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Qualitative Study of a Cholera Model

[1]Oghre E. O. and [2]Akhaze R. U.

**[1,2]Department of Mathematics,
University of Benin, Benin City;**

Abstract

A Mathematical model for the dynamics of cholera in an aquatic environment is developed. The model examines and analyses the effect of the growth rate of the V. cholera in the lower-infective class on the dynamics of the disease. The effect of this assumption was used to derive the basic reproduction number, R_0 which was used in analyzing the stability of the disease free equilibrium point. The results obtained show the strong likelihood of cholera outbreaks due to the growth of the lower-infective V. cholera and the contributions from the infective.

Keywords: Basic reproduction number, disease-free equilibrium, epidemic, cholera disease, , infective, mathematical model, population, removed, susceptible.

1.0 Introduction

Cholera is an acute intestinal infection caused by the ingestion of contaminated food and water with Vibrio cholerae bacterium. Vibrio cholera is a motile gram negative curved rod bacterium that causes cholera in humans [1]. Among more than 200 serogroups of Vibrio Cholerae, epidemic disease has been linked almost with serogroups 01 and 0139 [2].

The etiological agent, V. Cholerae 01 (and more recently V. Cholerae 0139) passes through and survives the gastric acid barriers of the stomach and then penetrates the muscle lining that coats the intestinal epithelial [3]. In volunteer studies, the infectious dose was determined to be $10^2 – 10^3$ cells [4]. Once they colonize the intestinal gut, they produce enterotoxin (which stimulates water and electrolyte secretion by the endothelial cells of the small intestine) that leads to watery diarrahoea and if left untreated, it leads to death within hours. Cholera is characterized in its most severe form, by the sudden onset of acute watery diarrhea that can lead to death by severe dehydration.

Cholera can either be transmitted through interaction between humans (i.e. Faecal – Oral), or through interaction between human and their environment (i.e. ingestion of contaminated water and food from the environment). Some of the recommended controlling mechanisms (by WHO) are providing safe and clean drinking water (chlorination), intensified promotion to improve the population awareness and sanitary practice like the washing of hands after defecation and before handling food, proper disposal of human excreta and sanitation practices especially in highly populated areas.

Recent experimental observations suggest that the V. cholerae ID_{50} (the infectious dose sufficient to produce frank disease in 50% of those exposed) depends upon the length of time the pathogen has existed outside the host. Passage of V. cholerae 01 Inaba EI Tor (one of the group in V. cholera 01) through the human host appears to transiently increase the infectivity of V. cholerae [5]. Laboratory experiments also demonstrate that when inoculated into the intestines of mice, freshly shed V. cholera greatly out-competes bacteria grown *in vitro*, as much as 700-fold. Which means that after some hours, freshly shed V. cholerae organism lose their competitive advantage. Comparing freshly shed vibrios to those not freshly shed, a different set of genes were up-regulated and these are thought to be responsible for faster bacterial growth in the gastrointestinal tract and increased shedding. Such observations suggest that passage of V. cholera 01 Inaba EL Tor through the human gastrointestinal tract results in a short-lived, hyperinfection (HI) state.[6] Hyperinfectivity is key to understanding the explosive nature of human-to-human transmission in out breaks. Hartley has model the picture of cholera, demonstrating the existence of a transient HI state and the attendant reduction in ID_{50} explains the explosiveness of cholera epidemics.

[1]Corresponding author: ***Oghre E. O.,*** E-mail: eoghre@yahoo.com, Tel. +234 8033551266 and 08181657432 (A. R. U.)

