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DYNAMIC ANALYSIS OF THE MATHEMATICAL MODEL OF THE SPREAD OF CHOLERA WITH VACCINATION STRATEGIES

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Abstract. *This research discusses the math model of spreading cholera disease with a mathematical model constructed by considering a vaccination strategy. In addition, there is a population of hyper infectious and less infectious bacteria, so the model of SVIR-$B_{hi}B_{li}$ type. The model is formed in fixed-point determination, basic reproductions numbers, analysis of the equilibrium point, and sensitivity analysis The equilibrium analysis produces two equilibrium points of disease-free equilibrium point is locally asymptotically stable if $R_0 < 1$ and endemic equilibrium points will be locally asymptotically stable if $R_0>1$. Furthermore, a numerical simulation that the increase in vaccination rate influences the decline in R_0 value while increased rate of vaccine depreciation can increase the value of R_0. In addition, sensitivity analysis shows that if the parameter ξ is enhanced while other contrast parameters will contribute to the increase in R_0 value, it can increase the rate of transmission of cholera disease. Whereas if the parameter μ_p is enhanced while other contrast parameters will contribute to the decrease in R_0 value, the dissemination of the disease can be pressed very significantly.*

Keywords: *cholera, vaccination, mathematical model, basic reproductive numbers, stability analysis.*

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1. INTRODUCTION

Cholera is an acute intestinal infection that occurs due to consuming food and water contaminated with Vibrio cholerae. This bacterium produces enterotoxins that cause excessive discharge of body fluids. Body fluids with the Vibrio cholerae bacteria have a high infection rate (hyper infectious). However, the infection will not last long, and the nature of the infection can decrease to less infectious (weak infection). It means that hyper infectious bacteria will only be digested if an infected individual uses the same toilet on the same day [1]. WHO has released data that there are 132.121 cases of cholera with 2,420 reported deaths [2-3].

The high number of reported cases shows that there needs to be a solution to control and prevent the spread of cholera. In mathematics, this problem can be studied from a modeling perspective. Mathematical modeling is a field of mathematics that simplifies problems in the real world into mathematical statements in the form of equations and inequalities so that the proper understanding is obtained [4]. Many mathematicians have mathematical modeling of cholera, which is still developing today.

The model of the spread of cholera discussed by Rahmi discusses the cholera model with the Hyper infectious type of Vibrio cholerae bacteria [5]. Tian involves a vaccination strategy by dividing the population into five compartments, namely the number of susceptible individuals (S), the number of individuals who are infected and can infect other individuals (I), the number of recovered individuals (R), the number of individuals vaccinated (V), and the concentration of toxigenic V. cholerae in water (B). In addition, Kokomo and Emvudu formulated an age-structured cholera model with vaccination and demographic movement [6]. Furthermore, Lin et al. investigated cholera transmission dynamics with hyperinfected vibrio by involving a control strategy [7]. A recent study conducted by Nuha and Resmawan discussed a mathematical model of the spread of cholera by considering the incubation period [8].

In this study, a new model is introduced, which refers to the Tian model [5] by modifying the concentration of toxigenic V. cholerae in water (B) into two sub-populations, namely the concentration of hyper infectious bacteria (B_{hi}) and the concentration of less infectious bacteria (B_{li}). B_{hi} is a class of bacterial population with a high infection rate, and B_{li} is a class of bacterial population with a low infection rate. The addition of the B_{hi} variable was to determine the spread of cholera from humans caused by using the same toilet simultaneously. It has a higher risk of transmission [5-9]. The addition of the B_{li} variable because Vibrio cholerae bacteria that have been in the environment within hours will become less infectious and have a lower infection rate [7]. Another modification was done by adding a mortality variable to hyper infectious bacteria (B_{hi}) using the water sanitation control method [10].

2. RESEARCH METHODS

This research used the literature study method with the following stages:

1. Determine the problem,
2. Formulate the problem,
3. Theoretical studies,
4. Analysis for problem-solving, and
5. Draw conclusions.

