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RESEARCH PAPER

Mathematical modeling for the transmission dynamics of cholera with an optimal control strategy

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Abstract

Cholera is an acute diarrheal disease caused by Vibrio cholera, its prevalence occurs in almost all the continents of the world, annually there are about 1.3 to 4.0 million cases of cholera and 21,000 to 143,000 deaths worldwide. In this paper, we propose a deterministic model for the transmission dynamics of cholera to assess the impact of vaccines in decreasing the spread of cholera infection in Nigeria. Moreover, we develop an optimal control strategy, in which we consider personal hygiene a control strategy on infection class, with $u(t)$ as the control function. The best values of the fitting parameters have been obtained using least square minimization to validate the model with the help of experimental data obtained from Nigeria. We perform sensitivity analysis to determine the key parameters that have impacts on the control of the spread of cholera infections in the population. In addition, the numerical simulation of the model reveals that the use of vaccines and personal hygiene will effectively control the spread of cholera infection.

Keywords: Basic reproduction number; treatment; model fitting; sensitivity analysis

AMS 2020 Classification: 34C23; 62P10; 92B05; 92D25

1 Introduction

Cholera is a short-term (acute) life-threatening disease caused by a bacterium called Vibrio cholera. The disease attracts the intestine and brings about diarrhea. Cholera exists in different serogroups, but only 01 and 0139 cause outbreaks [1]. Diarrhea is the main symptom of cholera and it is

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sometimes called acute diarrheal disease. The diarrhea is accompanied by severe dehydration and can lead to death within hours. The disease is asymptomatic between 12 hours to 5 days after its invasion into humans through ingesting contaminated food or water. However, infected individuals can still shed the bacterium (which can contaminate the environment) and can infect others [2]. People with low immunity "such as malnourished children or people living with HIV have a higher tendency to develop the infection [3].

Cholera is transmitted through ingestion of food or water contaminated with the Vibro cholera bacterium (which implies that unhygienic environments are more susceptible to cholera). The disease can also be transmitted directly through human-to-human contact such as shaking hands [4]. To avoid its transmission, proper sanitation of the environment is required to ensure clean water and food. In addition to ensuring proper hygiene, vaccination is used for the prevention of its prevalence [2]. The disease treatment is by quick replacement of the fluids and salt lost through diarrhea (Oral rehydration solution (ORS) is used) [2]. Recovered cholera patients acquired immunity that prevent them from being infected for many years [5].

Cholera prevalence occurs in almost all the continents of the world. It has been estimated that there are 1.3 to 4.0 million cases of cholera, and 21,000 to 143,000 deaths worldwide due to cholera annually [2]. Its pandemic started in 1961 in Indonesia, and it then spread into Europe, the South Pacific, and Japan at the end of 1970*s*. The prevalence reached South America in 1990*s*. Previously, there are many cholera outbreaks in India (2007), Congo, Zimbabwe and Iraq (2008), Zimbabwe and Vietnam (2009), Nigeria and Haiti (2010). In the year 2010 alone, it is estimated that 3–5 million people were infected with cholera which causes the death of 100,000–130,000 people worldwide [6]. In Nigeria, cholera is a recursive disease that occurs annually (during a rainy season). Its first epidemic occurred in 1970 and 1990 with high epidemics in 1992, 1995, 1996 and 1997. There were 37,289 cholera cases and the disease caused 1,434 deaths between January and October 2010 as reported by the Federal Ministry of Health. Furthermore, in 2011, 22,797 cases of cholera with 728 deaths were reported. Nigeria Centre for Disease Control (NCDC) reported 42,466 suspected cases with 830 deaths in 2018 [1]. The NCDC also reported in November 21, 2021 that Nigeria recorded 103,589 cholera infections and 3,566 deaths which is greater than the death caused by $covid-19$ (2977) in the same year [7].

Many mathematical models have been developed to study the transmission dynamic of cholera infection and come up with different measures, some of these are: the study by [8] shows that effective control of the epidemic can easily be achieved through vaccination, public health education, and treatment. Hove-Musekwa *et al.,* (2011) recommended that nutritional issues should be addressed in poor communities affected by cholera to reduce the burden of the disease. In order to avoid the cholera outbreak in China, Sun et al. (2017) stated that it might be better to increase the immunization coverage rate and make an effort to improve environmental management, especially for drinking water. Motivated by the aforementioned works, we developed a mathematical model of cholera infection with vaccination as a control measure.

2 Model description

We developed a mathematical model to study the spread of cholera in a human population at time $t > 0$, denoted by $N(t)$, and subdivided into four compartments: Susceptible individuals $S(t)$ (those who are healthy but can acquire the infection) with the infection rate λ; Vaccinated individuals $V(t)$ (those who take the vaccine) but some can acquire the infection at a slower rate $\sigma\lambda$; Infected individuals $I(t)$ (those who are infected with the disease) but can obtain immunity with recovery rate ϕ and Recovered individuals $R(t)$ (those who recovered from the disease). The susceptible individuals are vaccinated at a constant rate ω, while the vaccine wears off at a rate ψ. The population of the bacteria is denoted by $M(t)$ (the concentration of Vibrio Cholerae

(V.C) in contaminating the environment). We use ξ and θ to denote the rate of disinfection and the decay rate of V.C, respectively. We split the transmission rate into two parts. One is environment-to-human transmission rate β_1; and the other is human-to-human transmission rate β_2. The parameter k represents the concentration of the V.C in contaminating the environment which yields 50% chance of acquiring the cholera disease (half-saturation constant of the bacteria population). The force of infection denoted by λ (the rate at which the susceptible individuals acquire the infectious disease) is given by:

$$\lambda = \frac{\beta_1 M}{k + M} + \beta_2 I.$$

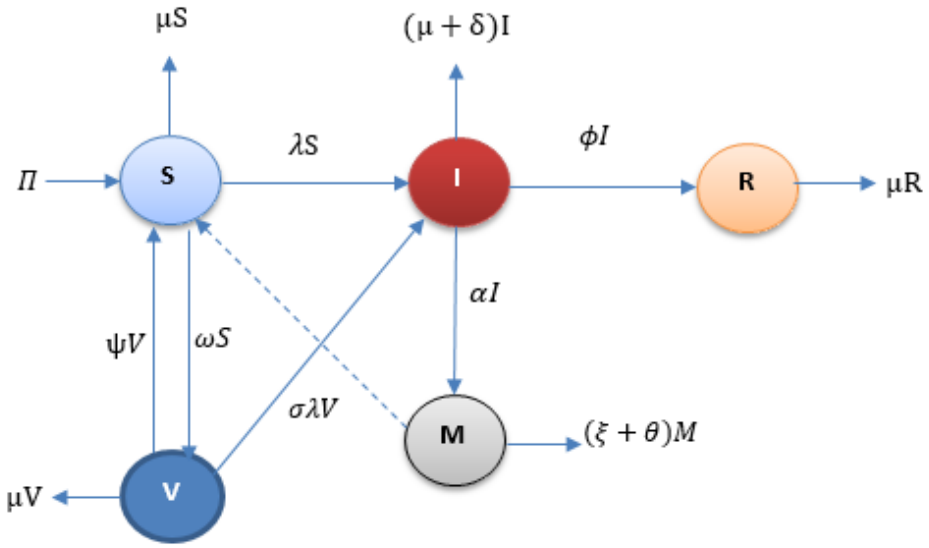


Figure 1. Schematic diagram of the model (1). Solid arrows indicate transitions and expressions next to arrows show the *per ca-pita* flow rate between compartments

According to the diagram above, the dynamics of cholera can be described by the following system of five differential equations.

