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Analysis of a Cholera Model With Treatment Noncompliance

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Abstract

A model for transmission dynamics of cholera infection between human host and environment is developed. We incorporate proportion of infectious individuals who do not comply with treatment into the human population. Stability analysis as well as simulation of the model is done. The results from the stability analysis show that the disease-free equilibrium solution is locally asymptotically stable if $R_0 < 1$ while the endemic equilibrium solution is globally asymptotically stable when $R_0 > 1$. The technical tool used for our analysis is the theory of competitive systems, compound matrices and stability of periodic orbits. Finally, we investigate, numerically, the influence of seasonal variation on the control of cholera.

Keywords: Cholera transmission, reproduction number, compound matrices, global stability
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1. Introduction

Cholera is a highly infectious disease which is endemic in many parts of Africa and Asia. It enters into a person through drinking of contaminated water and drinks or consumption of food contaminated with V. Cholerae [22]. The last few years have witnessed many cholera outbreaks in developing countries. According to the World Health Organization report globally, it is estimated that each year, there are about 1.4 to 4.3 million cases of cholera with 28000 to 142000 deaths due to cholera epidemic [1]. Due to its huge impact on public health and social economic development, cholera has been the subject of extensive studies in clinical, experimental and theoretical fields. It

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remains an important global cause of morbidity and mortality capable of causing periodic epidemic disease [19].

Since 1979, several mathematical models for the transmission of cholera have been proposed: see, e.g. [4, 5, 15] and references cited therein. In [2], the authors proposed and analysed a mathematical model for cholera considering vaccination compartment without proportion of infectious individuals who do not comply to treatment. Their model was proved for the existence and uniqueness of disease-free and endemic equilibria. Finally, they concluded that the number of infected individuals would have been much lower, provided the vaccination campaign had begun earlier. In another development, [7] developed a mathematical model for the transmission of cholera under the impact of available medical resources. They conducted asymptotic stability analysis of disease-free and endemic equilibria. They fitted their simulation results to the epidemic data published by the World Health Organization and found that different levels of disease prevalence and severity were linked to different geographical regions in the country. However, they did not consider a case where some infectious individuals are given medication but do not comply to it as prescribed by their doctors.

Kamuhanda et al [11] formulated an epidemic model for the dynamics of cholera infections. An analysis on the existence of all the equilibrium points, the disease-free and endemic equilibrium points are conducted. They established conditions for stability of disease-free and endemic equilibrium points. They carried out sensitivity analysis of the model to know the most sensitive parameter to R_o. They also performed numerical simulations which revealed that as the number of infectious population increases, the number of susceptible humans decreases in the system. Also, [30] investigated a cholera model with vaccination of the susceptible population only without investigating proportion of infectious individuals who are already placed on treatment but do not comply (i.e. they do not complete dosage or stop treatment as soon as they think that they feel better). They proved the global asymptotic stability of disease-free equilibrium point by means of Lyapunov functions and LaSalle's invariance principle. In addition, they used Pontryagin's maximum principle to obtain the optimal control strategies to prevent and control the cholera infection. [21] extended an SIR model by incorporating a compartment $W(t)$ that measures pathogen concentration in water reservoir, which is an essential compartment to consider in the transmission dynamics of cholera infection. They determined the important features of the model and analysed for stability. Furthermore, they carried out optimal control analysis by incorporating vaccination, treatment and water purification. The model was validated using a cholera outbreak in Haiti.

Non-drug compliance on the part of infectious individuals poses a great threat to the control of cholera. In this work, we modify the model developed in [21] by incorporating the proportion of infectious individuals who do not comply with treatment into the human population. Our goal is to investigate the role of noncompliance to treatment in cholera transmission and its relationship with other parameters. To achieve this, we obtain the basic reproduction number, R_0, which is then used as a threshold to prove the local and global stabilities of the disease-free equilibrium as well as global stability of endemic equilibrium. Global stability of the disease-free equilibrium is established by constructing a suitable Lyapunov function while that of endemic equilibrium is established using the theory of competitive systems, compound matrices and stability of periodic orbits. As the disease-free equilibrium is locally and globally asymptotically stable when $R_0 < 1$, the condition $R_0 < 1$ is sufficient for cholera eradication. Model simulation shows that compliance to treatment is necessary but not sufficient for the eradication of cholera. Therefore, as means of intervention, we considered reduction in the shedding rate of V. cholera in addition to compliance to treatment. Lastly, we investigate, numerically, the influence of seasonal variation on the control of cholera.

The remaining part of this paper is organised as follows: In Section 2, a system of ordinary differential equations which models the disease dynamics is presented. Stability analysis is done in

Table 1: Summary of the parameters

Parameter	Meaning	Value	Reference
μ_h	Natural human death rate	[0.012, 0.033](year)$^{-1}$	[6]
α	Contact rate between bacteria and susceptible host	[1.05, 10.5](day)$^{-1}$	[3]
k	50% chance of catching v.cholerae	[10^3, 10^6](cells/ms)	[13]
ν	Loss of immunity rate	[0.001, 0.03](day)$^{-1}$	[12]
τ	Treatment rate	[0.07, 0.20](day)$^{-1}$	[20]
θ	Decay rate of vibrios	[0.02, 1.0](day)$^{-1}$	[6]
β	Natural recovery rate	[0.01] (day)$^{-1}$	Estimated
σ	Shedding rate of pathogen	[1,100] (cells/ml/day^{-1} person^{-1})	[22]
λ_h	Recruitment rate of susceptible host	0.1 (year)$^{-1}$	Assumed
ρ	Fraction of infectious host with treatment noncompliance	0.5	Assumed
δ	Cholera-induced death rate	0.015 (day)$^{-1}$	[26]

Section 3 while the results are discussed in Section 4. We gave the concluding remarks in Section 5.

