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Stability Analysis of the Endemic Equilibrium Point of a Mathematical Model for Cholera

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Abstract

In this paper, we present the local and global stability analysis of the endemic equilibrium of a mathematical model for cholera that incorporates the death of hyperinfective V. cholerae, the pathogen responsible for cholera, in the transmission dynamics of cholera. The analyses show that the endemic equilibrium point (EEP) exists and is unique and is linearly globally asymptotically stable in the domain under consideration.

Keywords: Cholera, endemic equilibrium point, hyperinfective, V. cholerae

1.0 Introduction

Cholera is an ancient disease that continues to cause epidemic and pandemic infection despite ongoing efforts to limit its spread [1]. Historically, six out of the seven cholera pandemics have swept the globe since 1816[2 - 4]. Most recently, the seventh pandemic started from Indonesia in 1961, spread into Europe, South Pacific and Japan in the late 1970s, reached South America in 1990s, and has continued (though much diminished) to the present. The last few years have witnessed many cholera outbreaks in developing countries, including India (2007), Congo (2008), Iraq (2008), Zimbabwe (2008–2009), Vietnam (2009), Nigeria (2010), and Haiti (2010). In the year of 2010 alone, it is estimated that cholera affects 3–5 million people and causes 100,000–130,000 deaths in the world [4]. Particularly, cholera represents a significant public health burden to developing countries and cholera continues receiving worldwide attention [1].

Cholera is an infection of the small intestine caused by the gram-negative bacterium, *Vibrio cholerae*. Untreated individuals suffer severely from diarrhea and vomiting. It can cause a rapid dehydration and electrolyte imbalance, and can lead to death. As a water/food-borne disease, cholera is typically infected through pathogen ingestion, such as drinking sewage-contaminated water, or eating food prepared by an individual with soiled hands. Mean-while, different transmission pathways are possible. For example, a cholera outbreak in a Singapore psychiatric hospital indicated that the direct human-to-human transmission was a driving force [1]. In addition, several other aspects must be considered, including the pathogen ecology outside of human hosts [5] and climatological influence [6]. The present work aims to understand the global dynamics of cholera epidemiology in a general mathematical mod-el which has a potential to incorporate these different factors into a unified framework. Such understanding is crucial for effective prevention and intervention strategies against cholera outbreak.

Many mathematical models have already been proposed to investigate the complex epidemic and endemic behavior of cholera. One difficulty in studying cholera dynamics is the coupling between its multiple transmission pathways which involve bothdirect human-to-human and indirect environment-to-humanmodes and which lead to combined human-environment epidemiological models [1]. The earliest mathematical model was proposed byCapasso and Paveri-Fontana[7]to study the 1973 cholera epidemicin the Mediterranean region. The model consists of two components, the concentration of the pathogen in water and the population of the infected people. Codeço [8] in 2001 extended the work in [7] and explicitly accounted for the role of the aquatic reservoir in cholera dynamics. Codeço included the susceptible population into her model to consider the long-term dynamics. Similar to the work of Capasso and Paveri-Fontana [7], this model assumes the ingestion of contaminated water is the only transmission route. Using similar non-linear incidence in Codeço's model, Hartley *et al.* [9] incorporated a hyperinfective stage of *V. cholerae* (i.e., freshly shed vibrios) into their model. This model emphasizes the stage of ''explosive'' infectivity of *V. cholerae*, based on the laboratory measurements that freshly shed *V. cholerae* from human intestines outcompeted other *V. cholerae* by as much as 700-fold for the first few hours in the environment [9]. Consequently, this model tries to implicitly highlight the importance of human-to-human interaction in cholera epidemics. Oghre and Ako [10] modified the work of Hartley *et al.* [9] by the inclusion of the death rate of hyperinfective *V. cholerae*. Their model is given by.

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$$\left.\begin{aligned}
\frac{dS}{dt} &= \mu N - \beta_L S \frac{B_L}{K_L + B_L} - \beta_H S \frac{B_H}{K_H + B_L} - \mu S \\
\frac{dI}{dt} &= \beta_L S \frac{B_L}{K_L + B_L} + \beta_H S \frac{B_H}{K_H + B_H} - (\gamma + \mu) I \\
\frac{dR}{dt} &= \gamma I - \mu R \\
\frac{dB_H}{dt} &= \xi I - (\chi + \delta_H) B_H \\
\frac{dB_L}{dt} &= \chi B_H - \delta_L B_L
\end{aligned}\right\} \quad (1)$$

where $S(0) = N,\ I(0) = B_H(0) = B_L(0).$

The state variables (sub-populations) are: number of 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. In their paper, Oghre and Ako[10] computed the basic reproduction number, R_0 , and the critical susceptible population, S_C , to be:

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

and

$$S_C = \frac{(\gamma+\mu)(\chi+\delta_H) K_H K_L \delta_L}{\xi(\beta_H K_L \delta_L + \beta_L K_H \chi)} \quad (3)$$

respectively(see [10] for more details). Oghre and Ako [10] analyzed the local and global asymptotic stability of the infection-free equilibrium point in their work. In this paper, we extend the work in [10] by analyzing the local and global asymptotic stability of the endemic equilibrium point (EEP).