$$\begin{aligned}
\frac{dS}{dt} &= \Pi - \lambda S - (\mu + \omega)S + \psi V, \\
\frac{dV}{dt} &= \omega S - (\mu + \psi)V - \sigma\lambda V, \\
\frac{dI}{dt} &= \lambda S - (\mu + \delta + \phi)I + \sigma\lambda V, \\
\frac{dR}{dt} &= \phi I - \mu R, \\
\frac{dM}{dt} &= \alpha I - (\xi + \theta)M.
\end{aligned} \tag{1}$$

Table 1. Interpretation of the state variables and parameters used in the model (1)

Variable	Description
N	Total human population
S	Susceptible individuals
I	Infected individuals
V	Vaccinated individuals
R	Recovered individuals
M	Concentration of V.C in contaminating the environment
Parameter	
Π	Recruitment rate
μ	Natural death rate
λ	Force of infection
β_1	Environment to human transmission rate
β_2	Human to human transmission rate
k	Concentration of V.C in the environment
σ	Parameter for decrease of infectiousness in V
δ	V.C induced death rate
ϕ	Recovery rate
α	Rate of human contribution to V.C
θ, ξ	Rate of disinfection in the environment and decay rate of V.C respectively
ω	Vaccination rate
ψ	Vaccine withdrawing period

3 Basic properties of the model

Boundedness and positivity of solutions

The model consists of the human population and bacteria population (V.C). As such the variables and parameters of the model are non-negative.

Theorem 1 *The solution of the model* (1) *within the invariant region are feasible for all* $t > 0$,

$$\Omega = \left\{ (S(t), I(t), V(t), R(t), M(t)) \in R_+^5 : N \leq \frac{\pi}{\mu}, M \leq \frac{\alpha}{(\xi + \theta)^2} \right\}.$$

Proof It suffices to show that the solution of the model (1) initiated in Ω does not leave the region i.e R_+^5 is positively invariant under the flow of system (1). [9, Theorem 2.1.5]. From the boundedness of Ω it follows that $S(0) > 0, I(0) > 0, V(0) > 0, R(0) > 0$, and $M(0) > 0$. Suppose $S(0)$ and $V(0)$ are not positive, then there exists a time $\tilde{t} > 0$, such that $S(t) > 0$ and $V(t) > 0$ for $t \in [0, \tilde{t})$, and $S(\tilde{t}) = V(\tilde{t}) = 0$. Now, consider the second, and the last part of model (1), we have

$$\begin{aligned} \frac{dI(t)}{dt} &\geq -(\mu + \delta + \Phi)I(t), \quad \text{for } t \in [0, \tilde{t}), \\ \frac{dM(t)}{dt} &\geq -(\xi + \theta)M(t), \quad \text{for } t \in [0, \tilde{t}), \end{aligned}$$

so that $I(0) > 0$, and $M(0) > 0$ for $t \in [0, \tilde{t})$. Now, from the first and the second part of the model (1), we have

$$\begin{aligned} \frac{dS(t)}{dt} &\geq -(\mu + \lambda + \omega)S(t), \quad \text{for } t \in [0, \tilde{t}), \\ \frac{dV(t)}{dt} &\geq -(\mu + \psi)V(t), \quad \text{for } t \in [0, \tilde{t}). \end{aligned}$$

Now, $S(0) > 0$, and $V(0) > 0$ which contradict our hypothesis $S(\tilde{t}) = V(\tilde{t}) = 0$. Therefore $S(t)$, and $V(t)$ are positive. To determine the positivity of the remaining variables we can write the remaining part of the model (1) excluding first and the second equation in matrix form as follows:

$$\frac{dY(t)}{dt} = \mathcal{Q}Y(t) + B(t), \tag{2}$$

with

$$\begin{aligned} Y(t) &= \begin{pmatrix} I & R & M \end{pmatrix}^T, \\ \mathcal{Q} &= \begin{pmatrix} -(\mu+\delta+\Phi) & 0 & 0 \\ \Phi & \mu & 0 \\ \alpha & 0 & -(\xi+\theta) \end{pmatrix}, \\ B(t) &= \begin{pmatrix} 0 & 0 & 0 \end{pmatrix}^T. \end{aligned} \tag{3}$$

The above matrix $\mathcal{Q}$ is called a Metzler matrix for the fact that $S(t)$ is non-negative. Thus, subsystem (2) is a monotone system [10]. Hence we can conclude that $\mathbb{R}^4_+$ is invariant under the flow of subsystem (2). Therefore, $\mathbb{R}^5_+$ is positively invariant under the flow of system (1).

Disease-free equilibrium

In the absence of the disease, the model system (1) has a disease-free equilibrium which is obtained by setting the right-hand side of the model equations to zero. Thus we have,

$$\epsilon^0 = (S^0, V^0, I^0, R^0, M^0) = \left(\frac{(\mu+\psi)\,\pi}{\mu\,(\mu+\omega+\psi)}, \frac{\omega\,\pi}{\mu\,(\mu+\omega+\psi)}, 0, 0, 0 \right).$$

Now, the total population at disease-free equilibrium $N(t)$ is,

$$N^0 \leq \frac{\pi}{\mu}.$$

Basic reproduction number

The next generation operator method described by [11], was used to determine the basic reproduction number denoted by $R_0 = \rho(FV^{-1})$. The matrices F for the new infection terms and V for the remaining transition terms are given by:

$$F = \begin{bmatrix} \frac{\Pi\beta_2(\mu+\psi)}{(\mu+\omega)(\mu+\psi)-\psi\,\omega} + \frac{\Pi\beta_2\omega}{(\mu+\omega)(\mu+\psi)-\psi\,\omega} & \frac{\Pi\beta_1(\mu+\psi)}{k((\mu+\omega)(\mu+\psi)-\psi\,\omega)} + \frac{\Pi\beta_1\sigma\,\omega}{k((\mu+\omega)(\mu+\psi)-\psi\,\omega)} \\ 0 & 0 \end{bmatrix}, \tag{4}$$

$$V = \begin{bmatrix} \mu+\delta+\psi & 0 \\ -\alpha & \xi+\theta \end{bmatrix}, \tag{5}$$

$$V^{-1} = \begin{bmatrix} \frac{1}{\mu+\delta+\phi} & 0 \\ \frac{\alpha}{(\mu+\delta+\phi)(\xi+\theta)} & \frac{1}{\xi+\theta} \end{bmatrix}, \tag{6}$$

$$FV^{-1} = \begin{bmatrix} \frac{\Pi\left((\beta_2(\xi+\theta)k+\alpha\beta_1)\mu+\beta_2\psi(\xi+\theta)k+\beta_1\alpha(\omega\sigma+\psi)\right)}{k\mu(\mu+\psi+\omega)(\mu+\delta+\phi)(\xi+\theta)} & \frac{\Pi\beta_1(\omega\sigma+\mu+\psi)}{k\mu(\mu+\psi+\omega)(\xi+\theta)} \\ 0 & 0 \end{bmatrix}. \tag{7}$$

We determine the basic reproduction number as follows:

$$R_0 = \frac{\Pi\left(\left(\beta_2(\xi+\theta)k+\alpha\beta_1\right)\mu+\beta_2\psi(\xi+\theta)k+\alpha\beta_1(\omega\sigma+\psi)\right)}{k\mu(\mu+\psi+\omega)(\mu+\delta+\phi)(\xi+\theta)}.$$

Using the proof from Theorem 2 of [11], if the reproduction number is less than one, the disease-free equilibrium point is locally stable and the population can not be invaded by the disease. Hence, the proof of the following theorem holds.

Theorem 2 *The disease-free equilibrium (DFE) T_0, of the model (1), is locally-asymptotically stable (LAS) in Ω if $R_0 < 1$, and unstable if $R_0 > 1$.*

Interpretation of the basic reproduction number

The threshold parameter (R_0) is interpreted as the number of secondary cases produced by a single cholera-infected individual in a completely susceptible population.