The problem was determined and formulated through a literature study of scientific references related to cholera disease and mathematical modeling. Theoretical studies were carried out by collecting library resources to support the research. Furthermore, the stages and analytical procedures in this study were carried out as follows:

1. Determination of assumptions,
2. Finding the equilibrium point,
3. Determine the value of R_0,
4. Conduct research using the Jacobian matrix,
5. Finding the eigenvalues,
6. Perform equilibrium point analysis, and
7. Provide biological interpretation to obtain conclusions.

3. RESULTS AND DISCUSSION

3.1. Mathematical Model

The assumptions used in this model were:

1. The total human population is not constant because the death and birth rates are not the same.
2. The population is closed, with no migration either into or out of the population.
3. Newborn individuals will enter the population susceptible to cholera.
4. The vaccinated susceptible population will enter the vaccinated population.
5. Individuals who have been vaccinated will experience an increase in body resistance. However, the vaccines available in the human body will continue to decrease. Therefore, the population can return to the susceptible population.
6. The vaccinated population can enter the infected population because not all vaccines function effectively. The vaccine is not effective in preventing infection.
7. Individuals can become infected with cholera by consuming food or drink contaminated with *V. cholerae* hyper infectious bacteria (caused by an infected individual with a susceptible individual) or V. less infectious bacteria (consuming contaminated food or drink without encountering an infected individual with a susceptible individual).
8. Some individuals in the infected population can enter the recovered population because they are recovering.
9. Cholera can cause death.
10. Every population experiences a natural death.
11. Total population can be written as N = S + V + I + R

The pattern of spread of cholera can be seen in the compartment diagram Figure 1.

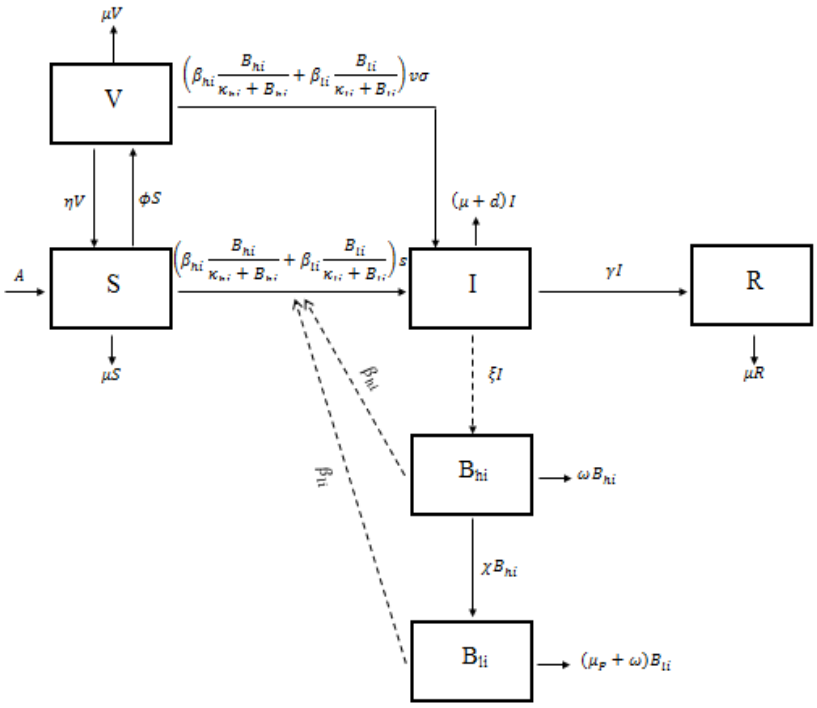


Figure 1. Compartment Diagram Model of the spread of cholera by the Hyper infectious type of *Vibrio cholerae* bacteria with Vaccination strategy