Capasso and Paveri-Fantana [7] describe the dynamics of the infected individuals in the community and the dynamics of the free-living bacteria population of the 1973 epidemic of cholera in Italy. Codeco [8] developed a model with an additional equation for the susceptible individual of the population. Thus the model is given

$$\left.\begin{aligned} \frac{dS}{dt} &= n(H-S) - a\lambda(B)S \\ \frac{dI}{dt} &= a\lambda(B)S - \gamma I \\ \frac{dB}{dt} &= B(nb-mb) + \ell l \end{aligned}\right\} \qquad (1.1)$$

With

$$\lambda(B) = \frac{B}{K+B}$$

The reproduction number was given by

$$R_O = \frac{a\ell}{rk(mb-nb)} S_O$$

Where,

H	total human population
n	Human birth and death rates (day-1)
	a rate of exposure to contaminated water (day-1)
K	concentration of V. cholerae in water that yields 50% chance of catching cholera (cells/ml)
r	rate at which people recover from cholera (day-1)
nb	growth rate of V. cholerae in the aquatic environment (day-1)
mb	loss rate of V. cholerae in the aquatic environment (day-1)
e	contribution of each infected person to the population of V. cholera in the aquatic environment (cell/ml day-1 person-1)

This means that there will be an outbreak of cholera due to individual coming in contact with contaminated water.

Hartley et al. [9] developed a more general model which took into account the different infective states of Vibrio cholerae. Liao and Wang [10] gave a mathematical analysis of the model in [9]. His model contains five equations which describe the dynamics of susceptible, infective and removed human population and the dynamics of a hyperinfective state and the lower infective state of V. cholerae population. The model was given by

$$\left.\begin{aligned} \frac{dS}{dt} &= \mu(N-S) - \beta_H \frac{SB_H}{B_H+K_H} - \beta_L \frac{SB_H}{B_H+K_H} \\ \frac{dI}{dt} &= \beta_H \frac{SB_H}{B_H+K_H} + \beta_L \frac{SB_H}{B_H+K_H} - (\mu+\gamma)I \\ \frac{dR}{dt} &= \gamma I - \mu R \\ \frac{d\beta_H}{dt} &= \xi I - \chi B_H \\ \frac{d\beta_L}{dt} &= \chi B_H - \delta_L B_L \end{aligned}\right\} \qquad (1.2)$$

Where,

S	-	S(t) is the susceptible class
I	-	I(t) is the infected and infectious class
R	-	R(t) is the dead or recovered and immune.
B_H	-	Is the concentration of the hyperinfectious (HI) of V. cholerae.
B_L	-	Is the concentration of the lower infectious (LI) of V. cholera
μ	=	Constant birth and death rate.
N	=	Total human population.
β_H	=	Rate of drinking HI, V. cholerae
β_L	=	Rate of drinking low infective V. cholerae
K_H	=	HI V. cholerae infectious concentration.
K_L	=	Non HI V. cholerae Infectious concentration
ξ	=	Rate of contribution to HI V. cholerae in aquatic environment.
χ	=	Rate of decay from hyperinfective to lower infective state.
γ	=	Rate of recovery from cholera
δ_L	=	Net death rate of non-HI V. cholerae in the environment

In this paper, we present a mathematical model for the dynamics of the disease. Steady states are examined and a threshold condition is obtained. Situations that could allow for endemicity were also examined.

2.0 The Mathematical Model

The model under consideration is S – I – R (Susceptible – Infectious – Removed) model for infectious diseases, with a combination from the aquatic environment due to contribution from V. cholerae in both the hyperinfectivity (HI) and Lower infectivity (LI) states represented by B_H and B_L respectively

The Figure 2.1 describes the process of our model

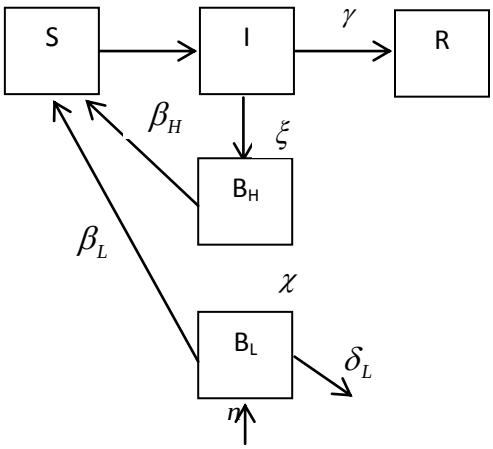

Fig. 2.1: The schematic diagram showing the relationship between the Susceptible class S, infected and infectious class I, and removed class R for our SIR model.