Global stability of disease-free equilibrium

Theorem 3 *The disease-free equilibrium (DFE) ϵ^0, of the model (1), is globally-asymptotically stable (GAS) in Ω if $R_0 < 1$, and unstable if $R_0 > 1$.*

Proof To show the GAS of DFE, the two condition $[F_1]$, and $[F_2]$ for $R_0 < 1$, need to be satisfied [12]. The system of (1) is re-write as.

$$\begin{aligned} \frac{dY_1}{dt} &= F_1(Y_1, Y_2), \\ \frac{dY_2}{dt} &= F_2(Y_1, Y_2) : F_2(Y_1, 0) = 0, \end{aligned} \tag{8}$$

where $Y_1 = (S^0, V^0, R^0)$, and $Y_2 = (I^0, M^0)$, with the elements of $Y_1 \in R^3_+$, representing the uninfected population and the elements of $Y_2 \in R^2_+$, representing the infected population.
The DFE is now denoted as, $\epsilon^0 = (Y_1^*, 0)$, where $Y_1^* = (N^0, 0)$.
Now for the first condition, that is GAS of Y_1^*, gives

$$\frac{dY_1}{dt} = F_1(Y_1, 0) = \begin{bmatrix} \pi - (\mu+\omega)S^0 + \psi V \\ \omega S - (\mu+\psi)V^0 \\ -\mu R \end{bmatrix}. \tag{9}$$

Solving the linear differential equations gives,

$$\begin{aligned} S^0(t) &= \frac{\pi+\psi V}{(\mu+\omega)} - \frac{\pi+\psi V}{(\mu+\omega)}e^{-(\mu+\omega)t} + S^0(0)e^{-(\mu+\omega)t}, \\ V^0(t) &= \frac{\omega S}{\mu+\psi} - \frac{\omega S}{\mu+\psi}e^{-(\mu+\psi)t} + V^0(0)e^{-(\mu+\psi)t}, \\ R^0(t) &= R(0)e^{-(\mu)t}. \end{aligned}$$

Now, it is easy to show that $S^0(t) + V^0(t) + R^0(t) \to N^0(t)$, as $t \to \infty$, regardless of the value of $S^0(t), V^0(t)$ and, $R^0(t)$. Thus, $Y_1^* = (N^0, 0)$ is globally asymptotically stable.
Furthermore, for the second condition, that is $\tilde{F}_2(Y_1, Y_2) = BY_2 - F_2(Y_1, Y_2)$, gives:

$$B = \begin{pmatrix} \beta_2 S - (\mu+\delta+\phi) + \sigma\beta_2 V & \frac{\beta_1 Sk}{(k+M)^2} + \frac{\sigma\beta_1 Vk}{(k+M)^2} \\ \alpha & -(\xi+\theta) \end{pmatrix}. \tag{10}$$

This is a Metziller matrix

$$F_2(Y_1, Y_2) = \begin{pmatrix} \lambda S - (\mu+\delta+\phi)I + \sigma\lambda V \\ \alpha I - (\xi+\theta)M \end{pmatrix}. \tag{11}$$

Then,

$$\tilde{F}_2(Y_1, Y_2) = BY_2 - F_2(Y_1, Y_2) = \begin{bmatrix} 0 \\ 0 \end{bmatrix}.$$

Thus, we have

$$\tilde{F}_2(Y_1, Y_2) = \begin{bmatrix} 0 & 0 \end{bmatrix}^T.$$

It is clear that $\tilde{F}_2(Y_1, Y_2) = 0$. Hence, the two conditions are satisfied, guaranteeing the global stability of the disease-free equilibrium.

Endemic equilibrium point

The conditions $I \neq 0$ and $M \neq 0$ imply that the cholera invades the population. As such, setting the vector field of (1) to zero, we obtain the equilibrium point at the endemic state as:

$$\epsilon^* = (S^*, V^*, I^*, R^*, S^*),$$

$$\begin{aligned} S^* &= \frac{\pi\ (\sigma\lambda+\mu+\psi)}{\sigma\lambda^2+\sigma\lambda\mu+\sigma\lambda\omega+\mu\lambda+\lambda\psi+\mu^2+\mu\omega+\mu\psi}, \\ V^* &= \frac{\pi\omega}{\sigma\lambda^2+\sigma\lambda\mu+\sigma\lambda\omega+\mu\lambda+\lambda\psi+\mu^2+\mu\omega+\mu\psi}, \\ I^* &= \frac{\lambda\pi\ (\sigma\lambda+\sigma\omega+\mu+\psi)}{(\mu+\delta+\phi)\ (\sigma\lambda^2+\sigma\lambda\mu+\sigma\lambda\omega+\mu\lambda+\lambda\psi+\mu^2+\mu\omega+\mu\psi)}, \\ R^* &= \frac{\phi\lambda\pi\ (\sigma\lambda+\sigma\omega+\mu+\psi)}{\mu\ (\mu+\delta+\phi)\ (\sigma\lambda^2+\sigma\lambda\mu+\sigma\lambda\omega+\mu\lambda+\lambda\psi+\mu^2+\mu\omega+\mu\psi)}, \end{aligned} \tag{12}$$

$$M^* = \frac{\alpha\,\lambda\,\pi\,(\sigma\,\lambda + \sigma\,\omega + \mu + \psi)}{(\xi+\theta)\,(\mu+\delta+\phi)\,(\sigma\,\lambda^2 + \sigma\,\lambda\,\mu + \sigma\,\lambda\,\omega + \mu\,\lambda + \lambda\,\psi + \mu^2 + \mu\,\omega + \mu\,\psi)}.$$

Existence of the endemic equilibrium

To determine the existence of the endemic equilibrium, Descartes's rule of sign is used. Now the force of infection at the endemic state is given by,

$$\lambda^* = \frac{\beta_1 M^*}{k + M^*} + \beta_2 I^*.$$

Substituting the endemic equilibrium points into the above force of infection gives $\lambda^* = 0$, and the polynomial of order four is obtained in the form of λ^*

$$A{\lambda^*}^4 + B{\lambda^*}^3 + C{\lambda^*}^2 + D\lambda^* + E = 0,$$

where

$$\begin{aligned}
A &= k(\xi+\theta)(\mu+\delta+\phi)^2\sigma^2 + \Pi\alpha(\mu+\delta+\phi)\sigma^2,\\
B &= 2k(\xi+\theta)(\mu+\delta+\psi)^2(\sigma\mu+\mu^2+\mu\omega+\mu\phi)\sigma + \Pi\alpha\sigma(\mu+\delta+\phi)(\sigma\mu+2\sigma\omega+2\mu+2\psi)\\
&\quad - \Pi\alpha\beta_1\sigma^2(\mu+\delta+\phi) - \Pi\beta_2\alpha k(\xi+\theta)(\mu+\delta+\phi)\sigma^2 - \Pi^2\beta_2\alpha\sigma^2,\\
C &= k(\xi+\theta)(\mu+\delta+\phi)[2\sigma(\mu^2+\mu\omega+\mu\psi) + (\sigma\mu+\sigma\omega+\mu+\psi)^2] + \Pi\alpha(\mu+\delta+\phi)[\sigma(\mu^2+\mu\omega+\mu\psi)\\
&\quad + (\sigma\omega+\mu+\psi)(\sigma\mu+\sigma\omega+\mu+\psi)] - \Pi\alpha\beta_1(\mu+\delta+\phi)(\sigma\mu+2\sigma\omega+2\mu+2\psi)\sigma\\
&\quad - \Pi\beta_2 k(\xi+\theta)(\mu+\delta+\phi)(\sigma\mu+2\sigma\omega+2\mu+2\psi)\sigma - 2\Pi^2\alpha\beta_2(\sigma\omega+\mu+\psi)\sigma,\\
D &= 2k(\xi+\theta)(\mu+\delta+\phi)^2(\sigma\mu+\sigma\omega+\mu+\psi)(\mu^2+\mu\omega+\mu\psi) + \Pi\alpha\beta_1(\mu+\delta+\phi)[(\mu^2+\mu\omega+\mu\psi)\sigma\\
&\quad + (\sigma\omega+\mu+\psi)(\sigma\mu+\sigma\omega+\mu+\psi)] - \Pi\beta_2 k(\xi+\theta)(\mu+\delta+\phi)[(\mu^2+\mu\omega+\mu\psi)\sigma\\
&\quad + (\sigma\omega+\mu+\psi)(\sigma\mu+\sigma\omega+\mu+\psi)] - \Pi^2\alpha\beta_2(\sigma\omega+\mu+\phi)^2,\\
E &= k(\xi+\theta)(\mu+\delta+\phi)^2(\mu^2+\mu\omega+\mu\psi)^2[1-R_0].
\end{aligned} \tag{13}$$

