A Mathematical Model of Cholera Outbreak With Type III Functional Response

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***Abstract*—** Several mathematical models of the Cholera epidemic have been proposed in response to outbreaks in many countries of the world. South Sudan offers the most example of the tragedy that befalls a country and its people when cholera stroked it in the past years. In this paper, we propose a cholera model that describes the disease outbreaks in South Sudan during 2016-2017. We formulated a SIR-type model with a pathogen class, a deterministic mathematical model using a system of ordinary differential equations. We conducted an analysis to verify the positivity and boundness of the model solution, then we conducted an analysis of the existence of both a disease-free and endemic equilibria. The basic reproduction number was computed by using the next-generation matrix approach. The local and global stabilities of both the disease-free and endemic equilibria are analyzed. Also, the model is used to fit the real disease situation of the cholera outbreak in South Sudan, and sensitivity analysis of the key parameters is carried out. Finally, the system of differential equations is solved numerically to show the numerical results.

Keywords: Cholera model; Basic reproduction number; Holling Type-III functional response; Stability analysis.

I. INTRODUCTION

Cholera disease is a bacteria disease caused by Vibrio cholerae bacteria [20]. The cholera bacterium has two reservoirs, humans and the aquatic environment, where saltwater serves as its natural habitat; and as a result, it is commonly found in oysters. Cholera diseases can be transmitted directly to humans by person-to-person contact or indirectly to humans via contaminated water [30, 32, 13, 33, 14, 38, 3, 16, 20, 39].

The mechanism of action of cholera Vibrio cholerae passes through the stomach acid barrier in the stomach and then penetrates the mucus lining that envelops the intestinal epithelium. Once it colonizes the intestines, it produces enterotoxins, which cause human cholera symptoms [39], such as the secretion of fluids and electrolytes by intestinal epithelial cells. Other symptoms may be nausea, muscle cramps, vomiting, and leg cramps. If infected individuals do not receive treatment, they become dehydrated and suffer from a breakdown of blood circulation. This condition can lead to death within 12 to 24 hours [3, 21, 26, 32, 29]. The period of infection of cholera ranges from a few hours to 5 [26]. Under normal circumstances, cholera is relatively easy to treat by treating oral dehydration using clear water and a modest amount of salt and sugar has saved millions of lives and reduced overall case fatality rates below 1%.

Antibiotics are also used for treatment, but their effects are unclear because they contribute to increasing antimicrobial resistance [41].

Although cholera is a disease that appeared about 200 years ago and combating it is still a challenge until now [13, 3, 26, 30]. Cholera is common in developing countries like Africa, parts of Asia, and South and Central America where there is inadequate sanitation and clean drinking water [38, 26].

Between 2007 and 2018, the world witnessed many cholera outbreaks in developing countries, specifically in Angola, Haiti, Zimbabwe, and Yemen, in particular India (2007), Congo (2008), Iraq (2008), Zimbabwe (2008-2009), Vietnam (2009), Nigeria (2010), Kenya (2010), Haiti (2010), Cameroon (2010-2011) and Yemen (2016-2018). It was the worst cholera outbreak in modern history [21, 33, 27, 14, 38, 3, 1, 35, 16, 41].

According to the WHO fact sheet 2018, between 1.3 to 4 million cases of cholera occurred and between 21 , 000 to 143,000 people died of cholera in the world [29, 30]. The global number of cholera cases reported to WHO during 2014 (190000), 2015 (170000), 2016 (130000) 2017 (1215000), 2018 (499447), and 2019 (923037) (see statista website). According to European Centre for Disease Prevention and Control (ECDC), Several countries in Africa and Asia have reported cholera outbreaks in 2021 approximately 13162 suspected cholera cases, including 101 deaths, have been reported worldwide (see ECDC webpage).

In this paper we develop a general SEIRB mathematical model that involves a Holling type III functional response, to describe the dynamics of cholera outbreak. We will analyze the model stability both locally and globally.

The rest of the paper is organized as follows. In Section 2, we formulate the

mathematical model and analyze it in Sects .3 and 4, we establish the Basic properties R0 of the model. In Section 5, the model is used to fit the real disease situation of a cholera outbreak in South Sudan and solve the resulting cholera model numerically. Finally, the conclusions are summarized in Section 6.

II. Model Formulation

Let N(t) be the total human population in any region under consideration at time t which is divided into five compartments with respect to their disease status in the system, Susceptible humans (S(t)), Infectious humans (I(t)), and Recovered humans (R(t)). Let B(t) be the density of vibrio cholera in the aquatic environment. The proposed model is based on the schematic diagram shown in Figure 1.

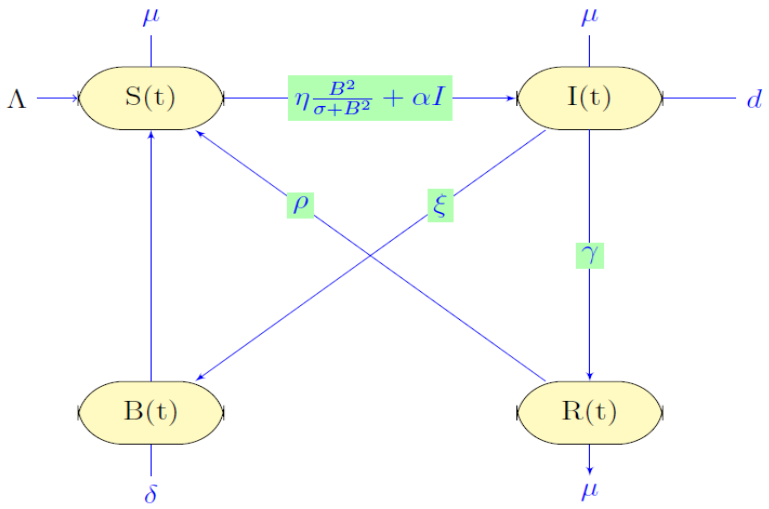

Fig 1. Flow diagram of the cholera model

The state equations which govern this model can be written as follow:

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - \eta\frac{SB^2}{\sigma+B^2} - \alpha SI + \rho R - \mu S \\
\frac{dI}{dt} &= \eta\frac{SB^2}{\sigma+B^2} + \alpha SI - (\gamma+\mu+d)I \\
\frac{dR}{dt} &= \gamma I - (\mu+\rho)R \\
\frac{dB}{dt} &= \xi I - \delta B
\end{aligned} \tag{2.1}$$

With initial conditions:

$$S(0) > 0, I(0) \geq 0, R(0) \geq 0, B(0) \geq 0 \tag{2.2}$$

The parameters of the model are described in Table 1.

Table 1: Description of the parameters in the SIRB model (2.1).

Parameters	Description
Λ	Constant human recruitment rate
μ	Natural human mortality rate
$\frac{1}{\rho}$	immune period
k	Half saturation constant
η	indirect transmission rate for humans and contaminated water
α	direct transmission rate between S and I
d	Disease induced death rate
$\frac{1}{\gamma}$	mean infectious period
ξ	Bacteria shed rate into the water supply by infected human
δ	Decay rate of vibrio

In this model, it is assumed that the incidence is represented by both direct (person-to-person) and indirect (environment-to-person) transmissions. The direct transmission is represented by the mass action term αSI, with a constant infection rate α. The indirect transmission is represented by Holling type-III functional response$\frac{SB^2}{\sigma+B^2}$, with constant infection rate η. The parameter Λ is the recruitment rate added to the population through the susceptible compartment and $\mu > 0$ is the natural death rate of individuals in the population. It is also assumed that infected individuals become recover at a rate $\gamma > 0$. Any recovered individual can lose the immunity after some while and the recovered individuals become susceptible again at a rate $\rho \geq 0$. The parameter $d \geq 0$ is the death rate associated with the disease. Each infected individual has a contribution to the bacteria concentration at rate ξ. The natural decay rate of V. cholera is $\delta > 0$ whereas $\sigma > 0$ is the concentration of vibrios in contaminated water in the environment (concentration of V. cholerae in water that yields 50%).

III. MODEL ANALYSIS

In this section we prove the positivity and boundness of the solution of the model (2.1)-(2.2) and discuss the existence of the endemic equilibria and its stability.

A. **Positivity and boundness of solution**:

A.1 Boundness of the solution

We show that the dynamic of the system (2.1) is uniformly bounded in a certain region Y defined as $\Upsilon = \Upsilon_H \times \Upsilon_B$ where

$$\Upsilon_H = \left\{(S, I, R) \in \mathbf{R}_+^3 \mid \frac{\Lambda}{\mu + d} \leq S(t) + I(t) + R(t) \leq \frac{\Lambda}{\mu}\right\}$$

and

$$\Upsilon_B = \left\{B \in \mathbf{R}_+ \mid 0 \leq B(t) \leq \frac{\Lambda\xi}{\mu\delta}\right\}$$

To show that all possible solutions are uniformly bounded in a certain region Υ, let

$$N(t) = S(t) + I(t) + R(t) \in \mathbf{R}_+^3$$

be any solution with non-negative initial conditions. From system (2.1) we have

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

Thus,

$$\left\{\frac{\Lambda}{\mu+d} + \left(N(0) - \frac{\Lambda}{\mu+d}\right)e^{-(\mu+d)t}\right\} \leq N(t) \leq \left\{\frac{\Lambda}{\mu} + \left(N(0) - \frac{\Lambda}{\mu}\right)e^{-\mu t}\right\}$$

where $N(0)$ is the initial population. Taking the limit when $t \to \infty$ gives

$$\frac{\Lambda}{\mu+d} \leq N(t) \leq \frac{\Lambda}{\mu} \tag{3.1}$$

Equation (3.1) shows that N (t) is bounded and all the feasible solutions of the human only component of model (2.1) starting in the region YH approach, enter or stay in the region.