Hence, our model can be expressed as follows:

$$\left.\begin{aligned}
\frac{dS}{dt} &= N\mu - \beta_H \frac{SB_H}{K_H + B_H} - \beta_L \frac{SB_L}{K_L + B_L} - \mu S \\
\frac{dI}{dt} &= \beta_H \frac{SB_H}{K_H + B_H} + \beta_L \frac{SB_L}{K_L + B_L} - (\gamma + \mu) I \\
\frac{dR}{dt} &= \gamma I - \mu R \\
\frac{dB_H}{dt} &= \xi I - \chi B_H \\
\frac{dB_L}{dt} &= \chi B_H + (n - \delta_L) B_L
\end{aligned}\right\} \qquad (2.1)$$

Where

n = Growth rate of V. cholerae in the aquatic environment.

With S (0), I (0), R(0) given as the initial condition and N = S + I + R.

The difference between Hartley model and our model, is the inclusion of growth term in last equation ie. ($(n - \delta_L) B_L$). The growth term was introduced due to environmental factor. Since bacteria are anaerobic in nature, they multiply very fast.

3.1 Model Analysis

The Disease-Free Equilibrium

When we write the above equation in a vector form, we have

$$\frac{d}{dt}(S, I, R, B_H, B_L)^T = F\left((S, I, R, B_H, B_L)^T\right)$$

So that $\frac{d}{dt} X = F(X)$ (3.1)

Where

$$X = (S, I, R, B_H, B_L)^T,$$

At the disease free equilibrium we have

$$X_0 = (N, O, O, O, O)^T \qquad (3.2)$$

The local stability of the DFE, which is directly related to the disease epidemics is analysed as follows using the Jacobian of the ordinary differential equation system

$$J^0 = \begin{bmatrix}
-\beta_L \frac{B_L}{K_L + B_L} - \beta_H \frac{B_H}{K_H + B_H} - \mu & O & O & -\beta_H \frac{SK_H}{(K_H + B_H)^2} - \beta_L \frac{SK_L}{(K_L + B_L)^2} \\
\beta_L \frac{B_L}{K_L + B_L} + \beta_H \frac{B_H}{K_H + B_H} & -(\gamma + \mu) & O & \beta_H \frac{SK_H}{(K_H + B_H)^2} \; \beta_L \frac{SK_L}{(K_L + B_L)^2} \\
O & \gamma & -\mu & O & O \\
O & \xi & O & -\chi & O \\
O & O & O & \chi & -(\delta_L - n)
\end{bmatrix}$$

$$J^0 = \begin{bmatrix} -\mu & O & O & -\beta_H \frac{N}{K_H} & -\beta_L \frac{N}{K_L} \\ O & -(\gamma+\mu) & O & \beta_H \frac{N}{K_H} & \beta_L \frac{N}{K_L} \\ O & \gamma & -\mu & O & O \\ O & \xi & O & -\chi & O \\ O & O & O & \chi & -(\delta_L - n) \end{bmatrix}$$

Where I is a 5 by 5 unit matrix and λ the eigenvalues. Thus

$$\left|\lambda I - J^o\right| = (\lambda+\mu)(\lambda+(\gamma+\mu)) \begin{vmatrix} \lambda+\mu & O & O \\ O & \lambda+\chi & O \\ O & -\chi & \lambda+(\delta_L - n) \end{vmatrix}$$

$$-(\lambda+\mu)\left(\beta_H \frac{N}{K_H}\right) \begin{vmatrix} -\gamma & \lambda+\mu & O \\ \xi & O & O \\ O & O & \lambda+(\delta_L - n) \end{vmatrix}$$

$$+(\lambda+\mu)\left(\beta_L \frac{N}{K_L}\right) \begin{vmatrix} -\gamma & \lambda+\mu & O \\ \xi & O & \lambda+\chi \\ O & O & -\chi \end{vmatrix}$$

$$+\left(\beta_H \frac{N}{K_H}\right)(\lambda+(\gamma+\mu)) \begin{vmatrix} O & \lambda+\mu & O \\ O & O & O \\ O & O & \lambda+(\delta_L - n) \end{vmatrix}$$

$$+\left(\beta_L \frac{N}{K_L}\right)\left(\beta_H \frac{N}{K_H}\right) \begin{vmatrix} O & -\gamma & \lambda+\mu \\ O & -\xi & O \\ O & O & O \end{vmatrix}$$

$$-\left(\beta_L \frac{N}{K_L}\right)(\lambda+(\gamma+\mu)) \begin{vmatrix} O & \lambda+\mu & O \\ O & O & \lambda+\chi \\ O & O & -\chi \end{vmatrix}$$

$$+\left(\beta_L \frac{N}{K_L}\right)\left(\beta_H \frac{N}{K_H}\right) \begin{vmatrix} O & -\gamma & \lambda+\mu \\ O & -\xi & O \\ O & O & O \end{vmatrix}$$