Global stability of endemic equilibrium

Theorem 4 *If $R_0 > 1$, the endemic equilibrium ϵ^* is globally asymptotically stable.*

Proof We construct a Lyapunov function

$$\begin{aligned}
F = &\left(S - S^* - S^* ln\left(\frac{S}{S^*}\right)\right) + \left(V - V^* - V^* ln\left(\frac{V}{V^*}\right)\right) + \left(I - I^* - I^* ln\left(\frac{I}{I^*}\right)\right)\\
&+ \left(R - R^* - R^* ln\left(\frac{R}{R^*}\right)\right) + \left(M - M^* - M^* ln\left(\frac{M}{M^*}\right)\right).
\end{aligned} \tag{14}$$

The derivative of along the solution of model Eq. (1) is:

$$\begin{aligned}
F' = &\Pi - \lambda S - (\mu+\omega)S - \frac{S^*}{S}(\Pi - \lambda S - (\mu+\omega)S) + \omega S - \sigma\lambda V - \mu V - \frac{V^*}{V}(\omega S - \sigma\lambda V - \mu V)\\
&+ \lambda S - (\mu+\phi)I + \sigma\lambda V - \frac{I^*}{I}(\lambda S - (\mu+\phi)I + \sigma\lambda V) + \phi I - \mu R - \frac{R^*}{R}(\phi I - \mu R)\\
&+ \alpha I - (\xi+\theta)M - \frac{M^*}{M}(\alpha I - (\xi+\theta)M).
\end{aligned}$$

At steady state:

$$\begin{aligned}\Pi &= \lambda S^* + (\mu+\omega)S^*,\\ (\mu+\phi)I^* &= \lambda S^* + \sigma\lambda V^*,\\ \omega S^* &= (\mu+\psi)V^* + \sigma\lambda V^*,\\ \phi I^* &= \mu R^*,\\ \alpha I^* &= (\xi+\theta)M^*.\end{aligned}$$

Using the above relation we have:

$$\begin{aligned}F' \leqslant (\mu+\omega)S^*\left(2-\frac{S}{S^*}-\frac{S^*}{S}\right)+\lambda S^*\left(3-\frac{S^*}{S}-\frac{I}{I^*}-\frac{I^*}{I}\right)+\mu V^*\left(2-\frac{V}{V^*}-\frac{V^*}{V}\right)\\ +\sigma\lambda V^*\left(3-\frac{I}{I^*}-\frac{I^*}{I}-\frac{V^*}{V}\right)+\mu R^*\left(2-\frac{R}{R^*}-\frac{R^*}{R}\right)+M^*(\xi+\theta)\left(2-\frac{M}{M^*}-\frac{M^*}{M}\right).\end{aligned}$$

Since the arithmetic mean is greater than the geometric mean we have:

$$\begin{gathered}\left(2-\frac{S}{S^*}-\frac{S^*}{S}\right)\leqslant 0,\left(3-\frac{S^*}{S}-\frac{I}{I^*}-\frac{I^*}{I}\right)\leqslant 0,\left(2-\frac{V}{V^*}-\frac{V^*}{V}\right)\leqslant 0,\\ \left(3-\frac{I}{I^*}-\frac{I^*}{I}-\frac{V^*}{V}\right)\leqslant 0,\left(2-\frac{R}{R^*}-\frac{R^*}{R}\right)\leqslant 0,\left(2-\frac{M}{M^*}-\frac{M^*}{M}\right)\leqslant 0,\end{gathered}$$

thus, we have that $F' \leqslant 0$ for $R_0 > 1$, since the relevant variables in the equations for $S(t)^*, V(t)^*, I(t)^*, R(t)^*, M(t)^*$ are at endemic steady state, it follows that these can be substituted into the equations for $S(t), V(t), I(t), R(t)$ and $M(t)$. Therefore, the result follows by applying the LaSalle's invariance principle [13]. Hence the endemic equilibrium (EE) ϵ^* of model (1) is globally asymptotically stable (GAS).

4 Designing the optimal control problem

Optimal control involves the determination of a piece-wise control variable $u(t)$, and the associated state variables $x(t)$, that minimize the number of infectious individuals and the cost of controlling the infection. In this paper, we use personal hygiene as a control strategy on the basic model of cholera transmission which symbolizes $u(t)$. Moreover, the controlled system is as follows:

$$\begin{aligned}\frac{dS}{dt} &= \Pi - u(t)\lambda S - (\mu+\omega)S + \psi V,\\ \frac{dV}{dt} &= \omega S - (\mu+\psi)V - u(t)\sigma\lambda V,\\ \frac{dI}{dt} &= u(t)\lambda S - (\mu+\delta+\phi)I + u(t)\sigma\lambda V,\\ \frac{dR}{dt} &= \phi I - \mu R,\\ \frac{dM}{dt} &= \alpha I - (\xi+\theta),\end{aligned} \tag{15}$$

with $S(0) = S_0, V(0) = V_0, I(0) = I_0, R(0) = R_0, M(0) = M_0$.
The single-objective function called the cost functional $J[x(t), u(t)]$ to be minimized for our

problem is given by:

$$J[x(t), u(t) = \int_0^{t_f} \left(aI + \frac{1}{2} wu^2 \right) \mathrm{d}t, \tag{16}$$

where $a > 0$, $w > 0$, and the terms aI and $\frac{1}{2}wu^2$ represent the cost of infection and the cost of personal hygiene, respectively. The condition associated with the cost is nonlinear, and therefore we perceive the cost expression to be quadratic $(\frac{1}{2}w_i u_i^2)$. $u(t)$ is a piece-wise continuous in the set of admissible control $U = \{(u(t)) : 0 \leq u(t) \leq 1\}$. The aim is to determine the optimal control u^* such that

$$J(u^*) = \min_{(u(t)) \in U} J(u(t)).$$

Thus, we show that an optimal control u^* for system (15) exists. Also, we are to highlight that the system (15) is bounded for finite time [14]. We extend to find the upper bound solutions (super solutions) of S, V, I, R and M in model (15). Now, we consider the first equation of (15).