2.0 Existence and Local Stability of the Endemic Equilibrium Point

The dynamics of a disease over a very long period of time is characterized and governed by the stability at the endemic equilibrium. Furthermore, endemicity refers to a situation whereby a disease seems to be locally persistent in a given community over a long period of time, thus making that community vulnerable [11].

Let the endemic equilibrium point (EEP) of system (1) denoted by

$$X^* = (S^*,\ I^*,\ R^*,\ B_H^*,\ B_L^*)^T \quad (4)$$

That is, generally, $\frac{dX^*}{dt} = F(X^*) = 0$ (5)

Thus, the components of the endemic equilibrium point, X^* , are

$$I^* = \frac{S^*}{\gamma + \mu} \left(\frac{\beta_L \xi \chi I^*}{K_L \delta_L (\chi + \delta_H) + \xi \chi I^*} + \frac{\beta_H \xi I^*}{K_H (\chi + \delta_H) + \xi I^*} \right) \quad (6)$$

$$S^* = N - \frac{(\gamma + \mu) I^*}{\mu} \quad (7)$$

$$R^* = \frac{\gamma I^*}{\mu} \tag{8}$$

$$B_H^* = \frac{\xi I^*}{\chi + \delta_H} \tag{9}$$

$$B_L^* = \frac{\xi\chi I^*}{\delta_L(\chi + \delta_H)} \tag{10}$$

These components (6 - 10) will aid us in showing the existence and uniqueness of the positive endemic equilibrium. We will do this in the following theorem.

Theorem 1

The positive endemic equilibrium point exists and is unique if and only if $R_0 > 1$.

Proof: Substituting Eq. (7) in Eq. (6) and expanding the result yields

$$U(I^*)^3 + V(I^*)^2 + WI^* = 0 \tag{11}$$

where

$$U = -\xi^2\chi(\gamma+\mu)(\beta_L+\beta_H+\mu) \tag{12}$$

$$V = \xi^2\chi\mu N(\beta_L+\beta_H) - \xi(\gamma+\mu)(\chi+\delta_H)(\beta_L\chi K_H + \beta_H K_L\delta_L + \mu K_L\delta_L + \mu\chi K_H) \tag{13}$$

$$W = (\chi+\delta_H)[\xi\mu N(\beta_L\chi K_H + \beta_H K_L\delta_L) - \mu(\gamma+\mu)(\chi+\delta_H)K_H K_L\delta_L] \tag{14}$$

Factorizing Eq. (14) gives

$$W = \xi\mu(\chi+\delta_H)(\beta_L\chi K_H + \beta_H K_L\delta_L)\left[N - \frac{(\gamma+\mu)(\chi+\delta_H)K_H K_L\delta_L}{\xi(\beta_L\chi K_H + \beta_H K_L\delta_L}\right] \tag{15}$$

Recalling Eq. (3) and substituting it in Eq. (15), gives

$$W = \xi\mu(\chi+\delta_H)(\beta_L\chi K_H + \beta_H K_L\delta_L)[N - S_C] \tag{16}$$

Eq. (11), on further simplification, yields

$$I^*\left[U(I^*)^2 + VI^* + W\right] = 0 \tag{17}$$

From Eq. (15), it is obvious that either

$$I^* = 0 \tag{18}$$

or

$$U(I^*)^2 + V(I^*) + W = 0 \tag{19}$$

The zero root of Eq. (18) i.e. $I^* = 0$, corresponds to the DFE.

The other two (non-zero) roots, I_1 *and* I_2, of Eq. (19) must satisfy:

$$I_1 I_2 = \frac{W}{U} \tag{20}$$

$$I_1 + I_2 = -\frac{V}{U} \tag{21}$$

The sign on U is negative, i.e. $U < 0$ since all the parameters are positive.When $R_0 > 1, \text{ then } N > S_C \text{ and } W > 0$, so that the RHS of Eq. (20) is negative. Therefore, there is one and only one positive real root for Eq. (19).Conversely, if $R_0 < 1, \text{ then } N < S_C$ and $W < 0$, so that the RHS of Eq. (21) is positive.

Next we prove that $V < 0$. Recall that

$$V = \xi^2\mu\chi N(\beta_L+\beta_H) - \xi(\gamma+\mu)(\chi+\delta_H)(\beta_L\chi K_H + \beta_H K_L\delta_L + \mu K_L\delta_L + \mu\chi K_H) \tag{22}$$

From Eq. (22), we have that

$$\xi^2\mu\chi N(\beta_L+\beta_H)<\frac{\xi^2\mu\chi(\gamma+\mu)(\chi+\delta_H)K_HK_L\delta_L}{\xi(\beta_L\chi K_H+\beta_HK_L\delta_L)} \quad (23)$$

Hence,

$$\xi^2\mu\chi N(\beta_L+\beta_H)<\frac{\xi^2\mu\chi(\gamma+\mu)(\chi+\delta_H)K_HK_L\delta_L}{\beta_L\chi K_H+\beta_HK_L\delta_L} \quad (24)$$

when $N<S_C$. Meanwhile,

$$\mu\chi(\beta_L+\beta_H)(\gamma+\mu)(\chi+\delta_H)K_HK_L\delta_L<(\gamma+\mu)(\chi+\delta_H)[(\beta_L\chi K_H+\beta_HK_L\delta_L+\mu K_L\delta_L+\mu\chi K_H(\beta_L\chi K_H+\beta_HK_L\delta_L)] \quad (25)$$

