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Understanding Cholera Transmission Dynamics: Local and Global StabilityAnalysis of the Disease-free Equilibrium

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Abstract

A deterministic mathematical model for the dynamics of cholera is presented. The model incorporates the effect and influence of the death of hyperinfective V. cholerae on the dynamics of cholera which was evaluated and the basic reproduction number, R_0, ***for the model computed and used in analyzing the local and global asymptotic stability of the disease-free equilibrium respectively. Analysis showed that the novel parameter, the death rate of hyperinfective V. cholerae, has a very significant effect on the transmission dynamics of cholera by providing a critical value or threshold which determines the onset, growth, sustenance or decay of the disease in the community.***

Keywords: Basic reproduction number, cholera, death rate,diarrhoea,disease-free equilibrium, epidemic, V. cholerae, vibrios

1.0 Introduction

Cholera is a waterborne gastro-intestinal disease caused by the bacterium *Vibrio cholerae* (commonly referred to as *V. cholerae*), i.e. the etiological agent, which colonizes the human intestine and produces an enterotoxin responsible for the disease. *V. cholerae* was first identified by the Italian anatomist Filippo Pacini in 1854, though his discovery was not known until Robert Koch thirty years later in 1884[1].The clinical description of cholera begins with sudden onset of massive diarrhoea. The patient may lose gallons of protein-free fluid and associated electrolytes, bicarbonates and ions within a day or two. This results from the activity of the cholera enterotoxin which activates the adenylate cyclase enzyme in the intestinal cells, converting them into pumps which extract water and electrolytes from blood and tissues and pump it into the lumen of the intestine. This loss of fluid leads to dehydration, anuria, acidosis and shock. The watery diarrhoea is speckled with flakes of mucus and epithelial cells ("rice-water stool") and contains enormous numbers of vibrios. The loss of potassium ions may result in cardiac complications and circulatory failure [2].

Cholera has claimed many lives throughout history and it has long been, and continues to be a global health threat regardless of the advancement of medical science and health care service and one of the key indicators of social development [3-5]. And because it continues to be such a threat to so much of the world, it is important to continue to try to understand the disease dynamics and how interactions with environmental and human factors contribute to the epidemic behaviour observed during current cholera outbreaks. As a consequence, the disease had found its place in the contemporary literary works in a number of instances where subtle intricacies of human relationship were craftily dealt with, in the backdrop of an ongoing epidemic[6].Cholera epidemics are still a major public health concern in many areas of the world, especially in developing countries like Nigeria.

Transmission of cholera is typically and predominantly through faecallycontaminated food and water [3, 7]. The disease transmission can occur in two distinct ways: human-human (i.e. faecal-oral) and environment-to-human (i.e. water or food contamination). Cholera has been found in only two other animal populations: shellfish and plankton[8]. In the developed world, seafood is the usual cause, while in the developing world it is more often water. Experiments also show that vibrios consumed with food are more likely to cause infection than those from water alone [9]. People infected with cholera often have diarrhoea, and if this highly liquid stool, colloquially referred to as "rice-water," contaminates water used by others, disease transmission may occur [10]. The source of the contamination is typically other cholera sufferers when their untreated diarrheal discharge is allowed to get into waterways or into groundwater or drinking water supplies. Drinking any infected water and eating any foods washed in the water, as well as shellfish living in the affected waterway, can cause a person to

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contract an infection. Cholera is rarely spread directly from person to person (i.e. faecal-oral), probably because the inoculum needed to cause disease is high, i.e., greater than 10^5 cells/ml in most cases. Despite a large body of clinical, experimental and theoretical studies, the fundamental mechanism of transmission for cholera is not well understood at present, which has hindered effective prevention and control strategies of the disease. The difficulty stems from the complex, multiple transmission pathways which include both direct human-to-human and indirect environment-to-human modes, and which distinct cholera from many other infectious diseases [11]. The World Health Organization (WHO) estimates that during any cholera epidemic, approximately 0.2-1% of the local population will contract the disease. Anyone can get cholera, but infants, children, and the elderly are more likely to die from the disease because they become dehydrated faster than adults [12]. Historically speaking, there are very few diseases that can match cholera in terms of its severity and explosive onset in the form of an outbreak or epidemic. Further, high mortality and morbidity rates associated with classical cholera had a tremendous tragic impact on the personal as well as social life of people living in the affected areas. The combination of war, poverty, lack of or destruction of infrastructure, weather, and natural disasters i.e. extreme environmental events, conditions in which cholera thrives and can contribute to the disease's ability to ravage communities.