For the pathogen population, it follows that

$$\frac{dB}{dt} = \xi I - \delta B$$

This yields

$$-\delta B \leq \frac{dB}{dt} \leq \xi\frac{\Lambda}{\mu} - \delta B$$

Therefore,

$$B(0)e^{-\delta t} \leq B(t) \leq \frac{\Lambda\xi}{\mu\delta} + B(0)e^{-\delta t}$$

where $B(0)$ is the initial population of bacteria. When $t \to \infty$ we have

$$0 \leq B(t) \leq \frac{\Lambda\xi}{\mu\delta} \tag{3.2}$$

Equation (3.2) shows that $B(t)$ is bounded and all the feasible solutions of the bacterium component of model (2.1) starting in the region Υ_B approach, enter or stay in the region.

Thus it follows from (3.1) and (3.2) that $N(t)$ and $B(t)$ are bounded and all the possible solutions of the model starting in Υ will enter or stay in the region $\Upsilon = \Upsilon_H \times \Upsilon_B$, for all $t \geq 0$.

A.2 Positivity of the solution

Theorem 1. *Let* $(S(0) > 0, I(0), R(0), B(0) \geq 0) \in \Upsilon$ *be non-negative real values then the solutions set* $\{S(t), I(t), R(t), B(t)\}$ *of the model* (2.1) *are non-negative for all* $t \geq 0$.

Proof. Considering $T = sup\{t > 0: S(t) > 0, I(t) \geq 0, R(t) > 0, B(t) \geq 0\}$. Considering the first equation in system (2.1), we have

$$\frac{dS}{dt} = \Lambda - \eta \frac{SB^2}{\sigma + B^2} - \alpha SI + \rho R - \mu S \geq \Lambda - \left(\eta \frac{B^2}{\sigma + B^2} + \alpha I + \mu\right) S$$

From which,

$$\frac{dS}{dt} \geq \Lambda - \left(\eta \frac{B^2}{\sigma + B^2} + \alpha I + \mu\right) S$$

multiplying both sides by the integration factor, yields

$$\frac{d}{dt}\left\{S(t) e^{\mu t + \left(\int_0^t \eta \frac{B^2(\tau)}{\sigma + B^2(\tau)} + \alpha I(\tau)\right) d\tau}\right\} \geq \Lambda e^{\mu t + \left(\int_0^t \eta \frac{B^2(\tau)}{\sigma + B^2(\tau)} + \alpha I(\tau)\right) d\tau}$$

Hence,

$$S(T) e^{\mu T + \left(\int_0^T \eta \frac{B^2(\tau)}{\sigma + B^2(\tau)} + \alpha I(\tau)\right) d\tau} - S(0) \geq \int_0^T \Lambda e^{\mu s + \int_0^s \left(\eta \frac{B^2(\tau)}{\sigma + B^2(\tau)} + \alpha I(\tau)\right) d\tau} ds \qquad (3.3)$$

This implies that

$$S(T) \geq S(0) e^{-\left(\mu T + \left(\int_0^T \eta \frac{B^2(\tau)}{\sigma + B^2(\tau)} + \alpha I(\tau)\right) d\tau\right)} + \Lambda e^{-\left(\mu T + \left(\int_0^T \eta \frac{B^2(\tau)}{\sigma + B^2(\tau)} + \alpha I(\tau)\right) d\tau\right)} \int_0^T e^{\mu s + \int_0^s \left(\eta \frac{B^2(\tau)}{\sigma + B^2(\tau)} + \alpha I(\tau)\right) d\tau} ds > 0 \qquad (3.4)$$

Now, we consider the second equation in system (2.1) we have

$$\frac{dI}{dt} = \eta \frac{SB^2}{\sigma + B^2} + \alpha S - (\gamma + \mu + d) I \geq -(\gamma + \mu + d) I$$

Separation of variables and then integrating both sides gives

$$\int_0^T \frac{dI}{I} \geq -\int_0^T (\gamma + \mu + d) dt$$

from which,

$$\ln\left(\frac{I(T)}{I(0)}\right) \geq -(\gamma T + \mu T + dT)$$

Hence,

$$\frac{dR}{dt} = \gamma I - (\mu + \rho)R \geq -(\mu + \rho)R$$

Similarly, it can be shown $R \geq 0$, by considering the third equation in system (2.1)

$$\frac{dR}{dt} = \gamma I - (\mu + \rho)R \geq -(\mu + \rho)R$$

which leads to

$$\frac{dR}{dt} \geq -(\mu + \rho)R$$

By separating the variables and then integrating both sides

$$\int_0^T \frac{dR}{R} \geq -\int_0^T (\mu + \rho)dt$$

from which,

$$\ln\left(\frac{R(T)}{R(0)}\right) \geq -(\mu + \rho)T$$

Hence,

$$R(T) \geq R(0)e^{-(\mu+\rho)T} \geq 0 \qquad (3.6)$$

Finally, we show $B > 0$, considering that the fifth equation in system (2.1), we have

$$\frac{dB}{dt} = \xi I - \delta B \geq -\delta B$$

Now,

$$\frac{dB}{dt} \geq -\delta B$$

By separation of variables and then integrating both sides we obtain

$$\int_0^T \frac{dB}{B} \geq -\int_0^T \delta dt$$

from which,

$$\ln\left(\frac{B(T)}{B(0)}\right) \geq -\delta T$$

Hence,

$$B(T) \geq B(0)e^{-\delta T} \geq 0 \qquad (3.7)$$

Therefore, any solution of system (2.1) is such that $(S(t), I(t), R(t), B(t)) \in \Upsilon$ for all $t \geq 0$. Hence, $S(t) > 0$, $I(t), R(t)$, and $B(t) \geq 0$ for all $t > 0$, given the initial conditions.

Theorem 1 can also be proven by using the method in Appendix B of [34].

In region Υ defined by $\Upsilon = \Upsilon_H \times \Upsilon_B$, model (2.1) is epidemiologically and mathematically well posed. In other words, every solution of the model (2.1) with initial conditions in Υ remains in Υ for all $t \geq 0$.

B. Existence of Equilibrium EEP

The equilibria points of model (2.1) can be obtained by equating the right-hand sides of the equations in (2.1) to zero:

$$\Lambda - \eta\frac{SB^2}{\sigma + B^2} - \alpha SI + \rho R - \mu S = 0 \quad (3.8)$$

$$\eta\frac{SB^2}{\sigma + B^2} + \alpha SI - (\gamma + \mu + d)I = 0 \quad (3.9)$$

$$\gamma I - (\mu + \rho)R = 0 \quad (3.10)$$

$$\xi I - \delta B = 0 \quad (3.11)$$

from equations (3.10) and (3.11) we get:

$$R^* = \frac{\gamma}{(\mu + \rho)}I^* \text{ and } B^* = \frac{\xi}{\delta}I^* \quad (3.12)$$

Adding equation (3.8) and (3.9) and solving for S, we get

$$S^* = \frac{\Lambda}{\mu} + \left(\frac{\rho\gamma}{\mu(\mu + \rho)} - \frac{\gamma + \mu + d}{\mu}\right)I^* \quad (3.13)$$

$$S^* = \frac{\Lambda}{\mu} - \kappa I^* \geq 0 \text{ iff } 0 \leq I^* \leq \frac{\Lambda}{\kappa\mu} \quad (3.14)$$

where,

$$r = \gamma + \mu + d$$

$$\kappa = \frac{1}{\mu}\left(r - \frac{\rho\gamma}{\mu + \rho}\right)$$

By multiplying equation (3.9) by μδ2(σ + B2), substituting $B = \xi I^*/\delta$ and S^* from (3.14) we obtain a fourth order equation in I^* given by:

$$-\alpha\kappa\xi^2\mu I^{*4} + \xi^2\big(\Lambda\alpha - \mu(\eta\kappa + r)\big)I^{*3} + (\Lambda\eta\xi^2 - \alpha\kappa\sigma\delta^2\mu)I^{*2} + \delta^2\sigma(\Lambda\alpha - r\mu)I^* = 0 \quad (3.15)$$

