A Mathematical Model Analysis for the Transmission Dynamics of Cholera with Control Strategy

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Abstract: *Cholera is an acute diarrheal disease caused by vibro-cholerae bacteria and the outbreak can occur in a situation where water supply, sanitation, food safety and hygiene are insufficient. We developed an epidemic model of SIQR-B, or Susceptible- Infectious-Quarantined-Recovered and Bacteria, type model for cholera infection. We incorporate control measures of treatment in quarantine and vaccination. The effective reproduction number is computed in terms of model parameters. The existence and stability of disease free and endemic steady statesare recognized and the stead states indicated to be locally and globally asymptotically stable whenever effective reproduction numberis less than unity and greater than unity respectively. The most influential parameter to the reproduction number is obtained by using sensitivity analysisand vaccination rate is found to be influential. Furthermore, we carried out numerical simulations to verify and support the impact of intervention measures on the reproduction number, which is seen in the analytical results. The findings indicates that applying combined control measures vaccination and treatment in quarantine will help to prevent and control cholera transmission in the community.*

Keywords: *Cholera, Dynamical systems, Reproduction number, stability,Vaccination*

I.   Introduction

Cholera is an acute diarrheal disease caused by vibro-cholerae bacteria and the outbreak can occur in a situation where water supply, sanitation, food safety and hygiene are insufficient. Since the incubation period of cholera is very short (2 hours -5 days), the number of cases can rise rapidly. The modes of transmission of cholera are direct from human-to-human (fecal-oral) and indirect from environment-to-human (exposure to the environmental reservoir to vibro-cholerae). The severity of the diarrhea and vomiting can lead to rapid dehydration and electrolyte imbalance [1-9].There are over 100 vibrio species but only the 'cholerae' species are responsible for Cholera epidemics. Vibrio cholerae species are divided in to 2 serogroups. These serogroups 01 and 0139 causes outbreak (Alexander 2008) V. cholerae 01 causes the majority of outbreak, while 0139 first identified in India in 1992 is confined to south-East Asia. Non-01 and non-0139 v. cholerae can cause mild diarrhea but do not generate epidemics [10-14].The etiological agent, *Vibrio cholera* 01 and vibrio cholera 0139, passesthrough and survives the gastric acid barrier of the stomach and then penetrates the mucus lining that coats the intestinal epithelial [15]. Once they colonise the intestinal gut, thenproduce enterotoxin (which stimulates water and electrolytesecretion by the endothelial cells of the small intestine) thatleads to copious, painless, and watery diarrhea that canquickly lead to severe dehydration and death if treatment isnot properly given [16-18].

A number of mathematical models have been used to study the transmission dynamicsof cholera. Capasso and Serio introduced an incidencerate in the form of $\frac{kSI}{(I+\alpha I)}$(with human(I)-to-human(S) transmission model only) in 1973. Codeco proposedan incidence form of $\frac{aSB}{(K+B)}$(with environment(B)-to human(S)transmission model only) in 2001 which, in thefirst time, explicitly incorporated the pathogen concentrationinto cholera modeling. Mukandavire et al. included bothtransmission pathways in the form of $\frac{\beta_e SB}{(K+B)} + \beta_h SI$ [19-25]. The major differences of these models are how the incidence rate is determined and how the environmental vibrio concentration is formulated. However, the goal of this paper is to propose cholera dynamics incorporating control strategies using only codeco's incidence form.

Experimental studies suggest that it is necessary a heavy inoculum of V. cholerae in order to develop cholera. Here, this dependence is represented by a logistic dose response curve$\lambda_0(B) = \frac{B}{k+B}$, where κ is the concentration of V. cholerae in water that yields 50% chance of catching cholera and B is the bacteria population [26-28].

The world health organization (WHO) recommends focusing on prevention, preparedness and response to combat the spread of Cholera. Purification of water used for drinking, washing, cooking and sterilizing contaminated material using chlorinated water or other effective anti-microbial agents are crucial in combating Cholera epidemic. In general, if good sanitation practices are continuously applied throughout the life, it is usually sufficient to stop the epidemic [14].

Vaccination has been a commonly used method for diseases control and works by reducing the number of susceptible individuals in a population.Since Koch found *Vibrio cholera* in 1883, the research for cholera vaccine had been going on for over one hundred years. People have developed a variety of vaccines. However, these vaccines were parenteral (by injection), which have short effective protection and big side effects. In 1973, the World Health Organization (WHO) canceled the vaccine inoculation, which attracted a major concern to oral vaccines. WHO recommends immunization of high -risk group such as children, people with HIV and in countries where this disease is endemic [5,28].

According to WHO 2010 report, every year there is an estimated 3-5 million Cholera cases and100,000-120,000 deaths due to Cholera [13,21]. In the year 2017 the Cholera pandemic recorded was the largest ever in history. Explosive country-wide epidemics of Cholera killed thousands of people in Yemen (2,261), the Democratic Republic of Congo (1,190) and Somalia (1,007) [29]. In Africa, the number of people affected by Cholera rose sharply, with the largest number of cases reported since 2011. In 2017,14 African countries reported a total of 179,835 cases and 3,220 deaths [29,30].

Mathematical models of epidemiology in particular of infectious disease enable the researchers to understand the status of the prevalence of the disease, find the optimal performance, appropriate public health intervention strategies and make predictions about the disease, which helps to prevent and control the disease.

The organization of this paper is as follows: We formulate our model for cholera-infection transmission dynamics by analyzing the positivity and boundedness of the solutions of the dynamical systems as basic properties of the model, which are essential in the proofs of stability.Existence of disease-free and endemic equilibria as well as their local and global stability and analysis of the sensitivity of the parameters of the reproduction number are treated. We present the numerical simulation to verify or support the analytical findings of the research.The result, discussion, conclusion and recommendation of the research are present consecutivelyafter numerical simulation. Finally, the paper ends with limitations of the research.

II.   Model formulation

In this model of cholera infection, public health intervention strategies are incorporated.All the recruited individuals are susceptible. The total human population is closed. Total human population is given by $N = S + I + Q_I + R_I$.The basic assumptions in developing this model are as follows.There is a positive recruitmentinto the susceptible class.Cholera infected individuals are subject to cholera treatment stay in quarantine.Cholera infection is caused by indirect (environment-to-human) way of infection i.eingestion of contaminated water and food with infective vibrio- cholera.Cholera recovered from Cholera infection loose immunity for further infection. The extended model incorporates additional assumptions: Cholera infection is caused by indirect (environment-to-human) mode of transmission, intervention strategies vaccination and antibiotic therapy for cholera-infected individuals in quarantinewill be taken in to account.

The variables and parameters of the model are defined as follows:

The total human population $N(t)$, susceptiblepopulation $S(t)$, infected with cholera $I(t)$, cholera treatment through quarantine $Q_I(t)$and cholera recovered from cholera infected individuals $R_I(t), \mu$ is the natural mortality rate in all classes at time t, for $t \geq 0$. Furthermore, a class $B(t)$that reflects the bacterial concentration at time t.We assumed that there is a positive recruitment rate Λinto the susceptible class. Susceptible individuals can become infected with cholera at rate $\lambda(B) = \frac{\vartheta B}{K+B}$ that is dependent on time t. Note that $\vartheta > 0$ is the ingestion rate of the bacteria throughcontaminated sources and k is the half saturation constant of the bacteria population (i.e the bacteria population that yields 50% chance of catching cholera).Cholera infected are assumed to suffer cholera related mortality at rate $\delta$and quarantined individuals suffered cholera related deathrate γ.The parameter *e* defines the average contribution of each cholera-infected individual to the aquatic population of V. cholerae. The pathogen population is generated or grows at a rate g and the pathogen natural death or loss rate is l and thus the net death rate of the vibros is $\xi = l - g$. Infected individuals are in quarantine for treatment at the rate ρ and quarantined individuals recover from infection by the rate α. Cholera recovered lose their immunity at the rat φ and move to susceptible for further infection. The schematic diagram is as follows:
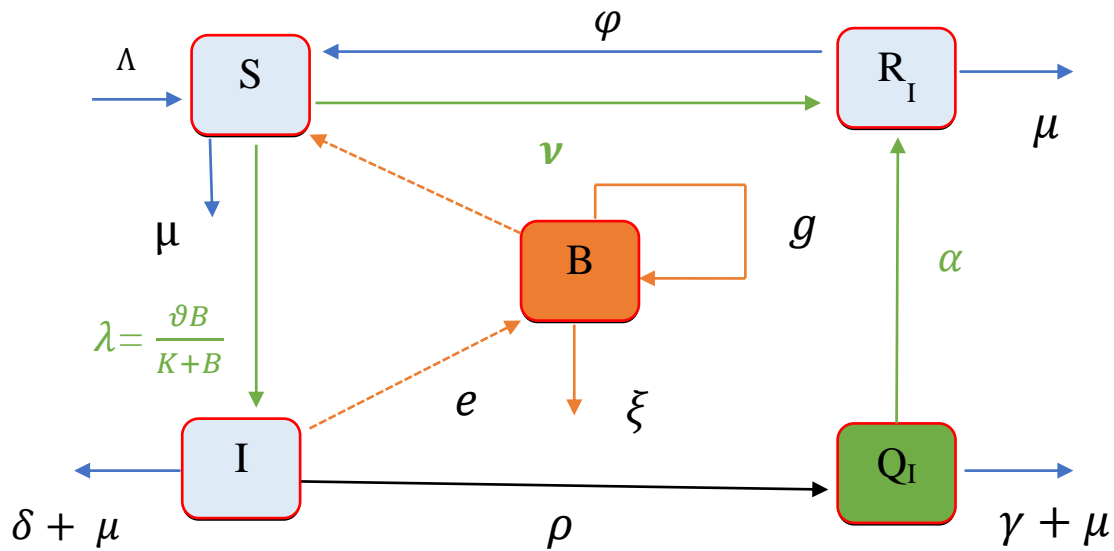
The corresponding dynamical systems is:

$$\frac{dS}{dt} = \Lambda + \varphi R_I - \frac{\vartheta B}{K+B}S - \mu S - \nu S \qquad 1.1$$

$$\frac{dI}{dt} = \frac{\vartheta B}{K+B}S - \rho I - (\delta + \mu)I \qquad 1.2$$

$$\frac{dQ_I}{dt} = \rho I - \alpha Q_I - (\gamma + \mu)Q_I \ 1.3 \qquad (1)$$

$$\frac{dR_I}{dt} = \alpha Q_I + \nu S - \varphi R_I - \mu R_I \qquad 1.4$$

$$\frac{dB}{dt} = eI - \xi B \ 1.5$$

III.   Model analysis

3.1 Positivity of the solutions

Theorem 1. The solutions $(S(t), I(t), Q_I(t), R_I(t)$ and $B(t))$ of model (1) are nonnegative for all t $>$ 0with non-negative initialconditions.