According to the WHO records, 45,159 cases and 3,488 deaths in ten African nations were reported up to July 1991. Since 2005, the reoccurrence of cholera is linked with the ever-increasing size of the population living in unsanitary conditions. For instance, from August 2008 to February 2009, more than 79,000 cases and 3,700 deaths were reported from a single country Zimbabwe. While the disease is not an issue in the developed nations where minimum hygiene standards are met, it still remains a threat in developing countries. In 2006, 236,896 cases were reported from 52 nations, including 6,311 deaths, which is 79% greater than the reported cases in 2005. In Haiti, the first cases of cholera after the 2010 earthquake were reported in the Centre department; 4 months later, 215, 936 cases had been reported across all 10 of Haiti's geographic departments, and among these, 1.9% (2, 6) of patients died. Because reporting capacity is weak in Haiti, these statistics probably underestimate the number of cases of cholera and the rate of spread. In the first months of the epidemic, case-fatality rates (CFR) varied by 10-fold across departments, ranging from 0.8% to 8% [13].It is estimated that only a small proportion of cases less than 10% were reported to WHO. The burden of the disease was therefore highly under-estimated because of poor surveillance and under-reporting [3], i.e. it is difficult to gauge the exact morbidity and mortality of cholera because the surveillance systems in many developing countries are rudimentary, and many countries are hesitant to report cholera cases to the WHO because of the potential negative economic impact of the disease on trade and tourism [13, 14].

Treatment of cholera involves the rapid intravenous replacement of the lost fluid and ions. Following this replacement, administration of isotonic maintenance solution should continue until the diarrhoea ceases. If glucose is added to the maintenance solution it may be administered orally, thereby eliminating the need for sterility and intravenous administration. By this simple treatment regimen, patients on the brink of death seem to be miraculously cured and the mortality rate of cholera can be reduced more than ten-fold. Most antibiotics and chemotherapeutic agents have no value in cholera therapy, although a few (e.g. tetracyclines) may shorten the duration of diarrhoea and reduce fluid loss [2].Untreated cholera frequently results in high (50-60%) mortality rates [2].

2.0 Model Formulation

We formulate a mathematical model which incorporates the contribution of the death rate of hyperinfective (HI)*V. cholerae*into the model in [1]. This inclusioninfluences the possibility of the reduction in the concentration of less-infective (LI)*V. cholerae*in the environment due to the death of some HI vibrios.

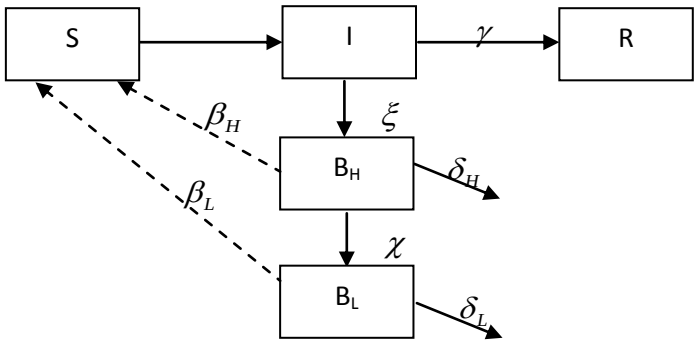

Figure 1: A schematic representation of our model with transition between the different possible states.

We have the following system of non-linear ordinary differential equations (ODE) for the cholera model:

$$\frac{dS}{dt} = \mu N - \beta_L S \frac{B_L}{K_L + B_L} - \beta_H S \frac{B_H}{K_H + B_L} - \mu S \quad (1a)$$

$$\frac{dI}{dt} = \beta_L S \frac{B_L}{K_L + B_L} + \beta_H S \frac{B_H}{K_H + B_H} - (\gamma + \mu) I \quad (1b)$$