One solution of equation (3.15) is $I^* = 0$, from which we obtain a disease free quilibrium (DFE):

$$E_0^* = (S^*, I^*, R^*, B^*) = \left(\frac{\Lambda}{\mu}, 0,0,0\right)$$

Other solutions can be obtained by solving the cubic equation:

$$I^{*3} + \frac{\mu(\eta\kappa + r) - \Lambda\alpha}{\alpha\kappa\mu}I^{*2} + \frac{\alpha\kappa\sigma\delta^2\mu - \Lambda\eta\xi^2}{\alpha\kappa\xi^2\mu}I^* + \frac{\delta^2\sigma(r\mu - \Lambda\alpha)}{\alpha\kappa\xi^2\mu} = 0 \quad (3.16)$$

to obtain three values of I^*, where we reject negative real or complex (non real) roots. Equation (3.16) has either one real root and two conjugate complex roots or three real roots. Let

$$A_2 = \frac{\mu(\eta\kappa + r) - \Lambda\alpha}{\alpha\kappa\mu}, A_1 = \frac{\alpha\kappa\sigma\delta^2\mu - \Lambda\eta\xi^2}{\alpha\kappa\xi^2\mu} \text{ and } A_0 = \frac{\delta^2\sigma(r\mu - \Lambda\alpha)}{\alpha\kappa\xi^2\mu}$$

then, Equation (3.16) becomes:

$$F(I) = I^{*3} + A_2 I^{*2} + A_1 I^* + A_0 = 0 \qquad (3.17)$$

The number of possible positive real roots of Equation (3.17) are determined using the Descartes rule of sign and the discrement $\Delta = (A_2^2 - 3A_1)$ of the derivitive equation

$$F'(I) = 3I^{*2} + 2A_2 I + A_1, \qquad (3.18)$$

where the roots of $F'(I)$ are comlex or real (depending on where the discrement is negative or complex respectively) . the roots of the quadratic equation (3.18) are

$$I_{1,2} = \frac{-A_2 \pm \sqrt{\Delta}}{3}$$

Now we will discuses different scenarios about the parameters A_1, A_2, A_0 and their relations to the nature of the roots of (3.17).

Case 1: $\Delta < 0$

In this case, $f'(I)$ does not have real roots, and hence, $f(I)$ does not have return points. Given the facts that $\lim_{I\to+\infty} f(I) = +\infty$ and $\lim_{I\to-\infty} f(I) = -\infty$ then $f(I)$ is strictly increasing function of I in $(-\infty, +\infty)$ and has one real root $I = I^*$. If $A_0 > 0$ then $I^* < 0$ and the system (2.1) does not have an endemic equilibrium point. If $A_0 < 0$, then $I^* > 0$ and in this case the system (2.1) has an endemic equilibrium if and only if I^* fulfills the condition $S^* = \frac{\Lambda}{\mu} - \kappa I^* \geq 0$.

Case 2: $\boldsymbol{\Delta = 0}$

In this case $f'(I)$ would have a single repeated root $I = \tilde{I}$, which is an inflection point of the function $f(I)$. Hence, $f(I)$ has again a single real root $I = I^*$. If $A_0 > 0$ then $I^* < 0$ and the system (2.1) does not have an endemic equilibrium. If $A_0 < 0$, then $I^* > 0$ and in this case, again the system (2.1) will have an endemic equilibrium if and only if I^* satisfies the condition $S^* = \frac{\Lambda}{\mu} - \kappa I^* \geq 0$.

Case 3: $\boldsymbol{\Delta > 0}$

In this case, $f'(I)$ has two roots $\tilde{I}_1$ and $\tilde{I}_2$, where

$$\tilde{I}_1 = \frac{-A_2 - \sqrt{\Delta}}{3}$$

$$\tilde{I}_2 = \frac{-A_2 + \sqrt{\Delta}}{3}$$

Now, $\tilde{I}_1$ and $\tilde{I}_2$ are turning points for $f(I)$, where $f(I)$ is increasing function in $(-\infty, \tilde{I}_1) \cup (\tilde{I}_2, \infty)$ and is decreasing function in $(\tilde{I}_1, \tilde{I}_2)$. Hence, all the roots of $f(I)$ are real. However, the signs of A_2, A_1 and A_0 play crucial roles in determining the natures of the roots of (2.1), which we summarize in the following points.

1. $A_2 < 0$: in this case $-A_2 > 0$. Now
   (i) if $A_1 < 0$, then $\Delta > A_2^2$ and hence $\sqrt{\Delta} > |A_2|$. Hence, $I_1 = \left(-A_2 - \sqrt{\Delta}\right)/3 < 0$ and $I_2 = \left(-A_2 + \sqrt{\Delta}\right)/3 > 0$. Now,
      a) . if $A_0 > 0$, then $f(I)$ will have to positive roots and one negative root.
      b) if $A_0 = 0$, then $f(I)$ will have one negative root, zero root and one positive root.
      c) if $A_0 < 0$, then $f(I)$ will have two negative roots and one positive root.
   (ii) if $A_1 = 0$:, then $\Delta = A_2^2$ and therefore $\sqrt{\Delta} = |A_2|$. Hence, both $I_1 = 0$ and $I_2 = \left(-A_2 + \sqrt{\Delta}\right)/3 > 0$. Now,
      a) if $A_0 > 0$, then $f(I)$ will have two positive roots and one negative root.
      b) if $A_0 = 0$, then $f(I)$ will have repeated zero root and one positive root.
      c) if $A_0 < 0$, then $f(I)$ will have one positive root.
   (iii) if $A_1 > 0$:, then $\Delta < A_2^2$ and therefore $\sqrt{\Delta} < |A_2|$. Hence, both $I_1 = \left(-A_2 - \sqrt{\Delta}\right)/3 > 0$ and $I_2 = \left(-A_2 + \sqrt{\Delta}\right)/3 > 0$. Now,
      a) if $A_0 > 0$, then $f(I)$ will have two positive roots and one negative root.
      b) if $A_0 = 0$, then $f(I)$ will have one zero root and two positive roots.
      c) if $A_0 < 0$, then all the three roots of $f(I)$ are positive.
2. $A_2 = 0$: In this case, $\Delta > 0$ when $A_1 < 0$ and $\Delta = 0$ when $A_1 = 0$. We consider these two cases.
   (i) if $A_1 < 0$: in this case $\Delta = -3A_1 = 3|A_1|$. Then, the two roots of $f'(I)$ are given by: $I_1 = -\sqrt{3|A_1|}/3 < 0$ and $I_2 = \sqrt{3|A_1|}/3 > 0$. Hence,
      a) if $A_0 > 0$, then $f(I)$ has two positive roots and one negative root.
      b) if $A_0 = 0$, then $f(I)$ has one negative root, one zero root and one positive root.
      c) if $A_0 < 0$, then $f(I)$ has two negative roots and one positive root.
   (ii) if $A_1 = 0$: in this case $\Delta = 0$. Then, $f'(I)$ has one repeated root $I_1 = 0$. The function $f(I)$ has an inflection point at $I = I_1$ and one real root $I^* = 0$. Hence,
      a) if $A_0 > 0$, then $f(I)$ has one negative root and no positive root. There is no endemic equilibrium point for model (2.1) in this case.

b) if $A_0 = 0$, then $f(I)$ has one zero root and no positive root. Also in this case, there is no endemic equilibrium point for model (2.1) in this case.

c) if $A_0 < 0$, then $f(I)$ has one positive root.

3. $A_2 > 0$: In this case $-A_2 < 0$. Following similar steps to the case $A_2 < 0$, we have the following results:

(i) if $A_1 < 0$, then $\Delta > A_2^2$ and hence $\sqrt{\Delta} > |A_2|$. Hence, $I_1 = \left(-A_2 - \sqrt{\Delta}\right)/3 < 0$ and $I_2 = \left(-A_2 + \sqrt{\Delta}\right)/3 > 0$. Now,

a) if $A_0 > 0$, then $f(I)$ will have two positive roots and one negative root.

b) if $A_0 = 0$, then $f(I)$ will have one negative root, zero root and one positive root.

c) if $A_0 < 0$, then $f(I)$ will have two negative roots and one positive root.

(ii) if $A_1 = 0$:, then $\Delta = A_2^2$ and therefore $\sqrt{\Delta} = |A_2|$. Hence, $I_1 < 0$ and $I_2 = 0$. Now,

a) if $A_0 > 0$, then $f(I)$ will have one negative root and no positive roots. In this case the model (2.1) does not have an endemic equilibrium point.

b) if $A_0 = 0$, then $f(I)$ has a repeated zero root and one negative root. In this case also the model (2.1) does not have an endemic equilibrium point.

c) if $A_0 < 0$, then $f(I)$ has two negative roots and one positive root.

(iii) if $A_1 > 0$:, then $\Delta < A_2^2$ and therefore $\sqrt{\Delta} < |A_2|$. Hence, both $I_1 = \left(-A_2 - \sqrt{\Delta}\right)/3 < 0$ and $I_2 = \left(-A_2 + \sqrt{\Delta}\right)/3 < 0$. Now,

a) if $A_0 > 0$, then all the three roots of $f(I)$ are negative. In this case, the model (2.1) does not have an endemic equilibrium.

b) if $A_0 = 0$, then $f(I)$ has one zero root and two negative roots. Again, in this case the model (2.1) does not have an endemic equilibrium.

c) if $A_0 < 0$, then $f(I)$ has two negative roots and one positive root.