This implies that

$$\left|\lambda I - J^o\right| = \left[\lambda^3 - \lambda^2((\delta_L - n)+\chi+\gamma+\mu) - \lambda[\chi(\delta_L - n) - \gamma(\delta_L - n) + \chi\gamma - \mu(\delta_L - n) + \chi\mu + \beta_H \frac{N\xi}{K_H}\right] -$$

$$\left(\chi\gamma \left(\delta_L - n\right) - \chi\mu \left(\delta_L - n\right) + \beta_H \frac{N}{K_H} \xi\left(\delta_L - n\right) - \beta_L \frac{N}{K_L} \chi\xi \right)] \left(\lambda + \mu\right)^2 \qquad (3.3)$$

3.2 Stability of The Disease Free Equilibrium Point

The equilibrium point of equation (3.1) is locally asymptotically stable if and only if all roots of the above polynomial have negative root of multiplicity 2.

We set the following;

$$\ell_1 = \left(\delta_L - n\right) + \chi + \gamma + \mu$$

$$\ell_2 = \chi\left(\delta_L - n\right) + \gamma\left(\delta_L - n\right) + \gamma\chi + \mu\left(\delta_L - n\right) + \mu\chi - \beta_H \frac{N\xi}{K_H}$$

$$\ell_3 = \gamma\chi\left(\delta_L - n\right) + \mu\chi\left(\delta_L - n\right) - \beta_H \frac{N\xi}{K_H}\left(\delta_L - n\right) - \beta_L \frac{N\xi\chi}{K_L}$$

To analyze the three roots of the cubic polynomial inside the square brackets, we use the sufficient and necessary condition for stability based on the Routh-Hurwitz criterion [11, 12].

$$\ell_1 > 0, \quad \ell_3 > 0, \quad \ell_1 \ell_2 - \ell_3 > 0 \qquad (3.4)$$

The first inequality

$$\ell_1 = \left(\delta_L - n\right) + \chi + \gamma + \mu > 0$$

The second inequality, $\ell_3 > 0$, holds if and only if

$$\left[-\chi\gamma \left(\delta_L - n\right) - \mu\chi \left(\delta_L - n\right) + \beta_H \frac{N\xi}{K_H}\left(\delta_L - n\right) \right] + \beta_L \frac{N\xi\chi}{K_L} < 0$$

Dividing through by $\left(\delta_L - n\right)$

$$\left[-\chi\gamma - \mu\chi + \beta_H \frac{N\xi}{K_H} \right] + \beta_L \frac{N\xi\chi}{K_L(\delta_L - n)} < 0$$

$$\left(-\chi \left(\gamma + \mu\right) + \beta_H \frac{N\xi}{K_H} \right) + \beta_L \frac{N\xi\chi}{K_L\left(\delta_L - n\right)} < 0 \qquad (3.5)$$

This yields

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

$$N < \frac{\left(\gamma + \mu\right)\chi\ K_H\ K_L\left(\delta_L - n\right)}{\xi\left(\beta_H\ K_L\left(\delta_L - n\right) + \beta_L\ \chi K_H\right)} \qquad (3.6)$$