Proof:-Since the system of equations (1) represents human populations, all parameters in the model are non-negative and the total human population is finite at time $t > 0$, we need to show that, given non-negative initial values

$S(0) \geq 0, I(0) \geq 0, Q_I(0) \geq 0, R_I(0) \geq 0,$ and$B(0) \geq 0$, the solutions of the system are non-negative.

Suppose $S(t) + I(t) + Q_I(t) + R_I(t) = N(t) \leq \frac{\Lambda}{\mu}$

Let us consider the region$\mathcal{H} = \Omega \ X \ \mathcal{B}$ where

$\Omega = \left\{(S, I, Q_I, R_I) \in \mathbb{R}^4 : N \leq \frac{\Lambda}{\mu}\right\}and\mathcal{B} = \{B \in \mathbb{R}^1\}$ for system (1).

From (1.1):$\frac{dS}{dt} = \Lambda + \varphi R_I - (\lambda + \nu + \mu)S$,$Where \ \lambda = \frac{\vartheta B}{K+B}$

$\Rightarrow \ \frac{dS}{dt} \leq \Lambda + \varphi R_I \leq \Lambda + \varphi\left(\frac{\Lambda}{\mu} - S\right)$, since $R_I \leq \frac{\Lambda}{\mu} - S \geq 1$

Let$\frac{dS}{dt} + \varphi S - \left(\Lambda + \frac{\Lambda}{\mu}\right) = 0$ which is the first order linear ordinary differential equation(ODE)

$\Rightarrow S(t) = e^{-\varphi t}\int_0^t (\Lambda + \frac{\varphi \Lambda}{\mu})e^{\varphi \tau} \, d\tau = e^{-\varphi t}(\Lambda + \frac{\varphi \Lambda}{\mu})\frac{1}{\varphi}[e^{\varphi t} - 1] \geq 0$

Therefore, since $S(0) \geq 0$, for $t \to \infty, 0 \leq S(t) \leq e^{-\varphi t}(\Lambda + \frac{\varphi \Lambda}{\mu})\frac{1}{\varphi}[e^{\varphi t} - 1]$

From (1.2):$\frac{dI}{dt} = \lambda S - (\rho + \delta + \mu)I$

$\Rightarrow \ \frac{dI}{dt} - \lambda\left(\frac{\Lambda}{\mu} - I\right) \leq 0$, since $S \leq \frac{\Lambda}{\mu} - I \geq 1$

$\Rightarrow I(t) = e^{-\lambda t}\frac{\lambda \Lambda}{\mu}\int_0^t e^{\lambda \tau} \, d\tau = e^{-\lambda t}\frac{\lambda \Lambda}{\mu}\frac{1}{\lambda}[e^{\lambda t} - 1] = e^{-\lambda t}\frac{\Lambda}{\mu}[e^{\lambda t} - 1] \geq 0$

Therefore, since $I(0) \geq 0$, for $t \to \infty, 0 \leq I(t) \leq e^{-\lambda t}\frac{\Lambda}{\mu}[e^{\lambda t} - 1]$

From (1.3):$\frac{dQ_I}{dt} = \rho I - (\alpha + \gamma + \mu)Q_I$

$\Rightarrow \frac{dQ_I}{dt} - \rho\left(\frac{\Lambda}{\mu} - Q_I\right) \leq 0$, since $I \leq \frac{\Lambda}{\mu} - Q_I$

$\Rightarrow Q_I(t) = e^{-\int_0^t (\rho)d\tau} \int_0^t \rho \frac{\Lambda}{\mu} e^{\int_0^t (\rho)d\tau} d\tau = e^{-(\rho)t} \frac{\rho\Lambda}{\mu}\frac{1}{\rho}[e^{\rho t} - 1] = e^{-\rho t}\frac{\Lambda}{\mu}[e^{\rho t} - 1] \geq 0$

Therefore, since $Q_I(0) \geq 0$, for $t \rightarrow \infty, 0 \leq Q_I(t) \leq e^{-\rho t}\frac{\Lambda}{\mu}[e^{\rho t} - 1]$

From (1.4): $\frac{dR_I}{dt} = \alpha Q_I - (\varphi + \mu)R_I$

$\Rightarrow \frac{dR_I}{dt} - \alpha\left(\frac{\Lambda}{\mu} - R_I\right) \leq 0$, since $Q_I \leq \frac{\Lambda}{\mu} - R_I$

$\Rightarrow R_I(t) = e^{-\alpha t}\alpha\frac{\Lambda}{\mu}\int_0^t e^{\alpha\tau} d\tau = e^{-\alpha t}\frac{\alpha\Lambda}{\mu}\frac{1}{\alpha}[e^{\alpha t} - 1] = e^{-\alpha t}\frac{\Lambda}{\mu}[e^{\alpha t} - 1] \geq 0$

Therefore, since $R_I(0) \geq 0$, for $t \rightarrow \infty, 0 \leq R_I(t) \leq e^{-\alpha t}\frac{\Lambda}{\mu}[e^{\alpha t} - 1]$

From (1.5): $\frac{dB}{dt} = eI - \xi B$

$\Rightarrow \frac{dB}{dt} - e\frac{\Lambda}{\mu} \leq 0$, since $I \leq \frac{\Lambda}{\mu}$ and $\frac{\Lambda}{\mu} \geq 1$.

$\Rightarrow B(t) = \int_0^t e\frac{\Lambda}{\mu}d\tau = e\frac{\Lambda}{\mu}t \geq 0$. Therefore, since $B(0) \geq 0$, as $t \rightarrow \infty, 0 \leq B(t) \leq e\frac{\Lambda}{\mu}t$

Hence, any solution of system $(1)(S(t), I(t), Q_I(t), R_I(t), B(t)) \in \mathbb{R}_+^5$ for all $t \geq 0$.

3.2 Boundedness of the solutions

Theorem 2. The Solutions$(S(t), I(t), Q_I(t), R_I(t), B(t))$of model (1) are bounded.

Proof:-The population is grouped into two parts, the human population $(S(t), I(t), Q_I(t), R_I(t))$ and pathogen population $B(t)$.

The total human population in our model is denoted by N and divided in to four subclass which are denoted by S, I, Q_I, R_I from this we have

$$N(t) = S(t) + I(t) + Q_I(t) + R_I(t)$$

By differentiating both side with respect to time t we get:

$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dI}{dt} + \frac{dQ_I}{dt} + \frac{dR_I}{dt} \leq \Lambda - \mu N$, from this we have $\frac{dN}{dt} \leq \Lambda - \mu N$.

If $\frac{dN}{dt} \geq 0$ then $\Lambda - \mu N \geq 0$. Thus $N(t) \leq \frac{\Lambda}{\mu}$ for $N(0) \leq \frac{\Lambda}{\mu}$, where at $t = 0, N(0)$ is initial population.

Therefore $\lim_{t\rightarrow\infty} \sup N(t) \leq \frac{\Lambda}{\mu}$. This shows that $N(t)$ is bounded above and monotonic. Since $N(t)$ is bounded above, each other state variable of human population $S(t), I(t), Q_I(t)$ and $R_I(t)$ is bounded above.

To show that the state variables of human population are bounded below, we need to show the boundedness of each state variable below for $N(0) \geq \frac{\Lambda}{\mu}$.

From equation (1.1) we have:

$\frac{dS}{dt} = \Lambda + \varphi R_I - (\lambda + \nu + \mu)S$

$\Rightarrow \frac{dS}{dt} \leq \Lambda + \varphi\frac{\Lambda}{\mu} - (\varphi + \lambda + \nu + \mu)S$

If $\Lambda + \varphi\frac{\Lambda}{\mu} - (\varphi + \lambda + \nu + \mu)S \leq 0$, then $\frac{dS}{dt} \leq 0$ and S(t) is decreasing with time $t > 0$,

that is $S(t) \geq \frac{\Lambda + \varphi\frac{\Lambda}{\mu}}{\varphi + \lambda + \nu + \mu}$. This shows that S(t) is bounded below and monotonic.

Therefore $\lim_{t\rightarrow\infty} \inf S(t) \geq \frac{\Lambda + \varphi\frac{\Lambda}{\mu}}{\varphi + \lambda + \nu + \mu}$.

From equation (1.2) we have:

$\frac{dI}{dt} = \lambda S - (\rho + \delta + \mu)I$

If $\lambda\frac{\Lambda}{\mu} - (\lambda + \rho + \delta + \mu)I \leq 0, \frac{dI}{dt} \leq 0$ and I(t) is decreasing with time $t > 0$ that is $I(t) \geq \frac{\Lambda}{\mu}\left(\frac{\lambda}{\lambda + \rho + \delta + \mu}\right)$. This shows that I(t) is bounded below and monotonic.

Therefore, $\lim_{t\rightarrow\infty} \inf I(t) \geq \frac{\Lambda}{\mu}\left(\frac{\lambda}{\lambda + \rho + \delta + \mu}\right)$.