Theorem 2. *An endemic equilibrium point exists if and only if condition (3.14) is fullfiled and there is one positive root we can get it under the conditions of discernment and Descartes rule of sign's of A_i where $i = 0,1,2$.*

Proposition 3.1. *The basic reproduction number of model (2.1) is given by*

$$\mathcal{R}_0 = \rho(F_0 V_0^{-1}) = \frac{\alpha\Lambda}{\mu(\gamma_1 + \mu + d)}$$

Proof. We will calculate the basic reproduction number $\mathcal{R}_0$ by using the method of the next generation matrix [37].

In this method the matrices $\check{F}_i(t), \check{V}_i^{+}(t)$ and $\check{V}_i^{-}(t)$ associated with model (2.1), are

given by

$$\check{\mathrm{F}}(\mathrm{t}) = \begin{pmatrix} \eta \dfrac{SB^2}{\sigma + B^2} + \alpha SI \\ 0 \end{pmatrix}, \check{\mathrm{V}}^{+}(\mathrm{t}) = \begin{pmatrix} 0 \\ \xi I \end{pmatrix} \text{ and } \check{\mathbf{V}}^{-}(\mathbf{t}) = \begin{pmatrix} (\gamma + \mu + d)I \\ \delta B \end{pmatrix}$$

Therefore

$$\mathrm{F}_0 = \begin{pmatrix} \alpha S_0 & 0 \\ 0 & 0 \end{pmatrix} \text{ and } \mathrm{V}_0 = \begin{pmatrix} (\gamma + \mu + d) & 0 \\ -\xi & \delta \end{pmatrix}$$

The basic reproduction number of model (2.1) is then given by

$$\mathcal{R}_0 = \rho(F_0 V_0^{-1}) = \frac{\alpha \Lambda}{\mu(\gamma_1 + \mu + d)}$$

The $\mathcal{R}_0$ describes how humans transmit cholera to other humans (α). This concludes the Proof.

IV. STABILITY ANALYSIS

In this section, we analyze the local and global stability of both endemic-free and endemic equilibria points.

A. Local stability analysis of the endemic free equilibrium point

Theorem 3. The disease-free equilibrium (DFE) of the model (2.1) is locally asymptotically stable if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$.

Proof. The Jacobian matrix for the model system (2.1) is as follows

$$\mathbf{J}_0 = \begin{pmatrix} -\mu & -\alpha S_0 & \rho & 0 \\ 0 & \alpha S_0 - \gamma_1 - \mu - d & 0 & 0 \\ 0 & \gamma & -\mu - \rho & 0 \\ 0 & \delta_1 & 0 & -\delta \end{pmatrix}$$

Characteristic polynomial of the matrix given by $\mathrm{Det}\,(J_0 - \lambda I) = 0$.

We can expand the matrix in terms of the first column, this will give an eigenvalue $\lambda_1 = -\mu$, and expand the remaining matrix around the last column will give an eigenvalue $\lambda_2 = -\delta$. The remaining two eigenvalues are the eigenvalues of the following matrix:

$$\mathbf{J}_0 = \begin{pmatrix} \mathcal{R}_0 - 1 & 0 \\ \gamma & -(\mu + \rho) \end{pmatrix}$$

Now we can easily apply the Theorem (3.2) conditions [25] that guarantee that the eigenvalues of J_0 have negative real part (Assume that J is a 2×2 matrix with constant entries and $\mathrm{Det}\ J_0 \neq 0$. Assume that J has been obtained as a linearization around the equilibrium (x^*, y^*). Then the equilibrium (x^*, y^*) is locally asymptotically stable if and only if $\mathrm{Tr}\ J < 0$

and Det $J > 0$. The equilibrium (x^*, y^*) is unstable if and only if Tr $J > 0$ or Det $J < 0$). The trace of this matrix is given by

$$(\mathcal{R}_0 - 1) - (\mu + \rho)$$

and the determinant of J_0 is given by

$$-(\mathcal{R}_0 - 1)(\mu + \rho)$$

We notice that the condition $\mathcal{R}_0 < 1$ implies both Tr $J_0 < 0$ and Det $J_0 > 0$. Therefore, if $\mathcal{R}_0 < 1$, the disease-free equilibrium is locally asymptotically stable. If $\mathcal{R}_0 > 1$, the disease-free is unstable. By Theorem 3.2 [25] the endemic equilibrium is locally asymptotically stable.

B. Global Stability of the Disease-Free Equilibrium

To study the global asymptotic stability of the Disease-Free Equilibrium, we follow the result introduced by Castillo-Chavez et al. [7]. We split the epidemic system into two groups of compartments: compartments of non-infected individuals, compartments of infected individuals including infectious.

Lemma 1. (see [7]. If a model system can be written in the form

$$\begin{aligned} \frac{dX}{dt} &= F(X, Y) \\ \frac{dY}{dt} &= G(X, Y)\,, G(X, 0) = 0 \end{aligned}$$

Where $X \in R^m$ be the vector whose components are the susceptible, recovered and $Y \in R^n$ be the vector whose components are the infected individuals including latent, infectious etc; Also assume the conditions (H_1) and (H_2) below:

H_1: For $\frac{dX}{dt} = f(X, 0), X^*$ is globally asymptotically stable.

H_2: $G(X, Y) = AY - \hat{G}(X, Y), \hat{G}(X, Y) \geq 0$ for $(X, Y) \in \Upsilon$, where the Jacobin $A = D_Y G(X^*, 0)$ is an M-matrix (the off diagonal elements of A are non negative) and Υ is the region where the model makes biological sense. Then the DFE $X_0 = (X^*, 0)$ is globally asymptotically stable provided that $\mathcal{R}_0 < 1$.

Theorem 4. *When $\mathcal{R}_0 < 1$ the disease-free equilibrium of the model (2.1) is globally asymptotic stable.*

Proof. We only need to show that the conditions (H_1) and (H_2) hold when $\mathcal{R}_0 < 1$. In our model, $X = (S, R), Y = (I, B)$. We note that the system

$$\frac{\mathrm{dX}}{\mathrm{dt}} = F(X, 0) = \begin{pmatrix} \Lambda + \rho R - \mu S \\ -(\mu + \rho)R \end{pmatrix}$$

is linear and its solution can be easily found as

$$R(t) = R(0)e^{-(\mu+\rho)t}\,, S(t) = \frac{\Lambda}{\mu} - R(0)e^{-(\mu+\rho)t} + \left(S(0) - \frac{\Lambda}{\mu} + R(0)\right)e^{-\mu t}$$

Clearly $R(t) \to 0$ and $S(t) \to \frac{\Lambda}{\mu}$ as $t \to \infty$, regardless of the values of $R(0)$ and $S(0)$. Thus $X^* = \left(\frac{\Lambda}{\mu}, 0\right)$ is globally asymptotically stable.

Next, we have

$$\mathrm{G(X,Y)} = \begin{pmatrix} \eta\dfrac{SB^2}{\sigma + B^2} + \alpha SI - (\gamma + \mu + d)I \\ \xi I - \delta B \end{pmatrix}$$

We can then obtain

$$\mathrm{A} = \begin{pmatrix} \alpha S_0 - (\gamma + \mu + d) & 0 \\ \xi & -\delta \end{pmatrix} = \begin{pmatrix} \dfrac{\alpha S_0}{(\gamma + \mu + d)} - 1 & 0 \\ \xi & -\delta \end{pmatrix} = \begin{pmatrix} R_0 - 1 & 0 \\ \xi & -\delta \end{pmatrix}$$

Matrix A can be written in the form $A = M - D$, with $M \geq 0$ and $D > 0$, a diagonal matrix [7]. So $\mathcal{R}_0 < 1$ to verify the D condition > 0. Obviously, A is an M-matrix (the off-diagonal elements of A are non-negative) and the set $Y = (I, B)$ is expressed as a column matrix to get

$$\mathrm{AY} = \begin{pmatrix} \alpha SI - (\gamma + \mu + d)I \\ \xi I - \delta B \end{pmatrix} \text{ and } \hat{\mathrm{G}}\mathrm{(X,Y)} = \begin{pmatrix} \eta\dfrac{SB^2}{\sigma + B^2} \\ 0 \end{pmatrix}$$

it is obvious that $\hat{G}(X, Y) \geq 0$.

The conditions 1 and 2 have been met and therefore E_0 is globally asymptotically stable.

C. Local Stability of the Endemic Equilibrium EE

Theorem 5. The endemic equilibrium of the model (3.1) $E_1 = (S^*, I^*, R^*, B^*)$ is locally asymptotically stable if $\mathcal{R}_0 > 1$.

