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DYNAMIC ANALYSIS OF THE MATHEMATICAL MODEL FOR THE CHOLERA DISEASE SPREAD INVOLVING MEDICATION AND ENVIROMENTAL SANITATION

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ABSTRACT

This study aims to analyze the mathematical model of the cholera disease spread involving medication and environmental sanitation. The model was analyzed by determining the equilibrium point and the basic reproduction number. The next step was to analyze the equilibrium point, sensitivity, and simulate numerically. Analysis of the stability of the disease-free and endemic equilibrium points used the Routh-Hurwitz criteria and the Castillo-Chaves and Song Theorem. The Analysis result of the model produced two equilibrium points; namely the disease-free equilibrium point (T_1) *for local asymptotic stability* $R_0 < 1$ *and the endemic equilibrium point* (T_2) *for local asymptotic stability if* $R_0 > 1$. *Furthermore, the sensitivity analysis indicated the most sensitive parameters for basic reproductive number changes in succession are the parameters for natural birth rates* (A), *the transmission rate of bacteria from the environment to humans* (β), *the saturated concentration of bacteria in water* (k), *an increase in the bacterial population caused by environmental pollution rate by humans* (ξ). *Numerical simulations suggest an increase to give vaccine can contribute to slowing the transmission of cholera where as the reduction of a vaccine able to promote the transmission of cholera diseases.*

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1. INTRODUCTION

Cholera, first appeared in 1817 in Jessore India, is an infectious disease caused by the bacterium *Vibrio cholerae*. Cholera is a global public health threat in several countries, and it is estimated that 21.000 to 43.000 death cases from 1.3 to 1.4 million infected by cholera in the world annually [1]. Cholera can attack the digestive tract so that someone infected will experience acute vomiting and diarrhea and even become dehydrated due to losing a lot of fluids in the body. Cholera is caused when a person consumes a drink or food infected with the *Vibrio cholerae* bacteria [2]. This disease is common in areas with limited clean water supply and poor sanitation [3].

Mathematical modeling is a way to describe complex problems in mathematical form. Mathematical modeling can also be interpreted as a process of understanding mathematics through the context of the real world to make it easier to find solutions to problems that are often faced everyday [4]. One of the topics that can be studied in prospective mathematical modeling in the field of science is disease modeling. The case of the spread of cholera can be formulated with a mathematical approach through the concept of mathematical modeling. The resulting mathematical model can help provide an overview and impact of population changes caused by cholera [5][6].

Various studies in the field of mathematics regarding cholera have been carried out, including the SIR type mathematical model by Fitrianah, et al. [7] which showed that an increase in the rate of bacterial growth (hyper infectious) caused the disease to become an endemic epidemic. The SEIRS-type epidemic model was developed by Side, at al. [3] with vaccination and treatment as an initial control that can reduce the number of infected individuals. Furthermore, there is a study that discusses the SVIR-B mathematical model by adding a factor V (Vaccinated) by Tian, et al. [8]. This research shows that the vaccine can suppress the spread of cholera. However, Erick and Kokomo [9] showed that the disease cannot be eradicated by using vaccines alone but that other treatments are needed. Abdul, et al. [6] developed a mathematical model of cholera type SVIR $-$ B$_{hi}B_{li}$ by considering vaccination strategies, hyper infectious bacteria and less infectious populations. Recent research on cholera modeling was conducted by Manaqib, et al. [10] by developing a mathematical model of the SIWR type added with the fly vector. The results of this study indicate that the dominant parameters influencing the spread of cholera are the contact rate of susceptible individuals with infected individuals and the cure rate of cholera.

Several other models are devoted to developing mathematical models that consider the impact of climatic factors and human behavior on the spread of cholera [11]. Several studies have also discussed the mathematical model of the spread of cholera by involving fractional derivatives [12][13][14][15]. Furthermore, Mukandavire, et al [16] used the Manifold theory to show the stability of the endemic equilibrium as well as the lyapunov function for its global stability. Some of these studies broadly discuss the spread of cholera in a population considering the effect of solutions such as vaccinations and treatments that are carried out to reduce the number of infected individuals. In previous studies, there were studies that discussed the spread of cholera with vaccination using the SVIRB model. To distinguish them, a different model will be formed from the previous one.

This study discusses the basic mathematical model of cholera transmission, which refers to Tian, et al. [8] by modifying the model by adding medication and environmental sanitation parameters. Medication given to patients with cholera is in the form of an ORS solution to replace lost body fluids so that patients do not become dehydrated. Patients will receive more medication in intravenous fluids, antibiotics, and *Zinc* supplements if the symptoms they experience continue to reduce the number of bacteria [17]. With medication for cholera, it can speed up the healing process and minimize the risk of death while simultaneously suppressing the source of disease transmission quickly. Meanwhile, environmental sanitation is an effort or effort made to improve and maintain healthy environmental health by controlling physical environmental factors. These conditions include the provision of clean water, waste disposal, sewerage, and the provision of latrines that must be owned by every family and must always be maintained or clean and healthy [18]. Environmental sanitation is very necessary to suppress and break the chain of transmission of cholera. It is assumed that in the population, environmental sanitation is carried out in the bacterial population class (B), where sanitation can suppress and reduce the number of bacterial populations in the environment. Environmental sanitation is also considered in the mathematical model of hepatitis in [19] where the parameters α and h respectively represent the percentage of sanitation success and the level of sanitation. From this model, the endemic and disease-free equilibrium points are determined with the basic reproduction number R_0 to see whether the population is endemic or not. Followed by a stability analysis of the equilibrium

point either free of disease or endemic and numerical simulations were also carried out to determine the population dynamics for the cholera disease spread involving medication and environmental sanitation.

2. RESEARCH METHODS

This research was conducted using a literature study with the following steps:

1. Literature review related to the mathematical model of the spread of cholera.
2. Modify the mathematical model for the cholera disease spread involving medication and environmental sanitation.
3. Determine the stability analysis of the equilibrium point on the mathematical model for the cholera disease that has been modified by involving medication and environmental sanitation.
4. Conduct numerical simulations to see population dynamics for the cholera disease by involving medication and environmental sanitation.

3. RESULTS AND DISCUSSION

3.1. Mathematical Model

The assumptions used in building the model are formulated as follows:

1. The population is closed, with no migration either into or out of the population.
2. Newborn individuals will enter the susceptible population (S).
3. The vaccinated susceptible population will be included in the vaccinated population (V).
4. Individuals who have received the vaccine will experience an increase in body resistance, but over time the vaccine in the human body will continue to decrease so that individuals can return to the susceptible population (S).
5. The vaccinated population can be included in the infected population because not all vaccines given function effectively in preventing disease infection.
6. Susceptible individuals can enter the infected population because they consume food or drink that has been contaminated with Vibrio cholerae bacteria
7. The presence of these infected individuals can increase the population of bacteria (B) in the environment.
8. Environmental sanitation is carried out on the bacterial population (B) to reduce the number of bacterial populations in the environment.
9. Some infected individuals will receive medication and experience healing to enter the cured population (R).
10. Every population has the possibility to experience death, namely natural death, human death due to disease, and bacterial death.

With the above assumptions, the mathematical model for the cholera disease can be seen in **Figure 1**.