Based on Figure 4.1, the differential equation of the mathematical model is obtained as follows,

$$\frac{dS}{dt} = A + \eta\, V - \phi\, S - \left(\beta_{hi}\frac{B_{hi}}{K_{hi}+B_{hi}} + \beta_{li}\frac{B_{li}}{K_{li}+B_{li}}\right)S - \mu\, S$$

$$\frac{dV}{dt} = \phi\, S - \left(\beta_{hi}\frac{B_{hi}}{K_{hi}+B_{hi}} + \beta_{li}\frac{B_{li}}{K_{li}+B_{li}}\right)\sigma\, V - (\eta+\mu)V$$

$$\frac{dI}{dt} = \left(\beta_{hi}\frac{B_{hi}}{K_{hi}+B_{hi}} + \beta_{li}\frac{B_{li}}{K_{li}+B_{li}}\right)(S+\sigma V) - (\mu+\gamma+d)I \quad (1)$$
$$\frac{dR}{dt} = \gamma I - \mu R$$
$$\frac{dB_{hi}}{dt} = \xi I - (\chi+\omega)B_{hi}$$
$$\frac{dB_{li}}{dt} = \chi B_{hi} - (\mu_p+\omega)B_{li}$$

With the following parameters and variables used, S, V, I, R are the population of Susceptible-Vaccinated-Infected-Recovered individuals. B_{hi} and B_{li} are the population of Hyper infectious-less infectious bacteria. A is the birth rate, ϕ is the vaccination rate, η is the vaccine shrinkage rate, μ is the natural death rate, σ is the rate of decline in vaccine effectiveness, γ is the recovery rate, d is the death rate from cholera, ξ is the contribution rate of each infected person to the population of hyper infectious V. cholerae bacteria in aquatic environment. χ is the rate of bacterial transition from hyper infectious to less infectious, ω is the rate of bacterial death due to water sanitation, μ_p is the natural death rate for bacteria, β_{hi} is the rate of hyper infectious bacteria ingested by individual S from contaminated water, β_{li} is the rate of ingestion of hyper infectious bacteria by individual S from contaminated water, K_{hi} is the concentration of hyper infectious bacteria in the water that causes a 50 percent chance of getting cholera, and K_{li} is the concentration of less infectious bacteria in the water that causes a 50 percent chance of getting cholera. Next, we will find the equilibrium point of the system of equations (1) and analyze the stability properties of the equilibrium point.

3.2. Equilibrium Point and Basic Reproductive Number

Solving equation (1) obtains two equilibrium points, namely, the disease-free equilibrium point $E_0(S,V,I,R,B_{hi},B_{li}) = \left(\frac{A(\eta+\mu)}{\mu(\eta+\mu+\phi)} + \frac{A\phi}{\mu(\eta+\mu+\phi)}, 0,0,0,0\right)$ and Endemic Equilibrium Point

$$E_1(S,V,I,R,B_{hi},B_{li}) = (S^*,V^*,I^*,R^*,{B_{hi}}^*,{B_{li}}^*)$$

where

$$S^* = \frac{A+V^*\eta}{\frac{B_{hi}^*\,\beta_{hi}}{B_{hi}^*+K_{hi}} + \frac{B_{li}^*\beta_{li}}{B_{li}^*+K_{li}} + \mu + \phi} \qquad R^* = \frac{I^*\gamma}{\mu}$$
$$V^* = \frac{s\phi}{\eta + \mu\left(\frac{B_{hi}^*\beta_{hi}}{B_{hi}^*+K_{hi}} + \frac{B_{li}^*\beta_{li}}{B_{li}^*+K_{li}}\right)\sigma} \qquad B_{hi}^* = \frac{I^*\xi}{\chi+\omega}$$
$$I^* = \frac{\left(B_{hi}^*\beta_{hi}(B_{li}^*+K_{li}) + B_{li}^*\beta_{li}(B_{hi}^*+K_{hi})\right)(S^*+V^*\sigma)}{\left(B_{hi}^*+K_{hi}\right)\left(B_{li}^*+K_{li}\right)(d+\mu+\gamma)} \qquad B_{li}^* = \frac{B_{hi}^*\chi}{\mu_p+\omega}$$