Proof. The Jacobian matrix of (2.1) evaluated in $E_1 = (S^*, I^*, R^*, B^*)$ is given by

$$\mathbf{J(E_1)} = \begin{pmatrix} -\dfrac{\eta B^{*2}}{B^* + \sigma} - \alpha I^* - \mu & -\alpha S^* & \rho & -2\dfrac{\eta BS}{B^2 + \sigma} + 2\dfrac{\eta B^3 S}{(B^2 + \sigma)^2} \\ \dfrac{\eta B^{*2}}{B^{*2} + \sigma} + \alpha I^* & \alpha S^* - (\gamma_1 + \mu + d) & 0 & 2\dfrac{\eta BS}{B^2 + \sigma} - 2\dfrac{\eta B^3 S}{(B^2 + \sigma)^2} \\ 0 & \gamma_1 & -(\mu + \rho) & 0 \\ 0 & \delta_1 & 0 & -\delta \end{pmatrix}$$

we can rewrite the matrix as

$$\mathbf{J}(\mathbf{E}_1) = \begin{pmatrix} -\frac{\eta B^{*2}}{B^{*2}+\sigma} - \alpha I^* - \mu & -\alpha S^* & \rho & -2\frac{\eta BS}{B^2+\sigma} + 2\frac{\eta B^3 S}{(B^2+\sigma)^2} \\ \frac{\eta B^{*2}}{B^{*2}+\sigma} + \alpha I^* & \mathcal{R}_0 - 1 + \frac{\alpha}{(\gamma_1+\mu+d)}Q & 0 & 2\frac{\eta BS}{B^2+\sigma} - 2\frac{\eta B^3 S}{(B^2+\sigma)^2} \\ 0 & \gamma_1 & -(\mu+\rho) & 0 \\ 0 & \delta_1 & 0 & -\delta \end{pmatrix}$$

where $Q = \left(\frac{\rho\gamma}{\mu(\mu+\rho)} - \frac{(\gamma+\mu+d)}{\mu}\right) I^*$.

To prove the local stability of the endemic equilibrium $E_1 = (S^*, I^*, R^*, B^*)$, Gershgorin's theorem is employed [5][36][4][17][27] [24]. We verify that

- If $a_{ii} < 0$ then the centers $(a_{ii}, 0)$ are located on the negative real half-axis of the complex plane, and the distance between $(a_{ii}, 0)$ and $(0,0)$ is $|a_{ii}|$ for $i = 1, \dots, n$.
- $R_i < |a_{ii}|$ which implies $C_i \subset \{\lambda \in C: |\lambda - (a_{ii}, 0)| < |a_{ii}|\}$ for $i = 1, \dots, n$. The first hypothesis $a_{ii} < 0$ is satisfied if and only if $\alpha S^* < (\gamma_1 + \mu + d)$ and $a_{11} = -\left(\frac{\eta B^{*2}}{B^{*2}+\sigma} + \alpha I^* + \mu\right)$, $a_{33} = -(\mu+\rho)$, $a_{44} = -\delta$.

The second hypothesis is verified if and only if the following inequalities are fulfilled.

$$\frac{\eta B^{*2}}{B^{*2}+\sigma} + \alpha I^* < \left|\frac{\eta B^{*^2}}{B^{*^2}+\sigma} + \alpha I^* + \mu\right| \quad (4.1)$$

$$\alpha S^* + \gamma + \xi < \left|R_0 - 1 + \frac{\alpha}{(\gamma_1+\mu+d)}Q\right| \quad (4.2)$$

$$\rho < |\rho + \mu| \quad (4.3)$$

$$0 < |\delta| \quad (4.4)$$

Corollary 1. [26] Any Gershgorin's disc with radius 0 is an eigenvalue.

That means that the matrix has at least one column with nondiagonal entries all equal to zero. If $\mathcal{R}_0 > 1$, The inequality (4.2) can be written as

$$\alpha S^* + (\gamma + \xi) < (\mathcal{R}_0 - 1) + \frac{\alpha}{(\gamma_1+\mu+d)}Q$$

Substituting Equation (3.13) in inequality (4.5)

$$\frac{\alpha\Lambda}{\mu} + \alpha Q + (\gamma + \xi) < (\mathcal{R}_0 - 1) + \frac{\alpha}{(\gamma_1+\mu+d)}Q \Rightarrow$$
$$(\gamma + \xi) < (\mathcal{R}_0 - 1) + \alpha\left(\frac{1}{(\gamma_1+\mu+d)} - 1\right)Q - \frac{\alpha\Lambda}{\mu}$$

Since $\mathcal{R}_0 > 1$ and $Q < 0$, the inequality (4.2) is satisfied, this shows that the endemic equilibrium is locally asymptotically stable.

D. Global Stability Analysis of the Endemic Equilibrium EE

Theorem 6. *The endemic equilibrium E_1 of the model (2.1) is globally asymptotically stable if $\mathcal{R}_0 > 1$.*

Proof. The global asymptotic stability property of E_1 will be explored using a Lyapunov function. Define a Lyapunov function:

$$V = \int_{S^*}^{S} \left(1 - \frac{S^*}{X}\right) dX + \int_{I^*}^{I} \left(1 - \frac{I^*}{X}\right) dX + \eta \frac{S^* B^{*2}}{\gamma I^* (\sigma + B^{*2})} \int_{R^*}^{R} \left(1 - \frac{R^*}{X}\right) dX + \eta \frac{S^* B^{*2}}{\xi I^* (\sigma + B^{*2})} \int_{B^*}^{B} \left(1 - \frac{B^*}{X}\right) dX$$

Then the derivative of V along solutions of system (2.1) with respect to t

$$\dot{V} = \left(1 - \frac{S^*}{S}\right) \dot{S} + \left(1 - \frac{I^*}{I}\right) \dot{I} + \eta \frac{S^* B^{*2}}{\gamma I^* (\sigma + B^{*2})} \left(1 - \frac{R^*}{R}\right) \dot{R} + \eta \frac{S^* B^{*2}}{\xi I^* (\sigma + B^{*2})} \left(1 - \frac{B^*}{B}\right) \dot{B}$$

and replace $\dot{S}, \dot{I}, \dot{R}$ and $\dot{B}$ with their equals from system (2.1) we have that:

$$\left(1 - \frac{S^*}{S}\right) \dot{S} = \left(1 - \frac{S^*}{S}\right) \left(\Lambda - \eta \frac{S B^2}{\sigma + B^2} - \alpha S I + \rho R - \mu S\right)$$

One of the classical first steps here is to replace Λ with its equal from the equilibrium equations [22] , that is

$$\left(\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}+\alpha S^*I^*-\rho R^*+\mu S^*\right)$$

$$= \left(1-\frac{S^*}{S}\right)\left(\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}+\alpha S^*I^*-\rho R^*+\mu S^*-\eta\frac{S^2}{\sigma+B^2}-\alpha SI+\rho R-\mu S\right)$$

$$= \left(1-\frac{S^*}{S}\right)\left(\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}-\eta\frac{S^2}{\sigma+B^2}\right)+\left(1-\frac{S^*}{S}\right)(\alpha S^*I^*-\alpha SI)+\left(1-\frac{S^*}{S}\right)$$

$$(\rho R-\rho R^*)+\left(1-\frac{S^*}{S}\right)(\mu S^*-\mu S)$$

$$= \left(1-\frac{S^*}{S}\right)\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(1-\frac{(\sigma+B^{*2})SB^2}{S^*B^{*2}(\sigma+B^2)}\right)+\alpha S^*I^*\left(1-\frac{S^*}{S}\right)\left(1-\frac{\alpha SI}{\alpha S^*I^*}\right)$$

$$+ \quad \rho\left(1-\frac{S^*}{S}\right)(R-R^*)+\mu\left(1-\frac{S^*}{S}\right)(S^*-S)$$

$$= \left(1-\frac{S^*}{S}\right)\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(1-\frac{(\sigma+B^{*2})SB^2}{S^*B^{*2}(\sigma+B^2)}\right)+\alpha S^*I^*\left(1-\frac{S^*}{S}\right)\left(1-\frac{\alpha SI}{\alpha S^*I^*}\right)$$

$$+ \quad \rho\left(1-\frac{S^*}{S}\right)(R-R^*)-\frac{\mu}{S}(S-S^*)^2$$

$$\leq \left(1-\frac{S^*}{S}\right)\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(1-\frac{(\sigma+B^{*2})SB^2}{S^*B^{*2}(\sigma+B^2)}\right)+\alpha S^*I^*\left(1-\frac{S^*}{S}\right)\left(1-\frac{\alpha SI}{\alpha S^*I^*}\right)+$$

$$\rho\left(1-\frac{S^*}{S}\right)(R-R^*)$$

$$\left(1-\frac{I^*}{I}\right)\dot{I} = \left(1-\frac{I^*}{I}\right)\left(\eta\frac{SB^2}{\sigma+B^2}+\alpha SI-(\gamma+\mu+d)I\right)$$

$$= \left(1-\frac{I^*}{I}\right)\left(\eta\frac{SB^2}{\sigma+B^2}+\alpha SI-\left(\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}+\alpha S^*I^*\right)\frac{I}{I^*}\right)$$

$$= \left(1-\frac{I^*}{I}\right)\left(\eta\frac{SB^2}{\sigma+B^2}-\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\frac{I}{I^*}\right)+\left(1-\frac{I^*}{I}\right)\left(\alpha SI-\alpha S^*I^*\frac{I}{I^*}\right)$$