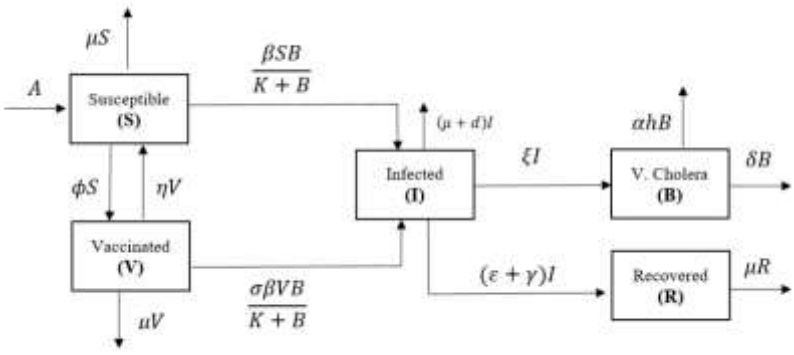


Figure 1. Compartment diagram for the cholera disease spread involving medication and environmental sanitation

Based on **Figure 1**. The following system of equations is obtained:

$$\begin{aligned}
\frac{dS}{dt} &= \mathrm{A} + \eta\mathrm{V} - \phi\mathrm{S} - \frac{\beta SB}{K+B} - \mu S \\
\frac{dV}{dt} &= \phi\mathrm{S} - \eta\mathrm{V} - \mu\mathrm{V} - \frac{\sigma\beta VB}{K+B} \\
\frac{dI}{dt} &= \frac{\beta SB}{K+B} + \frac{\sigma\beta VB}{K+B} - (\varepsilon + \gamma + \mu + d)I \\
\frac{dR}{dt} &= \varepsilon I + \gamma I - \mu R \\
\frac{dB}{dt} &= \xi I - (\delta + \alpha h)B
\end{aligned} \tag{1}$$

3.2. Areas of Solutions Model For The Cholera Disease Spread

The solution area of the cholera distribution model in **Equation (1)** is non-negative

Lemma 1. The set $\Omega = (S,V,I,R,B) \in \Re_+^5 : 0 \le S+V+I+R \le \frac{A}{\mu} + N_0$ and $0 \le B \le \frac{\xi I}{\alpha h} + B_0 e^{-\alpha h t}$ is the non-negative solution area of equation (1), where N_0 is the total human population at $t = 0$ and B_0 is the total bacterial population at $t = 0$.

Proof:

Let $N = S + V + I + R$ from equation (1) we get

$$\begin{aligned}
\frac{dN}{dt} &= \frac{dS}{dt} + \frac{dV}{dt} + \frac{dI}{dt} + \frac{dR}{dt} \\
\frac{dN}{dt} &= \mathrm{A} + \eta\mathrm{V} - \phi\mathrm{S} - \frac{\beta SB}{K+B} - \mu S + \phi\mathrm{S} - \eta\mathrm{V} - \mu\mathrm{V} - \frac{\sigma\beta VB}{K+B} \\
&\quad + \frac{\beta SB}{K+B} + \frac{\sigma\beta VB}{K+B} - (\varepsilon + \gamma + \mu + d)I + \varepsilon I + \gamma I - \mu R \\
\frac{dN}{dt} &= \mathrm{A} - \mu\mathrm{N} - \mathrm{dI}
\end{aligned} \tag{2}$$

Because $dI \ge 0$, then from **Equation (2)** we get

$$\begin{aligned}
\frac{dN}{dt} &\le A - \mu N \\
\frac{dN}{dt} + \mu N &\le A
\end{aligned} \tag{3}$$

Inequality (3) is solved using 1st order inhomogeneous linear PD so that we get

$$N \le \frac{A}{\mu}(1 - e^{-\mu t}) + N_0 e^{-\mu t} - \frac{c_1}{\mu}(1 - e^{-\mu t})$$

because $0 \le e^{-\mu t} \le 1$ for every $t \ge 0$ obtained

$$N \le \frac{A}{\mu} + N_0$$

or

$$S + V + I + R \le \frac{A}{\mu} + N_0$$

Cause $S(t), V(t), I(t), \text{and } R(t)$ is not negative, then for every $t \ge 0$ we get

$$0 \le S + V + I + R \le \frac{A}{\mu} + N_0 \tag{4}$$

next it will be determined that B_0 is not negative, obtained

$$\frac{dB}{dt} = \varepsilon I - (\delta + \alpha h)B \tag{5}$$

$$\frac{dB}{dt} + (\delta + \alpha h)B = \varepsilon I$$

Based on **Equation (4)** then $I \leq \frac{A}{\mu} + N_0$, so from **Equation (5)** we get

$$\frac{dB}{dt} + (\delta + \alpha h)B = \varepsilon \frac{A}{\mu} + N_0 \tag{6}$$

Inequality (6) produces a solution

$$B \leq \frac{A\xi}{\mu(\alpha h + \delta)}\left(1 - e^{-(\alpha h+\delta)}\right) + \frac{N_0\xi}{(\alpha h + \delta)}\left(1 - e^{-(\alpha h+\delta)}\right) + B_0 e^{-(\alpha h+\delta)} - \frac{C_2}{(\alpha h + \delta)}\left(1 - e^{-(\alpha h+\delta)}\right) \tag{7}$$

Since $0 \leq e^{-(\alpha h+\delta)} \leq 1$ for every $t \geq 0$ then we get

$$B \leq \frac{A\xi}{\mu(\alpha h + \delta)} + \frac{N_0\xi - C_2}{(\alpha h + \delta)} + B_0 \tag{8}$$

Since $B(t)$ is not negative for $t \geq 0$ we get

$$0 \leq B \leq \frac{A\xi}{\mu(\alpha h + \delta)} + \frac{N_0\xi - C_2}{(\alpha h + \delta)} + B_0 \tag{8}$$

Based on the inequalities (4) and (8) we get

$0 \leq S + V + I + R \leq \frac{A}{\mu} + N_0$ and $0 \leq B \leq \frac{A\xi}{\mu(\alpha h+\delta)} + \frac{N_0\xi - C_2}{(\alpha h+\delta)} + B_0$. ■

3.3. Equilibrium Points

The equilibrium point of the mathematical model stability analysis model in cholera in the presence of medication and environmental sanitation is obtained by setting the equations in the system to be constant with time or:

$$\frac{ds}{dt} = \frac{dv}{dt} = \frac{di}{dt} = \frac{dr}{dt} = \frac{db}{dt} = 0 \tag{9}$$

Therefore, from the results of the system analysis **Equation (2)** there are two types of equilibrium points, namely disease-free and endemic equilibrium points. The disease-free equilibrium point denoted by T_1 is:

$$T_1(s, v, i, r, b) = \left(\frac{a(\eta + \mu)}{\mu(\eta + \mu + \phi)}, \frac{a\,\phi}{\mu(\eta + \mu + \phi)} 0,0,0\right) \tag{10}$$

The point of reaching endemic is denoted by T_2 which is:

$$T_2 = (s^*, v^*, i^*, r^*, b^*) \tag{11}$$

With

$$s^* = \frac{\alpha(b + k)((b + k)(\eta + \mu) + b\beta\sigma)}{-(b + k)^2\eta\phi + ((b + k)(\eta + \mu) + b\beta\sigma)(k(\mu + \phi) + b(\beta + \mu + \phi))}$$

$$v^* = \frac{\alpha(b + k)^2\phi}{-(b + k)^2\eta\phi + ((b + k)(\eta + \mu) + b\beta\sigma)(k(\mu + \phi) + b(\beta + \mu + \phi))}$$

$$i^* = \frac{b(h\alpha + \delta)}{\xi}$$

$$r^* = \frac{b(h\alpha+\delta)(\gamma+\varepsilon)}{\mu\xi}$$

$$b^* = \frac{-a_2 \pm \sqrt{a_2^2 - 4a_1a_3}}{2a_1}$$

Which is

$$\begin{aligned} a_1 &= -(h\alpha+\delta)(d+\gamma+\varepsilon+\mu)((\beta+\mu)(\eta+\mu+\beta\sigma)+(\mu+\beta\sigma)\phi) < 0 \\ a_2 &= k(h\alpha+\delta)\mu(d+\gamma+\varepsilon+\mu)(\eta+\mu+\phi)(R_0-1) \\ &\quad -\left(\left(k(h\alpha+\delta)(d+\gamma+\varepsilon+\mu)(\eta+\mu+\phi)\right)\right) \\ &\quad + k(h\alpha+\delta)\mu(d+\gamma+\varepsilon+\mu)\beta(\eta+\mu+\mu\sigma+\sigma\phi) - \alpha\beta^2\xi\sigma \\ a_3 &= -k^2(h\alpha+\delta)\mu(d+\gamma+\varepsilon+\mu)(\eta+\mu+\phi)(1-R_0) \end{aligned}$$

Theorem 1. *For the system of* ***Equation (11)*** *The disease-free equilibrium point T_1 will always exist. Moreover, the endemic equilibrum point T_2 is unique and positive if and only if $R_0 > 1$.*