Manipulating both sides of Eq. (25) yields

$$\frac{\xi\mu\chi(\beta_L+\beta_H)(\gamma+\mu)(\chi+\delta_H)K_HK_L\delta_L}{\beta_L\chi K_H+\beta_HK_L\delta_L}<\xi(\gamma+\mu)(\chi+\delta_H)(\beta_L\chi K_H+\beta_HK_L\delta_L+\mu K_L\delta_L+\mu\chi K_H) \quad (26)$$

From the combination of Eq. (24) and (26), we obtain

$$\xi^2\mu\chi N(\beta_L+\beta_H)<\xi(\gamma+\mu)(\chi+\delta_H)(\beta_L\chi K_H+\beta_HK_L\delta_L+\mu K_L\delta_L+\mu\chi K_H) \quad (27)$$

which on further simplification, yields

$$\xi^2\mu\chi N(\beta_L+\beta_H)-\xi(\gamma+\mu)(\chi+\delta_H)(\beta_L\chi K_H+\beta_HK_L\delta_L+\mu K_L\delta_L+\mu\chi K_H)<0 \quad (28)$$

which implies that $V<0$ .Hence, the RHS of Eq. (21) is negative. In this case we either have two negative real roots, or two complex conjugate roots with negative real parts, for $U(I^*)^2+VI^*+W=0.$ which is a contradiction. Hence there is no positive endemic equilibrium given the condition that $R_0<1$ i.e. $N<S_C$ and $W<0$.

Finally, if $R_0=1$, then $N=S_C$ and $W=0$, i.e. Eq. (20) becomes

$$I_1\ I_2=\frac{W}{U}=0 \quad (29)$$

which implies that either $I_1=0\ or\ I_2=0$. Hence, if $I_1=0,$ then $I_2\neq 0$. Conversely, if $I_2=0,$ then $I_1\neq 0$ .Thus, Eq. (21) based on Eq. (29) gives us either for $I_1=0\ and\ I_2\neq 0,$

$$I_1+I_2=I_2=-\frac{V}{U} \quad (30)$$

or for $I_2=0\ and\ I_1\neq 0$,

$$I_1+I_2=I_1=-\frac{V}{U} \quad (31)$$

Hence, either

$$I_1=-\frac{V}{U}\ or\ I_2=-\frac{V}{U} \quad (32)$$

Hence, for $R_0=1$, Eq. (17) has only one non-zero root, $-\frac{V}{U}$, which is negative, which contradicts the statement of the theorem. Thus, the positive endemic equilibrium exists and is unique if and only if $R_0>1.$

Theorem 2

When $R_0>1$, the positive endemic equilibrium point of system (5) is locally asymptotically stable.

Proof: We consider the Jacobian ofEq. (5) at the endemic equilibrium point. In order to make the algebraic manipulation easier, we set:

$$A=\beta_L\frac{B_L^*}{K_L+B_L^*}+\beta_H\frac{B_H^*}{K_H+B_H^*},B=\beta_HS^*\frac{K_H}{(K_H+B_H^*)^2},C=\beta_LS^*\frac{K_L}{(K_L+B_L^*)^2} \quad (33)$$

where $A, B, C > 0$ .The Jacobian matrix, J^* ,at the EEP becomes

$$J^* = \begin{bmatrix} -A-\mu & 0 & 0 & -B & -C \\ A & -(\gamma+\mu) & 0 & B & C \\ 0 & \gamma & -\mu & 0 & 0 \\ 0 & \xi & 0 & -(\chi+\delta_H) & 0 \\ 0 & 0 & 0 & \chi & -\delta_L \end{bmatrix} \quad (34)$$

The characteristic polynomial of J^* is given as

$$Det\left|\lambda I - J^*\right| = (\lambda+\mu)\,[(\lambda + A+b)(\lambda+\gamma+\mu)(\lambda+\chi+\delta_H)(\lambda+\delta_L) - \xi B(\lambda+\mu)(\lambda+\delta_L) - C\xi\chi(\lambda+\mu)] = 0 \quad (35)$$

It is obvious that $\lambda = -\mu$ is a negative root of Eq. (35).

We then proceed to expand the expression in the square brackets to obtain

$$b_4\,\lambda^4 + b_3\lambda^3 + b_2\lambda^2 + b_1\lambda + b_0 = 0 \quad (36)$$

where

$$b_4 = 1 \quad (37)$$

$$b_3 = 2\mu + A + \gamma + \chi + \delta_H + \delta_L \quad (38)$$

$$b_2 = \mu^2 + \mu A + \mu\gamma + A\gamma - \xi C + 2\mu\chi + A\chi + \gamma\chi + 2\mu\delta_H + A\delta_H + \gamma\delta_H + 2\mu\delta_L + A\delta_L + \gamma\delta_L + \chi\delta_L + \delta_H\delta_L \quad (39)$$

$$b_1 = -C\xi\chi - \mu\xi B + \mu^2\chi + A\mu\chi + \mu\gamma\chi + A\gamma\chi + \mu^2\delta_H + A\mu\delta_H + \mu\gamma\delta + \mu^2\delta_L + A\mu\delta_L + \mu\gamma\delta_L + A\gamma\delta_L - \xi B\delta_L + 2\mu\chi\delta_L + A\chi\delta_L + \gamma\chi\delta_L + 2\mu\delta_H\delta_L + A\delta_H\delta_L + \gamma\delta_H\delta_L \quad (40)$$

$$b_0 = -\mu C\xi\chi - \mu\xi B\delta_L + \mu^2\chi\delta_L + \mu A\delta_L + \mu\gamma\chi\delta_L + A\gamma\chi\delta_L + \mu^2\delta_H\delta_L + \mu A\delta_H\delta_L + \mu\gamma\delta_H\delta_L + A\gamma\delta_H\delta_L \quad (41)$$