2. Model Formulation

In this section, a model for the spread of cholera disease in human and vector population, is formulated. The total human population denoted by N_H, is partitioned into three classes namely; the susceptible individual S_H, the infectious individual I_H and the recovered individual R_H so that $N_H = S_H + I_H + R_H$. We denote B as the compartment that measures pathogen concentration in the environment [28].

2.1. Assumptions of the Model

The following assumptions were made in order to formulate the equations of the model:

(a) Direct person-to-person transmission is not considered because environment-to-person transmission has been shown to be the major route of waterborne disease transmission [25];
(b) Proportion of infectious individuals who do not comply to treatment get treated partially thereby increase the infectious population;
(c) The remaining proportion of infectious individuals who comply to treatment get treated fully and move to the recovered compartment;
(d) All new born individuals and immigration of individuals are susceptible to Cholera disease;
(e) The total human population is not constant.

Susceptible individuals are recruited at a rate λ_h. They acquire cholera through contact with pathogen concentration in the environment at a rate α. Proportion of individuals who do not comply to treatment increases the infectious population while proportion of infectious individuals who comply to treatment get treated fully and move to the recovered compartment. Infectious individuals shed pathogen into water at a rate σ and are treated at a rate τ. Natural human deaths occur at a rate μ_h.

Applying the assumptions, nomenclature of parameters and definitions of variables, the following system of ODEs is formulated:

$$\frac{dS_H}{dt} = \lambda_h N_H - \frac{\alpha S_H B}{B+K} + \nu R_H - \mu_h S_H, \tag{2.1}$$

$$\frac{dI_H}{dt} = \frac{\alpha S_H B}{B+K} + \rho\tau I_H - \tau I_H - \beta I_H - \delta I_H - \mu_h I_H, \tag{2.2}$$

$$\frac{dR_H}{dt} = (1-\rho)\tau I_H - \nu R_H + \beta I_H - \mu_h R_H, \tag{2.3}$$

$$\frac{dB}{dt} = \sigma I_H - \theta B. \tag{2.4}$$

with initial conditions

$$S_H(0) = S_H^0 > 0, \quad I_H(0) = I_H^0 \geq 0, \quad R_H(0) = R_H^0 \geq 0, \quad B(0) = B^0 \geq 0,$$

where the model parameters are non negative.

For simplicity of analysis, we use fraction of population instead of population number. This is done by dividing each population class by the total population and hence, we have:

$$s_h = \frac{S_H}{N_H},\ i_h = \frac{I_H}{N_H},\ r_h = \frac{R_H}{N_H},\ b = \frac{B}{N_H},\ k = \frac{K}{N_H}.$$

With these, we obtain

$$\begin{aligned}
\frac{ds_h}{dt} &= \lambda_h(1-s_h) - \alpha s_h \frac{b}{b+k} + \nu r_h + \delta s_h i_h, && (2.5)\\
\frac{di_h}{dt} &= \alpha s_h \frac{b}{b+k} - (\tau + \delta + \beta + \lambda_h - \rho\tau) i_h + \delta i_h^2, && (2.6)\\
\frac{dr_h}{dt} &= \tau i_h - \rho\tau i_h - \nu r_h - \lambda_h r_h + \beta i_h + \delta i_h r_h, && (2.7)\\
\frac{db}{dt} &= \sigma i_h + \mu_h b - (\theta + \lambda_h) b + \delta i_h b. && (2.8)
\end{aligned}$$

To obtain (2.5), observe (by adding (2.1)−(2.3)) that

$$\frac{dN_H}{dt} = \lambda_h N_H - \mu_h N_H - \delta I_h.$$

Therefore

$$\begin{aligned}
\frac{ds_h}{dt} &= \frac{1}{N_H}\left[\frac{dS_H}{dt} - s_h \frac{dN_H}{dt}\right]\\
&= \frac{1}{N_H}\left[\lambda_h N_H - \frac{\alpha S_H B}{B+K} + \nu R_H - \mu_h S_H - s_h(\lambda_h N_H - \mu_h N_H - \delta I_H)\right]\\
&= \lambda_h(1-s_h) - \alpha s_h \frac{b}{b+k} + \nu r_h + \delta s_h i_h.
\end{aligned}$$

Equations (2.6)−(2.8) can be obtained similarly.

From the relation $s_h(t) + i_h(t) + r_h(t) = 1$, it implies that $r_h(t) = 1 - s_h(t) - i_h(t)$ which reduces to the following system of differential equations:

$$\begin{aligned}
\frac{ds_h}{dt} &= \lambda_h(1-s_h) - \alpha s_h \frac{b}{b+k} + \nu(1 - s_h - i_h) + \delta s_h i_h && (2.9)\\
\frac{di_h}{dt} &= \alpha s_h \frac{b}{b+k} + \rho\tau i_h - (\tau + \delta + \beta + \lambda_h) i_h + \delta i_h^2 && (2.10)\\
\frac{db}{dt} &= \sigma i_h + \mu_h b - (\theta + \lambda_h) b + \delta i_h b && (2.11)
\end{aligned}$$

For biological reasons, the model is analysed in the feasible region

$$T = \{(s_h, i_h, b) > \mathbf{0} : s_h + i_h \leq 1\},$$

that can be shown to be positively invariant with respect to the system (2.9)−(2.11). Thus, model is well posed mathematically and epidemiologically in $T < \infty$.

3. Stability Analysis

The equilibrium is obtained by setting the right hand side of (2.9)−(2.11) to zero and the system takes the form

$$\lambda_h(1-s_h^*)-\alpha s_h^*\frac{b^*}{b^*+k}+\nu(1-s_h^*-i_h^*)+\delta s_h^* i_h^*=0 \tag{3.1}$$

$$\alpha s_h^*\frac{b^*}{b^*+k}+\rho\tau i_h^*-(\tau+\delta+\beta+\lambda_h)i_h^*+\delta i_h^{*2}=0 \tag{3.2}$$

$$\sigma i_h^*+\mu_h b^*-(\theta+\lambda_h)b^*+\delta i_h^* b^*=0 \tag{3.3}$$

where $E_0=(s_h^*,i_h^*,b^*)=(1,0,0)$.