Proof:
Based on the system of **Equation (11)** we get

$$b^*(a_1b^2 + a_2b + a_3) = 0 \tag{12}$$

One of the three roots of **Equation (12)** is $b^* = 0$. The value $b^* = 0$ results in $i^* = 0, r^* = 0$. One solution (11) is the disease-free equilibrium point T_1. So it is evident that disease-free equilibrium point always exists. The other two roots (b_1^* and b_2^*) of **Equation (12)** are solutions of the following equation:

$$b_1^* + b_2^* = -\frac{a_2}{a_1} \tag{13}$$

$$b_1^* b_2^* = \frac{a_3}{a_1} \tag{14}$$

Since the basic reproduction number is $R_0 > 1$ or $\frac{\alpha\beta\xi(\eta+\mu+\sigma\phi)}{k(h\alpha+\delta)\mu(d+\gamma+\varepsilon+\mu)(\eta+\mu+\phi)} > 1$, then the value of $a_3 > 0$. Since $a_1 < 0$ and $a_3 > 0$, then $b_1^* b_2^* < 0$ provided that b_1^* and b_2^* must have different signs. So, there is only one positive root b_1^* so$b^* = 0, i^* = 0, r^* = 0$ exists and is unique with positive values. It is proved that if $R_0 > 1$ then the endemic equilibrium point T_2 is unique and ■ positive.

3.4. Basic Reproductive Numbers

The basic reproductive number (R_0) is obtained using the next-generation matrix method, which is defined as $K = FV^{-1}$ [20]. Based on the **Equation (1)** system, a system of equations is taken which includes the infected population class and the bacterial population class, namely:

$$\begin{aligned} \frac{dI}{dt} &= \frac{\beta SB}{K+B} + \frac{\sigma\beta VB}{K+B} - (\varepsilon+\gamma+\mu+d)I \\ \frac{dB}{dt} &= \varepsilon I - (\delta+\alpha h)B \end{aligned} \tag{15}$$

Based on **Equation (15)** above, the matrix F is obtained which is the rate of change resulting in an increase in the infected population, and V is the rate resulting in a decrease in the infected population.

$$F = \begin{pmatrix} \frac{bs\beta}{b+k} + \frac{bv\beta\sigma}{b+k} \\ 0 \end{pmatrix}$$

and

$$V = \begin{pmatrix} (d+\gamma+\varepsilon+\mu) \\ b(h\alpha+\delta) - i\xi \end{pmatrix}$$

Using the disease-free equilibrium point in **Equation (10)**, we get the Jacobian matrix F and V, namely

$$F = \begin{pmatrix} 0 & \frac{\alpha\beta(\eta+\mu)}{k\mu(\eta+\mu+\phi)} \\ 0 & 0 \end{pmatrix}$$

and

$$V = \begin{pmatrix} (d+\gamma+\varepsilon+\mu) & 0 \\ -\xi & h\alpha+\delta \end{pmatrix}$$

Furthermore, the basic reproduction number R_0 is obtained from the largest positive eigenvalue of the next generation matrix, $K = FV^{-1}$, is

$$R_0 = \frac{\alpha\beta\xi(\eta+\mu+\sigma\phi)}{k(h\alpha+\delta)\mu(d+\gamma+\varepsilon+\mu)(\eta+\mu+\phi)} \tag{16}$$

3.5. Local Stability Analysis

Analysis of the local stability of the equilibrium point is done by finding the eigenvalues of the Jacobi matrix system. The following is the Jacobi matrix from **Equation (1)**, namely:

$$J = \begin{pmatrix} J_{11} & J_{12} & 0 & 0 & J_{15} \\ J_{21} & J_{22} & 0 & 0 & J_{25} \\ 0 & 0 & J_{33} & 0 & J_{35} \\ 0 & 0 & J_{43} & J_{44} & 0 \\ 0 & 0 & J_{53} & 0 & J_{55} \end{pmatrix}$$

Which is

$$J_{11} = -\frac{b\beta}{b+k} - \mu - \phi \qquad J_{32} = \frac{b\beta\sigma}{b+k}$$
$$J_{12} = \eta \qquad J_{33} = -d-\gamma-\varepsilon-\mu$$
$$J_{15} = \frac{bs\beta}{(b+k)^2} - \frac{s\beta}{b+k} \qquad J_{35} = -\frac{bs\beta}{(b+k)^2} + \frac{s\beta}{b+k} + \frac{bv\beta\sigma}{(b+k)^2} - \frac{v\beta\sigma}{b+k}$$
$$J_{21} = \phi \qquad J_{43} = \gamma+\varepsilon$$
$$J_{22} = -\eta-\mu-\frac{b\beta\sigma}{b+k} \qquad J_{44} = -\mu$$
$$J_{25} = -\frac{bv\beta\sigma}{(b+k)^2} - \frac{v\beta\sigma}{b+k} \qquad J_{53} = \xi$$
$$J_{31} = \frac{b\beta}{b+k} \qquad J_{55} = -h\alpha-\delta$$

Stability of the cholera-free equilibrium point T_1 is presented in **Theorem 2**.

Theorem 2. *The local asymptotically stable cholera disease-free equilibrium point if* $R_0 < 1$.

Proof:

To obtain the stability of the system at the point T_1, an estimation is carried out around the equilibrium point T_1 so that the Jacobi matrix is obtained as follows

$$J_{T1} = \begin{pmatrix} J_{11} & J_{12} & 0 & 0 & J_{15} \\ J_{21} & J_{22} & 0 & 0 & J_{25} \\ 0 & 0 & J_{33} & 0 & J_{35} \\ 0 & 0 & J_{43} & J_{44} & 0 \\ 0 & 0 & J_{53} & 0 & J_{55} \end{pmatrix}$$

when

$$J_{11} = -\mu - \phi$$
$$J_{12} = \eta$$
$$J_{15} = \frac{\alpha\beta(\eta+\mu)}{k\mu(\eta+\mu+\phi)}$$
$$J_{21} = \phi$$
$$J_{22} = -\eta - \mu$$
$$J_{25} = \frac{\alpha\beta(\eta+\mu)}{k\mu(\eta+\mu+\phi)}$$
$$J_{33} = -d - \gamma - \varepsilon - \mu$$
$$J_{35} = \frac{\alpha\beta(\eta+\mu)}{k\mu(\eta+\mu+\phi)} + \frac{\alpha\beta\sigma\phi}{k\mu(\eta+\mu\phi)}$$
$$J_{43} = \gamma + \varepsilon$$
$$J_{44} = -\mu$$
$$J_{53} = \xi$$
$$J_{55} = -h\alpha - \delta$$

From the J_{T1}, Jacobi matrix, it is obtained the characteristic equation

$$(J_{44} - \lambda)\big(J_{12}J_{21} + (J_{11} - \lambda)(-J_{22} + \lambda)\big)(J_{35}J_{53} + (J_{33} - \lambda)(-J_{55} + \lambda)) = 0 \quad (17)$$

Based on the characteristic equation, obtained 5 eigenvalues with 1 negative eigenvalue, namely:

$$\lambda_1 = J_{44} = -\mu < 0$$

The two eigenvalues of **Equation (14)** can be seen in the equation below:

$$\begin{gathered} \big(J_{12}J_{21} + (J_{11} - \lambda)(-J_{22} + \lambda)\big) = 0 \\ J_{12}J_{21} - J_{11}J_{22} + \lambda(J_{11} + J_{22}) - \lambda^2 = 0 \\ -\lambda^2 + (J_{11} + J_{22})\lambda - J_{11}J_{22} + J_{12}J_{21} = 0 \\ \lambda^2 - (J_{11} + J_{22})\lambda + J_{11}J_{22} - J_{12}J_{21} = 0 \end{gathered} \quad (18)$$

Based on **Equation (18)** obtained

$$a_0\lambda^2 + a_1\lambda + a_2 = 0 \quad (19)$$

with

$$a_0 = 1$$
$$a_1 = -\eta - 2\mu - \phi$$
$$a_2 = -\mu(\eta + \mu + \phi)$$

The roots of **Equation (19)** are the eigen values of the characteristic **Equation (17)** namely λ_2 and λ_3. Based on the nature of the roots of the quadratic equation, the following system of equations is obtained:

$$\lambda_2 + \lambda_3 = -\frac{a_1}{a_0} = -a_1 < 0 \quad (20)$$

$$\lambda_2\lambda_3 = \frac{a_2}{a_0} > 0 \quad (21)$$

From **Equation (17)** it is possible that one of λ_2 and λ_3 is negative. Example

$$\lambda_2 < 0 \quad (22)$$

From Equation (18) it is known that λ_2 and λ_3 must have the same sign. Based on **Equation (19)**, if $\lambda_2 < 0$ then $\lambda_3 < 0$. Thus $\lambda_2 < 0$ and $\lambda_3 < 0$.