From equation (1.3) we have:

$\frac{dQ_I}{dt} = \rho I - (\alpha + \gamma + \mu)Q_I$

If $\rho \frac{\Lambda}{\mu} - (\rho + \alpha + \gamma + \mu)Q_I \leq 0$, then $\frac{dQ_I}{dt} \leq 0$ and $Q_I(t)$ is decreasing with time $t > 0$, that is $Q_I(t) \geq \frac{\Lambda}{\mu}\left(\frac{\rho}{\rho+\alpha+\gamma+\mu}\right)$. This shows that $Q_I(t)$ is bounded below and monotonic.

Therefore $\lim_{t\to\infty} \inf Q_I(t) \geq \frac{\Lambda}{\mu}\left(\frac{\rho}{\rho+\alpha+\gamma+\mu}\right)$

From equation (1.4) we have:

$$\frac{dR_I}{dt} = \alpha Q_I + \nu S - (\varphi + \mu)R_I$$

$$\Rightarrow \frac{dR_I}{dt} \leq \alpha\frac{\Lambda}{\mu} + \nu\frac{\Lambda}{\mu} - (\alpha + \nu + \varphi + \mu)R_I$$

If $R_I(t)$ is decreasing with time $t > 0$, $\frac{dR_I}{dt} \leq 0$ that is $R_I(t) \geq \frac{\Lambda}{\mu}\left(\frac{\alpha+\nu}{\nu+\alpha+\varphi+\mu}\right)$

Therefore, $\lim_{t\to\infty} \inf R_I(t) \geq \frac{\Lambda}{\mu}\left(\frac{\alpha+\nu}{\nu+\alpha+\varphi+\mu}\right)$. This shows that $R_I(t)$ is bounded below.

From equation (1.5) we have:

$$\frac{dB}{dt} = eI - \xi B$$

If $B(t)$ is increasing with time $t > 0$ and $N(0) \leq \frac{\Lambda}{\mu}$, then $\frac{dB}{dt} \geq 0$

$$eI - \xi B \geq 0 \Rightarrow B \leq \frac{eI}{\xi} \leq \frac{e}{\xi}\frac{\Lambda}{\mu}$$

Therefore $\lim_{t\to\infty} \sup B(t) \leq \frac{\Lambda e}{\xi\mu}$. This shows that $B(t)$ is bounded above.

If $B(t)$ is decreasing with time $t > 0$, then $\frac{dB}{dt} \leq 0 \Rightarrow eI - \xi B \leq 0 \Rightarrow B \geq \frac{\Lambda e}{\xi\mu}$

Therefore $\lim_{t\to\infty} \inf B(t) \geq \frac{\Lambda e}{\xi\mu}$. This shows that $B(t)$ is bounded below.

Thus, $B(t)$ is bounded. Hence, all solutions of the system (1) are bounded.

Theorem 3. The region $\Omega = \left\{(S, I, Q_I, R_I) \in \mathbb{R}_+^4 : N \leq \frac{\Lambda}{\mu}\right\}$ is positively invariant for the model (1) with non-negative initial conditions in $\mathbb{R}_+^4$.

Proof: -To proof the positive invariance of Ω (i.e., all solutions in Ω remain in Ω for all t).

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

$$\Rightarrow N(t) = \Lambda e^{-\mu t}\int_0^t e^{\int_0^t \mu t d\tau}d\tau = \Lambda e^{-\mu t}\int_0^t e^{\mu \tau}d\tau = \frac{\Lambda}{\mu}e^{-\mu t}[e^{\mu t} - 1] = \frac{\Lambda}{\mu}[1 - e^{-\mu t}] = \frac{\Lambda}{\mu} - \frac{\Lambda}{\mu}e^{-\mu t}$$

$\frac{dN}{dt} \leq \Lambda - \mu N \Rightarrow N(t) \leq \frac{\Lambda}{\mu} - N(0)e^{-\mu t}$, for $N(0) \leq \frac{\Lambda}{\mu}$

If $\frac{dN}{dt} \geq 0$ then $\Lambda - \mu N \geq 0$ and $\frac{dN}{dt} \geq 0 \Rightarrow N(t) \leq \frac{\Lambda}{\mu}$

Specifically, if $\frac{dN}{dt} \geq 0$ then $N(0) \leq \frac{\Lambda}{\mu}$. Thus $N(t) \leq \frac{\Lambda}{\mu}$ and this shows that $N(t)$ is increasing and bounded above by $\frac{\Lambda}{\mu}$ and if

$\Lambda - \mu N < 0$ then $\frac{dN}{dt} < 0$. Thus $N(t) > \frac{\Lambda}{\mu} \Rightarrow \frac{dN}{dt} < 0$. In particular, if $N(0) > \frac{\Lambda}{\mu}$, then $\frac{dN}{dt} < 0$ and this shows that $N(t)$ is decreasing and bounded below by 0 because of positivity. Thus, Ω is positive-invariant and attracting. Therefore, every solution of the human population dynamical system with initial conditions in Ω remains in Ω for $t > 0$. Hence, it is sufficient to consider the dynamics of human population for the system (1) in Ω and thus, in the region , the model system of the human population for the system (1) is epidemiologically and mathematically well posed.

From $\frac{dB}{dt} = eI - \xi B$, we have:

$\frac{dB}{dt} \geq 0$ Whenever $eI - \xi B \geq 0$

$\Rightarrow B \leq \frac{eI}{\xi} \leq \frac{eN}{\xi} \leq \frac{e\Lambda}{\xi\mu}$. Thus, $B(t)$ is increasing and bounded above. On the other hand $\frac{dB}{dt} < 0$, when $B(t) > \frac{e\Lambda}{\xi\mu}$. Thus $B(t)$ is decreasing and bounded below. Therefore $B(t)$ is monotone bounded. This leads us to accept the following corollary is also true.

Corollary 1. Let $\Omega = \left\{(S, I, Q_I, R_I) \in \mathbb{R}_+^4 : N \leq \frac{\Lambda}{\mu}\right\}$ and $\mathcal{B} = \left\{B \in R_+ : B \leq \frac{e\Lambda}{\xi\mu}\right\}$, then the region $\mathcal{H} = \Omega \, X \, \mathcal{B}$ is invariant and attracting for system (1).

The feasible region is $\mathcal{H} = \begin{cases} (S, I, Q_I, R_I) \in \mathbb{R}_+^4 : N \leq \frac{\Lambda}{\mu}, \\ \quad B \in R_+ : B \leq \frac{e\Lambda}{\xi\mu} \end{cases}$

3.3 Disease -free equilibrium point

The disease -free equilibrium point (E_{oc}) of the system (1) can be obtained by setting cholera related variables and parameters to zero $(I = Q_I = R_I = B = 0)$ then we have $\Lambda - (\mu + v)S = 0$. Therefor the disease-free equilibrium point of cholera model (1) is

$$E_{oc} = \left(S_0, I_0, Q_{I_0}, R_{I_0}, B_0\right) = \left(\frac{\Lambda}{\mu + v}, 0, 0, 0, 0\right)$$

3.4 Effective reproduction number

Theorem 4. The effective reproduction number (R_C) of cholera model (1) is given by

$$R_c = \frac{\vartheta\Lambda e}{k\xi(\mu + v)(\rho + \delta + \mu)}$$

Proof: -In order to compute R_c, it is important to distinguish new infections from all other changes in the host population. We apply the next generation approach in Diekmann et al. 1990 used in [31, 32]. Let $\mathcal{F}_i(t)$ be the rate of appearance of new infections in compartment i, $V_i^+(t)$ be the transfer rate of individuals into compartment i by all other means, and $V_i^-(t)$ be the rate transfer of individuals out of compartment i. It is assumed that each function is continuously differentiable at least twice in each variable. The model (1) of cholera dynamics can be formulated as follows and arrange in order from infected to non- infected.

$\frac{dx_i}{dt} = f_i(t) = \mathcal{F}_i(t) - \mathcal{v}_i(t)$ where $i = 1, \dots, 5$, as there are five classes and $x_i = (I, Q_I, B, R_I, S)$

$\mathcal{v}_i(t) = V_i^-(t) - V_i^+(t)$ and the matrices $\mathcal{F}(t), V^+(t)$ and $V^-(t)$ associated with model (2) are given by

$$\mathcal{F}(t) = \begin{bmatrix} \frac{\vartheta BS(t)}{K+B(t)} \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}, V^+(t) = \begin{bmatrix} 0 \\ \rho I(t) \\ eI(t) \\ \alpha Q_I(t) + vS \\ \Lambda + \varphi R_I(t) \end{bmatrix} \text{ and } V^-(t) = \begin{bmatrix} b_1 I(t) \\ b_2 Q_I(t) \\ \xi B(t) \\ b_3 R_I(t) \\ \left(\frac{\vartheta B}{K+B} + \mu + v\right)S(t) \end{bmatrix}$$

Where $b_1 = \rho + \delta + \mu, b_2 = \alpha + \gamma + \mu$ and $b_3 = \varphi + \mu$

Let, $\mathcal{v}(t) = V^-(t) - V^+(t)$

Then, we have $\left[\frac{dI(t)}{dt} \frac{dQ_I(t)}{dt} \frac{dB(t)}{dt} \frac{dR_I(t)}{dt} \frac{dS(t)}{dt}\right]^T = \mathcal{F}(t) - \mathcal{v}(t)$

The Jacobian matrices of $F(t)$ and $V(t)$ for $\mathcal{F}(t)$ and $\mathcal{v}(t)$ respectively are 3x3 matrices as there are three infected classes I, Q_I and B

$$F = \frac{\partial \mathcal{F}}{\partial x_i} = \begin{bmatrix} 0 & 0 & \frac{k\vartheta S(t)}{(k+B(t))^2} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \text{ and } V = \frac{\partial \mathcal{v}}{\partial x_i} = \begin{bmatrix} b_1 & 0 & 0 \\ -\rho & b_2 & 0 \\ -e & 0 & \xi \end{bmatrix}, \text{ where } x_i = (I, Q_I, B)$$

F and V at the infection-free equilibrium point E_{oc} are F_0 and V_0 respectively:

Thus. $R_c = \rho(F_0 V_0^{-1})$ Where $\rho(F_0 V_0^{-1})$ denotes the spectral radius of a matrix $F_0 V_0^{-1}$ (that is, the eigenvalue with the highest magnitude). To find the eigen values of $F_0 V_0^{-1}$, we consider $\det(F_0 V_0^{-1} - \varpi T) = 0$, where T is the identity matrix.