In addition we have

$$\ell_1\ \ell_2 - \ell_3 = \left(\left(\delta_L - n\right) + \chi + \gamma + \mu\right)\left[\left(\delta_L - n\right)\left(\chi + \gamma + \mu\right) + \chi\left(\gamma + \mu\right) - \beta_H \frac{N\xi}{K_H} \right]$$

$$- \gamma\chi\left(\delta_L - n\right) - \mu\chi\left(\delta_L - n\right) + \beta_H \frac{N\xi}{K_H}\left(\delta_L - n\right) + \beta_L \frac{N\xi}{K_L}$$

$$= (\chi + \gamma + \mu)\left[\left((\delta_L - n)^2 + (\delta_L - n)\,\chi + (\delta_L - n)\,\gamma + (\delta_L - n)\,\mu\right) - \chi\,(\gamma + \mu) + \beta_H \frac{N\xi}{K_H}\right] + \beta_L \frac{N\xi\chi}{K_L}$$

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

It is clear that $\ell_1 \ell_2 - \ell_3 > 0$ as long as the inequality

$$\left(-\chi\,(\gamma + \mu) + \beta_H \frac{N\xi}{K_H}\right) + \frac{\beta_L N\xi\chi}{K_L(\delta_L - n)} < 0$$

Or, equivalently,

$$N < \frac{(\gamma + \mu)\,\chi K_H\, K_L\,(\delta_L - n)}{\xi\,(\beta_H\, K_L\,(\delta_L - n) + \beta_L\,\chi K_H)}$$

holds. This provides a threshold for the total population (which was the susceptible initially)

$$S_c = \frac{(\gamma + \mu)\;\chi\, K_H K_L\,(\delta_L - n)}{\xi\,(\beta_H K_L\,(\delta_L - n) + \beta_L\,\chi K_H)} \qquad (3.7)$$

When N is below S_c, the Disease Free - Equilibrium is stable and no epidemicity would occur. In contrast, if N is above this critical value, the DFE becomes unstable and any infection entering the population would persist and lead to an epidemic.

An epidemic ensues if the basic reproductive number $R_0>1$: that is, the number of secondary infections which arise from a primary infection greater than 1. Van den Driessche–Watmough [13] defined the basic reproduction number as 'the number of new infections produced by a typical infective individual in a population at a disease-free equilibrium, with the condition that the disease-free equilibrium is locally asymptotically stable in the system.' Their definition is more general than other definitions of the basic reproduction number.

From the work of Diekmann [14], we compute the basic reproduction number to be

$$R_0 = \frac{\xi N}{\gamma + \mu}\left[\frac{\beta_H\, K_L(\delta_L - n) + \beta_L\,\chi K_H}{\chi K_H\, K_L\,(\delta_L - n)}\right] \qquad (3.8)$$

The basic reproduction number of Hartley's model was given by

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

Where $\frac{\xi}{\gamma + \mu}$ is the average amount of V. cholera shed per infected individual, $\frac{\beta_H}{K_H}\;\frac{1}{\chi}$ is the number of new infections caused by one case of hyper infective state, and $\frac{\beta_L}{K_L}\;\frac{1}{\delta_L}$ is the number of new infections caused by one case of the lower infective state.

According to our model, a permanent environmental reservoir of toxigenic V. cholera ($(\delta_L = n)$) should increase the basic reproduction number towards infinity equation (3. 8). It means that any susceptible human population exposed to this water would be prone to cholera outbreaks. The magnitude of the problem, in terms of public health, would vary according to the probability of secondary transmission. In a community with good sanitation, cholera would show up as occasional primary cases without secondary transmission. In poor communities, on the other hand, endemism would result from the close contact between susceptible and the source of contamination.

Endemic cholera, however, can be maintained even in the absence of a permanent reservoir $(\delta_L > n)$. Endemism is maintained if bacteria net loss rate $(\delta_L - n)$ is sufficiently low to maintain an aquatic population of V. cholerae until the susceptible pool crosses the threshold S_c again

4.1 Conclusion

Our model is an improvement of the existing model of Hartley et al [9] through the introduction of growth rate The basic reproduction number, R_0 was calculated, derived and employed in the analysis of the stability of the disease free equilibrium point. The positive endemic equilibrium of the model was found to exist and is unique for $R_0 > 1$ and unstable for $R_0 < 1$. The disease - free equilibrium of the model was locally asymptotically stable for $R_0 < 1$ and unstable for $R_0 > 1$, the results obtain show that There is a threshold parameter, R_0, and the disease can persist if and only if $R_0 > 1$.

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