While the other two eigenvalues can be found in the following equation:

$$\begin{aligned}(J_{35}J_{53} + (J_{33} - \lambda)(-J_{55} + \lambda)) &= 0\\ J_{35}J_{53} - J_{33}J_{55} + \lambda(J_{33} + J_{55}) - \lambda^2 &= 0\\ -\lambda^2 + (J_{33} + J_{55})\lambda - J_{33}J_{55} + J_{35}J_{53} &= 0\\ \lambda^2 - (J_{33} + J_{55})\lambda + J_{33}J_{55} - J_{35}J_{53} &= 0\end{aligned} \tag{23}$$

Based on **Equation (23)** obtained:

$$a_0\lambda^2 + a_1\lambda + a_2 = 0 \tag{24}$$

with

$a_0 = 1$
$a_1 = -d - h\alpha - \gamma - \delta - \varepsilon - \mu$
$a_2 = (R_0 - 1)(h\alpha + \delta)(d + \gamma + \varepsilon + \mu)$

The roots of **Equation (22)** are the eigen values of the characteristic **Equation (14)** namely λ_4 and λ_5. Based on the nature of the roots of the quadratic equation, the following system of equations is obtained:

$$\lambda_4 + \lambda_5 = -\frac{a_1}{a_0} = -a_1 \tag{25}$$

$$\lambda_4\lambda_5 = \frac{a_2}{a_0} \tag{26}$$

Furthermore, it is enough to determine the stability of the equilibrium point by paying attention to the values of λ_4 and λ_5. if $\lambda_4 < 0$ dan $\lambda_5 < 0$ then the equilibrium point will be stable, whereas if $\lambda_4 > 0$ dan $\lambda_5 > 0$ then the equilibrium point will be unstable. Pay attention to the shape

$$a_2 = (R_0 - 1)(h\alpha + \delta)(d + \gamma + \varepsilon + \mu) \tag{27}$$

If $R_0 < 1$ then $a_2 < 0$. Thus, the value of **Equations (23)** and **Equations (24)** obtained the condition

$$\lambda_4 + \lambda_5 < 0 \tag{28}$$

$$\lambda_4\,\lambda_5 > 0 \tag{29}$$

This indicates that between the two eigenvalues, there are always those who dare to be negative. Suppose $\lambda_4 < 0$, based on (27) we get

$$\lambda_5 < 0 \tag{30}$$

Thus obtained all negative eigenvalues. Thus, if $R_0 < 1$ causes the disease-free equilibrium point T_1 is locally asymptotically stable.

Furthermore, it will be proved if $R_0 > 1$ then

$$a_2 = (R_0 - 1)(h\alpha + \delta)(d + \gamma + \varepsilon + \mu) > 0 \tag{31}$$

So based on **Equation (23)** we get

$$\lambda_4\,\lambda_5 < 0 \tag{32}$$

This means that λ_4 and λ_5 have different signs or there are positive eigenvalues so that the disease-free equilibrum point T_1 for system (20) is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$. The stability properties of the endemic equilibrium point T_2 are presented in **Theorem 3.** ■

Theorem 3. *The endemic equilibrium point is locally asymptotically stable if* $R_0 > 1$

Proof:
Suppose the bifurcation parameter is $\varphi = \beta, x_1 = s, x_2 = v, x_3 = i, x_4 = r, x_5 = b,$ so that **Equation (1)** becomes

$$
\begin{aligned}
f_1(x_1,x_2,x_3,x_4,x_5) &= \mathrm{A} + \eta x_2 - \phi x_1 - \frac{\beta x_1 x_5}{K+x_5} - \mu x_1 \\
f_2(x_1,x_2,x_3,x_4,x_5,) &= \phi x_1 - \eta x_2 - \mu x_2 - \frac{\sigma\beta x_2 x_5}{K+x_5} \\
f_3(x_1,x_2,x_3,x_4,x_5) &= \frac{\beta x_1 x_5}{K+x_5} + \frac{\sigma\beta x_2 x_5}{K+x_5} - (\varepsilon+\gamma+\mu+d)x_3 \\
f_4(x_1,x_2,x_3,x_4,x_5) &= \varepsilon x_3 + \gamma x_3 - \mu x_4 \\
f_5(x_1,x_2,x_3,x_4,x_5) &= \xi x_3 - (\delta+\alpha h)x_5
\end{aligned}
\tag{33}
$$

Based on $R_0 = 1$ will correspond to

$$
\varphi = \varphi^* = \frac{a\beta\xi(\eta+\mu+\sigma\phi)}{k(h\alpha+\delta)\mu(d+\gamma+\varepsilon+\mu)(\eta+\mu+\phi)}
$$

and the disease-free equilibrium point T_1 with $R_0 = 1$ has four negative eigenvalues and one zero eigenvalue. The zero eigenvalues have right eigenvectors $(u_1, u_2, u_3, u_4, u_5)$ and left eigenvectors $(v_1, v_2, v_3, v_4, v_5)$.

For example, $u_5 > 0$ is free, then

$$
\begin{aligned}
u_1 &= \frac{a\beta(\eta+\mu)^2 + \eta\sigma\phi)}{k\mu^2(\eta+\mu+\phi)^2} u_5 > 0 \\
u_2 &= \frac{a\beta\phi(\eta+\mu+\mu\sigma+\sigma\phi)}{k\mu^2(\eta+\mu\phi)^2} u_5 > 0 \\
u_3 &= \frac{a\beta(\eta+\mu+\sigma\phi)}{k\mu(d+\gamma+\varepsilon+\mu)(\eta+\mu+\phi)} u_5 > 0 \\
u_4 &= \frac{a\beta(\gamma+\varepsilon)(\eta+\mu+\sigma\phi)}{k\mu^2(d+\gamma+\varepsilon+\mu)(\eta+\mu+\phi)} u_5 > 0
\end{aligned}
\tag{34}
$$

For example, $v_3 > 0$ is free, then

$$
\begin{aligned}
v_1 &= v_2 = v_4 = 0 \\
v_5 &= \frac{(d+\gamma+\varepsilon+\mu)}{\xi} v_3 > 0
\end{aligned}
\tag{35}
$$

By using the Castillo-Chaves theorem and Song **[21]** it is defined

$$
\begin{aligned}
a &= \sum_{k,i,j=1}^{n} v_k u_i u_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(T^1, \phi^*) \\
b &= \sum_{k,i,j=1}^{n} v_k u_i \frac{\partial^2 f_k}{\partial x_i \partial \phi}(T^1, \phi^*)
\end{aligned}
\tag{36}
$$

Based on **Equation (36)**, the term value for a is obtained

$$
\begin{aligned}
\frac{\partial^2 f_3}{\partial x_1 \partial x_5} &= \frac{\beta}{k} \\
\frac{\partial^2 f_3}{\partial x_2 \partial x_5} &= -\frac{\beta\sigma}{k}
\end{aligned}
\tag{37}
$$

Based on **Equation (37)**, the term value for a is obtained

$$\frac{\partial^2 f_3}{\partial x_1 \partial \varphi} = 0$$
$$\frac{\partial^2 f_3}{\partial x_2 \partial \varphi} = 0 \quad (38)$$
$$\frac{\partial^2 f_3}{\partial x_5 \partial \varphi} = \frac{a(\eta+\mu+\sigma\phi)}{k\mu(\eta+\mu+\phi)}$$