Thus, $R_c = \frac{\vartheta\Lambda e}{k\xi(\mu+v)(\rho+\delta+\mu)}$, which represent the average number of new secondary cases generated by a single cholera infected individual during his/her entire infectious period in a completely susceptible population, in the presence of cholera vaccination and treatment in quarantine intervention strategies.

3.5 Local stability of the disease-free steady state

Theorem 5. The infection-free equilibrium (E_{oc}) point of model (1) is locally asymptotically stable, if $R_c < 1$ i.e if $\vartheta\Lambda e < k(\mu + v)\xi(\rho + \delta + \mu)$ and unstable, if $R_c > 1$ i.e if $\vartheta\Lambda e > k(\mu + v)\xi(\rho + \delta + \mu)$.

Proof: -The Jacobian matrix $J(x_i)$ of the system (1) at the disease free equilibrium point is as follows, where $x_i = (S, I, Q_I, R_I, B)$

$$J(E_{0c}) = \begin{bmatrix} -\mu - v & 0 & 0 & \varphi & -\frac{\vartheta\Lambda}{k(\mu+v)} \\ 0 & -(\rho + \delta + \mu) & 0 & 0 & \frac{\vartheta\Lambda}{k(\mu+v)} \\ 0 & \rho & -(\alpha + \gamma + \mu) & 0 & 0 \\ v & 0 & \alpha & -(\varphi + \mu) & 0 \\ 0 & e & 0 & 0 & -\xi \end{bmatrix}$$

The characteristic polynomial of the matrix $J(E_{0c})$ is given by

$p(\varpi) = \det(J(E_{0c}) - \varpi T) = \det(F_0 - V_0 - \varpi T)$ and in order to find the roots of the
Polynomial p, we set

$$P(\varpi) = \begin{vmatrix} -(\mu+v)-\varpi & 0 & 0 & \varphi & -\dfrac{\vartheta\Lambda}{k(\mu+v)} \\ 0 & -b_1-\varpi & 0 & 0 & \dfrac{\vartheta\Lambda}{k(\mu+v)} \\ 0 & \rho & -b_2-\varpi & 0 & 0 \\ v & 0 & \alpha & -b_3-\varpi & 0 \\ 0 & e & 0 & 0 & -\xi-\varpi \end{vmatrix} = 0$$

$$P(\varpi) = (b_2+\varpi)\left[\varpi^2 + (b_3+(\mu+v))\varpi + b_3(\mu+v) + v\varphi\right]\left[\varpi^2 + (b_1+\xi)\varpi + b_1\xi - \dfrac{e\vartheta\Lambda}{k(\mu+v)}\right] = 0$$

That is, either $\varpi = -b_2 < 0$ or $\left[\varpi^2 + (b_3+(\mu+v))\varpi + b_3(\mu+v) + v\varphi\right] = 0$ or $\left[\varpi^2 + (b_1+\xi)\varpi + b_1\xi - e\vartheta\Lambda k\mu+v=0\right.$

By Routh-Hurwitz stability criterion, if all the coefficients of the quadratic polynomial have the same sign, then all the roots of the polynomial have negative real part, and thus the disease-free equilibrium point is locally asymptotically stable. The coefficients of the first quadratic polynomial are $1 > 0, (b_3+(\mu+v)) > 0$, and $b_3(\mu+v) + v\varphi > 0$. The coefficients of the second quadratic polynomial are $1 > 0, (b_1+\xi) > 0$, and $b_1\xi - \dfrac{e\vartheta\Lambda}{k(\mu+v)}$ Therefore, the infection-free equilibrium point E_{oc} is locally asymptotically stable, if $\left(b_1\xi - \dfrac{e\vartheta\Lambda}{k(\mu+v)}\right) > 0$ i.e $\vartheta\Lambda e < k(\mu+v)b_1\xi = k(\mu+v)\xi(\rho+\delta+\mu)$.

$$b_1\xi - \dfrac{e\vartheta\Lambda}{k(\mu+v)} = (\rho+\delta+\mu)\xi\left[1 - \dfrac{\vartheta\Lambda e}{k(\mu+v)(\rho+\delta+\mu)\xi}\right] = (\rho+\delta+\mu)\xi[1-R_c]$$

Therefore, if $R_c > 1$, then $\left(b_1\xi - \dfrac{e\vartheta\Lambda}{k(\mu+v)}\right) < 0$. This shows that $J(E_{0c})$ has at least one eigen value with non-negative real part. Thus E_{0c} is unstable for $R_c > 1$.
Hence, the proof is completed.
The biological interpretation of locally asymptotically stabile of the disease-free equilibrium point is that, the existence of small number of infectious individuals will not be the cause of the outbreak of the disease unless $R_c > 1$. Thus, we need to consider the global asymptotic stability of E_{0c} to control the disease effectively. To investigate the global stability, we define a Lyapunov function [12,13].

3.6 Global stability of the disease free equilibrium point
Theorem6. Disease-free equilibrium point (E_{0c}) is globally asymptotically stable, if $R_c < 1$
Proof:- Define a Lyapunov function by applying Lyapunov theorem.
$V(S, I, Q_I, R_I, B) = (\mu+v)eI + (\mu+v)b_1B$, where $b_1 = \rho + \delta + \mu$. Since all variables and parameters in V
are positive $V(S, I, Q_I, R_I, B) \geq 0$ and $V(S_0, I_0, Q_{I_0}, R_{I_0}, B_0) = V\left(\dfrac{\Lambda}{\mu+v}, 0,0,0,0\right) = 0$ is the minimum value.
$\dfrac{\partial V}{\partial S} = \dfrac{\partial V}{\partial Q_I} = \dfrac{\partial V}{\partial R_I} = 0, \dfrac{\partial V}{\partial I} = (\mu+v)e, \dfrac{\partial V}{\partial B} = (\mu+v)b_1$ are all constants and thus continuous partial derivatives.
$$\dfrac{dV}{dt} = \dfrac{\partial V}{\partial I}\dfrac{dI}{dt} + \dfrac{\partial V}{\partial B}\dfrac{dB}{dt} = (\mu+v)e\left[\dfrac{\vartheta B}{k+B}S - b_1I\right] + (\mu+v)b_1[eI - \xi B]$$
$$= (\mu+v)e\dfrac{\vartheta B}{k+B}S - (\mu+v)b_1\xi B$$
$$= \dfrac{e\vartheta B\Lambda}{k}\left[\dfrac{k}{k+B}\dfrac{(\mu+v)}{\Lambda}S - \dfrac{(\mu+v)b_1\xi k}{e\vartheta\Lambda}\right]$$
$$\leq \dfrac{e\vartheta B\Lambda}{k}\left[\dfrac{k}{k+B}\dfrac{S}{N} - \dfrac{(\mu+v)\xi k(\rho+\delta+\mu)}{e\vartheta\Lambda}\right], \text{ since,} \dfrac{\mu+v}{\Lambda} < \dfrac{1}{N}$$
$$\leq \dfrac{e\vartheta B\Lambda}{k}\left[\dfrac{k}{k+B} - \dfrac{1}{R_c}\right] \leq 0, \text{ as} \dfrac{k}{k+B} < 1, \dfrac{S}{N} < 1 \text{ and} R_c < 1$$
$\dfrac{dV}{dt} = 0$ if and only if $B = 0$
The largest compact invariant subsets in $\{(S, I, Q_I, R_I, B)\}$ is the singleton set $\{E_{0c}\}$. Therefore, by Lasalle's invariant principle (Lasalle 1976) E_{0c} is global attractor whenever $R_c < 1$.
3.7 Endemic equilibrium point
Theorem 7. The endemic equilibrium point of the system (1) exist, if $R_c > 1$.
Proof:-The endemic equilibrium point $E_c = (S^*, I^*, Q_I^*, R_I^*, B^*)$ of the system (1) can be obtained by setting
$\dfrac{dS}{dt} = \dfrac{dI}{dt} = \dfrac{dQ_I}{dt} = \dfrac{dR_I}{dt} = \dfrac{dB}{dt} = 0$. Therefore. $E_c = (S^*, I^*, Q_I^*, R_I^*, B^*) = \left(\dfrac{\Lambda abc}{H}, \dfrac{\lambda^*abc}{H}, \dfrac{\lambda^*\Lambda\rho c}{H}, \dfrac{\Lambda(\alpha\rho\lambda^*+abv)}{H}, \dfrac{e\lambda^*abc}{\xi H}\right)$

Where, $a = \rho + \delta + \mu$, $b = \alpha + \gamma + \mu$, $c = \varphi + \mu$, $H = abc(\lambda^* + \mu + \nu) - \varphi(\alpha\rho\lambda^* + ab\nu)$

Therefore, $\lambda^* = \frac{\vartheta B^*}{k+B^*} = \vartheta B^* \frac{1}{k+B^*} = \left(\frac{\vartheta e \lambda^* \Lambda bc}{\xi[abc(\lambda^*+\mu+\nu)-\varphi(\alpha\rho\lambda^*+ab\nu)]}\right)\left(\frac{\xi[abc(\lambda^*+\mu+\nu)-\varphi(\alpha\rho\lambda^*+ab\nu)]}{k\xi[abc(\lambda^*+\mu+\nu)-\varphi(\alpha\rho\lambda^*+ab\nu)]+e\lambda^* \Lambda bc}\right) =$