$$\frac{dR}{dt} = \gamma I - \mu R \quad (1c)$$

$$\frac{dB_H}{dt} = \xi I - (\chi + \delta_H) B_H \quad (1d)$$

$$\frac{dB_L}{dt} = \chi B_H - \delta_L B_L \quad (1e)$$

where the state variables (sub-populations) are: numberof individuals not infected but susceptible to infection, S ; number of individuals infected and infectious, I ; number of individuals recovered from infection, R ; concentration of hyperinfectious (HI) *V. cholerae*, B_H ;concentration of less-infections (LI) *V. cholerae*, B_L . The model parameters are:per-capita natural human birth/mortality rate, μ ;ingestion rate of hyperinfectious (HI) *V. cholerae* by susceptible individuals, β_H ;ingestion rate of less-infectious (LI) *V. cholerae* by susceptible individuals, β_L ; the hyperinfectious (HI) *V. cholerae* infectious concentration or half saturation rate, K_H ; the less-infectious (LI) *V. cholerae* infectious concentration or half saturation rate, K_L ; bacterial transition rate i.e., the rate of decay from hyper-to reduced infectiousness, χ ;shedding rate i.e., the rate of contribution to HI *V. cholerae* in aquatic environment, ξ ; net death rate of HI vibrios, δ_H ;net death rate of non-HI vibrios in the aquatic environment, δ_L ; rate of recovery from cholera, γ .

The mathematical model (1) is based on the typical hyperinfectious cholera model by Hartley *et al*. [3], given in Eq. (*)

$$\left.\begin{aligned}
\frac{dS}{dt} &= bN - \beta_H S \frac{B_H}{K_H + B_H} - \beta_L S \frac{B_L}{K_L + B_L} - bS \\
\frac{dI}{dt} &= \beta_H S \frac{B_H}{K_H + B_H} + \beta_L S \frac{B_L}{K_L + B_L} - (\gamma + b) I \\
\frac{dR}{dt} &= \gamma I - bR \\
\frac{dB_H}{dt} &= \xi I - \chi B_H \\
\frac{dB_L}{dt} &= \chi B_H - \delta_L B_L
\end{aligned}\right\} \quad (*)$$

In the model presented in (1), we incorporated into the hyperinfectious class, a net death rate for the HI vibrios, δ_H , which has the propensity to reducing the population of the less-infectious *V. cholerae*in Eq. (*) with the resultant effect of slowing down cholera onset.Each equation in Eq. (1) represents the rate of change, with respect to time, of the state variables or sub-populations.

1.0 Model Analysis

Here, we analyze the disease-free equilibrium (DFE) for both local and global stability respectively and in the process, compute the basic reproduction number, R_0 ,the epidemic threshold which is critical to the dynamics of the disease in both the short and long term. The nature of the results of the stability analysis will ultimately determine whether the disease will die out or continue indefinitely in the host community.

1.1 The Disease-Free Equilibrium (DFE)

The model in Eq. (3.1) can be written in a vector form

$$\frac{d}{dt} X = F(X) \tag{2}$$

with

$$X = (S, I, R, B_H, B_L)^T \tag{3}$$

It is obvious that equations (1a – 1e) have a unique DFE

$$X_0 = (N, 0, 0, 0, 0)^T \tag{4}$$

3.2 The Local Stability of the DFE

The local stability of the DFE, which is directly related to the disease epidemics[7, 15], is analyzed as follows:
The Jacobian of the ODE system (1a – 1e) is given by

$$J = \begin{bmatrix} -\frac{\beta_L B_L}{K_L + B_L} - \frac{\beta_H B_H}{K_H + B_H} - \mu & 0 & 0 & -\beta_H S \frac{K_H}{(K_H + B_H)^2} & -\beta_L S \frac{K_L}{(K_L + B_L)^2} \\ \frac{\beta_L B_L}{K_L + B_L} + \frac{\beta_H B_H}{K_H + B_H} & -(\gamma + \mu) & 0 & \beta_H S \frac{K_H}{(K_H + B_H)^2} & -\beta_L S \frac{K_L}{(K_L + B_L)^2} \\ 0 & \gamma & -\mu & 0 & 0 \\ 0 & \xi & 0 & -(\chi + \delta_H) & 0 \\ 0 & 0 & 0 & \chi & -\delta_L \end{bmatrix} \tag{5}$$

At DFE: $S = N, I = B_H = B_L = 0$. Thus, Eq. (5) becomes

$$J_0 = \begin{bmatrix} -\mu & 0 & 0 & -\beta_H \frac{N}{K_H} & -\beta_L \frac{N}{K_L} \\ 0 & -(\gamma + \mu) & 0 & \beta_H \frac{N}{K_H} & \beta_L \frac{N}{K_L} \\ 0 & \gamma & -\mu & 0 & 0 \\ 0 & \xi & 0 & -(\chi + \delta_H) & 0 \\ 0 & 0 & 0 & \chi & -\delta_L \end{bmatrix} \tag{6}$$