Based on the results of the system of **Equations (37)** and **Equations (38)**, the values of a and b are obtained as follows:

$$\begin{aligned} a &= v_3 u_1 u_5 \frac{\partial^2 f_3}{\partial x_1 \partial x_5} + v_3 u_2 u_5 \frac{\partial^2 f_3}{\partial x_2 \partial x_5} \\ &= u_5 \left(v_3 u_1 \frac{\partial^2 f_3}{\partial x_1 \partial x_5} + v_3 u_2 \frac{\partial^2 f_3}{\partial x_2 \partial x_5} \right) \\ &= u_5 \left(v_3 \frac{a\beta((\eta+\mu)^2+\eta\sigma\phi)}{k\mu^2(\eta+\mu+\phi)^2} u_5 \frac{\partial^2 f_3}{\partial x_1 \partial x_5} + v_3 \frac{a\beta\phi(\eta+\mu+\mu\sigma+\sigma\phi)}{k\mu^2(\eta+\mu\phi)^2} u_5 \frac{\partial^2 f_3}{\partial x_2 \partial x_5} \right) \\ &= -\frac{u_5^2 v_3 a\beta^2((\eta+\mu)^2+\sigma(2\eta+\mu+\mu\sigma)\phi+\sigma^2\phi^2)}{k^2\mu^2(\eta+\mu+\phi)^2} < 0 \end{aligned}$$

$$\begin{aligned} b &= v_3 u_1 \frac{\partial^2 f_3}{\partial x_1 \partial \varphi} + v_3 u_2 \frac{\partial^2 f_3}{\partial x_2 \partial \varphi} + v_3 u_5 \frac{\partial^2 f_3}{\partial x_5 \partial \varphi} \\ &= v_3 u_5 \frac{\partial^2 f_3}{\partial x_5 \partial \varphi} \\ &= \frac{a v_3 u_5 (\eta+\mu+\sigma\phi)}{k\mu(\eta+\mu+\phi)} > 0 \end{aligned}$$

The values of a and b obtained have case criteria 4 in the Castillo-Chaves and Song theorem **[21]**. Consequently, if $\varphi < \varphi^*(R_0 < 1)$ becomes $\varphi > \varphi^*(R_0 > 1)$, then the disease-free equilibrium point T_1 changes from stable to unstable and the unstable endemic T_2 changes from negative to positive and locally asymptotically stable, while the disease-free equilibrum point T_1 is unstable. ■

3.6. Sensitivity Analysis

Parameter R_0 basic reproduction number, which states the average number of new cases from infected individuals to susceptible individuals. This basic reproductive number can be used as a benchmark for the occurrence or not of the spread of cholera caused by Vibrio cholerae. From this sensitivity analysis, it can be seen that the value of R_0 is influenced by the parameters in the model. The basic reproduction number analyzed is when the condition is $R_0 > 1$. The basic reproduction number when $R_0 > 1$ illustrates that the occurrence of disease spread in an area. Based on this, it is necessary to conduct a sensitivity analysis of the parameters on the system to determine the efforts that must be made to suppress the spread of the disease.

This sensitivity analysis aims to determine the most influential or sensitive parameter to the value of R_0. Sensitivity analysis was performed by determining the parametric sensitivity index. The sensitivity index of the normalized base reproduction number referring to **[22] [23]** is defined as:

$$C_p^{R_0} = \frac{\partial R_0}{\partial p} \times \frac{p}{R_0}$$

where p is the various parameters in the basic reproduction number, namely A, $\phi, \beta, k, \mu, \eta, \sigma, \gamma, d, \xi, \delta, \varepsilon, \alpha, h$. For parameter A, it is described as follows

$$\frac{\partial R_0}{\partial p} = \frac{\beta\xi(\eta+\mu+\sigma\phi)}{k(h\alpha+\delta)\mu(d+\gamma+\varepsilon+\mu)(\eta+\mu+\phi)}$$

So, the sensitivity index A is obtained as follows

$$C_p^{R_0} = \frac{\partial R_0}{\partial p} \times \frac{A}{R_0}$$
$$= \frac{\beta\xi(\eta+\mu+\sigma\phi)}{k(h\alpha+\delta)\mu(d+\gamma+\varepsilon+\mu)(\eta+\mu+\phi)} \times \frac{A}{\frac{\beta\xi(\eta+\mu+\sigma\phi)}{k(h\alpha+\delta)\mu(d+\gamma+\varepsilon+\mu)(\eta+\mu+\phi)}}$$
$$= 1$$

By substituting the parameter values, we get $R_0 = 1{,}39685$ and the sensitivity index value of each parameter can be seen in **Table 1**.

Table 1. Sensitivity index for $R_0 > 1$

Parameter	Sensitivity Index	Parameter	Sensitivity Index
A	1	γ	-0.090796
ϕ	-0.291791	d	-0.340485
β	1	ξ	1
k	-1	δ	-0.970588
η	0.288628	ε	-0.567475
M	-0.998081	α	-0.0294118
σ	0.372449	h	-0.0294118

Based on **Table 1**, it can be explained that for every one unit increase in parameter A or natural birth rate, it will cause R_0 to increase by 1 unit. Meanwhile, if the value of parameter A or the natural birth rate is reduced by one unit, it will result in R_0 being reduced by 1 unit. The positive value of the sensitivity index indicates the effect of changes in the parameter values that are directly proportional to changes in the basic reproduction number value.

The value of the sensitivity index ϕ or vaccination rate in **Table 1** is -0.291791, which means that if the parameter increases by one unit, it will cause R_0 to decrease by $0{,}291791$ units. Meanwhile, if the parameter ϕ is reduced by one unit, it will result in an increase in R_0 of 0.291791. The negative value of the sensitivity index indicates the effect of changes in the parameter value which is inversely proportional to the change in the value of the basic reproduction number.

Sensitivity analysis shows that A, β, k, ξ are natural birth rates, transmission rates of bacteria from the environment to humans, saturated concentrations of bacteria in water and the rate of environmental pollution by humans resulting in an increase in bacterial population are parameters that are sensitive to changes in reproductive numbers base.

3.7. Numerical Simulation

Numerical simulations are carried out using *Python Software* to show stability and show the stability properties of each equilibrium point by entering the parameter values in **Table 2** from each equilibrium point in the numerical system. There is a numerical simulation so that we can see how the population dynamics in the model is based on the existing parameter values. The values of the existing parameters are also to vary according to the possibilities that exist in the real world.

Table 2. Parameter Value

Parameter	$R_0 < 1$	$R_0 > 1$	Source
A	0.1	0.1	[8]
ϕ	0.01	0.01	[8]
β	0.2143	0.2143	[8]
k	10^6	10^6	[8]
η	0.005	0.005	[8]
μ	$5.48(10^{-5})$	$5.48(10^{-5})$	[8]
σ	0.1	0.3	[8]

Parameter	$R_0 < 1$	$R_0 > 1$	Source
γ	0.015	0.015	[8]
d	0.004	0.004	[8]
ξ	20	100	[8]
δ	0.33	0.33	[8]
ε	0.025	0.025	Assumption
α	$2.4(10^{-4})$	$2.4(10^{-4})$	Assumption
h	0.25	0.25	Assumption

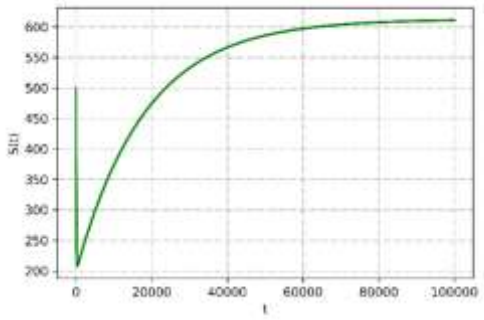
Population dynamics of the spread of cholera with medication and environmental sanitation will be observed under conditions $R_0 < 1$ and $R_0 > 1$The initial value used is $\mathrm{S}(0) = 500, \mathrm{V}(0) = 90, \mathrm{I}(0) = 350, \mathrm{R}(0) = 0, \mathrm{B} = 3000$.