The primary reproductive number is used to determine how big the potential spread of disease is. The primary reproduction number is determined by referring to equation (1) using *The next generation matrix* method, which is denoted by K [11-12]. The next generation matrix is defined as $K = FV^{-1}$, where the matrix F represents the matrix of the increasing number of individuals who are included in the population infected with cholera and matrix V represents the matrix of the increase in the population of infected individuals due to death and recovery from the disease so that R_0 value was obtained as follows

$$R_0 = \frac{A\xi(\eta+\mu+\sigma\phi)\left(K_{hi}\chi\beta_{li} + K_{li}\beta_{hi}\left(\mu_p+\omega\right)\right)}{K_{hi}K_{li}\mu(d+\mu+\gamma)(\eta+\mu+\phi)(\chi+\omega)\left(\mu_p+\omega\right)} \quad (2)$$

or $R_0 = R_1 + R_2$ with

$$R_1 = \frac{A\xi\chi\beta_{li}(\eta+\mu+\sigma\phi)}{K_{li}\mu(d+\mu+\gamma)(\eta+\mu+\phi)(\chi+\omega)\left(\mu_p+\omega\right)} \text{ and } R_2 = \frac{A\xi\beta_{hi}(\eta+\mu+\sigma\phi)}{K_{hi}\mu(d+\mu+\gamma)(\eta+\mu+\phi)(\chi+\omega)}$$

3.3. Stability Analysis

Theorem 1. *The disease-free equilibrium fixed point* (E_0) *is locally asymptotically stable if* $R_0 < 1$ *and unstable if* $R_0 > 1$.

Proof. The disease-free equilibrium point jacobian matrix is obtained by substituting the equilibrium point (E_0) into the jacobian matrix of equation (1), and is defined as follows

$$J(E_0) = \begin{bmatrix} A_{11} & A_{12} & 0 & 0 & A_{15} & A_{16} \\ A_{21} & A_{22} & 0 & 0 & A_{25} & A_{26} \\ 0 & 0 & A_{33} & 0 & A_{35} & A_{36} \\ 0 & 0 & A_{43} & A_{44} & 0 & 0 \\ 0 & 0 & A_{53} & 0 & A_{55} & 0 \\ 0 & 0 & 0 & 0 & A_{65} & A_{66} \end{bmatrix} \tag{3}$$

with

$A_{11} = -\mu - \phi$
$A_{12} = \eta$
$A_{15} = -\frac{A\beta_{hi}(\eta+\mu)}{K_{hi}\mu(\eta+\mu+\phi)}$
$A_{16} = -\frac{A\beta_{li}(\eta+\mu)}{K_{li}\mu(\eta+\mu+\phi)}$
$A_{21} = \phi$
$A_{22} = -\eta - \mu$
$A_{25} = -\frac{A\beta_{hi}\sigma\phi}{K_{hi}\mu(\eta+\mu+\phi)}$
$A_{26} = -\frac{A\beta_{li}\sigma\phi}{K_{li}\mu(\eta+\mu+\phi)}$
$A_{33} = -d - \mu - \gamma$
$A_{35} = \frac{A\beta_{hi}(\eta+\mu)}{K_{hi}\mu(\eta+\mu+\phi)} + \frac{A\beta_{hi}\sigma\phi}{K_{hi}\mu(\eta+\mu+\phi)}$
$A_{36} = \frac{A\beta_{li}(\eta+\mu)}{K_{li}\mu(\eta+\mu+\phi)} + \frac{A\beta_{li}\sigma\phi}{K_{li}\mu(\eta+\mu+\phi)}$
$A_{43} = \gamma$
$A_{44} = -\mu$
$A_{53} = \xi$
$A_{55} = -\chi - \omega$
$A_{65} = \chi$
$A_{66} = -\mu_p - \omega$