$$= \eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(1-\frac{I^*}{I}\right)\left(\frac{\eta\frac{SB^2}{\sigma+B^2}}{\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}}-\frac{I}{I^*}\right)+\alpha S^*I^*\left(1-\frac{I^*}{I}\right)\left(\frac{\alpha SI}{\alpha S^*I^*}-\frac{I}{I^*}\right)$$

$$\eta\frac{S^*B^{*2}}{\gamma I^*(\sigma+B^{*2})}\left(1-\frac{R^*}{R}\right)\dot{R} = \eta\frac{S^*B^{*2}}{\gamma I^*\left(\sigma+B^{*^2}\right)}\left(1-\frac{R^*}{R}\right)(\gamma I-(\mu+\rho)R)$$

$$= \eta\frac{S^*B^{*2}}{\gamma I^*(\sigma+B^{*2})}\left(1-\frac{R^*}{R}\right)\left(\gamma I-\gamma I^*\frac{R}{R^*}\right)$$

$$= \eta\frac{S^*B^{*2}}{\sigma+B^{*^2}}\left(1-\frac{R^*}{R}\right)\left(\frac{I}{I^*}-\frac{R}{R^*}\right)$$

and

$$\eta\frac{S^*B^{*2}}{\xi I^*\left(\sigma+B^{*^2}\right)}\left(1-\frac{B^*}{B}\right)\dot{B} = \eta\frac{S^*B^{*2}}{\xi I^*(\sigma+B^{*2})}\left(1-\frac{B^*}{B}\right)(\xi I-\delta B)$$
$$= \eta\frac{S^*B^{*2}}{\xi I^*(\sigma+B^{*2})}\left(1-\frac{B^*}{B}\right)(\xi I-\delta B)$$
$$= \eta\frac{S^*B^{*2}}{\xi I^*(\sigma+B^{*2})}\left(1-\frac{B^*}{B}\right)\left(\xi I-\frac{\xi I^*}{B^*}B\right)$$
$$= \eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(1-\frac{B^*}{B}\right)\left(\frac{I}{I^*}-\frac{B}{B^*}\right)$$

By direct calculations, we have that:

$$\dot{V}=\left(1-\frac{S^*}{S}\right)\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(1-\frac{(\sigma+B^{*2})SB^2}{S^*B^{*2}(\sigma+B^2)}\right)+\alpha S^*I^*\left(1-\frac{S^*}{S}\right)\left(1-\frac{\alpha SI}{\alpha S^*I^*}\right)+$$
$$\rho\left(1-\frac{S^*}{S}\right)(R-R^*)+\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(1-\frac{I^*}{I}\right)\left(\frac{\eta\frac{SB^2}{\sigma+B^2}}{\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}}-\frac{I}{I^*}\right)+\alpha S^*I^*\left(1-\frac{I^*}{I}\right)\left(\frac{\alpha SI}{\alpha S^*I^*}-\frac{I}{I^*}\right)$$
$$+\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(1-\frac{R^*}{R}\right)\left(\frac{I}{I^*}-\frac{R}{R^*}\right)+\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(1-\frac{B^*}{B}\right)\left(\frac{I}{I^*}-\frac{B}{B^*}\right)$$

We will extract the common factors

$$\dot{V}=\left(\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\right)$$
$$\left(\left(1-\frac{S^*}{S}\right)\left(1-\frac{(\sigma+B^{*2})SB^2}{S^*B^{*2}(\sigma+B^2)}\right)+\left(1-\frac{I^*}{I}\right)\left(\frac{\eta\frac{SB^2}{\sigma+B^2}}{\eta\frac{S^*B^*2}{\sigma+B^{*2}}}-\frac{I}{I^*}\right)\right)+\left(\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\right)$$
$$\left(\left(1-\frac{R^*}{R}\right)\left(\frac{I}{I^*}-\frac{R}{R^*}\right)+\left(1-\frac{B^*}{B}\right)\left(\frac{I}{I^*}-\frac{B}{B^*}\right)\right)+\rho\left(1-\frac{S^*}{S}\right)(R-R^*)$$
$$+\alpha S^*I^*\left(\left(1-\frac{S^*}{S}\right)\left(1-\frac{\alpha SI}{\alpha S^*I^*}\right)+\left(1-\frac{I^*}{I}\right)\left(\frac{\alpha SI}{\alpha S^*I^*}-\frac{I}{I^*}\right)\right)$$

We collect the similar terms

$$\dot{V} = \left(\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\right)\left(1-\frac{(\sigma+B^{*2})SB^2}{S^*B^{*2}(\sigma+B^2)}-\frac{S^*}{S}+\frac{(\sigma+B^{*2})S^*SB^2}{SS^*B^{*2}(\sigma+B^2)}+\frac{\eta\frac{SB^2}{\sigma+B^2}}{\eta\frac{S^*B^*}{\sigma+B^{*2}}}-\frac{I}{I^*}-\frac{I^*}{I}\frac{\eta\frac{SB^2}{\sigma+B^2}}{\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}}+\frac{II^*}{II^*}\right)$$
$$+\left(\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\right)\left(\frac{I}{I^*}-\frac{R}{R^*}-\frac{IR^*}{RI^*}+\frac{RR^*}{RR^*}+\frac{I}{I^*}-\frac{B}{B^*}-\frac{IB^*}{BI^*}+\frac{BB^*}{BB^*}\right)+\rho\left(1-\frac{S^*}{S}\right)(R-R^*)$$
$$+(\alpha S^*I^*)\left(1-\frac{\alpha SI}{\alpha S^*I^*}-\frac{S^*}{S}+\frac{\alpha SS^*I}{\alpha SS^*I^*}+\frac{\alpha SI}{\alpha S^*I^*}-\frac{I}{I^*}-\frac{\alpha I^*SI}{\alpha IS^*I^*}+\frac{II^*}{II^*}\right)$$
$$\dot{V} = \left(\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\right)\left(4-\frac{S^*}{S}+\frac{I}{I^*}-\frac{B}{B^*}-\frac{R}{R^*}-\frac{IR^*}{RI^*}-\frac{IB^*}{BI^*}+\frac{(\sigma+B^{*2})B^2}{B^{*2}(\sigma+B^2)}-\frac{(\sigma+B^{*2})I^*SB^2}{S^*B^{*2}(\sigma+B^2)I}\right)$$
$$+\alpha S^*I^*\left(2-\frac{S^*}{S}-\frac{S}{S^*}\right)+\rho\left(1-\frac{S^*}{S}\right)(R-R^*)$$

For the function $g(x) = 1 - x + \ln x$, we know that $x > 0$ leads to $g(x) \leq 0$. And if $x = 1$, then $g(x) = 0$.

Note that

$$\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(1-\frac{S^*}{S}\right)\left(1-\frac{(\sigma+B^{*2})SB^2}{S^*B^{*2}(\sigma+B^2)}\right)+\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(1-\frac{I^*}{I}\right)\left(\frac{SB^2(\sigma+B^{*2})}{(\sigma+B^2)(S^*B^{*2})}-\frac{I}{I^*}\right)$$
$$=\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(\left(1-\frac{S^*}{S}\right)\left(1-\frac{(\sigma+B^{*2})SB^2}{S^*B^{*2}(\sigma+B^2)}\right)+\left(1-\frac{I^*}{I}\right)\left(\frac{SB^2(\sigma+B^{*2})}{(\sigma+B^2)(S^*B^{*2})}-\frac{I}{I^*}\right)\right)$$
$$=\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(1-\frac{S^*}{S}-\frac{(\sigma+B^{*2})SB^2}{S^*B^{*2}(\sigma+B^2)}+\frac{(\sigma+B^{*2})S^*SB^2}{SS^*B^{*2}(\sigma+B^2)}+\frac{SB^2(\sigma+B^{*2})}{(\sigma+B^2)(S^*B^{*2})}-\frac{I}{I^*}\right)$$
$$-\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(\frac{I^*SB^2(\sigma+B^{*2})}{I(\sigma+B^2)(S^*B^{*2})}-\frac{II^*}{II^*}\right)$$
$$=\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(2-\frac{S^*}{S}+\frac{(\sigma+B^{*2})B^2}{B^{*2}(\sigma+B^2)}-\frac{I}{I^*}-\frac{I^*SB^2(\sigma+B^{*2})}{I(\sigma+B^2)(S^*B^{*2})}\right)$$
$$=\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(\left(\frac{B^2(\sigma+B^{*2})}{B^{*2}(\sigma+B^2)}-1\right)\left(1-\frac{(\sigma+B^2)}{(\sigma+B^{*2})}\right)+g\left(\frac{S^*}{S}\right)+g\left(\frac{I^*SB^2(\sigma+B^{*2})}{S^*B^{*2}I(\sigma+B^2)}\right)\right)$$
$$+\left(\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\right)\left(g\left(\frac{(\sigma+B^2)}{(\sigma+B^{*2})}\right)+\frac{B^2}{B^{*2}}-\ln\left(\frac{B^2}{B^{*2}}\right)-\frac{I}{I^*}+\ln\left(\frac{I}{I^*}\right)\right)$$
$$\leq\left(\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\right)\left(\frac{B^2}{B^{*2}}-\ln\left(\frac{B^2}{B^{*2}}\right)-\frac{I}{I^*}+\ln\left(\frac{I}{I^*}\right)\right)$$