Dinamics of Population Proportion in $R_0 < 1$

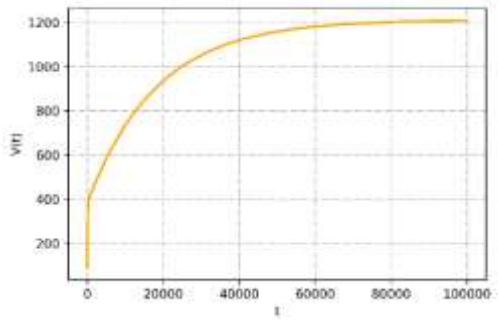
Based on **Equations (2)**, the disease-free equilibrium point is obtained. Where the disease-free equilibrium point is obtained by substituting the parameter values in **Table 2** into the model with a value of $R_0 = 0{,}216327$. The disease-free equilibrium point is obtained as follows:

$$T_1 = (612.701, 1212.12, 0, 0, 0)$$

The following shows the dynamics of the population proportion in the condition $R_0 < 1$ which can be seen in **Figure 2**.



(a)



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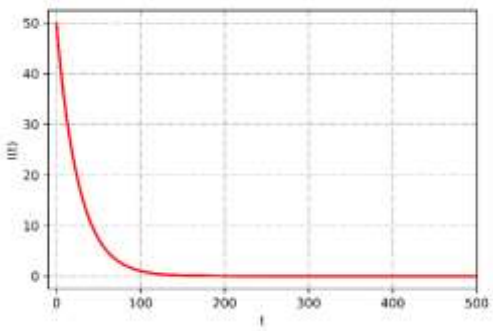
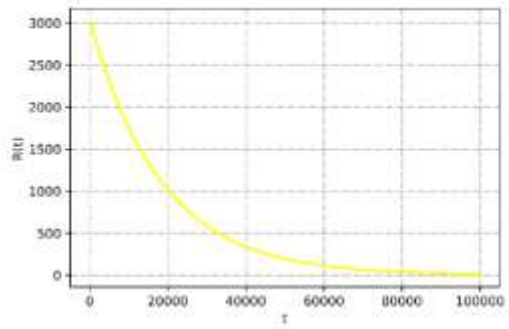
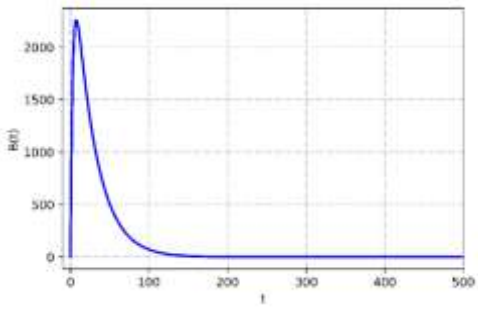


(c)



(d)



(e)

Figure 2. Numerical simulation for the disease-free equilibrium for $R_0 < 1$ that representative of: (a) susceptible population, (b) vaccinated population, (c) infected population, (d) recovered population, and (e) bacterial population

Figure 2 shows that each population is stable towards a disease-free equilibrium point. Susceptible population experienced a decrease in population from the initial value = 500 then increased in population until it reached a stable condition around $S = 612$ people. Meanwhile, the vaccinated population experienced an increase in population from the initial value until it reached a stable point at $V = 1.212$ people. while for the infected population, the population recovered and the bacterial population decreased from the initial point until it reached a stable point at $I = R = B = 0$.

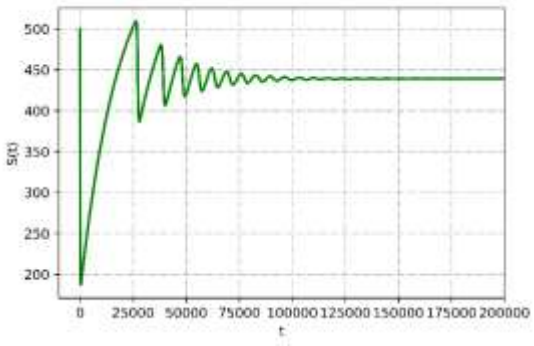
Dynamics of Population Proportion in $R_0 > 1$

Based on **Equation (2)** which is substituted with the values of the parameters contained in **Table 2** with the basic reproduction number $R_0 = 1{,}39685$, the following endemic equilibrium points are obtained

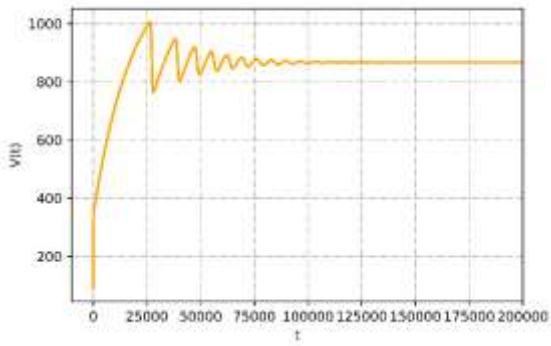
$$T_2 = (439.108, 866{,}603, 0.64572, 341.713, 189.918)$$

The following shows the dynamics of the population proportion in the condition $R_0 > 1$ which can be seen in **Figure 3**.

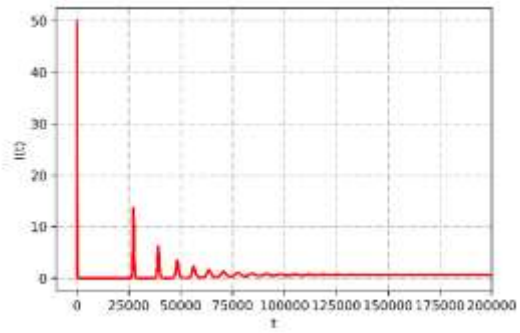
Figure 3 shows that each population at one time is not immediately stable but still fluctuates, where at a certain time the population will increase or decrease depending on the factors that influence it until a certain time (t) will be stable. And it shows that each population is approaching the endemic equilibrium point, the population susceptible to the spread of cholera has decreased in population until it reaches a stable point when S = 439.108 or about 439 people and (population vaccinated) V = 866.603 or about 866 people. For infected pollution I = 0.64572 or about 1 person, the population recovered from cholera is stable at R = 341.713 or about 341 people. while for the bacterial population B = 189.918.



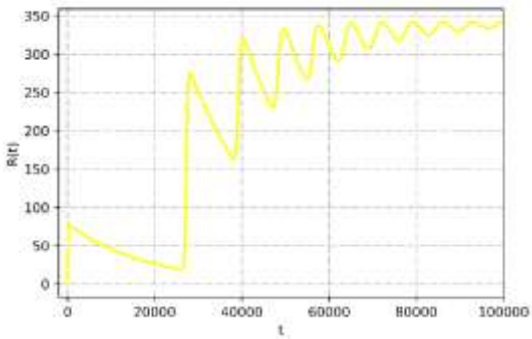
(a)



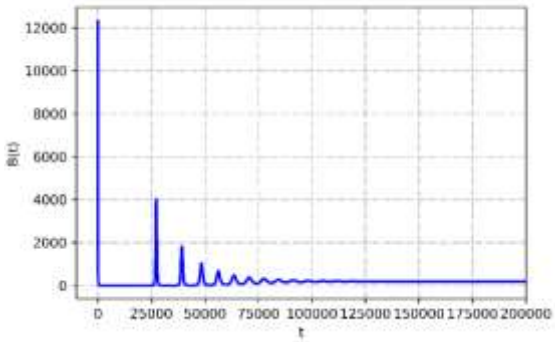
(b)



(c)



(d)



(e)

Figure 3. Numerical simulation of the endemic equilibrium point $R_0 > 1$ that representative of: (a) susceptible population, (b) vaccinated population, (c) infected population, (d) recovered population, and (e) bacterial population

Population Dynamics with Variation of Vaccine Parameters

This simulation was conducted to show the effect of vaccination rate on the spread of cholera. Where if the value of ϕ is increased it will have an effect on increasing the value of R_0. Changes in the value of R_0can be observed in **Table 3**.