Next, find the eigenvalues of the Jacobian matrix in equation (3), based on the characteristic equation

$$\det(\lambda I - JE_0) = 0$$

generate equation

$$(A_{44} - \lambda)\Big(\big((A_{33} - \lambda)(A_{55} - \lambda) - A_{35}A_{53}\big)(A_{66} - \lambda) + A_{36}A_{53}A_{65}\Big)\big(A_{12}A_{21} + (A_{11} - \lambda)(\lambda - A_{22})\big) = 0 \tag{4}$$

Based on equation (4), six eigenvalues are obtained. One of them is

$$\lambda_1 = A_{22} = -\mu < 0$$

The other two eigenvalues are obtained from the equation

$$a_0\lambda^2 + a_1\lambda + a_2 = 0 \tag{5}$$

with

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

Since all parameters are positive and based on the nature of the roots of the quadratic equation in equation (5), we get

$$\lambda_2 + \lambda_3 = -\frac{a_1}{a_0} = -a_1 < 0 \tag{6}$$

$$\lambda_2\lambda_3 = \frac{a_2}{a_0} = a_2 > 0 \tag{7}$$

From equation (7) it is known that λ_2 and λ_3 have the same sign. Based on equation (6) it is known that $\lambda_2 < 0$ and $\lambda_3 < 0$.

Furthermore, the other three eigenvalues are obtained from the equation

$$a_0\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0 \tag{8}$$

where

$$a_0 = 1$$
$$a_1 = d + \chi + \mu + \mu_p + \gamma + 2\omega$$
$$a_2 = \Big((1 - R_2)(\chi + \omega) + (\mu_p + \omega)\Big)(d + \mu + \gamma) + (\mu_p + \omega)(x + \omega)$$
$$a_3 = (1 - R_0)(d + \mu + \gamma)(\mu_p + \omega)(\chi + \omega)$$

Before determining the eigenvalues, it is necessary to ensure that a_0, a_1, a_2, a_3 are positive. Since all parameter values are positive, a_0 and a_1 are definitely positive. Note that if $R_0 < 1$, so a_2 has positive value. Likewise, with a_3 has positive value if only the condition $1 - R_0 > 0$ which means $R_0 < 1$.

Next, 3 eigenvalues will be identified from equation (8), namely λ_4, λ_5 dan λ_6. Based on the nature of the cubic equations, the following system of equations is obtained:

$$\lambda_4 + \lambda_5 + \lambda_6 = -\frac{a_1}{a_0} = -a_1 < 0 \tag{9}$$
$$\lambda_4\lambda_5 + \lambda_4\lambda_6 + \lambda_5\lambda_6 = \frac{a_2}{a_0} = a_2 > 0 \tag{10}$$
$$\lambda_4\lambda_5\lambda_6 = -\frac{a_3}{a_0} = -a_3 < 0 \tag{11}$$

From equation (9), because all parameters are positive then

$$\lambda_4 + \lambda_5 + \lambda_6 < 0 \tag{12}$$

From the equation (10),

$$\lambda_4(\lambda_5 + \lambda_6) + \lambda_5\lambda_6 > 0 \tag{13}$$

From the equation (11),

$$\lambda_4\lambda_5\lambda_6 < 0 \tag{14}$$

The conditions in equation (12) are met if at least one of $\lambda_4, \lambda_5,$ and λ_6 is negative. For example, $\lambda_4 < 0$, then based on equations (13) and (14), λ_5 and λ_6 must be negative. Conversely, if $R_0 < 1$, so $a_3 < 0$ which results in one of $\lambda_4, \lambda_5,$ and λ_6 has positive value. Thus, the equilibrium point E_0 is locally asymptotically stable, if $R_0 < 1$ and unstable if $R_0 > 1$. □

Theorem 2. *Endemic fixed point E^* is locally asymptotically stable if $R_0 > 1$ and unstable if $R_0 < 1$.*