$\frac{\vartheta e \lambda^* \Lambda bc}{k\xi H + \lambda^* \Lambda bce}$

$\Rightarrow \lambda^* - \frac{\vartheta e \lambda^* \Lambda bc}{k\xi H + \lambda^* \Lambda bce} = 0 \Rightarrow \lambda^*\left(1 - \frac{\vartheta e \Lambda bc}{k\xi H + \lambda^* \Lambda bce}\right) = 0,$

Since the disease exist $\lambda^* \neq 0$. Thus, $k\xi H + \lambda^* \Lambda bce - \vartheta e \Lambda bc = 0$

$\Leftrightarrow k\xi[abc(\lambda^*+\mu+\nu)-\varphi(\alpha\rho\lambda^*+ab\nu)] + \lambda^* \Lambda bce - \vartheta e \Lambda bc = 0$

$\Leftrightarrow k\xi abc(\lambda^*) + k\xi abc(\mu+\nu) - k\xi\varphi\alpha\rho\lambda^* - k\xi\varphi ab\nu + \lambda^* \Lambda bce = \vartheta \Lambda bce$

$\Leftrightarrow \lambda^*[k\xi abc - k\xi\varphi\rho + \Lambda bce] = \vartheta \Lambda bce - k\xi abc(\mu+\nu) + k\xi\varphi ab\nu$

$\Leftrightarrow \lambda^* \geq \frac{\vartheta \Lambda bce - k\xi abc(\mu+\nu)}{k\xi(abc - \varphi\alpha\rho) + \Lambda bce} = \frac{k\xi abc(\mu+\nu)\left(\frac{\vartheta \Lambda e}{k\xi(\mu+\nu)a} - 1\right)}{k\xi(abc - k\xi\varphi\alpha\rho) + \Lambda bce} = \frac{k\xi(\mu+\nu)abc\left(\frac{\vartheta \Lambda e}{k\xi(\mu+\nu)(\rho+\delta+\mu)} - 1\right)}{k\xi(abc - k\xi\varphi\alpha\rho) + \Lambda bce}$

$= \frac{k\xi(\mu+\nu)abc[R_c - 1]}{k\xi(abc - \varphi\alpha\rho) + \Lambda bce}$

It is true that $abc - \varphi\alpha\rho = (\rho+\delta+\mu)(\alpha+\gamma+\mu)(\varphi+\mu) - \varphi\alpha\rho > 0$ *as*
$\delta, \gamma \geq 0$ *and* $\mu > 0$ *and since* $k, \xi, \Lambda, e, \nu > 0$, *we have also* $k\xi(\mu+\nu)abc > 0$ *and*
$k\xi(abc - \alpha\rho\varphi) + \Lambda bce > 0$. *This shows that* $\lambda^* > 0$, *if* $R_c > 1$.

Thus, the dynamical systems (1) has an endemic equilibrium point given by $E_c = (S^*, I^*, Q_I^*, R_I^*, B^*)$.
Thus, the proof is completed.

3.8 Local stability of the endemic equilibrium point

Theorem 8. The endemic equilibrium point (E_c) of model (1)is locally asymptotically stable in the region $\mathcal{H}$ if $R_c > 1$

Proof:-The Jacobian matrix $J(x_i)$ of the system (1) at the endemic equilibrium point is as follows:

$$J(E_c) = \begin{bmatrix} -p_1 - (\mu+\nu) & 0 & 0 & \varphi & -p_2 \\ p_1 & -a & 0 & 0 & p_2 \\ 0 & \rho & -b & 0 & 0 \\ \nu & 0 & \alpha & -c & 0 \\ 0 & e & 0 & 0 & -\xi \end{bmatrix}, \text{ Where, } p_1 = \frac{\vartheta B^*}{K+B^*} \text{ and } p_2 = \frac{k\vartheta,S^*}{(K+B^*)^2},$$

The characteristic polynomial of the matrix $J(E_c)$is given by $h(\varpi) = \det(J(E_c) - \varpi T)$, where T is identity matrix and in order to find the roots of the polynomial h, we set

$$h(\varpi) = \begin{vmatrix} -p_1 - (\mu+\nu) - \varpi & 0 & 0 & \varphi & -p_2 \\ p_1 & -a-\varpi & 0 & 0 & p_2 \\ 0 & \rho & -b-\varpi & 0 & 0 \\ \nu & 0 & \alpha & -c-\varpi & 0 \\ 0 & e & 0 & 0 & -\xi-\varpi \end{vmatrix} = 0$$

$\Rightarrow h_0\varpi^5 + h_1\varpi^4 + h_2\varpi^3 + h_3\varpi^2 + h_4\varpi + h_5 = 0$

Where, $y = p_1 + \mu + \nu$, $p_1 = \frac{\vartheta B^*}{K+B^*}$ and $p_2 = \frac{k\vartheta,S^*}{(K+B^*)^2}$, $h_0 = 1$, $h_1 = \xi + ab + yc$

$h_2 = -ep_2 + ab + ycab + yc + \xi ab + \xi yc$

$h_3 = ep_2p_1 - ep_2(yc+b) + \xi ab + \xi ycab + \xi yc + 2ycab$

$h_4 = ep_2p_1bc - ep_2(yc+byc) + \xi 2ycab + ycab - \varphi p_1\rho\alpha + ep_2\nu\varphi$

$h_5 = \xi ycab - \xi\varphi p_1\rho\alpha + ep_2p_1bc - ep_2byc + ep_2b\nu\varphi$

The endemic steady state is locally asymptotically stable, if the necessary and sufficient conditions that all the roots of the polynomial $h(\varpi)$have negative real parts (to be located in the left half plane) are all the polynomial coefficients must have the same sign, nonzero and the first column of the Routh's array positive should be satisfied.This can be check by applying Routh-Hurwitz stability criterion.

3.9Global stability of the endemic equilibrium point

Theorem 9. Endemic equilibrium point(E_c) is globally asymptotically stable,if $R_c > 1$

Proof:- By applying Lyapunov theorem. Define a Lyapunov function

$$V(S, I, Q_I, R_I, B) = \left[S - S^* - S^* ln\left(\frac{S^*}{S}\right)\right] + \left[I - I^* - I^* ln\left(\frac{I^*}{I}\right)\right]$$

$$+ \left[Q_I - Q_I^* - Q_I^* ln\left(\frac{Q_I^*}{Q_I}\right)\right]\left[R_I - R_I^* - R_I^* ln\left(\frac{R_I^*}{R_I}\right)\right] + \left[B - B^* - B^* ln\left(\frac{B^*}{B}\right)\right]$$

$\frac{\partial V}{\partial S} = 1 - \frac{S^*}{S}$, $\frac{\partial V}{\partial I} = 1 - \frac{I^*}{I}$, $\frac{\partial V}{\partial Q_I} = 1 - \frac{Q_I^*}{Q_I}$, $\frac{\partial V}{\partial R_I} = 1 - \frac{R_I^*}{R_I}$, $\frac{\partial V}{\partial B} = 1 - \frac{B^*}{B}$ are all continuous partial derivatives for $(S, I, Q_I, R_I, B) \neq 0$.

Let $(x) = x - u - u\, ln\left(\frac{u}{x}\right)$, then $for\ x = u, f(x) = 0$ and for $x > u, f(x) > 0$, thus

$V(S^*, I^*, Q_I^*, R_I^*, B^*) = V\left(\frac{\Lambda abc}{H}, \frac{\lambda^*\Lambda bc}{H}, \frac{\lambda^*\Lambda\rho c}{H}, \frac{\Lambda(\alpha\rho\lambda^* + v)}{H}, \frac{e\lambda^*\Lambda bc}{\xi H}\right) = 0$ is minimum functional value.

Hence $V(S, I, Q_I, R_I, B) \geq 0$. The derivative of V along the solution is $\frac{dV}{dt} = \frac{\partial V}{\partial S}\frac{dS}{dt} + \frac{\partial V}{\partial I}\frac{dI}{dt} + \frac{\partial V}{\partial Q_I}\frac{dQ_I}{dt} + \frac{\partial V}{\partial R_I}\frac{dR_I}{dt} + \frac{\partial V}{\partial B}\frac{dB}{dt}$

$$\frac{dV}{dt} = \Lambda - \mu S - \frac{S^*}{S}\Lambda - \frac{S^*}{S}\varphi R_I + \frac{S^*}{S}\frac{\vartheta BS}{K+B} + \frac{S^*}{S}\mu S + v\frac{S^*}{S}S - (\delta + \mu)I - \frac{I^*}{I}\frac{\vartheta BS}{K+B} + \frac{I^*}{I}(\rho + \delta + \mu)I$$

$$- (\gamma + \mu)Q_I - \frac{Q_I^*}{Q_I}\rho I + \frac{Q_I^*}{Q_I}(\alpha + \gamma + \mu)Q_I - \mu R_I - \frac{R_I^*}{R_I}\alpha Q_I - \frac{R_I^*}{R_I}vS + \frac{R_I^*}{R_I}(\varphi + \mu)R_I + eI$$

$$- \xi B - \frac{B^*}{B}eI + B^*\xi$$

Now let, $m = \Lambda + \frac{S^*}{S}\frac{\vartheta BS}{K+B} + \frac{S^*}{S}\mu S + \frac{S^*}{S}vS + \frac{I^*}{I}(\rho + \delta + \mu)I + \frac{Q_I^*}{Q_I}(\alpha + \gamma + \mu)Q_I + \frac{R_I^*}{R_I}(\varphi + \mu)R_I + eI + B^*\xi$

$n = \mu S + \frac{S^*}{S}\Lambda + \frac{S^*}{S}\varphi R_I + (\delta + \mu)I + \frac{I^*}{I}\frac{\vartheta BS}{K+B} + (\gamma + \mu)Q_I + \frac{Q_I^*}{Q_I}\rho I + \mu R_I + \frac{R_I^*}{R_I}\alpha Q_I + \frac{R_I^*}{R_I}vS + \xi B + \frac{B^*}{B}eI$

Then, $\frac{dV}{dt} = m - n$ and $\frac{dV}{dt} \leq 0\ if\ m < n$.