and

$$
\begin{aligned}
&\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(1-\frac{B^*}{B}\right)\left(\frac{I}{I^*}-\frac{B}{B^*}\right)\\
&=\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(\frac{I}{I^*}-\frac{IB^*}{I^*B}-\frac{B}{B^*}+\frac{B^*B}{BB^*}\right)\\
&=\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(1+\frac{I}{I^*}-\frac{IB^*}{I^*B}-\frac{B}{B^*}\right)\\
&=\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(g\left(\frac{IB^*}{I^*B}\right)+\frac{I}{I^*}-\frac{B}{B^*}-\ln\frac{I}{I^*}+\ln\frac{B}{B^*}\right)\\
&\le\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(\frac{I}{I^*}-\ln\frac{I}{I^*}-\frac{B}{B^*}+\ln\frac{B}{B^*}\right)\\
&=\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(\frac{I}{I^*}-\frac{R}{R^*}-\frac{IR^*}{I^*R}+\frac{RR^*}{RR^*}\right)\\
&=\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(1+\frac{I}{I^*}-\frac{R}{R^*}-\frac{IR^*}{I^*R}\right)\left(\frac{I}{I^*}-\frac{R}{R^*}\right)\\
&=\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(g\left(\frac{IR^*}{I^*R}\right)+\frac{I}{I^*}-\ln\frac{I}{I^*}-\frac{R}{R^*}+\ln\frac{R}{R^*}\right)\\
&\le\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(\frac{I}{I^*}-\ln\frac{I}{I^*}-\frac{R}{R^*}+\ln\frac{R}{R^*}\right)
\end{aligned}
$$

Moreover, we can obtain

$$
\begin{aligned}
&\alpha S^*I^*\left(1-\frac{S^*}{S}\right)\left(1-\frac{\alpha SI}{\alpha S^*I^*}\right)+\alpha S^*I^*\left(1-\frac{I^*}{I}\right)\left(\frac{\alpha SI}{\alpha S^*I^*}-\frac{I}{I^*}\right)\\
=\;&\alpha S^*I^*\left(1-\frac{\alpha SI}{\alpha S^*I^*}-\frac{S^*}{S}+\frac{\alpha SS^*I}{\alpha SS^*I^*}+\frac{\alpha SI}{\alpha S^*I^*}-\frac{I}{I^*}-\frac{\alpha SII^*}{\alpha S^*I^*I}+\frac{II^*}{II^*}\right)\\
=\;&\alpha S^*I^*\left(2-\frac{S^*}{S}-\frac{S}{S^*}\right)\\
=\;&-\alpha S^*I^*\frac{(S-S^*)^2}{SS^*}\le 0
\end{aligned}
$$

As a result, we get

$$
\begin{aligned}
\dot{V}\;&\le\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(\frac{B^2}{B^{*2}}-\ln\left(\frac{B^2}{B^{*2}}\right)-\frac{I}{I^*}+\ln\left(\frac{I}{I^*}\right)\right)+\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(\frac{I}{I^*}-\ln\frac{I}{I^*}-\frac{B}{B^*}+\ln\frac{B}{B^*}\right)\\
&+\eta\frac{S^*B^{*2}}{\sigma+B^{*2}}\left(\frac{I}{I^*}-\ln\frac{I}{I^*}-\frac{R}{R^*}+\ln\frac{R}{R^*}\right)+\rho\left(1-\frac{S^*}{S}\right)(R-R^*)
\end{aligned}
$$

Consequently, we gain

$$\dot{V} \leq \eta \frac{S^* B^{*2}}{\sigma + B^{*2}} \left(\frac{B^2}{B^{*2}} - \ln \left(\frac{B^2}{B^{*2}} \right) - \frac{B}{B^*} + \ln \frac{B}{B^*} + \frac{I}{I^*} - \ln \frac{I}{I^*} - \frac{R}{R^*} + \ln \frac{R}{R^*} \right) + \rho \left(1 - \frac{S^*}{S} \right) (R - R^*)$$

Hence, $\dot{V}$ is non positive, and it is zero whenever $(S, I, R, B) = (S^*, I^*, R^*, B^*)$.

Now have to apply the LaSalle Theorem [15] [22] We consider the set where the Lyapunov function is equal to zero:

$$M = \{x \in R^n \mid \dot{V}(x) = 0\}$$

It is clear that $\dot{V}(x) = 0$ if and only if

$$S = S^*, I = I^*, R = R^*, B = B^*$$

The largest invariant subset at $\dot{V} = 0$ is E_1, hence, the set M consists of the singleton (S^*, I^*, R^*, B^*), therefore, by La Salle's invariance principle [22][15], E_1 is globally asymptotically.

v. NUMERICAL SIMULATIONS

In this section, we apply the proposed epidemic cholera model to the case of cholera outbreak in South Sudan during 2016 − 2017, by fitting the model to the epidemic data published by the WHO. These data sets contain the weekly reported new cases and cumulative cases for each governorate as well as the entire country (Relief website). The other parameter values used in the simulation are obtained from literature and are explained in Table 2.

The cholera outbreak in South Sudan during 2016 − 2017 started in 18th June 2016 and continued to 29 December 2017. So, the estimation of the parameters σ and η is established based on the available weekly data from the 43th week of 2016 to the 13th week of 2017. By using the Least square method, we could fit the model to the data (see Fig 2, which illustrates the actual cumulative data of infected individuals versus the infected compartment obtained from the solution of system (2.1). The good agreement between the model solution and the actual cholera cases, verifies the rationality of the model established in this paper.

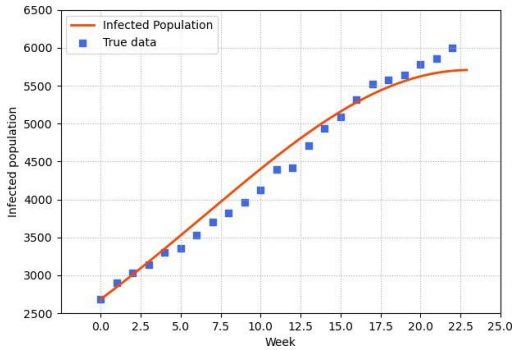

Fig 2: Cumulative cases in South Sudan in 23

By using the parameters of Table 2, model (2.1) is solved for a period of 40 weeks from the beginning of the outbreak. The solution of the model is illustrated in figures 3-6.

Table 2: parameter values (week).

Parameter	Value	Units	Source
Λ	680.9052	week	Click Here
μ	0.0002055769	week	Click Here
ρ	0.006410256	weeks	[38, [16,19,2,7]
σ	10^6	cells /mL	[20,9,25]
η	2.69×10^{-8}	week	estimated
α	4.22×10^{-7}	week	estimated
d	9.1111	week	Click Here
γ	0.7142857	week	[28][20][12][36]
ξ	70	cells ml week per person	[25,9]
δ	2.31	week	[?,6]