The characteristic polynomial of the matrix is given as

$$Det\left|\lambda I - J_o\right| = \begin{bmatrix} \lambda + \mu & 0 & 0 & \beta_H \frac{N}{K_H} & \beta_L \frac{N}{K_L} \\ 0 & \lambda + (\gamma + \mu) & 0 & -\beta_H \frac{N}{K_H} & \beta_L \frac{N}{K_L} \\ 0 & -\gamma & \lambda + \mu & 0 & 0 \\ 0 & -\xi & 0 & \lambda + (\chi + \delta_H) & 0 \\ 0 & 0 & 0 & -\chi & \lambda + \delta_L \end{bmatrix} = 0 \tag{7}$$

where I is a 5 x 5 unit matrix and λ represents the eigenvalues.Thus, Eq. (7) becomes

$$Det\left|\lambda I - J_0\right| = (\lambda + \mu)^2 \left[(\lambda + \delta_L) \left\{ (\lambda + \gamma + \mu)(\lambda + \chi \ \delta_H) - \beta_H \frac{N\xi}{K_H} \right\} - \beta_L \frac{N\xi\chi}{K_L} \right] = 0 \tag{8}$$

Further simplification of Eq. (8) gives us

$$Det\left|\lambda I - J_0\right| = (\lambda+\mu)^2\left[\lambda^3 + \lambda^2\left(\gamma+\chi+\mu+\delta_H+\delta_L\right) + \lambda\left(\gamma\chi + \gamma\delta_H + \mu\chi + \mu\delta_H + \gamma\delta_L + \chi\delta_L + \mu\delta_L + \delta_H\delta_L - \beta_H\frac{N\xi}{K_H}\right) + \left(\gamma\chi\delta_L + \gamma\delta_H\delta_L + \mu\chi\delta_L + \mu\delta_H\delta_L - \beta_L\frac{N\xi\delta_L}{K_H} - \beta_L\frac{N\xi\chi}{K_L}\right)\right] = 0 \quad (9)$$

The equilibrium Eq. (4) is locally asymptotically stable if and only if all roots of the polynomial in Eq. (9) have negative real parts. Obviously $\lambda = -\mu$ is a negative root of multiplicity 2.

To analyze the three roots of the cubic polynomial inside the square brackets of Eq. (9), we set

$$d_1 = \delta_H + \delta_L + \chi + \gamma + \mu \quad (10)$$

$$d_2 = \gamma\chi + \gamma\delta_H + \mu\chi + \mu\delta_H + \gamma\delta_L + \chi\delta_L + \mu\delta_L + \delta_H\delta_L - \beta_H\frac{N\xi}{K_H} \quad (11)$$

$$d_3 = \gamma\chi\delta_L + \gamma\delta_H\delta_L + \mu\chi\delta_L + \mu\delta_H\delta_L - \beta_H\frac{N\xi\delta_L}{K_H} - \beta_L\frac{N\xi\chi}{K_L} \quad (12)$$

On the premise of the Routh-Hurwitz criterion [15], the sufficient and necessary condition for stability is

$$d_1 > 0, \qquad d_3 > 0, \qquad d_1 d_2 - d_3 > 0 \quad (13)$$

It is observed that the first inequality of Eq. (13) is automatically satisfied given that all the model parameters are positive, i.e. $\beta_H, \beta_L, \delta_H, \delta_L, \chi, \gamma, \mu, K_H, K_L > 0$. The second inequality, $d_3 > 0$, holds true if and only if

$$\gamma\chi\delta_L + \gamma\delta_H\delta_L + \mu\chi\delta_L + \mu\delta_H\delta_L - \beta_H\frac{N\xi\delta_L}{K_H} - \beta_L\frac{N\xi\chi}{K_L} > 0 \quad (14)$$

Manipulating Eq. (14), we obtain

$$-(\chi+\delta_H)(\gamma+\mu) + \beta_H\frac{N\xi}{K_H} + \beta_L\frac{N\xi\chi}{\delta_L K_L} < 0 \quad (15)$$

Hence, on rearranging Eq. (15), we arrive at

$$N < \frac{(\gamma+\mu)(\chi+\delta_H)K_H K_L\delta_L}{\xi\left(\beta_H K_L\delta_L + \beta_L K_H\chi\right)} \quad (16)$$