3.1. Local Stability of Disease-Free Equilibrium Solution

At the steady state of the model, the Jacobian matrix is given by

$$J_E=\begin{bmatrix} -(\lambda_h+\frac{\alpha b^*}{b^*+k}+\nu-\delta i_h^*) & -\nu+\delta s_h^* & \frac{-\alpha s_h^* k}{(b^*+k)^2} \\ \frac{\alpha b^*}{b^*+k} & -G_T+\rho\tau+2\delta i_h^* & \frac{\alpha s_h^* k}{(b^*+k)^2} \\ 0 & \sigma+\delta b^* & \mu_h-\theta-\lambda_h+\delta i_h^* \end{bmatrix} \tag{3.4}$$

where $G_T=\tau+\delta+\beta+\lambda_h$. Evaluating the Jacobian matrix in (3.4) at E_0 gives

$$J_{E_0}=\begin{bmatrix} -(\lambda_h+\nu) & -\nu+\delta & -\frac{\alpha}{k} \\ 0 & -G_T+\rho\tau & \frac{\alpha}{k} \\ 0 & \sigma & \mu_h-\theta-\lambda_h \end{bmatrix} \tag{3.5}$$

From (3.5), we have three eigenvalues. One being $-(\lambda_h+\nu)$. The other two are obtained from the sub-matrix

$$J_{E_0}=\begin{bmatrix} -(G_T-\rho\tau) & \frac{\alpha}{k} \\ \sigma & -(\theta+\lambda_h-\mu_h) \end{bmatrix} \tag{3.6}$$

whose

$$\text{trace}(J_{E_0})=-\left((G_T-\rho\tau)+(\theta+\lambda_h)-\mu_h\right)<0 \quad \text{and}$$

$$\det(J_{E_0})=1-\frac{\sigma\alpha}{k(G_T-\rho\tau)(\theta+\lambda_h-\mu_h)}=1-R_0>0 \text{ if } R_0<1.$$

Defining $R_0=\dfrac{\sigma\alpha}{k(G_T-\rho\tau)(\theta+\lambda_h-\mu_h)}$, then, E_0 is locally asymptotically stable if and only if $R_0<1$, and we have thus established the following Lemma:

Lemma 3.1. *The disease-free equilibrium E_0 is locally stable if $R_0<1$ and unstable if $R_0>1$.*

3.2. Global Stability of Disease-Free Equilibrium Solution

The following result investigates the global behaviour of the model as its solution trajectory approaches the disease-free equilibrium solution.

Theorem 3.2. *The disease-free equilibrium E_0 is globally asymptotically stable if $\delta=0$, $R_0<1$ and unstable if $R_0>1$.*

Proof . Consider the Lyapunov function

$$V = s_h - 1 - \ln s_h + R_0 i_h + \frac{\alpha}{k(\theta + \lambda_h - \mu_h)} b.$$

Its time derivative is

$$\begin{aligned}
\dot{V} &= \left(1 - \frac{1}{s_h}\right)\frac{ds_h}{dt} + R_0\frac{di_h}{dt} + \frac{\alpha}{k(\theta + \lambda_h - \mu_h)}\frac{db}{dt} \\
&= \left(1 - \frac{1}{s_h}\right)\left(\lambda_h(1 - s_h) - \alpha s_h \frac{b}{b+k} + \nu(1 - s_h - i_h)\right) \\
&\quad + R_0\left(\alpha s_h \frac{b}{b+k} + \rho\tau i_h - (\tau + \beta + \lambda_h) i_h\right) \\
&\quad + \frac{\alpha}{k(\theta + \lambda_h - \mu_h)}\left(\sigma i_h + \mu_h b - (\theta + \lambda_h) b\right) \\
&= (R_0 - 1)\alpha s_h \frac{b}{b+k} + \lambda_h(1 - s_h)\left(1 - \frac{1}{s_h}\right) - \alpha b\left(\frac{1}{k} - \frac{1}{b+k}\right) \\
&\quad + \nu\left(1 - \frac{1}{s_h}\right)(1 - s_h - i_h).
\end{aligned}$$

Since $0 < s_h \leq 1$, $\left(1 - \frac{1}{s_h}\right) \leq 0$. Therefore

$$\dot{V} < 0 \qquad \text{whenever} \quad R_0 < 1.$$

By Lyapunov-Lasalle's Theorem [14], the disease-free equilibrium point is globally asymptotically stable in Γ if $R_0 < 1$. It implies that $(s_h, i_h, b) \to (1, 0, 0)$ as $t \to \infty$. . □

Remark 3.3. *The global stability of the DFE was proved in Theorem 3.2 with the assumption that $\delta = 0$, however, the result still holds if $\delta > 0$. This is because $\delta i_h^2 \leq \delta i_h$ in* (2.10) *leading to a decrease in infectious human population.*

3.3. Existence of Endemic Equilibrium Point

We shall show the interval where the endemic equilibrium exists using the idea of Tumwiine et al.[27]. Hence, for the existence and uniqueness of endemic equilibrium $E_1 = (s_h^*, i_h^*, b^*)$, its coordinates should satisfy the conditions $s_h^* > 0, i_h^* > 0, b^* > 0$. Adding (3.1)−(3.3), we have

$$\lambda_h(1 - s_h^* - i_h^*) + \nu(1 - s_h^* - i_h^*) - \delta i_h^*(1 - s_h^* - i_h^*) + \sigma i_h^* + \mu_h b^* - \theta b^* - \lambda_h b^* + \delta i_h^* b^* + \rho\tau i_h^* - \tau i_h^* - \beta i_h^* = 0$$