Table 3. Simulation Result of the Variation of parameter ϕ value R_0

Simulation	ϕ	$R_0 < 1$
1	0.01	$0.2163276 < 1$
2	0.02	$0.151453 < 1$
3	0.03	$0.123593 < 1$
4	0.04	$0.108099 < 1$

Based on the sensitivity index, the value is -0.291791. This value shows that the change in the parameter value is inversely proportional to the change in the value of R_0. This means that if the value of the parameter is enlarged, it will contribute to a decrease in the value of R_0. This means that the vaccine is appropriate to suppress the spread of cholera.

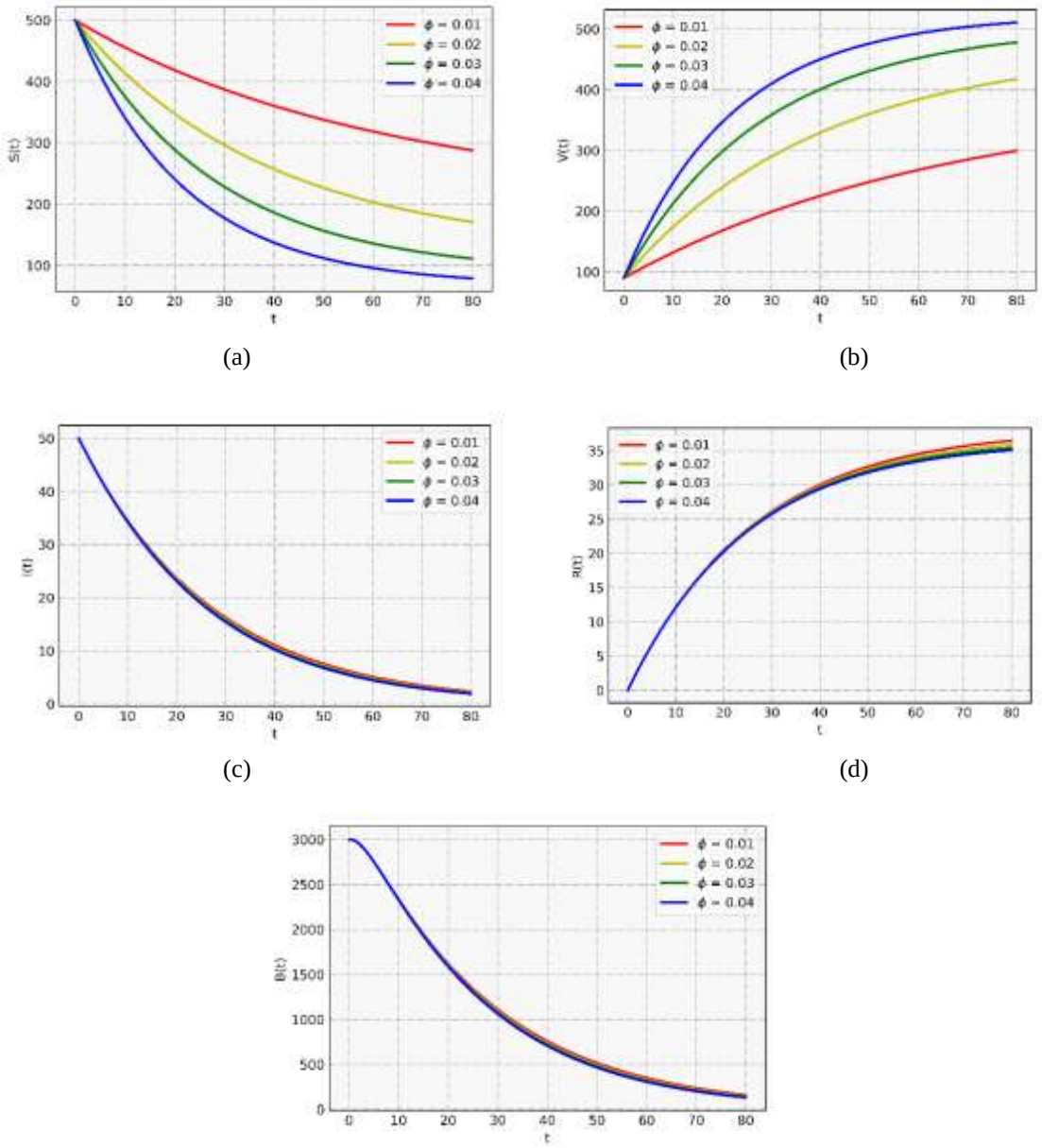


Figure 4. Simulation of vaccination rate that representative of: (a) susceptible population, (b) vaccinated population, (c) infected population, (d) recovered population, and (e) bacterial population

Figure 4 shows that changes in the value of the vaccination rate ϕ can affect population dynamics. If the vaccination rate is increased and the parameter values are constant or unchanged, it causes the number of vaccinated individual populations to increase. Meanwhile, the population of susceptible individuals, the population of infected individuals, the population of recovered individuals, and the population of bacteria decreased. This shows that by suppressing the rate of vaccination can reduce the number of infected individuals and the number of bacterial populations. Thus, it can be stated that increasing vaccination is a way that can be done to reduce the spread of cholera.

Population Dynamics with Variation of Vaccine Depletion Parameters

This simulation was carried out to show the effect of the vaccine shrinkage rate on the spread of cholera. Where if the value of is increased it will affect the increase in the value of R_0. Changes in the value of R_0 can be observed in **Table 4**.

Table 4. Simulation Result of the Variation of parameter η value R_0

Simulasi	η	$R_0 < 1$
1	0.005	$0.216327 < 1$
2	0.006	$0.236355 < 1$
3	0.007	$0.254035 < 1$
4	0.008	$0.269756 < 1$

Based on the sensitivity analysis, the value of 0.288628 was obtained. This value shows the change in the parameter value is directly proportional to the change in the value of R_0. This means that if the value of the parameter is enlarged, it will contribute to an increase in the value of R_0. This can be a consideration in making vaccines, the need for vaccines that can last a long time in the human body.