Existence of an optimal control on the system

We can prove the existence of optimal control by using the method used by [15]. For more details, see [[16], Theorem 6, pp. 6].
Let S_{max}, be the super solution associated with S. Given that $S(t) \geq 0$, and $V(t) \geq 0$ as proved in Theorem 1, then

$$\frac{dS_{max}}{dt} = \Pi + \psi V.$$

Similarly, Let V_{max}, I_{max}, R_{max}, and M_{max} be the super solution associated with V, I, R, and M respectively in (15). Given that $I(t) \geq 0$, $R(t) \geq 0$, and $I(t) \geq 0$ then,

$$\begin{aligned}
\frac{dV_{max}}{dt} &= \omega S, \\
\frac{dI_{max}}{dt} &= \lambda S + \sigma \lambda V, \\
\frac{dR_{max}}{dt} &= \phi I, \\
\frac{dM_{max}}{dt} &= \alpha S.
\end{aligned}$$

We can formulate a set of super solutions for system (15), by using the bounds. Denoting these super solutions by $\overline{S}, \overline{V}, \overline{I}, \overline{R}$, and $\overline{M}$ such as:

$$\begin{bmatrix} \frac{d\overline{S}}{dt} \\ \frac{d\overline{V}}{dt} \\ \frac{d\overline{I}}{dt} \\ \frac{d\overline{R}}{dt} \\ \frac{d\overline{M}}{dt} \end{bmatrix} = \begin{pmatrix} 0 & \psi & 0 & 0 & 0 \\ \omega & 0 & 0 & 0 & 0 \\ \lambda_{max} & \sigma\lambda_{max} & 0 & 0 & 0 \\ 0 & 0 & \psi & 0 & 0 \\ 0 & 0 & \alpha & 0 & 0 \end{pmatrix} \begin{pmatrix} \overline{S} \\ \overline{V} \\ \overline{I} \\ \overline{R} \\ \overline{M} \end{pmatrix} + \begin{pmatrix} \pi \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}. \tag{17}$$

It shows that this is a linear system in finite time with bounded coefficients, hence, the super-

solutions $\overline{S}, \overline{V}, \overline{I}, \overline{R}$, and $\overline{M}$ are uniformly bounded. Likewise, our original system is ultimately bounded. It shows that an optimal control exists.

Hamiltonian and optimality of the system

We used Pontryagin's Maximum Principle, which provides the necessary and sufficient conditions for optimality, to prove the optimality of the system. To obtain that, we need to write in detail, the Hamiltonian. The Hamiltonian (H) is generally symbolized as:

$$H = L + \lambda_1 \frac{dS}{dt} + \lambda_2 \frac{dV}{dt} + \lambda_3 \frac{dI}{dt} + \lambda_4 \frac{dR}{dt} + \lambda_5 \frac{dM}{dt}, \tag{18}$$

where L is the Lagrangian, obtained from the objective function. The Hamiltonian associated with the system under study is given by:

$$\begin{aligned} H =& aI + \frac{1}{2} w u^2 + \lambda_1 \left(\Pi - u(t)\lambda S - (\mu + \omega)S + \psi V\right) + \lambda_2 \left(\omega S - (\mu + \psi)V - u(t)\sigma\lambda V\right) \\ &+ \lambda_3 \left(u(t)\lambda S - (\mu + \delta + \phi)I + u(t)\sigma\lambda V\right) + \lambda_4 \left(\phi I - \mu R\right) + \lambda_5 \left(\alpha I - (\xi + \theta)\right), \end{aligned} \tag{19}$$

where $\lambda_1, \lambda_2, \lambda_3, \lambda_4$, and λ_5 are called the adjoint variables to be determined. We now state the following theorem.

Theorem 5 *Given the optimal control set $u(t)$ together with the corresponding solution, S, V, I, R, and M which minimize $J(u(t))$ over U, then there exist adjoint variables $\lambda_1, \lambda_2, \lambda_3, \lambda_4$, and λ_5 such that*

$$\begin{aligned} \frac{d\lambda_1}{dt} &= \lambda_1 \left(u(t)\lambda + \mu + \omega\right) - \lambda_2\omega - \lambda_3 u(t)\lambda, \\ \frac{d\lambda_2}{dt} &= -\lambda_1\psi + \lambda_2(\mu + \psi + u(t)\sigma\lambda) - \lambda_3 u(t)\sigma\lambda, \\ \frac{d\lambda_3}{dt} &= -a + u(t)\beta_2[\lambda_1 S + \lambda_2\sigma V - \lambda_3(S + \sigma V)] + (\mu + \sigma + \phi)\lambda_3 - \phi\lambda_4 - \alpha\lambda_5, \\ \frac{d\lambda_4}{dt} &= \mu\lambda_4, \\ \frac{d\lambda_5}{dt} &= -\frac{\beta_1 k}{(k + M)^2}[S\lambda_1 + u(t)\sigma\lambda_2 V - (S + \sigma V)u(t)\lambda_3] + (\xi + \theta)\lambda_5, \end{aligned} \tag{20}$$

with transversality conditions $\lambda_i(t_f) = 0, i = 1, ..., 5$. Moreover,

$$u^* = \min\left(\max\left(\frac{\lambda[\lambda_1 S + \lambda_2\sigma V - \lambda_3(S + \sigma V)]}{w}, 0\right), 1\right). \tag{21}$$

Proof As stated above, we applied the Pontraygin's Maximum Principle to determine the adjoint variables and the representations of the control functions Since the control functions exist. For the adjoint variables we proceed as follows:

$$\begin{aligned} \frac{d\lambda_1}{dt} &= -\frac{\partial H}{\partial S} = -[\lambda_1(-u(t)\lambda - (\mu + \omega)) + \lambda_2\omega + \lambda_3 u(t)\lambda] = \lambda_1\left(u(t)\lambda + \mu + \omega\right) - \lambda_2\omega - \lambda_3 u(t)\lambda, \\ \frac{d\lambda_2}{dt} &= -\frac{\partial H}{\partial V} = -[-\lambda\psi - \lambda_2(\mu + \psi + u(t)\sigma\lambda) + \lambda_3 u(t)\sigma\lambda] \\ &= -\lambda_1\psi + \lambda_2(\mu + \psi + u(t)\sigma\lambda) - \lambda_3 u(t)\sigma\lambda, \end{aligned}$$

$$\begin{aligned}
\frac{d\lambda_3}{dt} &= -\frac{\partial H}{\partial I} = -a + u(t)\beta_2[\lambda_1 S + \lambda_2\sigma V - \lambda_3(S+\sigma V)] + (\mu+\sigma+\phi)\lambda_3 - \phi\lambda_4 - \alpha\lambda_5,\\
\frac{d\lambda_4}{dt} &= -\frac{\partial H}{\partial R} = -(-\mu\lambda_4) = \mu\lambda_4,\\
\frac{d\lambda_5}{dt} &= -\frac{\partial H}{\partial M} = -\left(-\frac{\lambda_1\beta_1 Sk}{(k+M)^2} - \frac{\lambda_2\beta_1\sigma u(t)Vk}{(k+M)^2} + \frac{\lambda_3\beta_1 u(t)Sk}{(k+M)^2} + \frac{\lambda_3\beta_1\sigma u(t)Vk}{(k+M)^2} - (\xi+\theta)\lambda_5\right)\\
&= -\frac{\beta_1 k}{(k+M)^2}[S\lambda_1 + u(t)\sigma\lambda_2 V - (S+\sigma V)u(t)\lambda_3] + (\xi+\theta)\lambda_5.
\end{aligned} \tag{22}$$

The illustrations of the controls is given by:

$$\frac{\partial H}{\partial u(t)} = 0,$$

at $u(t) = u(t)^*$. Thus, the standard optimality argument is:

$$u(t)^* = \min\left(\max\left(\frac{\lambda[\lambda_1 S + \lambda_2\sigma V - \lambda_3(S+\sigma V)]}{w}, 0\right), 1\right). \tag{23}$$

Based on the results of the above Theorem 5, which imply that after obtaining the terms for the control function u^*, as well as the adjoint equations with their transversality conditions. We suggest the optimal control terms for minimizing the spread of cholera transmission.

5 Model fitting and parameter estimation

This section is devoted to fitting some unavailable biological parameters of the proposed five-dimensional epidemic model for cholera disease. It also assists one to have built confidence in the model proposed, for the validation comes along. Such vital analyses are possible only when some authentic information for the real experimental data for the disease under investigation is available. When the data set for the actual infected cases is arranged, there comes the question of a method that could be chosen for validation of the model with the help of an experimental data set. It may be noted that several methods exist in the present literature for the fitting of a nonlinear system of ordinary differential equations to the experimental results, we resort to least-squares minimization. Under this method, the best values of the fitting parameters can be obtained, including respective standard errors, statistical estimators (like the t-statistic and p-value), and confidence intervals.