From (3.3), $\sigma i_h^* + \mu_h b^* - (\theta + \lambda_h) b^* + \delta i_h^* b^* = 0$
This yields

$$(\lambda_h + \nu - \delta i_h^*)(1 - s_h^* - i_h^*) = (\tau - \rho\tau) i_h^*.$$

Since $(1 - s_h^* - i_h^*) > 0$ and $(\tau - \rho\tau + \beta) i_h^* > 0$, then

$$\lambda_h + \nu - \delta i_h^* > 0 \tag{3.7}$$

Further simplification gives

$$i_h^* < \frac{\lambda_h + \nu}{\delta}.$$

Therefore, an endemic equilibrium point exists, where i_h^* lies in the interval $\left(0, \min\left\{1, \frac{\lambda_h+\nu}{\delta}\right\}\right)$. If $\delta < \lambda_h + \nu$, the interval becomes large and this means that cholera disease persists in the population.

In order to study the global stability of unique endemic equilibrium, we apply the noble approach of convergence of trajectories within an invariant manifold in R^n found in [16, 18]. The Jacobian matrix of (2.9)−(2.11) is given as

$$J_E = \begin{bmatrix} -(\lambda_h + \frac{\alpha b^*}{b^*+k} + \nu - \delta i_h^*) & -\nu + \delta s_h^* & \frac{-\alpha s_h^* k}{(b^*+k)^2} \\ \frac{\alpha b^*}{b^*+k} & -G_T + \rho\tau + 2\delta i_h^* & \frac{\alpha s_h^* k}{(b^*+k)^2} \\ 0 & \sigma + \delta b^* & \mu_h - \theta - \lambda_h + \delta i_h^* \end{bmatrix}. \tag{3.8}$$

From [18], the second additive compound matrix for a 3 by 3 system is defined as

$$\begin{bmatrix} a_{11} + a_{22} & a_{23} & -a_{13} \\ a_{32} & a_{11} + a_{33} & a_{12} \\ -a_{31} & a_{21} & a_{22} + a_{33} \end{bmatrix}$$

From the Jacobian matrix J_E, the second additive compound matrix is given by

$$J_E^{[2]} = \begin{bmatrix} -(E - 3\delta i_h^*) & \frac{\alpha s_h^* k}{(b+k)^2} & \frac{\alpha s_h^* k}{(b+k)^2} \\ \sigma + \delta b^* & -(F - 2\delta i_h^*) & -\nu + \delta s_h^* \\ 0 & \alpha\frac{\alpha b^*}{b^*+k} & -(H - 3\delta i_h^*) \end{bmatrix} \tag{3.9}$$

where

$$\begin{aligned} E &= \lambda_h + \frac{\alpha b^*}{b^*+k} + \nu + G_T - \rho\tau \\ F &= 2\lambda_h + \frac{\alpha b^*}{b^*+k} + \nu + \theta - \mu_h \\ H &= G_T + \theta + \lambda_h - \rho\tau - \mu_h \\ G_T &= \tau + \lambda_h + \delta + \beta \end{aligned}$$

3.4. Global Stability of Endemic Equilibrium E_1

We need to establish the global stability of the unique endemic equilibrium point of the disease when it persists using the idea of [27]. Since (2.9)−(2.11) is a 3-dimensional asymptotical autonomous differential system, we use the property of competitive systems [23, 24, 10]) and additive compound matrices and differential equations[18] for the analysis.

We begin by giving the definition of a competitive system. Let $x \mapsto f(x)$ be a smooth vector field defined for x in an open set $D \subset R^n$. The differential equation

$$x' = f(x), \quad x \in D$$

is said to be competitive in D, if for some diagonal matrix $H = diag(\epsilon_1, \epsilon_2, ..., \epsilon_n)$ where each ϵ_i is either 1 or -1, $H(\frac{\partial f}{\partial x})H$ has non-positive off-diagonal elements for all $x \in D$. If D is convex, the flow of a competitive system (2.9)−(2.11) preserves, for $t < 0$, the partial ordering in R^n defined by the orthant $K = (x_1, ..., x_n) \in R^n : \epsilon_i x_i \geq 0$.

We choose the matrix H as

$$H = \begin{bmatrix} 1 & 0 & 0 \\ 0 & -1 & 0 \\ 0 & 0 & 1 \end{bmatrix}.$$

Then from the matrix H and the Jacobian given in (3.8), we get

$$H(J_E)H = \begin{bmatrix} -(\lambda_h + \frac{\alpha b^*}{b^*+k} + \nu - \delta i_h^*) & \nu - \delta s_h^* & -\frac{\alpha s_h^* k}{(b+k)^2} \\ -\frac{\alpha b^*}{b^*+k} & -G_T + 2\delta i_h^* & \frac{\alpha s_h^* k}{(b+k)^2} \\ 0 & -\sigma - \delta b^* & -\mu_h - \theta - \lambda_h + \delta i_h^* \end{bmatrix} \tag{3.10}$$

It is observed that the system is competitive in T with respect to the partial ordering defined by the orthant

$$K = (s_h^*, i_h^*, B^*) \in R^3 : s_h^* \geq 0, i_h^* \leq 0, B^* \geq 0.$$

This property is satisfied if the conditions $\delta < \lambda_h + \nu, \nu < \beta + \delta$ hold.

Let $p(t)$ with minimal period u and orbit $T = P(t) : 0 \leq t \leq u$ be the periodic solution of competitive system. The following definitions [8] are used to establish the stability of the orbit.