In addition,

$$d_1 d_2 - d_3 = (\delta_H+\delta_L+\chi+\gamma+\mu)(\gamma\chi+\gamma\delta_H+\mu\chi+\mu\delta_H+\gamma\delta_L+\chi\delta_L+\mu\delta_L+\delta_H\delta_L-\beta_H\frac{N\xi}{K_H}) - (\gamma\chi\delta_L+\gamma\delta_H\delta_L+\mu\chi\delta_L+\mu\delta_H\delta_L-\beta_H\frac{N\xi\delta_L}{K_H}-\beta_L\frac{N\xi\chi}{K_L})$$

$$= (\delta_H+\chi+\gamma+\mu)[\delta_L(\delta_H+\delta_L+\chi+\gamma+\mu)+(\chi+\delta_H)(\gamma+\mu)-\beta_H\frac{N\xi}{K_H}]+\beta_L\frac{N\xi\chi}{K_L}$$

It is obvious that $d_1 d_2 - d_3 > 0$ provided the inequality (15) or equivalently, (16) holds.The condition in Eq. (17) provides us with a threshold for the total population (which is assumed to be completely susceptible initially):

$$S_C = \frac{(\gamma+\mu)(\chi+\delta_H)K_H K_L\delta_L}{\xi\left(\beta_H K_L\delta_L + \beta_L K_H\chi\right)} \quad (17)$$

When $N < S_C$, the DFE is stable and no epidemicity would occur.If $N > S_C$, the DFE becomes unstable and any infection entering the population would persist and lead to an epidemic.

3.3 The Basic Reproduction Number

For our model in Eq. (1), based on [16] we define the basic reproduction number, R_0, by

$$R_0 = \frac{N}{S_C} = \frac{\xi(\beta_H K_L \delta_L + \beta_L K_H \chi)}{(\gamma+\mu)(\chi+\delta_H) K_H K_L \delta_L} N \quad (18)$$

Rearranging Eq. (22), we obtain a better expression for our R_0, i.e.

$$R_0 = \frac{\xi N}{(\gamma + \mu)} \left[\frac{\beta_H}{K_H} \frac{1}{\chi + \delta_H} + \frac{\beta_L}{K_L} \frac{1}{\delta_L} \frac{\chi}{\chi + \delta_H} \right] \quad (19)$$

Where $\frac{\xi}{\gamma + \mu}$ is the average amount of *V. cholerae* shed per individual, $\frac{1}{\chi + \delta_H}$ is the death-induced expected time that the *V. cholerae* remain in HI state, $\frac{1}{\delta_L}$ is the expected time that the *V. cholerae* remain in the non-HI state, $\frac{\beta_H}{K_H}$ is the number of new cases generated in terms of HI vibrios, $\frac{\beta_L}{K_L}$ is the number of new cases generated in terms of non-HI vibrios, $\frac{\chi}{\chi + \delta_H}$ is the probability that the HI vibrios will lose viability.

Equation (19) is a new result which is remarkably different from that obtained in[8], which is given in Eq. (24)

$$R_0 = \left(\frac{\xi N}{\gamma + \mu} \right) \left[\frac{\beta_H}{K_H} \frac{1}{\chi} + \frac{\beta_L}{K_L} \frac{1}{\delta_L} \right] \quad (20)$$

The effect of the saturating function $\frac{1}{\chi + \delta_H}$ and the quotient $\frac{\chi}{\chi + \delta_H}$ obtained in the R_0 forour model (See Eq. (19)) will be investigated, in order to check the significance of their presence and effect on the overall dynamics of the disease. We shall pause at this juncture to carry out our investigation in Section 3.3.1 before continuing our discussion of the basic reproduction number, R_0.

$$R_0^{(1)} = \frac{\xi N}{(\gamma + \mu)} \left[\frac{\beta_H}{K_H} \cdot \frac{1}{\chi} + \frac{\beta_L}{K_L} \cdot \frac{1}{\delta_L} \right] \quad (21)$$

3.3.1The Significance of the Effect of the Saturating Function $\chi/\chi+\delta_H$ and the Quotient $1/\chi+\delta_H$ on the Basic Reproduction Number, R_0

Here, we proceed to investigate the presence and the effect of the saturating function $\chi/\chi+\delta_H$ and the quotient $1/\chi+\delta_H$ on the basic reproduction number of our model; this investigation shall serve as a sensitivity analysis for the death rate of hyperinfective *V. cholerae* in our model. In order to achieve this, we compare the basic reproduction number for our model with the one obtained in[3].