The available parameters of the model (1) are shown in Table 2 wherein their units and the sources where-from they are taken are also mentioned. The two most important parameters β_1, and β_2 are fitted with their best estimates as shown in Table 3 that accompanies some statistical estimators as well. The p-values are < 0.05 with 95% confidence intervals for both estimated parameters, including reasonably small standard error with acceptable t-statistic.

Moreover, the descriptive statistical measures for both real and predicted cases are shown in Table 4 where minimum, three quartiles, mean, maximum and standard deviation can be observed. Each value from the real cases is found to have good agreement with what is obtained via simulations for the I compartment including the smaller standard deviation in the predicted cases. It may also be noted the interquartile range (IQR) for both cases is identical to be 5.7750×10^2, thereby containing middle 50% of the data. Figure 2 further confirms the better agreement of the predicted cholera cases with the real cases of the disease having R-squared (coefficient of determination) value to be about 0.9376, including some residuals which are uniformly distributed as shown in

multiple types of residuals in Figure 3. Some outliers are observed in the cholera cases (real and predicted) as shown by the box and whisker plot in Figure 4.

Table 2. Baseline values, units, and references for parameters of model (1)

Parameter	Baseline	Units	Sources
N	20616716	Persons	[17]
μ	$1/(11.4 \times 52)$	week^{-1}	[18]
Π	$36.855 \times \mu$	week^{-1}	[17]
k	1	$Cells.mL^{-1}$	[18]
σ	0.127	week^{-1}	[17]
δ	0.47	week^{-1}	[17]
ϕ	1.4	week^{-1}	[18]
α	2000	$Cells.mL^{-1}$.week^{-1}	[18]
θ	0.07	week^{-1}	[18]
ξ	0.2331	week^{-1}	[18]
ω	0.149	week^{-1}	[8]
ψ	0.021	week^{-1}	[8]

Table 3. The best fit parameters of the model (1) with the respective statistical estimators

	Estimate	Standard Error	t-Statistic	P-Value	Confidence Interval
β_1	4.3208×10^{-5}	1.2003×10^{-5}	3.5998	2.0480×10^{-3}	$(1.7991 \times 10^{-5}, 6.8425 \times 10^{-5})$
β_2	7.0320×10^{-8}	6.6760×10^{-9}	1.0533×10^{1}	3.9918×10^{-9}	$(5.6294 \times 10^{-8}, 8.4345 \times 10^{-8})$

Table 4. The descriptive statistical summary for both real experimental data and the simulations predicted from model (1) for I compartment

	Min	Q1	Q2	Q3	Mean	Max	SD
Real	4.600×10^{1}	7.800×10^{1}	2.540×10^{2}	6.330×10^{2}	5.535×10^{2}	2.127×10^{3}	6.406×10^{2}
Predicted	1.554×10^{2}	1.821×10^{2}	2.661×10^{2}	6.145×10^{2}	5.783×10^{2}	2.127×10^{3}	6.077×10^{2}

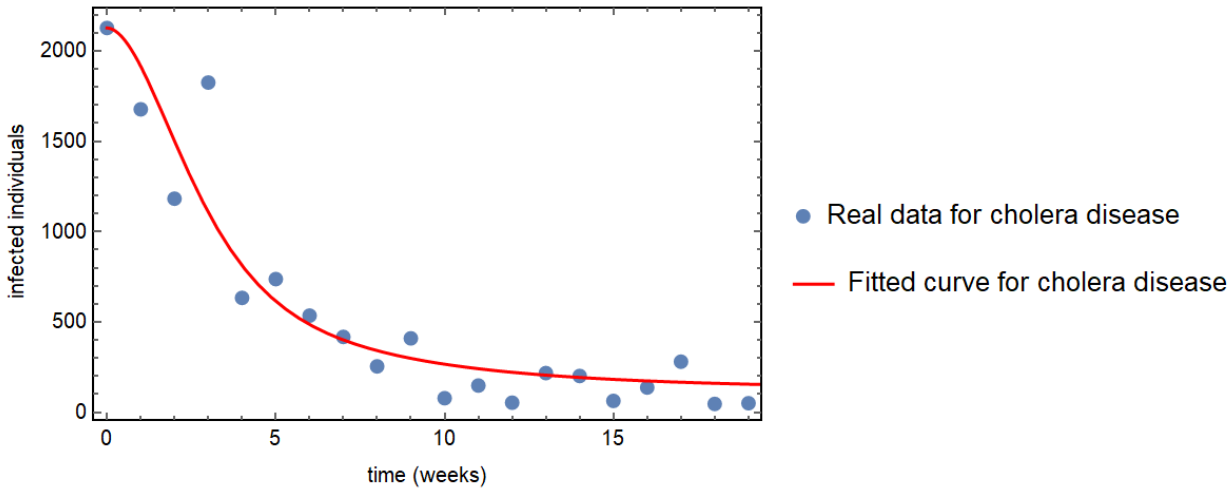


Figure 2. The best curve fitting for the real cases of the infected individuals from the proposed cholera model (1)

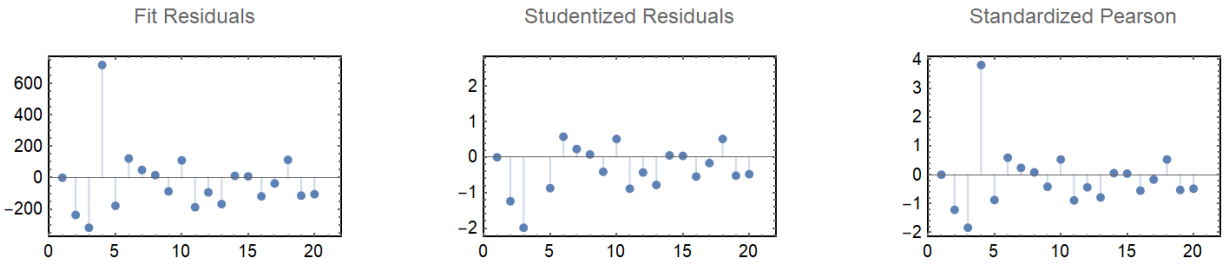


Figure 3. The residuals for the real cases of the infected individuals from the proposed cholera model (1)

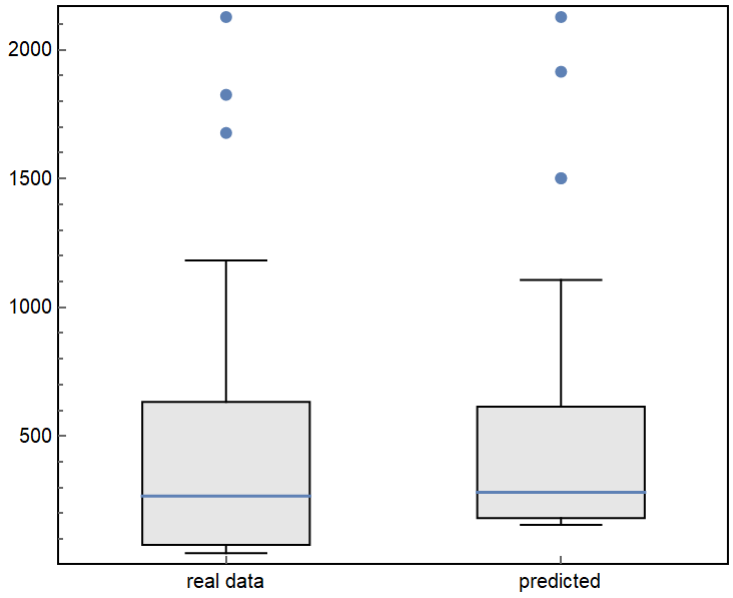


Figure 4. The comparison between real and predicted symptomatically infected individuals via BoxWhisker plot

