R_c} = \frac{\partial R_c}{\partial \psi} \times \frac{\psi}{R_c}. \tag{19}$$

where Ψ denotes model parameters contained in R_C. It is obtained from (19) the sensitivity indices of the parameters associated with the reproduction number as presented in Table 4.2. The parameters with positive sensitivity indices signify a high impact burden of Chlamydia in the population if their values keep increasing. In a similar manner, parameters in which their sensitivity indices are negative have a great effect in reducing Chlamydia burden in the population as their values increase while the others remain constant. Hence, as their values increase, the reproduction number decreases thus reducing the endemicity of the disease in the population.

Table 4.1: The parameter values of model (1)

Parameter	Nominal value ($year^{-1}$)	Reference
Λ	1000	Sharomi and Gumel, (2011)
β_1	0.1	Sharma and Samanta (2014)
β_2	0.15	Sharma and Samanta (2014)
μ	0.15	Sharma and Samanta (2014)
ψ	0.75	Ashezua *et al*. (2023)
ρ	0.70	Sharma and Samanta (2014)
η	0.50	Sharma and Samanta (2014)
κ	0.70	Sharma and Samanta (2014)
m	0.80	Sharma and Samanta (2014)
c_0	0.20	Alshammari and Khan (2021)
c_1	0.21	Alshammari and Khan (2021)
α	0.20	Alshammari and Khan (2021)

Table 4.2: Sensitivity indices of some parameter values

Parameter	Sensitivity indices
Λ	+1.0000
β_1	+0.2947
β_2	+0.7053
K	−0.6018
P	−0.4912
H	+0.2308
M	−0.1972
c_1	−0.4114
D	−1.0000

From the results of the sensitivity analysis presented in Table 4.2, some of the parameters with high negative indices are the intervention levels (d) and maximum per capita recovery rate due to effective treatment (c_1). These are the top parameters that significantly drive the dynamics of

Chlamydia in the population. Consequently, to control the spread of the disease, these top parameters must be effectively targetted by policy makers in the health sector so that the sensitivity indices of these parameters must be kept negative for an effective control of the disease in the community. This means that the advocacy for the use of condoms by susceptible individuals and proper treatment of infected individuals must be priotized if Chlamydia must be controlled in the population.

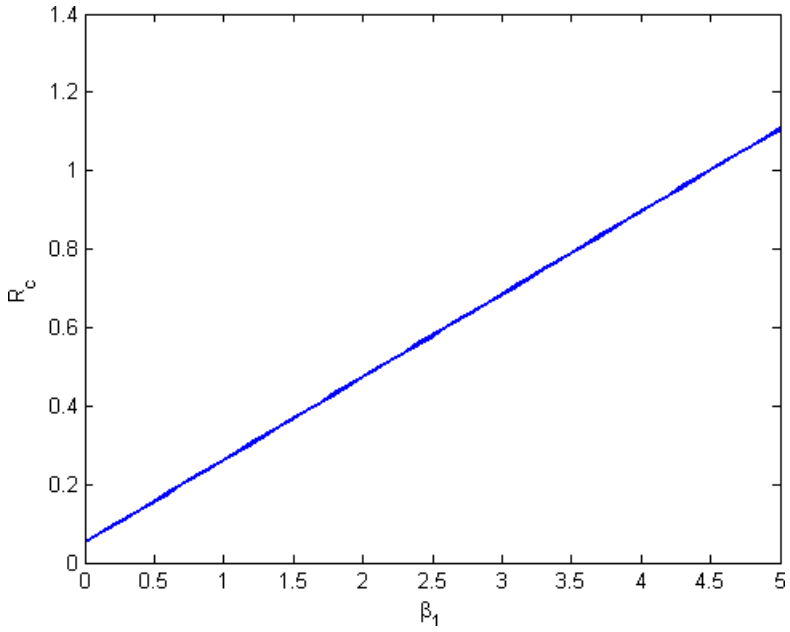

Figure 2: Plot of reproduction number, R_C as a function of progression rate, β_1. Parameter values used are as in Table 4.1.