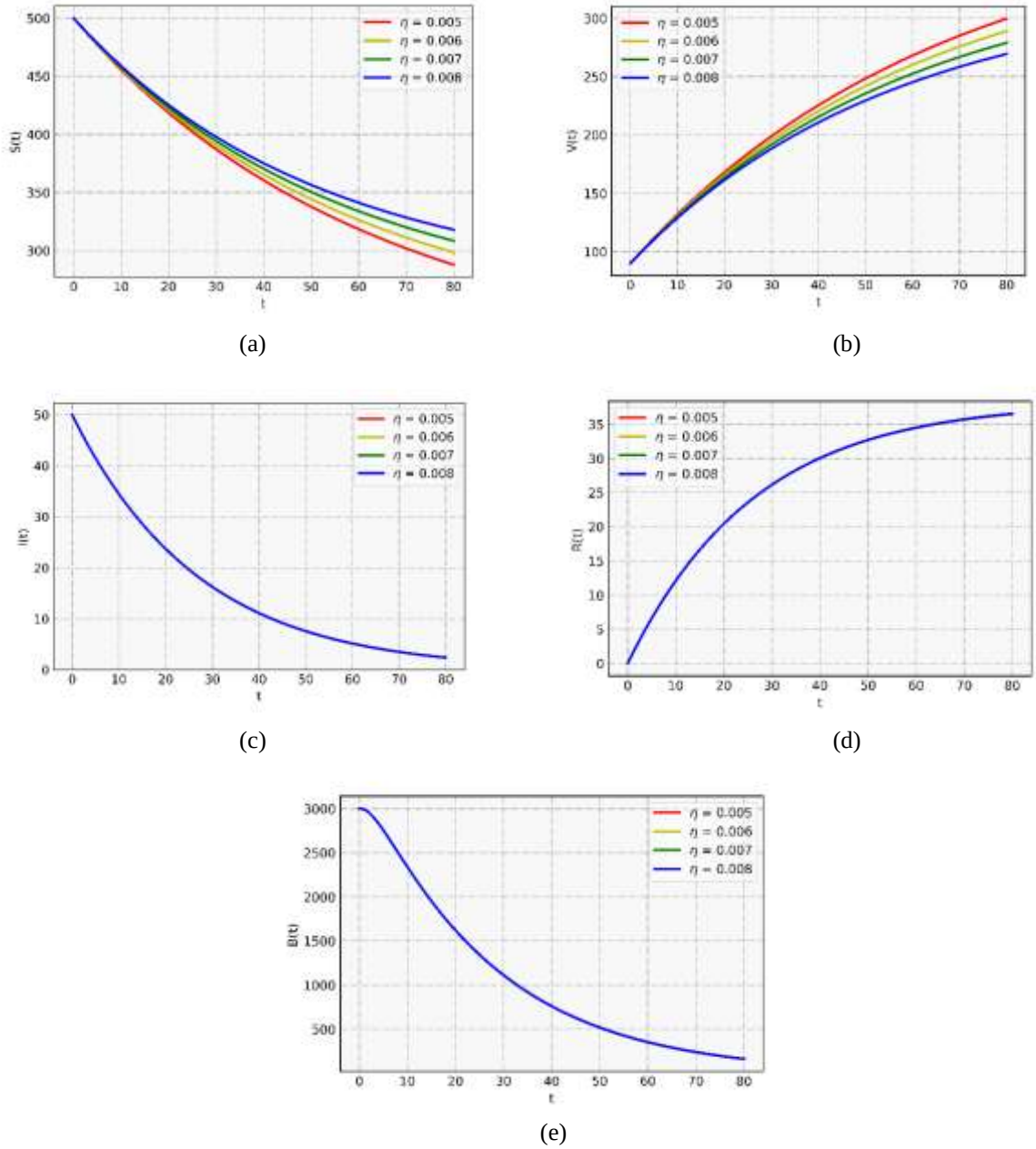


Figure 5. Simulation of vaccine depletion that representative of: (a) susceptible population, (b) vaccinated population, (c) infected population, (d) recovered population, and (e) bacterial population

Figure 5 shows that changes in the value of the vaccination shrinkage rate η can affect population dynamics. If the vaccination shrinkage rate is increased and the parameter values are constant or unchanged, it will cause the number of susceptible individuals to increase and the number of vaccinated individuals to decrease. This shows that vaccine shrinkage can potentially increase the occurrence of disease transmission.

Population Dynamics with Variation in Medication Rate

This simulation was conducted to show the effect of medication rate on the spread of cholera. Where if the value of is increased it will affect the increase in the value of R_0. Changes in the value of R_0. can be observed in **Table 5**.

Table 5. Simulation Result of the Variation of parameter ε value R_0

Simulasi	ε	$R_0 < 1$
1	0.025	$0.216327 < 1$
2	0.029	$0.19832 < 1$
3	0.033	$0.183081 < 1$
4	0.037	$0.170016 < 1$

Based on the sensitivity index, the value is -0.567475. This value shows that the change in the parameter value is inversely proportional to the change in the value of R_0. This means that if the value of the parameter ε is enlarged, it will contribute to a decrease in the value of R_0. It can be said that the provision of medication is appropriate to suppress the spread of cholera.

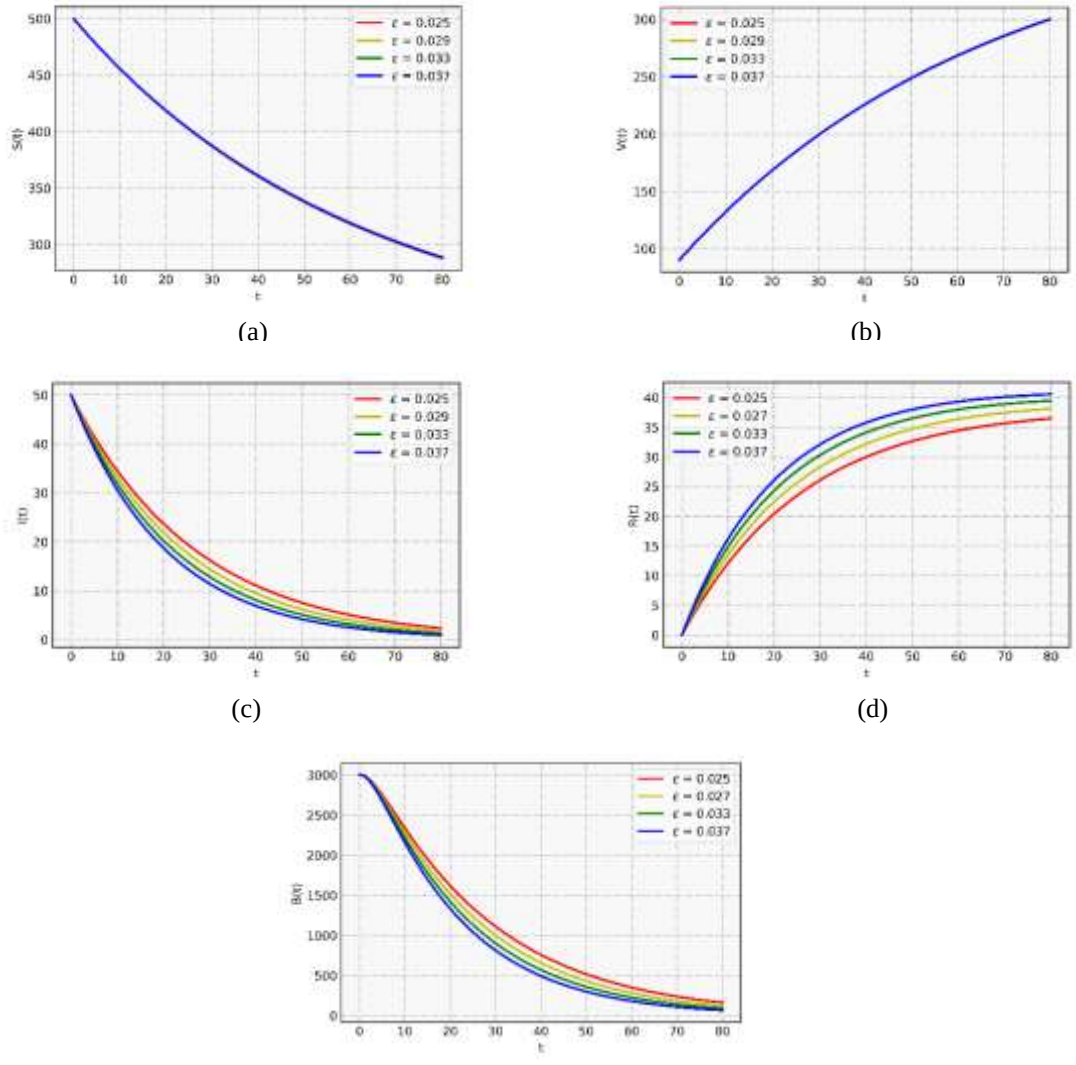


Figure 6. Simulation of medication rate that representative of: (a) susceptible population, (b) vaccinated population, (c) infected population, (d) recovered population, and (e) bacterial population

Figure 6 shows that changes in the value of medication rate can affect population dynamics. If the rate of medication is increased and the parameter values are constant or unchanged, it causes the number of recovered individual populations to increase. Meanwhile, the population of infected individuals and the population of bacteria decreased. This shows that reducing the rate of medication can reduce the number of

infected individuals and bacterial populations. Thus, it can be stated that increasing medication is an effective thing to reduce the spread of cholera.

4. CONCLUSIONS

Modification of the model in this study was carried out by adding medication and environmental sanitation parameters to the reference model so as to produce a model for the spread of cholera type SVIRB. The stability analysis of the mathematical model shows that there are two types of equilibrium points, namely the disease-free equilibrium point, T_1 and the endemic equilibrium point, T_2. The disease-free equilibrium point is locally asymptotically stable when $R_0 < 1$ and the endemic equilibrium point is locally asymptotically stable when $R_0 > 1$. The results of numerical simulations show that changes in the value of sensitive parameters, namely parameters A, β, k, ξ have a significant effect on basic reproduction numbers. By suppressing the rate of vaccination and the rate of medication, it can reduce the basic reproduction number. This means that suppression of vaccination rates and medication rates can suppress the transmission of cholera.

ACKNOWLEDGMENTS

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