In order to prove the local asymptotic stability of Eq. (36), we employ a result from the work of Heffernan *et al*.[12], which states that for more complex models (like Eq. (1)), the characteristic equation may be of the form

$$\lambda^n + P_{n-1}\,\lambda^{n-1} + \ldots + P_1\,\lambda + P_0 = 0, \quad (42)$$

with $P_1, P_2, \ldots, P_{n-1} > 0$. In this special case, $n-1$ roots of the polynomial (Eq. (42)) have negative real part. When $P_0 = 0$, the nth root, or largest eigenvalue, is zero, when $P_0 > 0$, all eigenvalues are negative, whereas when $P_0 < 0$, the largest eigenvalue has positive real part. Thus, the stability (i.e. the local asymptotic stability in this case) is determined solely by the sign of the constant term of the characteristic equation. It, therefore, behooves us to show that Eq. (36) fits the description in Heffernan *et al*.[12].

Obviously, $b_3 > 0$, since all the parameters are positive. Now, we need to show that $b_2 > 0$. Thus,

$$b_2 = \mu^2 + \mu\mathrm{A} + \mu\gamma + \mathrm{A}\gamma - \xi C + 2\mu\chi + \mathrm{A}\chi + \gamma\chi + 2\mu\delta_H + \gamma\delta_H + 2\mu\delta_L + \mathrm{A}\delta_L + \gamma\delta_L + \chi\delta_L + \delta_H\delta_L$$

can be rewritten as

$$b_2 = \mathrm{A}(\gamma + \mu + \chi + \delta_H + \delta_L) + \delta_L(\gamma + \mu + \chi + \delta_H) + \mu(\mu + \chi + \delta_H + \delta_L) + \gamma\delta_H + (\chi + \delta_H)(\gamma + \mu) - \xi B \quad (43)$$

Considering the last part of Eq. (43), we have

$$(\chi + \delta_H)(\gamma + \mu) - \xi B \quad (44)$$

To resolve Eq. (44), we will be requiring appropriate substitutions for $(\gamma+\mu)$ and B respectively. Now, from Eq. (6), we obtain an expression for $\gamma+\mu$, i.e.

$$\gamma+\mu = \xi S^* \left(\frac{\beta_L \chi}{K_L \delta_L (\chi+\delta_H) + \xi\chi I^*} + \frac{\beta_H}{K_H (\chi+\delta_H) + \xi I^*} \right) \quad (45)$$

Recall, from Eq. (3.90), that

$$B = \beta_H S^* \frac{K_H}{(K_H + B_H^*)^2} = \beta_H S^* \frac{K_H (\chi+\delta_H)^2}{\left[K_H (\chi+\delta_H) + \xi I^*\right]^2} \quad (46)$$

and

$$C = \beta_L S^* \frac{K_L}{(K_L + B_L^*)^2} = \beta_L S^* \frac{K_L \delta_L^2 (\chi+\delta_H)^2}{\left[K_L \delta_L (\chi+\delta_H) + \xi I^*\right]^2} \quad (47)$$

Thus, substituting Eqs. (45) and (46) in Eq. (44), we obtain

$$(\chi+\delta_H)(\gamma+\mu) - \xi B = \xi S^* (\chi+\delta_H) \left[\frac{\beta_L \chi}{K_L \delta_L (\chi+\delta_H) + \xi\chi I^*} + \frac{\beta_H \xi I^*}{[K_H (\chi+\delta_H) + \xi I^*]^2} \right] > 0 \quad (48)$$

Hence, substituting Eq. (48) into Eq. (43), we obtain

$$b_2 = A(\gamma+\mu+\chi\ \delta_H+\delta_L) + \delta_L\ (\gamma+\mu+\chi+\delta_H) + \mu\ (\mu+\chi+\delta_H+\delta_L) + \gamma\delta_H + \xi S^*\ (\chi+\delta_H) \left[\frac{\beta_L \chi}{K_L \delta_L\ (\chi+\delta_H) + \xi\chi I^*} + \frac{\beta_H \xi I^*}{\left[K_H\ (\chi+\delta_H) + \xi I^*\right]^2} \right] > 0 \quad (49)$$

Hence, $b_2 > 0$.