Definition 3.4. *The orbit T is orbitally stable if and only if for each $\epsilon > 0$, there exists a δ such that any solution $\tilde{x}$, for which the distance of $\tilde{x}(0)$ from T is less than δ, remains a distance less than ϵ from T, for all $t \geq 0$.*

Definition 3.5. *The orbit T is asymptotically orbitally stable, if it orbitally stable and the distance of $\tilde{x}(t)$ from T also tends to zero as $t \to \infty$.*

Since (2.9)−(2.11) is a 3-dimensional competitive system that is convex in D, the following theorem stated and proved in [17] for a system of an SEIR model, is used to generalize results of systems that are competitive, persistent and have the property of stability of periodic orbits.

Theorem 3.6. *For $n = 3$ and D convex and bounded and suppose that (2.9)−(2.11) is competitive, permanent and have the property of stability of periodic orbits. If $\tilde{x}_0$ is the only equilibrium point in intD, and if it is locally asymptotically stable, then it is globally asymptotically stable in intD.*

Proof . According to [18], the asymptotic orbital stability of a periodic orbit of a general autonomous system, it is sufficient to prove that the linear non-autonomous system

$$u'(t) = (J_E^{[1]}(p(t)))u(t)$$

is asymptotically stable, where $J_E^{[1]}$ is the second additive compound matrix of the Jacobian matrix J_E. From the second additive compound matrix in (3.9) given by

$$J_E^{[2]} = \begin{bmatrix} -(E - 3\delta i_h) & \frac{\alpha s_h k}{(b+k)^2} & \frac{\alpha s_h k}{(b+k)^2} \\ \sigma + \delta b & -(F - 2\delta i_h) & -\nu + \delta s_h \\ 0 & \alpha\frac{\alpha b}{b+k} & -(H - 3\delta i_h) \end{bmatrix},$$

we have a linear system with respect to the solutions (s_h, i_h, b) written as

$$\begin{aligned} u_1'(t) &= -(E - 3\delta i_h(t))u_1(t) + (\frac{\alpha s_h k}{(b+k)^2})u_2(t) + (\frac{\alpha s_h k}{(b+k)^2})u_3(t), \\ u_2'(t) &= (\sigma + \delta b)u_1(t) - (F - 2\delta i_h(t))u_2(t) + (\delta s_h(t) - \nu)u_3(t), \\ u_3'(t) &= (\frac{\alpha b}{b+k})u_2(t) - (H - 2\delta i_h(t))u_3(t). \end{aligned}$$

In order to prove that the system (2.9)−(2.11) is asymptotically stable, we shall use the following Lyapunov function that is positive but not differentiable everywhere:

$$V(u_1(t), u_2(t), u_3(t); s_h(t), i_h(t), b(t)) = sup\{|u_1|, \frac{i_h(t)}{b(t)}(|u_2| + |u_3|)\}.$$

Denoting the left-hand side derivative of $V(t)$ by $D_+V(t)$, we get the following inequalities:

$$\begin{aligned} D_+(|u_1(t)|) &\leq -(E - 3\delta i_h(t))|u_1(t)| + (\frac{\alpha s_h k}{(b+k)^2})(|u_2(t)| + |u_3(t)) \\ &\leq -(E - 3\delta i_h(t))|u_1(t)| + \frac{\frac{\alpha s_h k}{(b+k)^2} b(b+k)}{i_h(t)} \left(\frac{k i_h(t)}{kb(b+k)}|u_2(t)| + |u_3(t)|\right), \end{aligned} \quad (3.11)$$

$$D_+(|u_2(t)|) \leq (\sigma + \delta b)|u_1(t)| - (F - 2\delta i_h(t))|u_2(t)| + (\delta s_h(t) - \nu)|u_3(t)|, \quad (3.12)$$

and

$$D_+(|u_3(t)|) \leq \left(\frac{\alpha b}{b+k}\right)|u_2(t)| - (H - 2\delta i_h(t))|u_3(t)|. \quad (3.13)$$

We also have

$$\begin{aligned} D_+\frac{i_h(t)}{b(t)}(|u_2(t)| + |u_3(t)|) &= \left[\frac{i_h'(t)}{i_h(t)} - \frac{b'(t)}{b(t)}\right]\frac{i_h(t)}{b(t)}(|u_2(t)| + |u_3(t)|) \\ &\quad + \frac{i_h(t)}{b(t)} D_+(|u_2(t)| + |u_3(t)|). \end{aligned} \quad (3.14)$$

Adding (3.12) and (3.13), we have

$$\begin{aligned} D_+(|u_3(t)| + |u_4(t)|) &= (\sigma + \delta b)|u_1(t)| - (F - \alpha bb + k - 2\delta i_h(t))|u_2(t)| \\ &\quad + (\delta s_h(t) - \nu + 2\delta i_h(t) - H)|u_3(t)|, \\ &= (\sigma + \delta b)|u_1(t)| - (2\lambda_h + \nu + \theta - 2\delta i_h(t))|u_2(t)| \\ &\quad - [2\lambda_h + \nu + \theta - 2\delta i_h(t) + \delta i_h(t) + \tau + \beta - \rho\tau - \mu_h \\ &\quad -\delta(-1 + s_h(t) + i_h(t))]\,|u_3(t)|, \\ &\leq (\sigma + \delta b)|u_1(t)| - (2\lambda_h + \nu + \theta - 2\delta i_h(t))(|u_2(t)| + |u_3(t)|). \end{aligned} \quad (3.15)$$

Substituting (3.15) into (3.14) yields

$$\begin{aligned} &D_+\frac{i_h(t)}{b(t)}(|u_2(t)| + |u_3(t)|) \\ &\leq \left[\frac{i_h'(t)}{i_h(t)} - \frac{b'(t)}{b(t)}\right]\frac{i_h(t)}{b(t)}(|u_2(t)| + |u_3(t)|) + \frac{i_h(t)}{b(t)}(|u_3(t)| + |u_2(t)|) \\ &\quad + \frac{i_h(t)}{b(t)}\left[(\sigma + \delta b)|u_1(t)| - (2\lambda_h + \nu + \theta - 2\delta i_h(t))(|u_2(t)| + |u_3(t)|)\right], \\ &\leq (\sigma + \delta b)\frac{i_h(t)}{b(t)}|u_1(t)| + \\ &\quad \left[\frac{i_h'(t)}{i_h(t)} - \frac{b'(t)}{b(t)} - 2\lambda_h - \nu - \theta + 2\delta i_h(t)\right]\frac{i_h(t)}{b(t)}(|u_2(t)| + |u_3(t)|). \end{aligned} \quad (3.16)$$