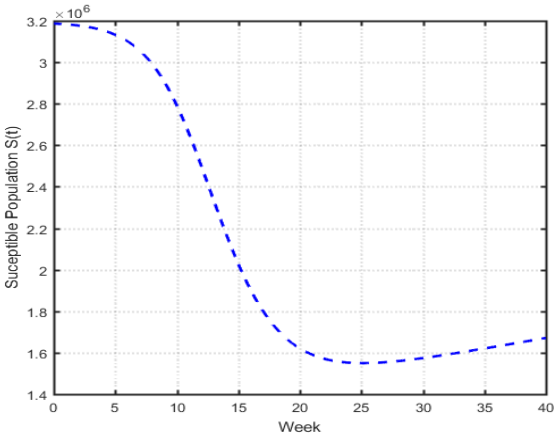

Fig 3: Susceptible population

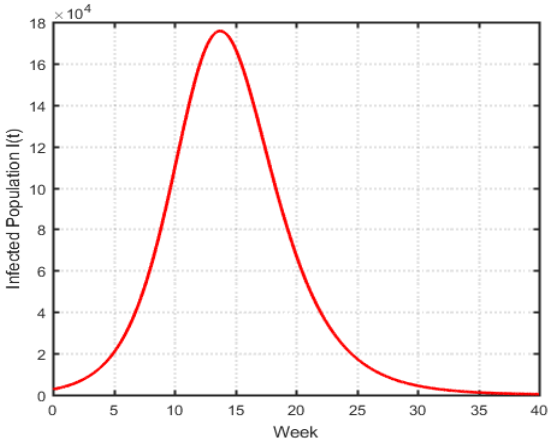

Fig 4: Infected population

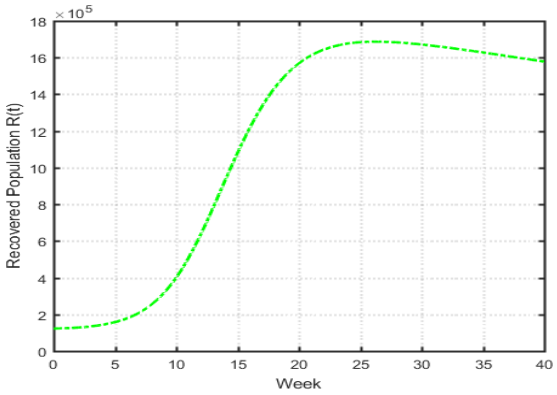

Fig 5: Recovered population

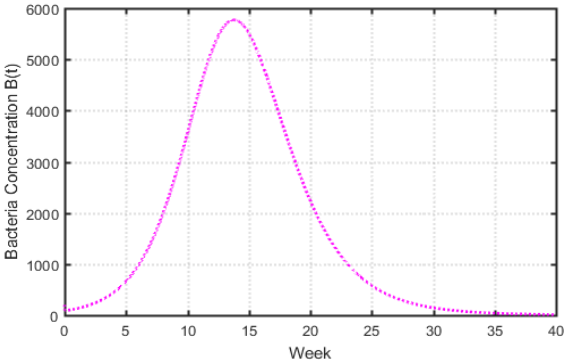

Fig 6: Vibro Bacteria

A. Sensitivity Analysis

In this section we would determine how best to reduce mortality and infectious people due to Cholera, it is necessary to know the relative importance of the different factors responsible for its transmission and prevalence. The basic reproduction number is very important in the effort required to eradicate a disease. We carry out sensitivity analysis of the Basic reproduction number with respect to the model parameters to assess the relative impact of each of the parameters in the transmission and prevalence of the disease. The normalized forward sensitivity index is used to calculate [8][27].

A.1 Sensitivity analysis indices of R_0

The explicit expression of R_0 is given by the equation

$$\mathcal{R}_0 = \rho(F_0 V_0^{-1}) = \frac{\alpha\Lambda}{\mu(\gamma_1 + \mu + d)}$$

Since R_0 depends only on five parameters, we derive an analytical expression for its sensitivity to each parameter using the normalized forward sensitivity index as by Chitnis[8]. The indices of the parameters of $\mathcal{R}_0$ are computed as follows:

$$\Upsilon_{\Lambda}^{R_0} = \frac{\partial R_0}{\partial \Lambda} \times \frac{\Lambda}{R_0} = 1$$

$$\Upsilon_{\alpha}^{R_0} = \frac{\partial R_0}{\partial \alpha} \times \frac{\alpha}{R_0} = 1$$

$$\Upsilon_{\gamma}^{R_0} = \frac{\partial R_0}{\partial \gamma} \times \frac{\gamma}{R_0} = -\frac{\gamma}{(\gamma + \mu + d)} = -0.13318992486277$$

$$\Upsilon_{\mu}^{R_0} = \frac{\partial R_0}{\partial \mu} \times \frac{\mu}{R_0} = -\frac{(\gamma + 2\mu + d)}{(\gamma + \mu + d)} = -1.0000195576963844$$

$$\Upsilon_{d}^{R_0} = \frac{\partial R_0}{\partial d} \times \frac{d}{R_0} = -\frac{d}{(\gamma + \mu + d)} = -0.8667905174408457$$

From Table 3, we can note that $\Upsilon_{\Lambda}^{\mathcal{R}_0} = 1$, this means that an increase in Λ will cause an increase of exactly the same proportion in $\mathcal{R}_0$. Similarly, a decrease in Λ will cause a decrease in R_0, $\Upsilon_{\alpha}^{\mathcal{R}_0} = 1$ also means that an increase in α will cause an increase of exactly the same proportion in $\mathcal{R}_0$. Similarly, a decrease in α will cause a decrease in $\mathcal{R}_0$.

The index $\Upsilon_{\gamma}^{\mathcal{R}_0} = -0.1332$ means that an increase in γ will cause a decrease of the same proportion in $\mathcal{R}_0$. Similarly, a decrease in γ will cause an increase in $\mathcal{R}_0$. We can also note that μ and d are negative, and hence these parameters are inversely proportional to $\mathcal{R}_0$.

By reducing the value of α from 7.22×10^{-7} to the value 1.00×10^{-7}, we see that cholera cases will drop rapidly during the 40 weeks, as illustrated in figures 7-10. These figures show radical change in the dynamics of model (2.1) obtained by taking $\alpha = 7.22 \times 10^{-7}$.

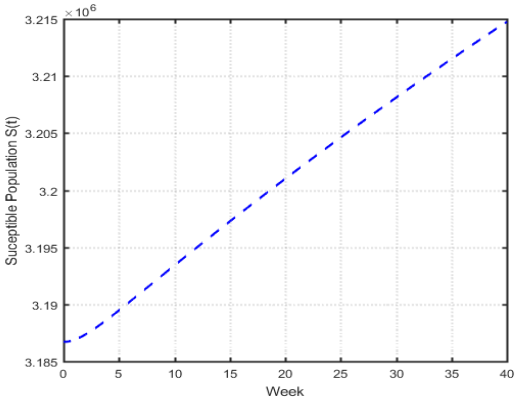

Fig 7: Susceptible population

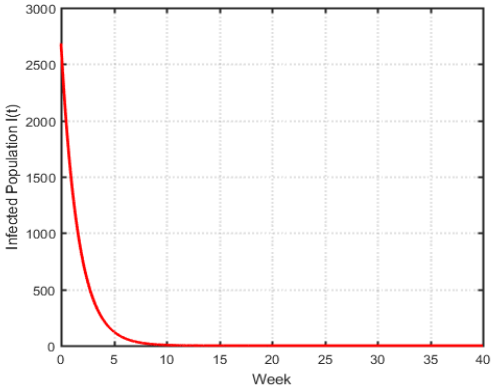

Fig 8: Infected population

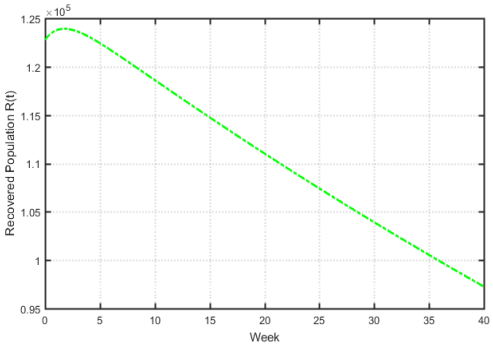

Fig 9: Recovered population

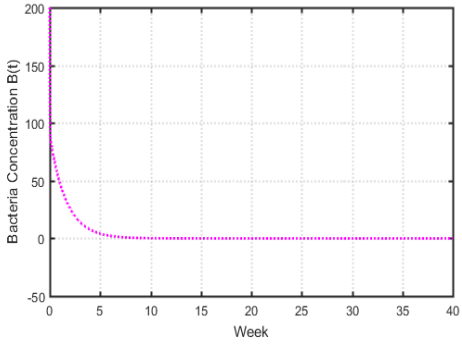

Fig 10: Vibro Bacteria

VI. Conclusions and remarks

In this paper, we proposed and analyzed an epidemiological deterministic model that describes the dynamical behaviour of cholera outbreak, based on Holling functional response of type III. The process of infection transmission is represented by both the directly (from person to person) and the indirectly (from environment to person). The indirect transmission is represented by Holling type (III) functional response. The model assumes loss of acquired immunity from infection among recovered individuals.

The model was analyzed thoroughly, where boundedness and positivity of the system solution have been discussed. The model is found to always have a disease-free equilibrium and the conditions of existence of endemic equilibrium point are derived. The basic reproduction number $\mathcal{R}_0$ of the model is computed. Then, we proved that when $\mathcal{R}_0 < 1$, the endemic-free equilibrium is locally (Theorem 3) and globally (Theorem 5) asymptotically stable. Also, the endemic equilibrium (when exists) is proved to be locally asymptotically stable, when $\mathcal{R}_0 > 1$ (Theorem 6) and globally-asymptotically stable when $\mathcal{R}_0 > 1$ (Theorem 7).

The proposed model is fitted to the data of South Sudan, where the parameters representing directed and indirect transmission rates of the epidemic are estimated. Then, numerical simulations are carried out to illustrate the dynamics of Cholera outbreak. Then sensitivity analysis is carried out to measure how the model parameters affect the basic

reproduction number, where we found that the recruitment rate and the direct transmission parametersplay the key roles in changing the basic reproduction number and hence the model's dynamics. Further numerical simulations were carried out to illustrate the effect of changing someof these parameters.

From such numerical simulations, we deduce the following:

- Entry of people to places where cholera outbreaks occur should be restricted, this will help limit the spread of the disease (parameter Λ).

- Reducing contact between the susceptible and the infected populations can limit the spread of cholera (α). It is usual to isolate the infected individual with the main purpose of reducing the contact rate and thus limiting the spread of cholera.

Because cholera kills in a very short time, early treatment of all cholera patients is highly recommended to save the lives of human patients (γ).

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