Next, we proceed by rewriting b_1 into the sum of three parts, i.e.

$$\begin{aligned} b_1 = {} & \left(\mu^2\chi + \mu^2\delta_H + \mu\gamma\chi + \mu\gamma\delta_H - \xi\mu B\right) \\ & + (\delta_L\chi\gamma + \gamma\delta_H\delta_L + \mu\chi\delta_L + \mu\delta_H\delta_L - \xi\delta_L B - \xi\chi C) \\ & + (\mu\chi\mathrm{A} + \mu\delta_H\mathrm{A} + \mu\delta_L\mathrm{A} + \gamma\delta_H\mathrm{A} + \delta_H\delta_L\mathrm{A} + \chi\delta_L\mathrm{A} + \gamma\chi\mathrm{A} + \gamma\chi\mathrm{A} \\ & + \mu\chi\delta_L + \mu\delta_H\delta_L + \mu^2\delta_L + \mu\gamma\delta_L) \end{aligned} \quad (50)$$

NB: It is obvious that the last part of Eq. (50) is positive.

Considering the first bracket of Eq. (50),

$$\mu^2\chi + \mu^2\delta_H + \mu\gamma\chi + \mu\gamma\delta_H - \xi\mu B = \mu\ (\chi+\delta_H)(\gamma+\mu) - \xi\mu B \quad (51)$$

Substituting Eqs. (45) and (46) into the RHS of Eq. (51) and simplifying the result yields

$$\mu\ (\chi+\delta_H)(\gamma+\mu) - \xi\mu B = \xi\mu\ (\chi+\delta_H)\ S^* \left[\frac{\beta_L \chi}{K_L\delta_L\ (\chi+\delta_H) + \xi\chi I^*} + \frac{\beta_H \xi I^*}{[K_H\ (\chi+\delta_H) + \xi I^*]^2} \right] > 0 \quad (52)$$

Considering the second bracket in Eq. (50),

$$\delta_L\chi\gamma + \gamma\delta_H\delta_L + \mu\chi\delta_L + \mu\delta_H\delta_L - \xi\delta_L B - \xi\chi C = \delta_L\ (\chi+\delta_H)\ (\gamma+\mu) - \xi\delta_L\ B - \xi\chi C \quad (53)$$

Substituting Eqs. (45), (46) and (47) into the RHS of Eq. (53) and simplifying the result yields

$$\delta_L\ (\chi+\delta_H)\ (\gamma+\mu) - \xi\delta_L\ B - \xi\chi C = \xi S^* \delta_L\ (\chi+\delta_H) \left[\frac{\beta_L \xi\chi^2\ I^*}{[K_L\delta_L\ (\chi+\delta_H) + \xi\chi I^*]^2} + \frac{\beta_H \xi I^*}{[K_H\ (\chi+\delta_H) + \xi I^*]^2} \right] > 0 \quad (54)$$

Thus, $b_1 > 0$.

Thus far, we have been able to establish that

$$b_1 , b_2 , b_3 > 0 \quad (55)$$

Finally, we need to establish that $b_0 > 0$.

Rearranging and factorizing Eq. (41), we obtain

$$b_0 = \left(A\delta_L (\chi + \delta_H)(\gamma + \mu)\right) + \left(\mu\delta_L (\chi + \delta_H)(\gamma + \mu) - \mu\xi\chi C - \mu\xi\delta_L B\right) \quad (56)$$

Substituting Eqs. (45), (46) and (47) into the second part of the RHS of Eq. (56) and simplifying yields

$$b_0 = \mathrm{A}\delta_L (\chi + \delta_H)(\gamma + \mu) + \mu\xi (\chi + \delta_H)\delta_L S^* \left[\frac{\beta_L \xi\chi^2 I^*}{[K_L\delta_L (\chi + \delta_H) + \xi\chi I^*]^2} + \frac{\beta_H \xi I^*}{[K_H(\chi + \delta_H) + \xi I^*]^2}\right] > 0 \quad (57)$$

Thus, $b_0 > 0$.

Recall, from Heffernan *et al*. [12], that

1. When $b_0 = 0$, the fourth root, or largest eigenvalue, is zero;
2. When $b_0 > 0$ all eigenvalues are negative and;
3. When $b_0 < 0$, the largest eigenvalue has positive real part.

Thus, since our $b_0 > 0$ and the stability, i.e. the local asymptotic stability, is determined by the sign of the constant term of the characteristic equation, the positive endemic equilibrium of system (5) is LAS (i.e. locally asymptotically stable), when $R_0 > 1$.

3.0 Linear Global Stability

The classical Poincare-Bendixson theory is a powerful tool to study global stability of non-linear autonomous systems. However, this framework cannot be directly extended to higher dimensional systems. Consequently, the global stability analysis of endemic equilibria, for non-linear higher-dimensional problems, such as the one in Eq. (1), is generally difficult despite the efforts made by several authors [11]. For some special differential equation systems, one might be able to find a suitable Lyapunov function [13, 14] to prove the global stability. Unfortunately, there is no systemic way to construct or find Lyapunov functions, which hinders the application of this approach to more general model systems [11]. We propose that the unique positive endemic equilibrium of system (1) is globally asymptotically stable when $R_0 > 1$ [11]. We will employ a special linear case to illustrate this point.