$\frac{dV}{dt} = 0$ if and only if $(S, I, Q_I, R_I, B) = (S^*, I^*, Q_I^*, R_I^*, B^*)$.

The largest compact invariant subsets in $\{(S, I, Q_I, R_I, B)\}$ is the singleton set $\{E_c\}$.

Therefore, by Lasalle's invariant principle (Lasalle 1976), E_c is global attractor whenever $R_c > 1$.

Table 1. Definition and values of parameter values for the SIQR-Bmodel

Para-meter	Description	Value	Reference
Λ	Recruitment rate	$0.559(day^{-1})$	[16]
μ	Death rate of unrelated cholera	$0.000022493\ (day^{-1})$	[31]
ϑ	Bacteria ingestion rate	$0.8(day^{-1})$	[31]
e	Human contribution to v. cholerae	$10\ (cell/ml\ day^{-1}person^{-1})$	[12]
κ	Half saturation constant	$10^6\ (cell/ml)$	[27]
α	Recovery rate	$0.2\ (day^{-1})$	[5]
φ	Immunity waning rate	$9.13x10^{-4}(day^{-1})$	[12]
δ	Disease induced death rate	$0.015\ (day^{-1})$	[31]
γ	Death rate of quarantined	$0.0001(day^{-1})$	[31]
v	Vaccination rate	0.2	[2]
ρ	Quarantine rate for treatment	$0.05\ (day^{-1})$	[31]
ξ	Bacteria net death rate	$0.33\ (day^{-1})$	[31]

3.10 Sensitivity analysis of the effective reproduction number

Sensitivity analysis assess the degree of the influence of parameters on the reproductive number. To conduct the sensitivity analysis, we adopt the normalized forward sensitivity index. The partial derivative is the rate of change of prediction with respect to each parameter using the approach in (Chitns et.al 2008), (Edward and Nyerere 2015), (Numfor 210)[15]. The degree of sensitivity index of the reproduction number with respect to a parameter say h, measures the relative change in variable when the parameter h changes as $\varphi_h^{R_c} = \frac{\partial R_c}{\partial h}\left(\frac{h}{R_c}\right)$.

The value $\varphi_h^{R_c} = 1$, shows an increase (decrease) of h results in an increase (decrease) of R_c and $\varphi_h^{R_c} = -1$, shows an increase (decrease) of h results in a decrease (increase) of R_c. The most sensitive or most influential parameter positively or negatively is the one with highest in magnitude. We calculate the sensitivity indices of the parameters using the values of the parameters from different literatures in TABLE 1, using $\varphi_h^{R_c} = \frac{\partial R_c}{\partial h}\left(\frac{h}{R_c}\right)$ for parameter h.

Table 2. Sensitivity indices of the effective reproduction number to model parameters

parameter	Sensitivity index
Λ	1
ϑ	1
e	1
k	-1

ξ	-1
δ	-0.23069
μ	-0.00046
ρ	-0.76896
ν	-0.99988

From the values of sensitivity indices in TABLE 2, we can suggest that an increase human recruitment, ingestion of bacteria, bacteria shedding may increase the magnitude of reproduction number. On the other hand, cholera related mortality, natural human mortality, medical treatment of cholera in quarantineand vaccination have negative influence on the magnitude of reproduction number. An increase in medical treatment in quarantine and vaccination control strategies have positive impact in controlling cholera transmission. Since the sensitivity index of our control measure vaccination is highest in magnitude than treatment in quarantine in TABLE 2, the effective reproduction number is more sensitive to parameter ν than parameter ρ.

3.11 Basic reproduction number

Theorem 10. The basic reproduction number(R_0) of cholera transmission model (1)is given by $R_0 = \frac{\vartheta \Lambda e}{k \xi \mu (\delta + \mu)}$

Proof: -We apply the next generation approach in Diekmannet al. 1990 used in [31, 32]. The model (1) of cholera dynamics can be formulated as follows and arrange in order from infected to non- infected model by setting $\rho = \nu = \alpha = \varphi = \gamma = Q_I = R_I = 0$ in SIQR-B to get SI-B model. From SI-B model

$$\mathcal{F}(t) = \begin{bmatrix} \frac{\vartheta B S(t)}{K+B(t)} \\ 0 \\ 0 \end{bmatrix}, V^+(t) = \begin{bmatrix} 0 \\ eI(t) \\ \Lambda \end{bmatrix} \text{and} V^-(t) = \begin{bmatrix} bI(t) \\ \xi B(t) \\ \left(\frac{\vartheta B}{K+B} + \mu\right) S(t) \end{bmatrix}, \text{Where } b = \delta + \mu$$

Let, $\mathscr{v}(t) = V^-(t) - V^+(t)$, then we have $\left[\frac{dI(t)}{dt} \frac{dB(t)}{dt} \frac{dS(t)}{dt}\right]^T = \mathcal{F}(t) - \mathscr{v}(t)$

The Jacobian matrices of $F(t)$ and $V(t)$ for $\mathcal{F}(t)$and $\mathscr{v}(t)$respectively are 2x2 matrices as there are three infected classes $I \text{ and } B$

$$F = \frac{\partial \mathcal{F}}{\partial x_i} = \begin{bmatrix} 0 & \frac{k\vartheta S(t)}{(k+B(t))^2} \\ 0 & 0 \end{bmatrix} \text{and} V = \frac{\partial \mathscr{v}}{\partial x_i} = \begin{bmatrix} b & 0 \\ -e & \xi \end{bmatrix}, \text{where } x_i = (I, B)$$

F and V at the infection-free equilibrium point $E_o = (\frac{\Lambda}{\mu}, 0, 0)$are F_0andV_0 respectively:

Thus. $R_0 = \rho(F_0 V_0^{-1})$, Where $\rho(F_0 V_0^{-1})$ denotes the spectral radius of a matrix$F_0 V_0^{-1}$ (that is, the eigenvalue with the highest magnitude). To find the eigen values of$F_0 V_0^{-1}$, we consider$\det(F_0 V_0^{-1} - \varpi T) = 0$, where T is the identity matrix.

Thus,$R_0 = \frac{\vartheta \Lambda e}{k \mu \xi (\delta + \mu)}$, which represent the average number of new secondary cases generated by a single cholera infected individual during his/her entire infectious period in a completely susceptible population, in the absence of cholera intervention strategy.

Now let us express the effective reproduction number(R_c) in terms of the basic one (R_o) and compare their magnitude.

$$R_c = \frac{\vartheta e \Lambda}{k \xi (\mu + \nu)(\rho + \delta + \mu)} = \frac{\vartheta e \Lambda}{k \xi (\mu \rho + \mu \delta + \mu^2 + \nu \rho + \nu \delta + \nu \mu)}$$

$$= \frac{\vartheta e \Lambda}{k \xi \mu (\delta + \mu)} \left[\frac{1}{1 + \frac{(\mu \rho + \nu(\rho + \delta + \mu))}{\mu(\mu + \delta)}} \right] = R_o \left[\frac{\mu(\mu + \delta)}{\mu(\mu + \delta) + (\mu \rho + \nu(\rho + \delta + \mu))} \right]$$

Since all parameters are positive,$\mu(\mu + \delta) < \mu(\mu + \delta) + (\mu \rho + \nu(\rho + \delta + \mu))$ and thus,

$\frac{\mu(\mu+\delta)}{\mu(\mu+\delta)+(\mu\rho+\nu(\rho+\delta+\mu))} < 1$. From this, we can conclude that$R_C < R_0$. To verify this, we use the parameter values present in TABLE 1, the basic reproduction number R_O, of the dynamics without public health intervention strategy is

$$R_o = \frac{\vartheta e \Lambda}{k \xi \mu (\delta + \mu)} = \frac{0.8 \times 10 \times 0.559}{10^6 \times 0.33 \times 0.000022493 \times 0.015022493} = 40.11$$

Whereas the effective reproduction number $R_c$with two control strategiesis given as

$$R_c = \frac{\vartheta e \Lambda}{k \xi (\mu + \nu)(\rho + \delta + \mu)} = \frac{0.8 \times 10 \times 0.559}{10^6 \times 0.33 \times 0.200022493 \times 0.065022493} = 0.001$$

From the above results, the basic reproduction number tells us a single cholera infected individual can generate about40.11 new secondary infections in the community during his/her entire infection period in a completely susceptible population. The effective reproduction number tells us 0.001 new infections generated by a single infected individual in the community where vaccination and therapeutic treatment in quarantine are used as intervention strategies.Therefore, we can observe that $R_c <<< R_0$

IV. Numerical Simulation

We carried out numerical simulations to verify and support the impact of the model parameters on the reproduction number, which is seen in the analytical results by using set of model parameters whose values are taken from literature. The model parameter values and respective sources are present in TABLE 1.

$$R_c(\vartheta) = \vartheta \left(\frac{\Lambda e}{k\xi(\mu+v)(\rho+\delta+\mu)} \right) = \vartheta \frac{10x0.559}{4291.96} = \vartheta \frac{5.59}{4291.96} = \vartheta 0.0013$$
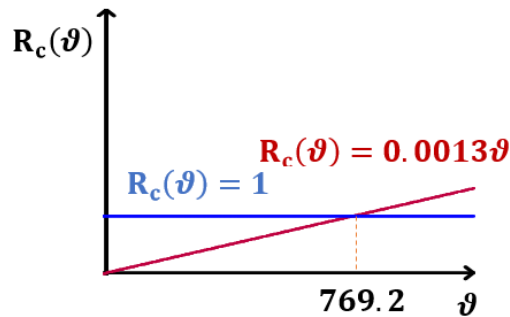
Figure 1: Effective reproduction number R_c versus ingestion rate ϑ with interventions