Proof. The proof of this theorem refers to the Castillo-Chaves theorem and Song [13]. For example, $\beta_{li} = \varphi$ is a bifurcation parameter that is chosen randomly as a threshold for changing stability properties. Define new variables $x_1, x_2, x_3, x_4, x_5,$ and x_6 which represent $S, V, I, R, B_{hi}, B_{li}$ respectively. Based on equation (1) a new system of equations is formed

$$f_1(x_1, x_2, x_3, x_4, x_5, x_6) = A + \eta\, x_2 - \phi\, x_1 - \left(\beta_{hi}\frac{x_5}{K_{hi} + x_5} + \beta_{li}\frac{x_6}{K_{li} + x_6}\right) x_1 - \mu\, x_1$$
$$f_1(x_1, x_2, x_3, x_4, x_5, x_6) = \phi\, x_1 - \left(\beta_{hi}\frac{x_5}{K_{hi} + x_5} + \beta_{li}\frac{x_6}{K_{li} + x_6}\right)\sigma\, x_2 - (\eta + \mu)x_2$$
$$f_1(x_1, x_2, x_3, x_4, x_5, x_6) = \left(\beta_{hi}\frac{x_5}{K_{hi} + x_5} + \beta_{li}\frac{x_6}{K_{li} + x_6}\right)(x_1 + \sigma\, x_2) - (\mu + \gamma + d)x_3 \tag{15}$$
$$f_1(x_1, x_2, x_3, x_4, x_5, x_6) = \gamma\, x_3 - \mu\, x_4$$
$$f_1(x_1, x_2, x_3, x_4, x_5, x_6) = \xi\, x_3 - (\chi + \omega)x_5$$
$$f_1(x_1, x_2, x_3, x_4, x_5, x_6) = \chi\, x_5 - (\mu_p + \omega)x_6$$

Note that, $R_0 = 1$ is equivalent to

$$\varphi^* = \frac{K_{li}\mu(d + \mu + \gamma)(\eta + \mu + \phi)(\chi + \omega)(\mu_p + \omega)(1 - R_2)}{Ax\xi(\eta + \mu + \sigma\phi)}$$

And the equilibrium point E_0 has five negative eigenvalues and one zero eigenvalue. The zero eigenvalues have a right eigenvector $(u_1, u_2, u_3, u_4, u_5, u_6)$, namely:

$$u_1 = -\frac{A((\eta+\mu)^2+\eta\sigma\phi)\left(K_{hi}\,\chi\,\beta_{li}+K_{li}\beta_{hi}(\mu_p+\omega)\right)}{K_{hi}K_{li}\mu^2(\eta+\mu+\phi)^2(\mu_p+\omega)}u_5 < 0$$

$$u_2 = -\frac{A\phi(\eta+\mu+\mu\sigma+\sigma\phi)\left(K_{hi}\,\chi\,\beta_{li}+K_{li}\beta_{hi}(\mu_p+\omega)\right)}{K_{hi}K_{li}\mu^2(\eta+\mu+\phi)^2(\mu_p+\omega)}u_5 < 0$$

$$u_3 = \frac{(\chi+\omega)}{\xi}u_5 > 0$$

$$u_4 = \frac{\gamma(\chi+\omega)}{\mu\xi}u_5 > 0$$

$u_5 > 0$ bebas

$$u_6 = \frac{\chi}{\mu_p+\omega}u_5 > 0$$

and the left eigenvector$(v_1, v, v_3, v_4, v_5, v_6)$ which is formulated as follows:

$$v_1 = \frac{\phi}{\mu+\phi}v_2 > 0$$

$v_2 > 0$ free

$$v_3 = \frac{A\xi\phi(\eta+\mu+\mu\sigma+\sigma\phi)\left(K_{hi}\,\chi\,\beta_{li}+K_{li}\,\beta_{hi}(\mu_p+\omega)\right)}{K_{hi}(\mu+\phi)K_{li}\mu(d+\mu+\gamma)(\eta+\mu+\phi)(x+\omega)(\mu_p+\omega)(R_0-1)}v2$$