Recall, the basic reproduction number for the model in[3] (which we shall denote by $R_0^{(1)}$) is given by

And the basic reproduction number for our model is represented by

$$R_0^{(2)} = \frac{\xi N}{(\gamma + \mu)} \left[\frac{\beta_H}{K_H} \frac{1}{\chi + \delta_H} + \frac{\beta_L}{K_L} \cdot \frac{1}{\delta_L} \cdot \frac{\chi}{\chi + \delta_H} \right] \quad (22)$$

Let $Z^{(0)} = \frac{1}{\chi + \delta_H}$ and $Z^{(1)} = \frac{\chi}{\chi + \delta_H}$ (23)

Case 1:

We assume that the rate at which the HI vibrios lose infectiousness, χ, is much more greater than the death rate of the HI vibrios, δ_H. That is, when $\chi >> \delta_H$ (δ_H fixed), and $Z^{(1)} \to 1$, as $\chi \to \infty$. Then

$$R_0^{(2)} \to R_0^{(1)} \to \frac{\xi N}{(\gamma + \mu)} \left[\frac{\beta_L}{K_L} \cdot \frac{1}{\delta_L} \right] \quad (24)$$

Thus, the result of our assumption reveals that the basic reproduction number will surely be a function of the contribution of the interaction of the human population, the HI and the LI vibrios respectively. Hence, the HI and LI vibrios, collectively, do have a very significant contribution to the disease transmission dynamics.

Case 2:
Here, we assume that the rate at which the HI vibrios lose their hyperinfectivity is very much smaller than the rate at which the HI vibrios die in the environment in the course of an epidemic i.e. $\chi << \delta_H \quad (\delta_H \quad fixed)$.Thus,

$Z^{(0)} \to \infty \; and \; Z^{(1)} \to \infty,$ which inadvertently leads to the situation where $R_0^{(1)} \to \infty \; and \; R_0^{(2)} \to \infty$. Hence, the disease will significantly and infinitely invade and persist in the population under consideration. This result establishes the endemicity of the disease transmission dynamics in the target population.

NB: the basic reproduction number, given in Eq. (19), can also be derived by the next generation matrix analysis or approach [17].Recall, from Section 3.3.1, the condition given in Eq. (16), we observe that this condition is equivalent to

$$R_0 < 1 \qquad (25)$$

Thus, we have established the result below:

Theorem 1[18]

The disease-free equilibrium of the model (1) is locally asymptotically stable if $R_0 < 1$, and unstable if $R_0 > 1$.

3.4 The Global Asymptotic Stability of the DFE

To ascertain the nature of the global asymptotic stability of the DFE, i.e. to analyze it, a common approach is to construct an appropriate Lyapunov function [9]. However, due to the complex nature of our model, we have found that it is much simpler to apply the following result developed and introduced in[19]and discussed in [11].

Lemma 2 [19]

Consider a model system written in the form

$$\frac{dX_1}{dt} = F(X_1, X_2) \qquad (26)$$
$$\frac{dX_2}{dt} = G(X_1, X_2), \qquad G(X_1, 0) = 0$$

where $X_1 \in \Re^m$ denotes (its components) the number of uninfected individuals and $X_2 \in \Re^n$ denotes (its components) the number of infected individuals including latent, infectious, etc; $X_0 = (X_1^*, 0)$ denotes the disease-free equilibrium of the system.

Also assume the conditions (H_1) and (H_2) below;

(H_1) *For* $\frac{dX_1}{dt} = F(X_1, 0)$, X_1^* is globally asymptotically stable;

(H_2) $G(X_1, X_2) = AX_2 - \hat{G}(X_1, X_2), \hat{G}(X_1, X_2) \geq 0 \quad for \; (X_1, X_2) \in \Omega,$

where the Jacobian $A = \frac{\partial G}{\partial X_2}(X_1^*, 0)$ is an M-matrix (the off diagonal elements of A are nonnegative) and Ω is the region where the model makes biological sense. Then the DFE $X_0 = (X_1^*, 0)$ is globally asymptotically stable provided that $R_0 < 1.$

Lemma 3[11]

The DFE of model (1) is globally asymptotically stable if $R_0 < 1.$

Proof: It behoves us to show that conditions (H_1) and (H_2) hold when $R_0 < 1$.