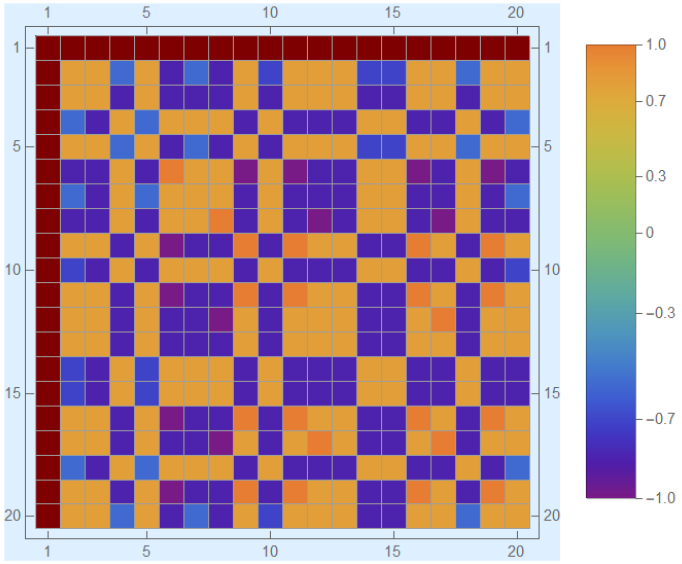


Figure 5. Contour plots of the basic reproduction number in terms of parameter values

6 Sensitivity analysis

In this section, the proposed cholera model associated with the basic reproduction number R_0 with respect to the biological parameters of the model is analyzed using the forward sensitivity index. This method is applied to determine the most sensitive parameters of the model, parameters with positive signs are considered the most sensitive for increasing the value of R_0 while those with negative signs are sensitive to the decrease of R_0 [15, 19]. We determine the sensitivity status of each parameter and their impacts on the control of the spread of cholera infections in the population to obtain the optimal result [20, 21]. The normalized local sensitivity index of R_0 with respect to ξ is denoted by $\chi_{\xi}^{R_0}$ which is written as

$$\chi_{\xi}^{R_0} = \frac{\xi}{R_0} \times \frac{\partial R_0}{\partial \xi}, \tag{24}$$

Table 5 shows the indices for R_0 with respect to parameters.

Table 5. Forward normalized sensitivity indices

Parameter	Elasticity Indices	Values of the Elasticity index
β_1	$\chi_{\beta_1}^{R_0}$	1.0000
k	$\chi_{k}^{R_0}$	-1.0000
ω	$\chi_{\omega}^{R_0}$	-0.4132
α	$\chi_{\alpha}^{R_0}$	1.0000
ξ	$\chi_{\xi}^{R_0}$	-0.7691
ϕ	$\chi_{\phi}^{R_0}$	-0.7480
θ	$\chi_{\theta}^{R_0}$	-0.2310
δ	$\chi_{\delta}^{R_0}$	-0.2511
ψ	$\chi_{\beta_2}^{R_0}$	0.3822
σ	$\chi_{\sigma}^{R_0}$	0.4546

7 Numerical scenarios

This is the section in which the behavior of the model is examined. The transmission dynamics of the governing model may be effectively explored using numerical simulations with the aid of state variables of interest. The numerical simulations are used to understand the behavior of the model under investigation. The parameters generated by the nonlinear minimum-squares fitting technique are used in the immediate section to determine different types of time series graphs. $S[0] = 20614589, I[0] = 2127, V[0] = 0, R[0] = 0, M[0] = 0$.

8 Discussion and conclusions

This research describes a deterministic model for the transmission dynamics of cholera infection incorporating vaccine and personal hygiene as strategies for controlling its spread. Analysis of the model shows that the disease-free equilibrium is locally and globally asymptotically stable when $R_0 < 1$, and unstable when $R_0 > 1$. Lyapunov function method is used in verifying the stability of the endemic equilibrium point which is found to be globally asymptotically stable when $R_0 > 1$, and unstable when $R_0 < 1$. The numerical simulations have been carried out using the data published by the Nigeria Centre for Disease Control [17]. A detailed explanation of the

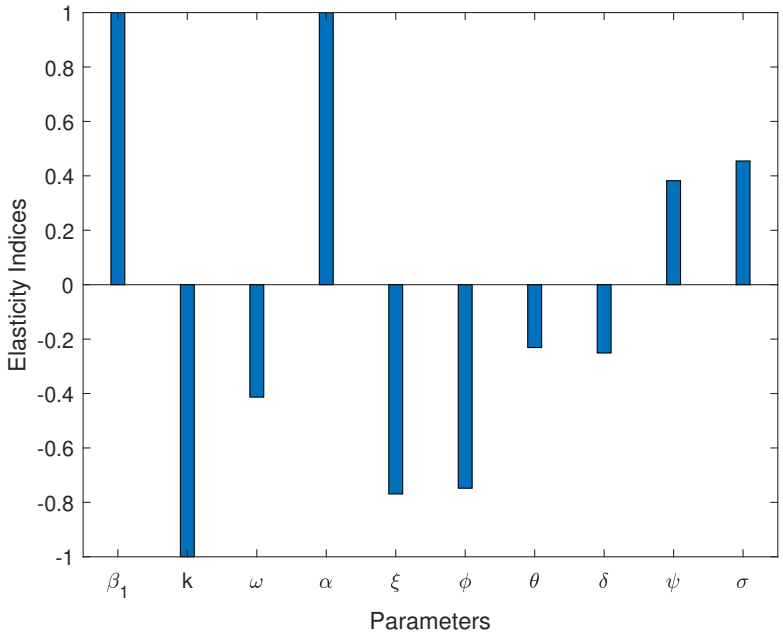
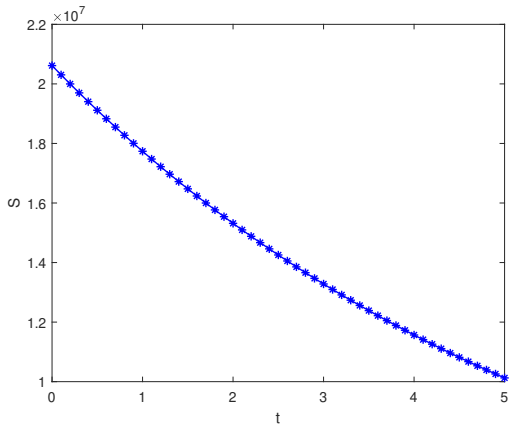
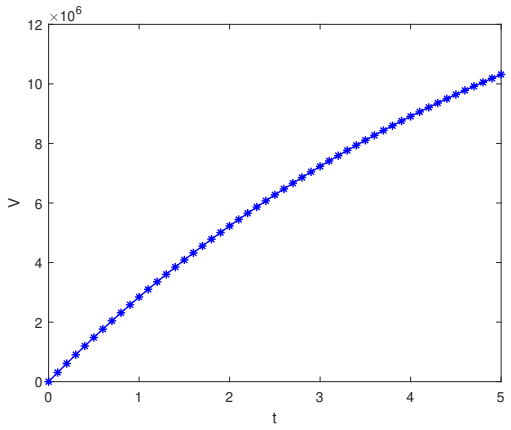