Case 1: We assume that the pathogen concentrations in the environment are far beyond the HI and LI half saturation rates (ID_{50}), i.e. $B_L >> K_L \ and \ B_H >> K_H$. Under this assumption, the incidence rates in the model become

$$\frac{B_L}{K_L + B_L} \approx 1 \ \ and \ \ \frac{B_H}{K_H + B_H} \approx 1 \quad (58)$$

That is, the possibility of infection is about 100% to those exposed to pathogens. Since $R = N - I - S$, the model (1) is reduced to a two-dimensional linear system:

$$\frac{dS}{dt} = \mu N - (\beta + \mu) S \quad (59)$$

$$\frac{dI}{dt} = \beta S - (\gamma + \mu) I \quad (60)$$

with $\beta = \beta_L + \beta_H$. It is straightforward to determine the unique positive endemic equilibrium of this system ((59) and (60)):

$$S^* = \frac{\mu N}{\beta + \mu} \quad (61)$$

and

$$I^* = \frac{\beta\mu N}{(\beta + \mu)(\gamma + \mu)} \quad (62)$$

There is no DFE in this case since I^* exists and is positive since all the parameters are positive. Meanwhile, the exact solution of the system ((59), (60)) can be obtained as follows:

Integrating Eq. (59) yields

$$S(t)=\frac{\mu N}{\beta+\mu} + \left(S(0) - \frac{\mu N}{\beta+\mu}\right) e^{-(\beta+\mu)t} \quad (63)$$

Integrating Eq. (60), we have

$$I(t) = \frac{\beta\mu N}{(\beta+\mu)(\gamma+\mu)} + \varphi_1 e^{-(\beta+\mu)t} + \varphi_2 e^{-(\gamma+\mu)t} \quad (64)$$

where

$$\phi_1 = \frac{\beta}{\gamma-\beta}\left(S(0) - \frac{\mu N}{\beta+\mu}\right) e^{-(\beta+\mu)t}$$

$$\phi_2 = I(0) - \frac{\beta\mu N}{(\beta+\mu)(\gamma+\mu)} - \frac{\beta}{\gamma-\beta}\left(S(0) - \frac{\mu N}{\gamma+\mu}\right)$$

Hence, we observe from Eqs. (63) and (64) that as $t\to\infty, S(t) \to S^* \text{ while } I(t) \to I^*$ regardless of the initial values of S and I respectively. Thus, the endemic equilibrium (S^*, I^*) is linearly globally asymptotically stable.

Case 2: In this case, we assume the pathogen concentrations are much lower than the half saturation rates, i.e., $B_L << K_L \text{ and } B_H << K_H$. This leads us to

$$\frac{B_L}{K_L + B_L} \approx 0 \quad and \quad \frac{B_H}{K_H + B_H} \approx 0 \quad (65)$$

That is, the possibility or chance of getting new infection is about 0. Our model system (1) is then reduced to

$$\frac{dS}{dt} = \mu N - \mu S \quad (66)$$

$$\frac{dI}{dt} = -(\gamma+\mu) I \quad (67)$$

We observe that there is no endemic equilibrium point in this case and the only equilibrium point of system ((66), (67)) is a DFE, i.e.

$$S(0) = N \quad (68)$$

and

$$I(0) = 0 \quad (69)$$

The exact solution of Eqs. (66) and (67) can be obtained as follows:Considering Eq. (66),

$$\frac{dS}{dt} = \mu N - \mu S$$

Integrating Eq. (66) yields

$$S(t) = N + (S(0) - N)e^{-\mu t} \quad (70)$$

Integrating Eq. (67) yields

$$I(t) = I(0) e^{-(\gamma+\mu)t} \quad (80)$$

Clearly, from Eqs. (67) and (80), $S(t) \to S(0) \text{ and } I(t) \to I(0) \text{ as } t \to \infty$, confirming the global stability of the DFE.

4.0 Parameter Estimation and Numerical Results

4.1 Parameter Estimation

We set the week as the unit of time. The constant mortality (μ) is estimated as the inverse of life expectancy at birth which

is about 49 years in Nigeria [15]. Hence μ = 1/49 = 0.02041 yr^{-1} = 0.000392465 wk^{-1}. We shall assume an arbitrary value for the net death rate of HI vibrios in the environment (δ_H).Among the many parameters in our model (1), K_L, K_H, χ, ξ, δ_L, β_H and β_L have been estimated by various literatures[11]; their values are listed in Table 1 and treated as reliable in our work. Since the total population of Nigeria is about 155 million [16] we scale down this number by a factor of 15,500 to match the hypothetical population of 10,000 in [9]. This figure is assumed to be constant i.e. births equals deaths.

Table 1: Model parameters and values. Source: [9, 11]

Model Parameter	**Symbol**	**Value**
Rate of drinking LI *V. cholerae*	β_L	1.50wk^{-1}
Rate of drinking HI *V. cholerae*	β_H	1.15wk^{-1}
Non-HI *V. cholerae* infectious concentration (ID_{50})	K_L	10^6 cells/ml
HI *V. cholerae* infectious concentration (ID_{50})	K_H	$K_H = K_L \div 700$ $= 1428.571429$ cells/ml
Natural human birth and death rate	μ	0.000392465wk^{-1}
Rate of decay from hyper- to reduced infectiousness	χ	33.60wk^{-1}
Rate of contribution to HI *V. cholerae* in the aquatic environment	ξ	70wk^{-1}
Net death rate of non-HI vibrios in the environment	δ_L	0.23333wk^{-1}
Net death rate of HI vibrios	δ_H	$*\delta_H = \delta_L$
Rate of recovery from cholera	γ	1.40wk^{-1}