In our ODE system (1),

$$X_1 = (S, R)^T, \; X_2 = (I, B_H, B_L)^T, \; and \; X_1^* = (N, 0) \qquad (27)$$

We observe that the system

$$\frac{dX_1}{dt} = \begin{bmatrix} \frac{dS}{dt} \\ \frac{dR}{dt} \end{bmatrix} = F(X_1, 0) = \begin{bmatrix} \mu N - \mu S \\ -\mu R \end{bmatrix} \qquad (28)$$

That is,

$$\frac{dS}{dt} = \mu N - \mu S \qquad (29)$$

$$\frac{dR}{dt} = -\mu R \tag{30}$$

is linear and its solution can be obtained as

$$R(t) = R(0)e^{-\mu t} \text{ and } S(t) = N - (N - S(0))e^{-\mu t} \tag{31}$$

Obviously, $R(t) \to 0$ *and* $S(t) \to N$ *as* $t \to \infty$, regardless of the values of $R(0)$ and $S(0)$.

Thus, $X_1^* = (N, 0)$ is globally asymptotically stable.

Next, we consider

$$\frac{dX_2}{dt} = \begin{bmatrix} \frac{dI}{dt} \\ \frac{dB_H}{dt} \\ \frac{dB_L}{dt} \end{bmatrix} = G(X_1, X_2) = \begin{bmatrix} \beta_L S \frac{B_L}{K_L + B_L} + \beta_H S \frac{B_H}{K_H + B_H} - (\gamma + \mu) I \\ \xi I - (\chi + \delta_H) B_H \\ \chi B_H - \delta_L B_H \end{bmatrix} \tag{32}$$

Now, $A = \frac{\partial G}{\partial X_2}(X_1^*, 0) = \begin{bmatrix} -(\gamma + \mu) & \beta_H \frac{N}{K_H} & \beta_L \frac{N}{K_L} \\ \xi & -(\chi + \delta_H) & 0 \\ 0 & \chi & -\delta_L \end{bmatrix}$ (33)

Recall, $G(X_1, X_2) = AX_2 - \hat{G}(X_1, X_2)$. *Hence,*

$$\hat{G}(X_1, X_2) = AX_2 - G(X_1, X_2) \tag{34}$$

$$= \begin{bmatrix} -(\gamma + \mu) & \beta_H \frac{N}{K_H} & \beta_L \frac{N}{K_L} \\ \xi & -(\chi + \delta_H) & 0 \\ 0 & \chi & -\delta_L \end{bmatrix} \begin{bmatrix} I \\ B_H \\ B_L \end{bmatrix} - \begin{bmatrix} \beta_L S \frac{B_L}{K_L + B_L} + \beta_H S \frac{B_H}{K_H + B_H} - (\gamma + \mu) I \\ \xi I - (\chi + \delta_H) B_H \\ \chi B_H - \delta_L B_L \end{bmatrix} \tag{35}$$

This on further simplification and manipulation yields

$$= \left[\frac{\beta_H B_H K_H (N - S) + \beta_H N B_H^2}{K_H (K_H + B_H)} + \frac{\beta_L B_L K_L (N - S) + \beta_L N B_L^2}{K_L (K_L + B_L)}, 0, 0 \right]^T \tag{36}$$

Since $0 \le S \le N$, it is clear that $\hat{G}(X_1, X_2) \ge 0$. Thus, the DFE $X_0 = (X_1^*, 0)$, *where* $X_1^* = (N, 0)$, is globally asymptotically stable provided that $R_0 < 1$.

4 Conclusion

The model we have presented in this paper is an improvement of the model in [3] via the introduction of the death rate of hyperinfective *V. cholerae* into their model. This inclusioninfluences the possibility of the reduction in the concentration of LI vibrios in the environment due to the death of some HI vibrios.In this study, we had confined our research to the stability of the disease-free equilibrium due to the sudden explosiveness observed at the onset of a cholera epidemic. We had computed the basic reproduction number, R_0 and employed it in the analysis of the DFE, which we found to be stable for $R_0 < 1$and unstable for $R_0 > 1$in conformity with the postulation in [18].A sensitivity analysis carried out on our model showed that the transmission dynamics of cholera is sensitive to the death rate of hyperinfective *V. cholerae.*We shall shift focus to the analysis of the endemic equilibrium of our model in a subsequent paper.

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