From fig. 1, Since two intervention strategies vaccination and treatment in quarantine are implemented simultaneously, the effective reproduction number to be greater than unity (disease to spread in the community) the ingestion rate must exceed a very much huge ingestion rate 769.2, If the ingestion rate is between 0 and 769.2, the effective reproduction number is less than unity. It also verifies that the ingestion rate ϑ has positive impact on the magnitude of effective reproduction number R_c.

$$R_c(\Lambda) = \Lambda \left(\frac{\vartheta e}{k\xi(\mu+v)(\rho+\delta+\mu)} \right) = \Lambda \frac{0.8x10}{4291.96} = \frac{8}{4291.96}\Lambda = 0.0019\Lambda$$
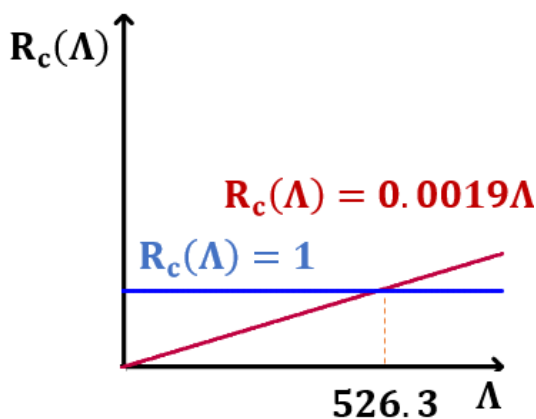

Figure 2: Effective reproduction number R_c versus recruitment rate Λ with interventions

From fig. 2, Since two intervention strategies vaccination and treatment in quarantine are implemented simultaneously, the effective reproduction number to be greater than unity the recruitment rate must exceed a very much huge recruitment rate 526.3, If the recruitment rate is between 0 and 526.3, the effective reproduction number is less than unity. It also support the analytical result that the recruitment rate Λ has positive impact on the effective reproduction number R_c.

$$R_c(e) = e \left(\frac{\vartheta\Lambda}{k\xi(\mu+v)(\rho+\delta+\mu)} \right) = e \frac{0.8 \times 0.559}{4291.96} = \frac{0.4472}{4291.96}e = 0.0001e$$
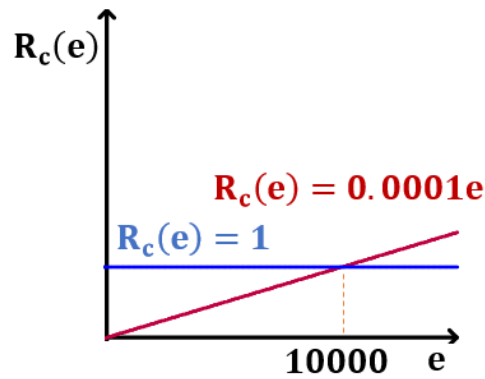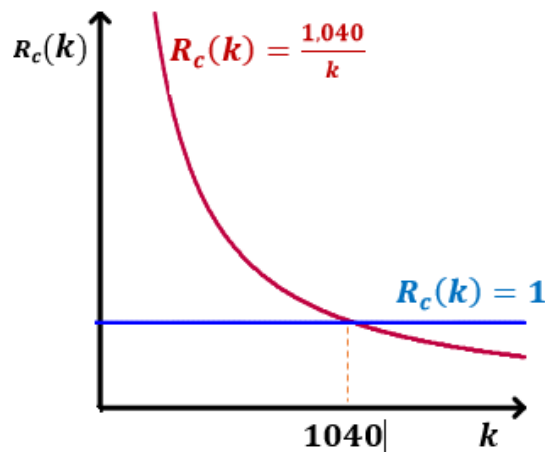
Figure 3: Effective reproduction number R_c versus shedding rate e with interventions

From fig. 3, Since two intervention strategies vaccination and treatment in quarantine are implemented simultaneously, the effective reproduction number to be greater than unity the shedding rate (contribution of each infected individual to the environment) must exceed the shedding rate 10,000. If the shedding rate is between 0 and 10,000, the effective reproduction number is less than unity. It also verifies that the shedding rate e has positive impact on the magnitude of effective reproduction number R_c.

$$R_c(k) = \frac{1}{k}\left(\frac{\vartheta \Lambda e}{\xi(\mu + v)(\rho + \delta + \mu)}\right) = \frac{1}{k}\left(\frac{4.472}{0.0043}\right) = \frac{1,040}{k}$$

Figure 4: Effective reproduction number R_c versus half saturation constant k with interventions

From fig. 4, Since two intervention strategies vaccination and treatment in quarantine are implemented simultaneously, the effective reproduction number to be less than unity the half saturation constant (number of bacteria causing 50% chance of catching cholera infection) must exceed 1040 amount of bacteria number. If the half saturation constant is between 0 and 1040, the effective reproduction number is greater than unity provided that the two control strategies are implemented. It also verifies that the half saturation constant k has negative impact on the magnitude of effective reproduction number R_c.

$$R_c(\xi) = \frac{1}{\xi}\left(\frac{\vartheta \Lambda e}{k(\mu + v)(\rho + \delta + \mu)}\right) = \frac{1}{\xi}\left(\frac{4.472}{13006}\right) = \frac{0.00034}{\xi}$$
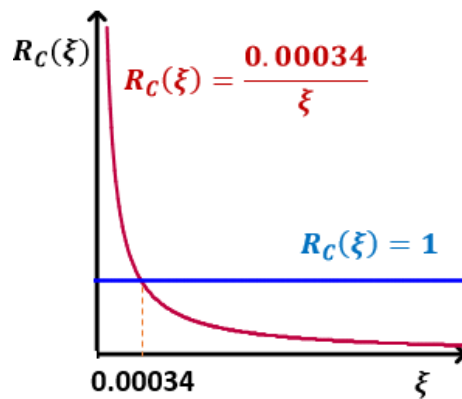
Figure 5: Effective reproduction number R_c versus bacteria net death rate ξ with interventions

From fig. 5, if the bacteria net death rate is greater than 0.00034, the effective reproduction number is less than unity and decreases (the disease dies out) but when the bacteria net death rate is between 0 and 0.00034, the effective reproduction number is greater than unity provided that the two control strategies are implemented. It also verifies that the bacteria net death rate has negative impact on the effective reproduction number.

$$R_c(\mu) = \frac{1}{(\mu + \nu)(\rho + \delta + \mu)}\left(\frac{\vartheta \Lambda e}{k\xi}\right) = \frac{1}{(\mu + \nu)(\rho + \delta + \mu)}\left(\frac{4.472}{10^6 \times 0.33}\right) = \frac{0.000014}{(\mu + 0.2)(0.065022493 + \mu)}$$

$$= \frac{0.000014}{\mu^2 + 0.265\mu + 0.013}$$

And $\frac{0.000014}{\mu^2 + 0.265\mu + 0.013} = 1$ implies that $\mu^2 + 0.265\mu + 0.0129 > 0$, for all $\mu > 0$
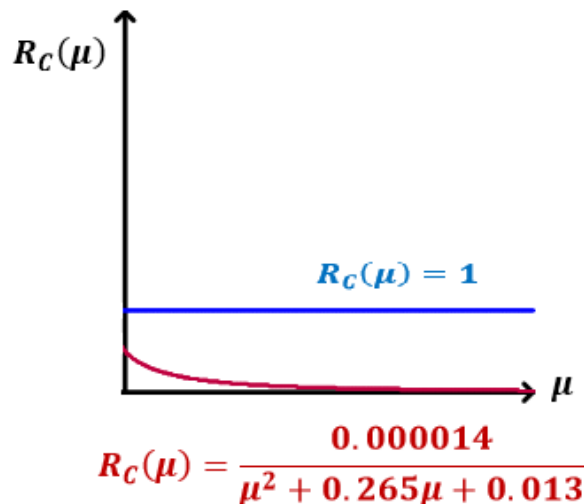

Figure 6: Effective reproduction number R_c versus human natural mortality rate μ.

From fig. 6, when the natural mortality rate increase, the effective reproduction number decreases and less than unity. This verifies that human natural mortality rate has negative impact on the effective reproduction number, but we cannot reduce the effective reproduction number by killing people as our objective is saving life.

$$R_c(\delta) = \frac{1}{(\rho + \delta + \mu)}\left(\frac{\vartheta \Lambda e}{k\xi(\mu + \nu)}\right) = \frac{1}{(\delta + 0.05 + 0.000022493)}\left(\frac{4.472}{330000 \times 0.200022493}\right)$$
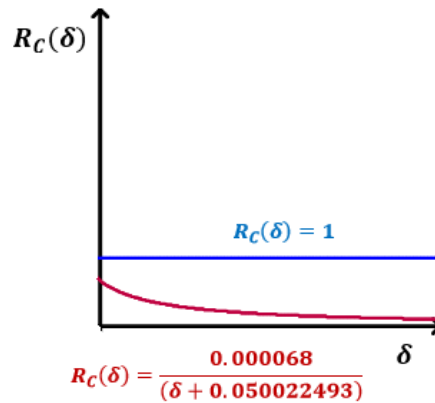
$$= \frac{0.000068}{(\delta + 0.050022493)}$$

Figure 7: Effective reproduction number R_c versus disease induced death rate rate δ.