By substituting the values of the model parameters in Table 1 into equations (2) and (3), we find that the basic reproduction number

$$R_0 = 15.083 \qquad (81)$$

and that the population threshold

$$S_C = 663 \qquad (82)$$

The fact that $R_0 > 1$, justifies the development of the cholera epidemics. The relatively large value of R_0 for the Nigerian cholera outbreak is attributed to the fact that the frequent exposure to and high consumption rate of *V. cholerae* infested water in Nigeria which is the resultant effect of the inadequate provision of potable water for her citizens and poor sanitation facilities due to overcrowding in areas ravaged by the disease. Although nearly 0.064 million cases of cholera between January 2010 and October 2011 have been reported, the overall percentage of infection with respect to the total population is still very low (less than 0.0004%). The R_0 estimated here is regarded as a nationally averaged reproduction rate. It is worthy of note that, scientifically, when the rate of drinking HI *V. cholerae*, β_H, is almost equal to the rate of drinking LI *V. cholerae*, β_L, i.e. $\beta_H \approx \beta_L$, then the value of R_0 will be quite large [9]. Meanwhile, we substitute these parameter values into equations (6 - 10) and find the unique positive endemic equilibrium:

$$S^* = 665,\ I^* = 2.6160,\ R^* = 9332,\ B_H{}^* = 5.4140,\ B_L{}^* = 779.50 \qquad (83)$$

Note again that we have scaled down the total population in Nigeria by a factor of 15,500 to match the hypothetical population $N = 10{,}000$. Thus, our model predicts that the realistic endemic infection number in Nigeria is about 40,548.

4.2 Numerical Results

To verify the model prediction, we run the numerical simulation for a large period of time (up to 2,000 weeks) with the initial conditions: $I(0) = 1,\ S(0) = 9999,\ R(0) = B_H(0) = B_L(0) = 0$ and present the results for I, S and R in Figures 1, 2 and 3.The first peak of the infection curve in Figure 1 represents the 2010-2011 cholera outbreaks.

The infection number (I) starts to decline once the susceptible population (S) falls below the threshold, $S_C = 665$. After this outbreak I drops to almost zero, meaning that the majority of the infected population have recovered and entered the recovered class, R, so that we observe a significant increase of R in Figure 3. Then I stays at zero level for the next 131 weeks or so (almost 3 years). During this period, the value of R gradually decreases due to the natural death of recovered individuals whereas the value of S gradually increases due to continuous birth of new susceptibles. Once the susceptible population exceeds the threshold $S_C = 665$, another cholera outbreak is triggered but with much lower magnitude. This pattern continues for a few more outbreaks with decaying magnitudes. After about 900 weeks, the infection curve rests at the endemic value, $I^* = 2.6160$; the S and R curves also converge to their endemic values, $S^* = 665$ and $R^* = 9332$ respectively.Figures 4, 5 and 6 show the results of another numerical run with different initial conditions: $I(0) = 5$, $S(0) = 8995$, $R(0) = 1000$, $B_H(0) = B_L(0) = 0$. We observe a very similar pattern to that which we had earlier obtained. In particular, the I, S and R curves all approach their endemic equilibrium values after about 900 weeks. This pattern demonstrates the global asymptotic stability of the endemic equilibrium when $R_0 > 1$. Meanwhile, these results also justify the instability of the disease-free equilibrium, as cholera outbreaks occur whenever the susceptible population S exceeds the critical value S_C. It is worthy of note that Figures 1 and 4 exhibit low endemicity.

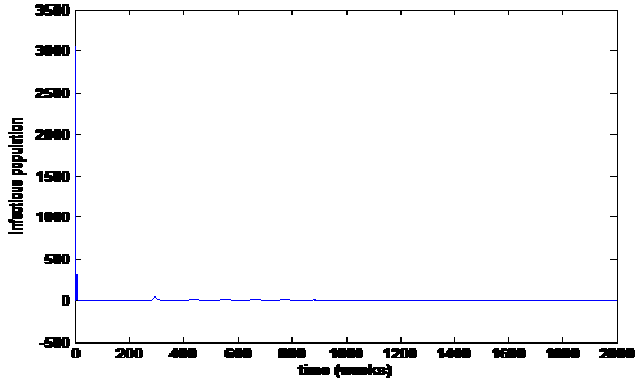

Figure 1: The infected population vs. time with the initial setting: $I(0) = 1$, $S(0) = 9999$, $R(0) = B_H(0) = B_L(0) = 0$. This curve exhibits several epidemic oscillations and then approaches the endemic equilibrium: $I^* = 2.6160$ over time.

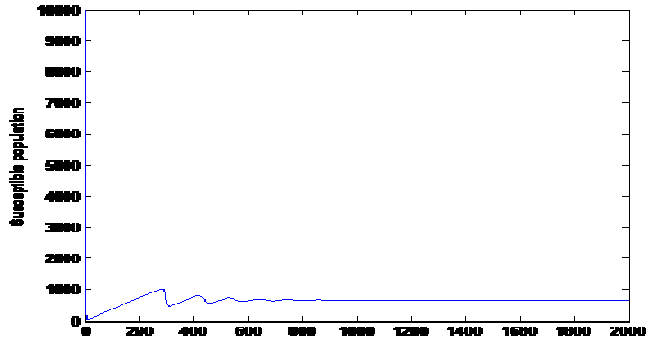

Figure 2: The susceptible population vs. time with the initial setting: $I(0) = 1$, $S(0) = 9999$, $R(0) = B_H(0) = B_L(0) = 0$. This curve exhibits several epidemic oscillations before approaching the endemic equilibrium: $S^* = 665$ over time.