From (3.11) and (3.16), we have

$$D_+V(t) \leq \sup\{g_1(t), g_2(t)\}V(t),$$

in which

$$g_1(t) = -(E - 3\delta i_h(t))|u_1(t)| + \frac{\frac{\alpha s_h b}{b+k}}{i_h} \quad \text{and} \tag{3.17}$$

$$g_2(t) = (\sigma + \delta b)\frac{i_h(t)}{b(t)} + \left(\frac{i_h'(t)}{i_h(t)} - \frac{b'(t)}{b(t)} - 2\lambda_h - \nu - \theta + 2\delta i_h(t)\right). \tag{3.18}$$

Using the following expressions from (3.2) and (3.3) given by

$$\begin{aligned} \frac{\frac{\alpha s_h b}{b+k}}{i_h} &= \frac{i_h'(t)}{i_h(t)} + (\tau + \delta + \beta + \lambda_h) - \delta i_h - \rho\tau, \\ (\sigma + \delta i_h)\frac{i_h}{b} &= \frac{b'}{b} + \theta + \lambda_h - \mu_h, \end{aligned}$$

(3.17) and (3.18) simplify to

$$\begin{aligned} g_1(t) &= -(E - 3\delta i_h(t)) + \frac{\frac{\alpha s_h b}{b+k}}{i_h}, \\ &= -\left(\lambda_h + \frac{\alpha b}{b+k} + \nu + G_T - \rho\tau - 3\delta i_h\right) + \frac{i_h'(t)}{i_h(t)} + G_T - \delta i_h(t) - \rho\tau, \\ &= \frac{i_h'(t)}{i_h(t)} + \left(2\delta i_h - (\lambda_h + \frac{\alpha b}{b+k} + \nu)\right), \end{aligned} \tag{3.19}$$

$$\begin{aligned} g_2(t) &= (\sigma + \delta b) + \frac{i_h'(t)}{i(t)} + \left(\frac{i_h'(t)}{i_h(t)} - \frac{b'(t)}{b(t)} - 2\lambda_h - \nu - \theta + 2\delta i_h(t)\right), \\ &= -\frac{b'}{b} + \theta + \lambda_h - \mu_h + \frac{i_h'}{i_h} - \frac{b'}{b} - 2\lambda_h - \nu - \theta + 2\delta i_h, \\ &= \frac{i_h'(t)}{i_h(t)} + (2\delta i_h - (\lambda_h + \mu_h + \nu)), \end{aligned} \tag{3.20}$$

so that

$$\sup\{g_1(t), g_2(t)\} \leq \frac{i_h'(t)}{i_h(t} - \delta. \tag{3.21}$$

From (3.21), we have

$$\int_0^\omega \sup\{g_1(t), g_2(t)\}dt \leq [\ln i_h(t)]_0^\omega - \delta\omega = -\delta\omega < 0. \tag{3.22}$$

This shows that the periodic solution $(s_h(t), i_h(t), b(t))$ is asymptotically stable. This establishes the fact that the endemic equilibrium point of the disease is globally stable. □

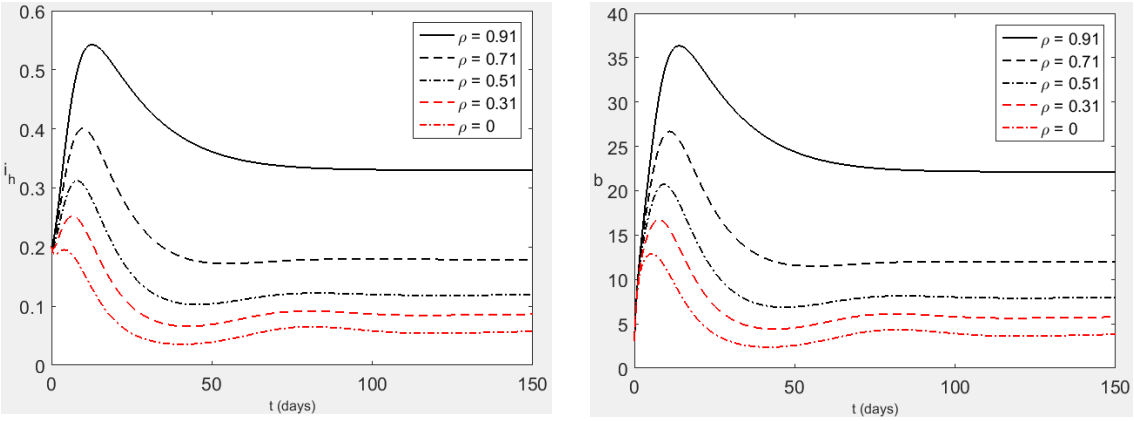

Figure 1: Solution of model (2.9)−(2.11) for different values of ρ.

4. Discussion of Results

System (2.9)−(2.11) is simulated on MATLAB platform using fourth order Runge-Kutta scheme for system of ordinary differential equations. Parameter values in Table 1 with initial values $s_h(0) = 0.5$, $i_h(0) = 0.2$, $b(0) = 3$ are used for the simulation. Figure 1 shows the time series plot of (2.9)−(2.11) with different values of ρ. Decrease in the value of ρ suggests a decrease in the peak and the spread of the disease. We investigate the relationship between infectious and susceptible human populations in Figure 2. At the initial stage, the number of susceptible individuals decreases while the number of infectious individuals increases. The case is later reversed until a stable equilibrium is reached although the situation becomes better as ρ decreases from 0.91 to 0. This figure confirms the existence of a unique endemic equilibrium.