From fig. 7, when the cholera induced death rate increase, the effective reproduction number decreases and less than unity. This verifies that cholera induced death rate has negative impact on the effective reproduction number, but we cannot control the disease by killing people as our objective is preventing people from dying of the disease and saving life.

$$R_c(\nu) = \frac{1}{\mu + \nu}\left(\frac{\vartheta \Lambda e}{k\xi(\rho + \delta + \mu)}\right) = \frac{1}{\mu + \nu}\left(\frac{4.472}{10^6 \times 0.33 \times 0.065022493}\right)$$

$$= \frac{1}{0.000022493 + \nu}\left(\frac{4.472}{0.33 \times 65022.493}\right) = \frac{0.00021}{\nu + 0.000022493}$$

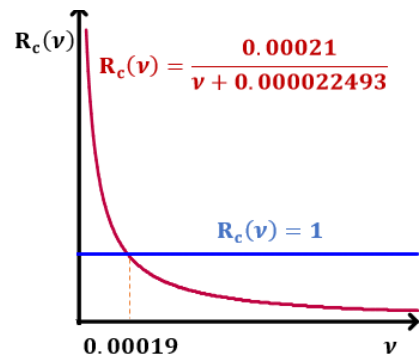$$\frac{0.00021}{\nu + 0.000022493} = 1 \quad \nu = 0.00019$$

Figure 8: Effective reproduction number R_c versus vaccination rate ν with constant treatment intervention in quarantine

From fig. 8, if vaccination rate is greater than 00019, the effective reproduction number is less than unity and decreases (the disease dies out) but when the vaccination is between 0 and 0.00019, the effective reproduction number is greater than unity provided that treatment in quarantine is implemented. It also verifies that vaccination has negative impact on the effective reproduction number

$$R_c(\nu) = \frac{1}{\mu + \nu}\left(\frac{\vartheta \Lambda e}{k\xi(\delta + \mu)}\right) = \frac{1}{\mu + \nu}\left(\frac{4.472}{10^6 \times 0.33 \times 0.015022493}\right)$$

$$= \frac{1}{0.000022493 + \nu}\left(\frac{4.472}{0.33 \times 15022.493}\right) = \frac{0.0009}{\nu + 0.000022493}$$
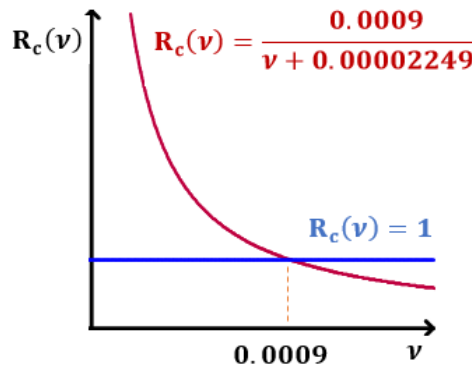
Figure 9: Effective reproduction number R_c versus vaccination rate v with no treatment in quarantine

From fig. 9, if vaccination rate is greater than 0009, the effective reproduction number is less than unity and decreases (the disease dies out) but when the vaccination is between 0 and 0.0009, the effective reproduction number is greater than unity(the disease persist) provided that treatment in quarantine is not implemented. Therefore, we can observe that $R_c(v)$ reduces faster (less effort on vaccination) to become less than unity in figure 8(with treatment in quarantine) than figure 9(with no treatment in quarantine). Which means if there is no treatment in quarantine, we need more additional vaccination. This shows that combined implementation of control strategies is more effective than single intervention to prevent and control the spread of cholera transmission.

$$R_c(\rho) = \frac{1}{(\rho + \delta + \mu)}\left(\frac{\vartheta \Lambda e}{k\xi(\mu + v)}\right) = \frac{1}{(\rho + \delta + \mu)}\left(\frac{4.472}{0.33x10^6 x0.200022493}\right)$$

$$= \frac{1}{(\rho + 0.015 + 0.000022493)}\left(\frac{4.472}{0.33x200022.493}\right) = \frac{1}{(\rho + 0.015022493)}\left(\frac{4.472}{66007.42}\right)$$
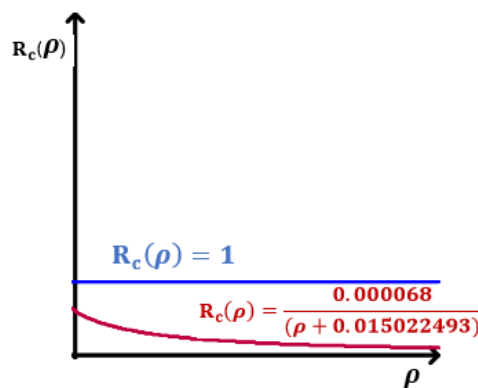
$$= \frac{0.000068}{(\rho + 0.015022493)}$$

Figure 10: Effective reproduction number R_c versus treatment in quarantine rate ρ with constant vaccination.

From fig.10, if treatment in quarantine with constant vaccination is implemented, the effective reproduction number never be above unity. This shows that combined implementation of control strategies will reduce the effective reproduction number and make the effective reproduction number to stay below unity. Thus, treatment in quarantine intervention strategy has negative impact on the magnitude of effective reproduction number.

$$R_c(\rho) = \frac{1}{(\rho + \delta + \mu)}\left(\frac{\vartheta \Lambda e}{k\xi\mu}\right) = \frac{1}{(\rho + \delta + \mu)}\left(\frac{4.472}{0.33 \times 10^6 \times 0.000022493}\right)$$

$$= \frac{1}{(\rho + 0.015022493)}\left(\frac{4.472}{0.33 \times 22.493}\right) = \frac{0.6}{(\rho + 0.015022493)}$$
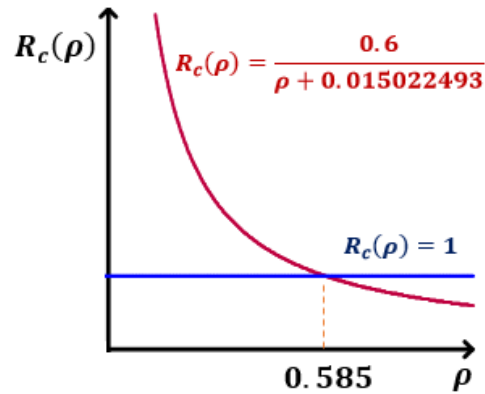
Figure 11: Effective reproduction number R_c versus treatment in quarantine rate ρ with no vaccination.

From fig. 11, if treatment in quarantine rate is greater than 0.585, the effective reproduction number is less than unity and decreases but when treatment in quarantine rate is between 0 and 0.585, the effective reproduction number is greater than unity provided that vaccination is not implemented. Therefore, we can observe that $R_c(\nu)$ reduces faster(less effort on vaccination) to become less than unity in figure 9(with no treatment in quarantine) than $R_c(\rho)$ to become less than unity in figure 11(with no vaccine). Which means vaccination control strategy is more preferable than treatment in quarantine to prevent and control the spread of cholera transmission. This shows that vaccination control parameter is the most influential parameter. Moreover, figure 11 supports that treatment in quarantine has negative impact on the magnitude of effective reproduction number. Above all, if there is no economic constrained, combined implementation of the two control strategies is advisable to prevent and control the spread of the disease.

V. Conclusion

Cholera, as atypical endemic disease around the world, brings huge physical psychological harm to human beings. Even though there are many potential prevention measures, it still causes a lot of damage in many countries specially developing countries [12]. In this paper, we proposed SIQR-B (Susceptible— Infectious-Quarantined-Recovered-Bacteria) type model by modifying the regular SIR-B cholera epidemiological model [28]. We tried to understand the effect of two control measures with one mode of transmission pathway (environment-to-human) of cholera, to gain useful strategies to the effective prevention and intervention strategies against cholera prevalence. We also incorporated no permanent immunity for the recovered group in order to assess the impact of vaccination, therapeutic treatment in quarantine on the transmission dynamics of cholera infection.

The basic reproduction number(R_0) and the effectivereproduction number(R_c) are determined. The disease free (E_{0c}) and endemic(E_C) equilibria are indicated to be locally and globally asymptotically stable for $R_c < 1$ and $R_c > 1$ respectively in the mathematical results. This shows that cholera disease dies out in the community, if the control strategies bring (R_c) less than unity and the disease persist in the community, if $R_c > 1$. We have shown that$R_c < R_0$, and $R_c = R_0$ if vaccination rate and treatment in quarantine rate are equal to zero($\nu = \rho = 0$). This mean that vaccination and therapeutic treatment in quarantine will reduce the basic reproduction number and thus they are important to control cholera epidemics. However, vaccination does not always work well due to the limitation of medical development and financial constrained (some vaccines are very expensive and some portion of population cannot afford) [5]. On the other hand, in the absence of these two intervention the spread of disease will be high.

By evaluating the sensitivity indices of the effective reproduction number with respect to model parameters,the influential parameters for the spread of the disease are identified and thus vaccination rate and treatment in quarantine rate are influential parameters. The most influential one is vaccination rate.From the values of sensitivity indices, an increase human recruitment, ingestion of bacteria, bacteria shedding may increase the magnitude of reproduction number. On the other hand, cholera related mortality, natural human mortality, medical treatment of cholera in quarantine and vaccination have negative influence on the magnitude of reproduction number. However, we cannot control cholera prevalence by disease and natural mortality, since our objective is preventing people from dying of the disease and save life. Therefore,We recommend primarily giving emphasis on preventionby expanding accessto improvedsources ofdrinking water, improved sanitation and hygiene, and working withcommunities to encourage behavioural change to avoid the risk of cholera infection.However, once the disease emerge in the community,implementing vaccination campaign is primarily advisable during the outbreak of cholera to prevent the spread of the disease. Since both control strategies vaccination and treatment in quarantine had negative impact on the spread of the disease,we

recommendcombined implementation of both public health intervention strategies. Thus, the stakeholders should design policies, planning, budgeting finance and resource allocations primarily focusing on prevention and then all possible public health interventions as much as possibleto combat against cholera transmission and prevalence.

This paper work consider only two mechanisms (vaccination and treatment in quarantine) of many public health preventive and intervention strategies like education campaign, sanitation and hygiene.The work also do not incorporate the climatic impacts on cholera epidemics (such as rainfall, flood, drought and water temperature). Combining human hosts and environment (Bacteria population) in the epidemiological model makes cholera dynamics different from most other disease dynamics and difficult to understand easily.There are two means of transmission of cholera, direct from human-to-human (fecal-oral) and indirect from environment-to-human. However, this researchfocusonly on indirect means. Therefore,other researchers may extend this research by including direct mode of transmission and additional public health intervention strategies.

Acknowledgment

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