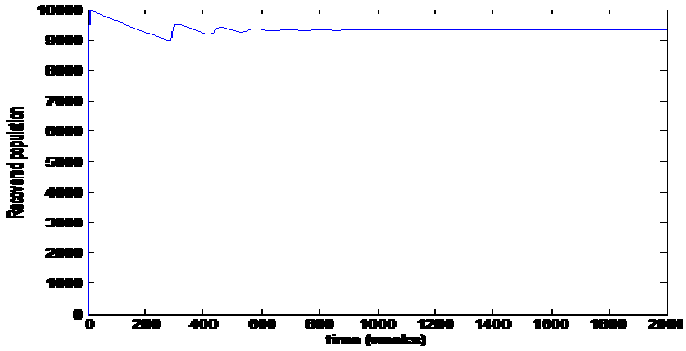

Figure 3: The recovered population vs. time with the initial setting: $I(0)=1,\ S(0)=9999,\ R(0)=B_H(0)=B_L(0)=0$. This curve exhibits several epidemic oscillations and then approaches the endemic equilibrium: $R^*=9332$ over time.

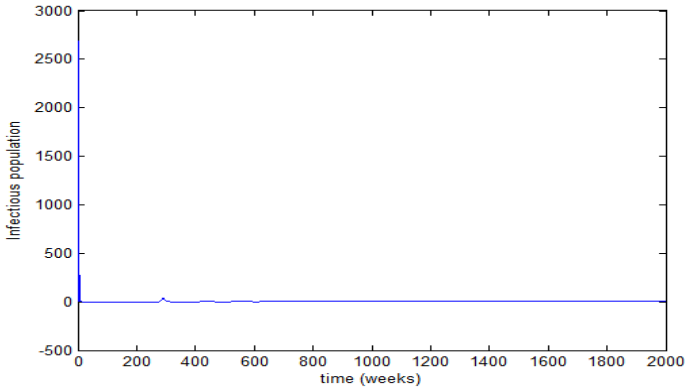

Figure 4: The infected population vs. time with the initial setting: $I(0)=5,\ S(0)=8995,\ R(0)=1000,\ B_H(0)=B_L(0)=0$. This curve exhibits several epidemic oscillations and then approaches the endemic equilibrium over time.

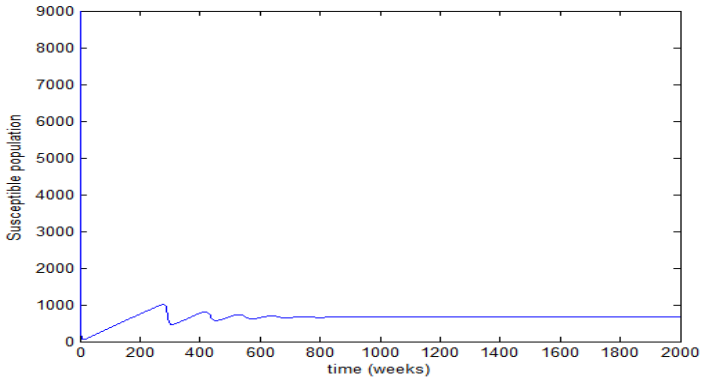

Figure 5: The susceptible population vs. time with the initial setting: $I(0)=5,\ S(0)=8995,\ R(0)=1000,\ B_H(0)=B_L(0)=0$. This curve exhibits several epidemic oscillations before approaching the endemic equilibrium over time.

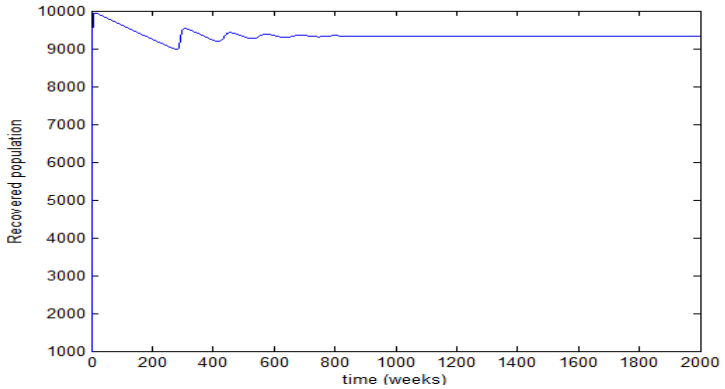

Figure 6: The recovered population vs. time with the initial setting: $I(0)=5,\ S(0)=8995,\ R(0)=1000,$ $B_H(0)=B_L(0)=0$. This curve exhibits several epidemic oscillations and then approaches the endemic equilibrium over time.

5.0 Conclusion

This work showed the stability of the EEP of the cholera mathematical model [10]. We showed that the positive EEP of the model in [10] exists and is unique where the associated reproduction number is greater than unity. The endemic equilibrium point was shown to be locally asymptotically stable while, for the special linear case, it was globally asymptotically stable. Numerically, we also demonstrated cases of low and high endemicity depending on the value of the basic reproduction number.

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