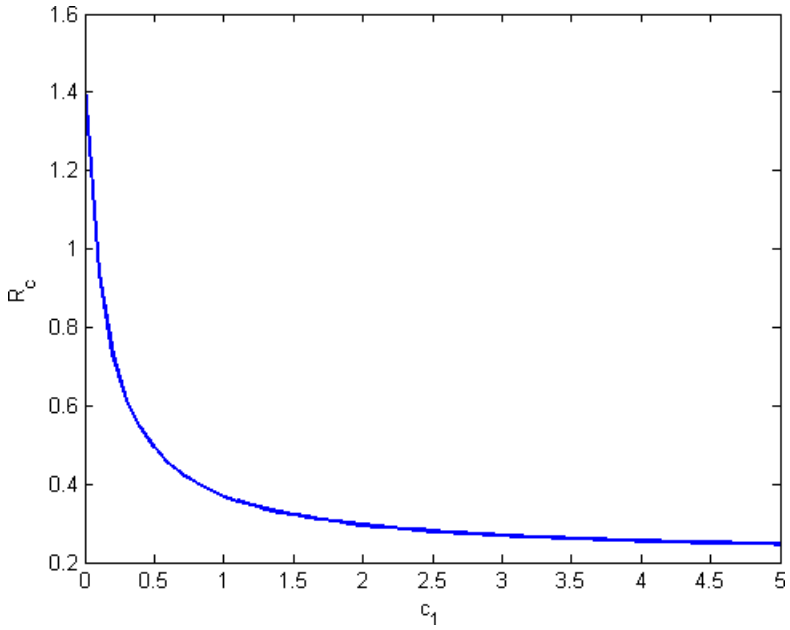

Figure 3: Plot of reproduction number, R_C as a function of progression rate, c_1. Parameter values used are as in Table 4.1.

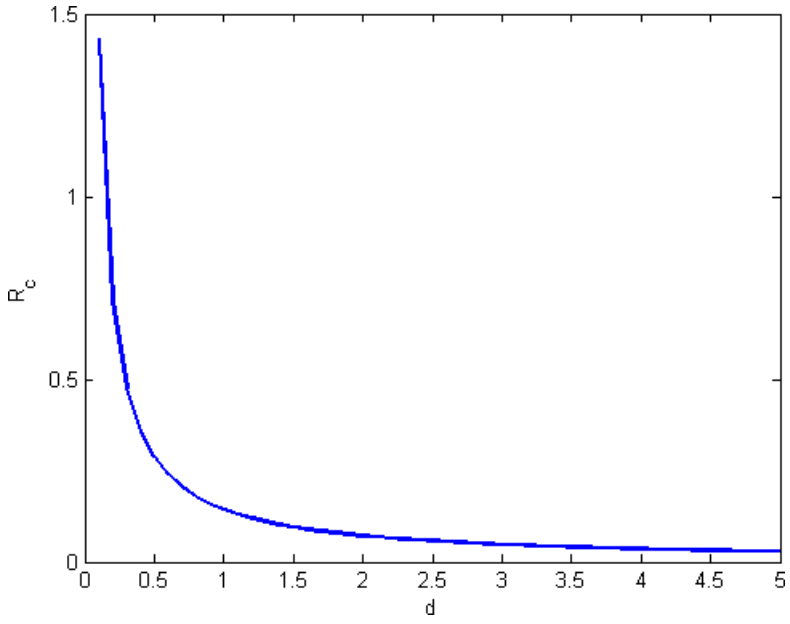

Figure 4: Plot of reproduction number, R_C as a function of progression rate, d. Parameter values used are as in Table 4.1.

5 Conclusion

In this paper, a deterministic mathematical model for gaining insights into the transmission dynamics of Chlamydia trachomatis in a population with nonlinear incidence and recovery rates is developed and analyzed. The aim of this study is to mathematically establish the impact of intervention levels and maximum per capita recovery rate due to effective treatment which are embedded in the nonlinear incidence and recovery rates, respectively. Qualitative analysis of the model shows that the disease-free equilibrium is locally asymptotically stable using the method of linearization. Further, using the comparison theorem method, the disease-free equilibrium was found to be globally asymptotically stable whenever the associated reproduction number is less or equal to unity. Furthermore, mathematical analysis of the reproduction number shows that the intervention levels and the maximum per capita recovery rate due to effective treatment has a significant impact in reducing the burden of Chlamydia in the population. This implies that susceptible individuals should be introduced to the available preventive measures e.g. abstaining from sex and the use of condoms correctly before engaging in any form of sexual activity. Also, effective treatment should be given to the infected individuals in order to control the spread of the disease in the population. Numerical results show a relationship between the transmission rate, intervention levels, maximum per capita recovery rate and the reproduction number. Sensitivity analysis was conducted on the parameters connected to the reproduction number, R_C and results reveal that the top parameters that significantly drive the dynamics of Chlamydia trachomatis in the population are the transmission rates, intervention levels and the maximum per capita recovery rate. These parameters need to be targetted by health policy makers if the disease must be controlled in the population. The present study can be further analyzed to establish the type of bifurcation the model exhibits and carry out cost-effectiveness analysis of the control strategies of Chlamydia trachomatis in the model.

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