It can also be observed from Figures 1 and 2 that compliance to treatment is necessary but not sufficient for the eradication of cholera. In other words, making sure that cholera patients complete treatment by proper follow-up, is of great significance but not enough in the fight against cholera. Therefore some other intervention strategies, in addition to compliance to treatment, are needed. Having a safe place for defecation will reduce shedding of vibrios to the environment (σ). This, in addition to treatment compliance, could make $R_0 < 1$ and thus lead to cholera eradication (see Figure 3). Numerical solution of model (2.9)−(2.11) taking $\rho = 0.1$ & $\sigma = 17.5$ (which makes $R_0 = 0.9943$) is presented in Figure 4. With this choice of ρ and σ, the populations of infectious human and V. cholerae decrease to zero.

Hartley et al. [9] reported that the interactions between the host, V. cholerae and environment are associated with the seasonal epidemics of cholera seen in endemic regions. Next, we investigate, numerically, the effects of seasonal variation on the disease dynamics. Seasonality in the transmission rate is added to the model (2.9)−(2.11) via a sine function with a period of 365 days, ie

$$\alpha(t) = \alpha\left(1 + \alpha_0 \sin\left(\frac{2\pi t}{365}\right)\right),$$

where $0 \leq \alpha_0 \leq 1$ accounts for the seasonal variation. For our computation, we choose $\alpha_0 = 0.7$ and other parameters as contained in Table 1. Figure 5 shows that the oscillation in the contact rate causes oscillation in the dynamics of the disease. However if we choose $\rho = 0.1$ & $\sigma = 17.5$ such that $R_0 = 0.9943$, the oscillation dies out and the disease vanishes (see Figure 6).

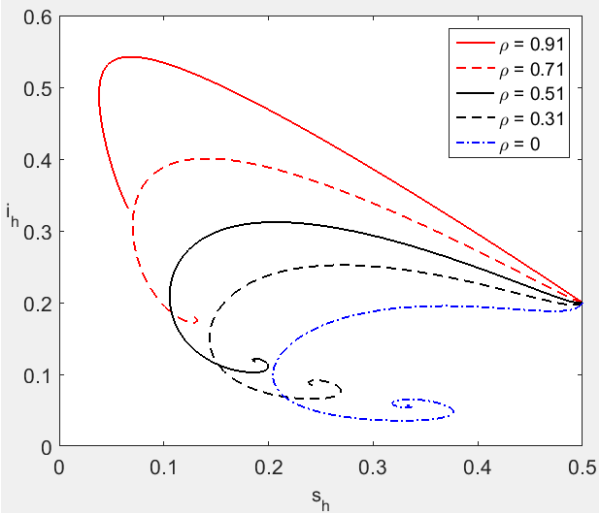

Figure 2: Relationship between the populations of the susceptible individuals and infectious individuals.

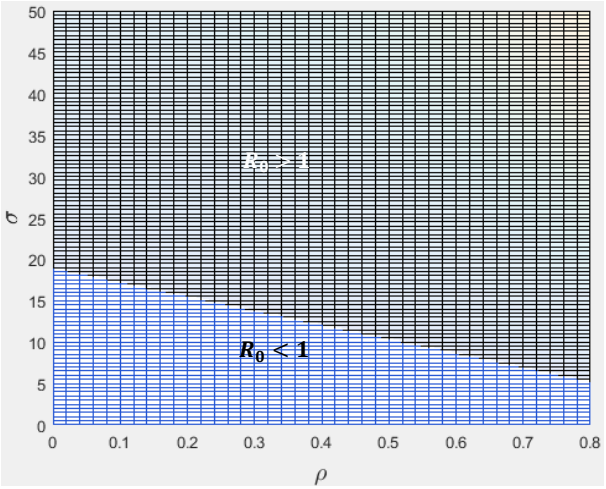

Figure 3: Region on $\rho - \sigma$ plane where $R_0 < 1$

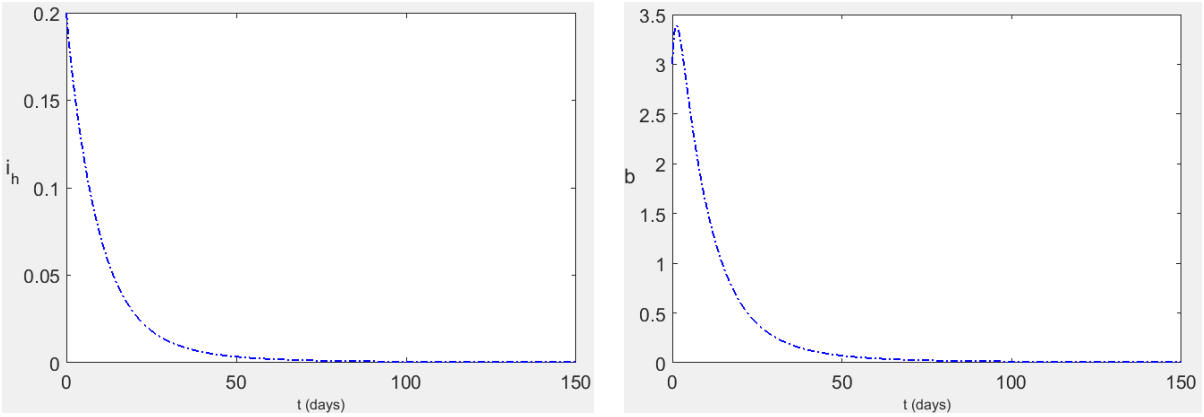

Figure 4: Solution of model (2.9)−(2.11) taking $\rho = 0.1$ & $\sigma = 17.5$ (which makes $R_0 = 0.9943$). Other parameter values are as contained in Table 1