Figure 6. Elasticity indices versus parameters

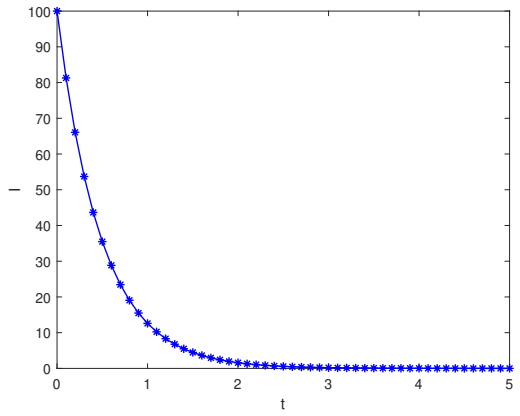


(a) Behavior of the state variable susceptible individual S

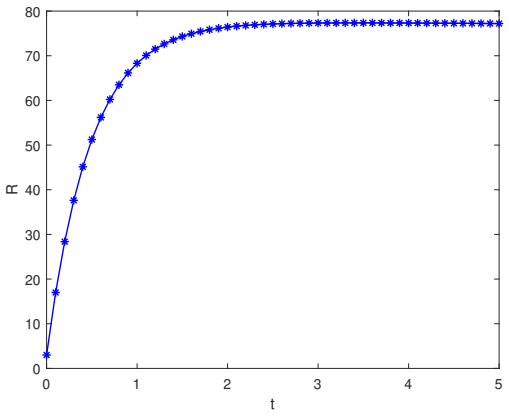


(b) Behavior of the state variable vaccinated individual V

method followed for the model fitting was described in Section 4. The fitted parameters of the model are summarized in Table 2. The most sensitive parameters for controlling the spread of cholera infection are determined using the forward sensitivity index method, these parameters with their elasticity index are summarized in Table 5. Patterns of the susceptible, vaccinated, infected, recovered and concentration of V.C in contaminating the environment are described in Figure 7a, Figure 7b, Figure 8a, Figure 8b and Figure 9, respectively. The effect of the rate of human contribution to V.C on the concentration of V.C in contaminating the environment is shown in Figure 10a. The figure shows that a decrease in contaminating the environment can reduce environmental transmission. Figure 10b shows that as the chance of becoming infected by vaccinated individuals decreases, the number of infected individuals also decreases, which implies that the disease control is dependent on the efficacy of the vaccine. Figure 11a shows that an increase in the rate of disinfection of the environment results to the decrease in the environmental cholera transmission. This implies that proper sanitation can control the environmental transmission of V.C. Nevertheless, the optimal control described in Section 4 shows that proper sanitation will



(a) Behavior of the state variable infected individual I



(b) Behavior of the state variable recovered individual R

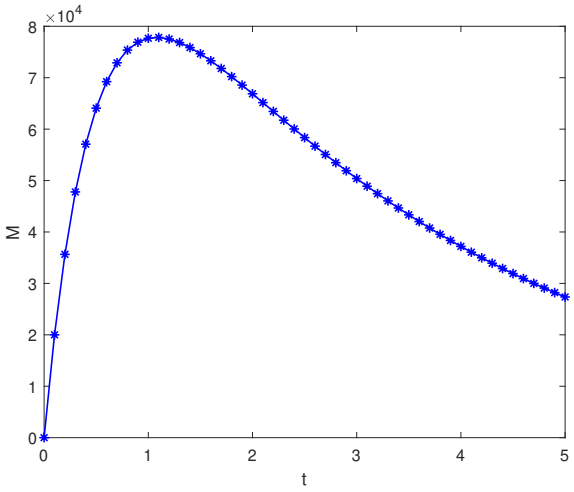
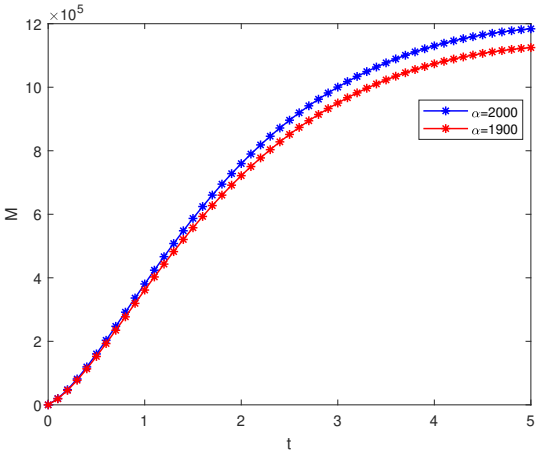
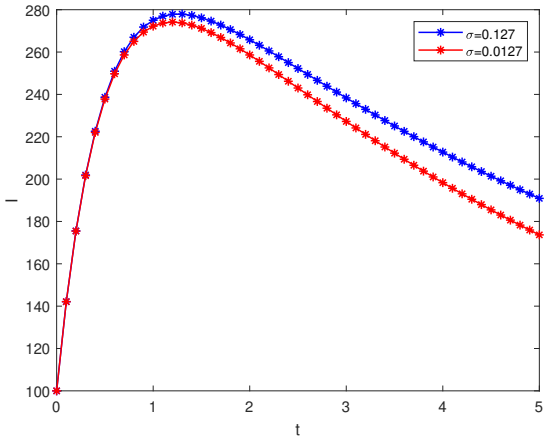


Figure 9. Behavior of the state variable Concentration of V.C in Contaminating the Environment M

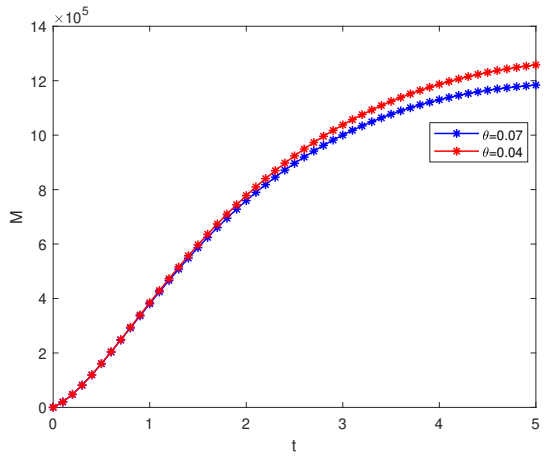


(a) pattern of M with different values of the rate of human contribution to V.C

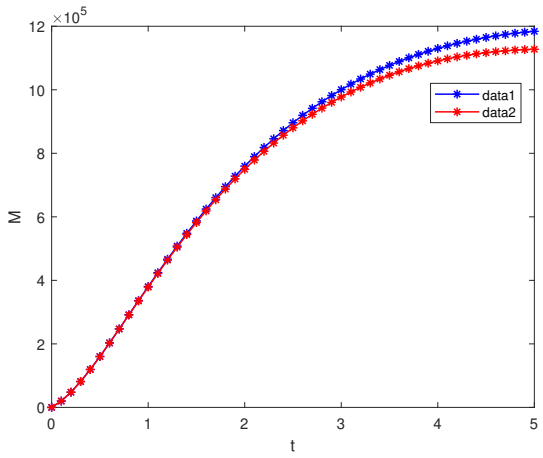


(b) pattern of I with different values of the modification parameter that decreases the infectiousness of V

cost less and the same time effective in controlling the recurrence of the disease. So to eradicate cholera disease in Nigeria, an efficient vaccine and proper sanitation should be enhanced.



(a) pattern of M with different values of the rate of disinfection of environment



(b) Behavior of the state variables (A) Infected individuals with undetectable viral load I_3, (B) Infected individuals under treatment I_t

Declarations

Use of AI tools

The authors declare that they have not used Artificial Intelligence (AI) tools in the creation of this article.

Data availability statement

All data generated or analyzed during this study are included in this article.

Ethical approval

The authors state that this research complies with ethical standards. This research does not involve either human participants or animals.

Consent for publication

Not applicable

Conflicts of interest

The authors declare that they have no conflict of interest.

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Not applicable

Author's contributions

U.T.M.: Methodology, Software, Validation, Y.A.M.: Formal Analysis, Investigation, Writing - Original Draft, Visualization, A.Y. and S.Q.: Software, Validation, Supervision, Project Administration. The authors have read and agreed to the published version of the manuscript.

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