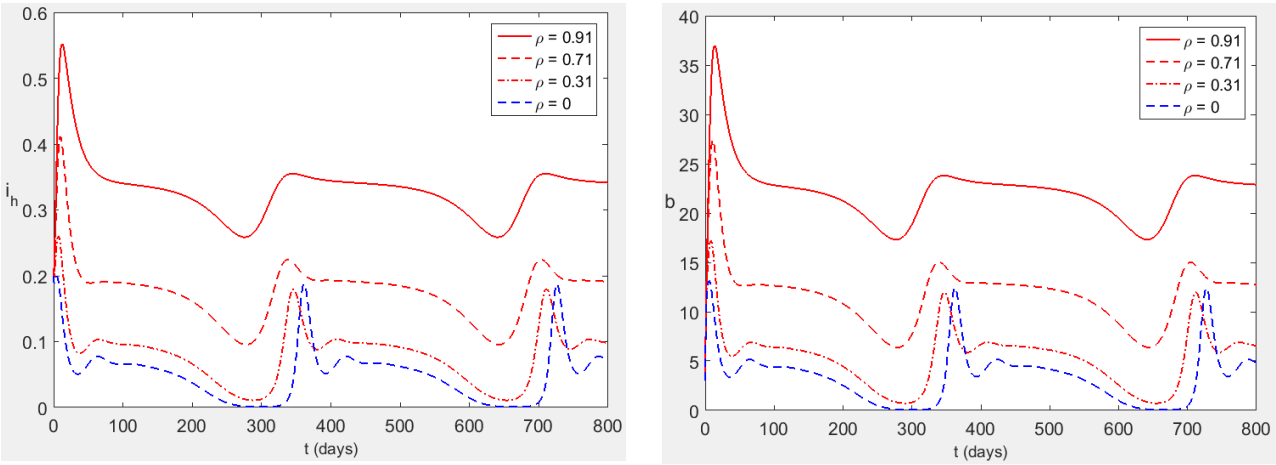

Figure 5: Solution of model (2.9)−(2.11) with seasonal variation in contact rate.

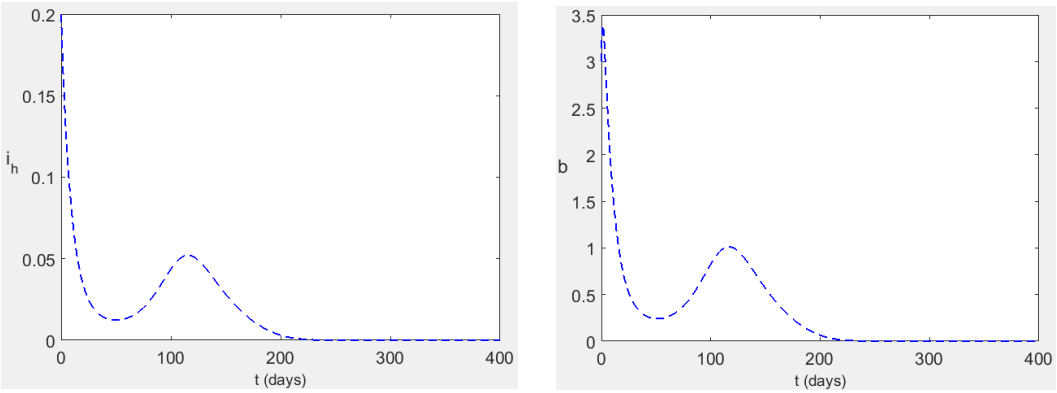

Figure 6: Solution of model (2.9)−(2.11) with seasonal variation in contact rate, taking $\rho = 0.1$ & $\sigma = 17.5$ (which makes $R_0 = 0.9943$). Other parameter values are as contained in Table 1.

5. Conclusion

In this work, a mathematical model that monitors the dynamics of cholera has been proposed. The model considers human population that incorporates proportion of infectious individuals who do not comply to treatment in the infectious class. The reproduction number as well as equilibrium points were obtained and stabilities examined. The technical tool used to establish the global stability of the endemic equilibrium is the theory of competitive systems, compound matrices and stability of periodic orbits. Model analysis showed that cholera may persist infinitely unless adequate control measures are taken. Since the DFE is globally asymptotically stable, the possibility of backward bifurcation in the dynamics of the disease is ruled out. Therefore, the condition $R_0 < 1$ is sufficient for cholera eradication.

Model simulation shows that compliance to treatment is necessary but not sufficient for the eradication of cholera. We therefore considered reduction in the shedding rate of V. cholera in addition to compliance to treatment as means of intervention. It was obtained numerically that the disease can be controlled when reduction in the rate of shedding V. cholera to the environment is achieved and infectious human's compliance to treatment is improved (through public health sensitization). Lastly, the impact of the seasonal variation in the transmission rate on the dynamics of cholera is investigated numerically. It was shown that seasonal variation in the transmission has great effects on the spread of cholera.

5.1. Application of this research

Noncompliance to treatment/medication supports the spread of cholera, however complying to treatment strategies is not sufficient for the control of the disease. Therefore other control measures (in addition to treatment compliance) should be implemented. This research can therefore inform the kind of public health education and intervention measures given to a population where cholera is endemic.

5.2. Open problems

This study can be extended in several ways, eg. the infectious class can be divided into two - asymptomatic and symptomatic groups. Asymptomatic infectious individuals could have great impact on the spread of cholera. Incorporating "infectious immigrant" in our model could be another interesting research. With recruitment of infected immigrants, eradication of the disease may not be possible as disease-free equilibrium solution does not exist in such situation. This work can further be extended by considering random effects on the model parameters. Cholera dynamics could be affected by influences that are not completely understood and thus make the spread of the disease inherently random.

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