$$v_4 = 0$$

$$v_5 = \frac{A\phi(\eta+\mu+\mu\sigma+\sigma\phi)\left(K_{hi}\;\chi\,\beta_{li}+K_{li}\beta_{hi}(\mu_p+\omega)\right)}{\mu(\mu+\phi)K_{hi}K_{li}(\eta+\mu+\phi)(x+\omega)(\mu_p+\omega)(R_0-1)}v2$$

$$v_6 = \frac{A\beta_{li}(d+\mu+\gamma\,)\phi(\eta+\mu+\mu\sigma+\sigma\phi)(x+\omega)}{(\mu+\phi)K_{li}\mu(d+\mu+\gamma)(\eta+\mu+\phi)(x+\omega)(\mu_p+\omega)(R_0-1)}v_2$$

Using the Castillo-Chavez Theorem and Song [13], it is defined

$$a = \sum_{k,i,j=1}^{6} v_k u_i u_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(E^0,\varphi^*)\; b = \sum_{k,i,j=1}^{6} v_k u_i \frac{\partial^2 f_k}{\partial x_i \partial \varphi}(E^0,\varphi^*) \tag{16}$$

Based on equations (15) and (16), the values of a and b are obtained as follows

$$a = \frac{A^2\xi\phi(\eta+\mu+\mu\sigma+\sigma\phi)((\eta+\mu)^2+\sigma(2\eta+\mu+\mu\sigma)\phi+\sigma^2\phi^2)\left(K_{hi}\,\chi\,\beta_{li}+K_{li}\beta_{hi}(\mu_p+\omega)\right)^3}{K_{hi}^3K_{li}^3\mu^3(d+\mu+\gamma)(\mu+\phi)(\eta+\mu+\phi)^3(x+\omega)(\mu_p+\omega)^3(1-R_0)}u_5^2v_2 \tag{17}$$

$$b = \frac{Ax\phi(\eta+\mu+\mu\sigma+\sigma\phi)}{(\mu+\phi)K_{li}\mu(\eta+\mu+\phi)(\mu_p+\omega)(R_0-1)}u_5v_2 \tag{18}$$

Based on equations (17) and (18), the values of a and b depend on the value of R_0. The condition $R_0 < 1$ will result $a > 0$ and $b < 0$ dan $0 < \varphi \ll 1$. This fulfills case 3 of the Castillo-Chaves and Song theorem [11] which states that E_0 is locally asymptotically stable and a positive fixed point E^* is unstable. On the other hand, the condition $R_0 > 1$ resulted in values $a < 0$ and $b > 0$ which fulfills case 4 of the Castillo-Chaves and Song theorem [11]. This shows that if φ changes from $\varphi < 0$ ($R_0 < 1$) to > 0 ($R_0 > 1$), it causes the fixed point E_0 change from stable to unstable. Besides, the endemic fixed point E^* changed from negative to positive and locally asymptotically stable. In other words, if $R_0 > 1$, the endemic point E^* is locally asymptotically stable. □

Stability properties are presented completely in Table 1.

Table 1. Table Point Stability Properties

Condition	Fixed Point Without Disease	Endemic Fixed Point
$R_0 < 1$	Exist and Locally asymptotically stable	Exist and Unstable
$R_0 > 1$	Exist and Unstable	Exist and Locally asymptotically stable

3.4. Numerical Simulation

Numerical simulations were carried out using python software to show the stability properties of each fixed point in the numerical system. Furthermore, the stability properties of each fixed point in the numerical system are shown. There is a numerical simulation to see how the population dynamics in the model are based on the parameter values in Table 2.

Table 2. Parameter value used

Parameter	$R_0 < 1$	$R_0 > 1$	Sources
χ	0.8	0.2	[1]
K_{li}	$2(10^6)$	10^6	[1]
A	0.1	0.1	[5]
ϕ	0.01	0.01	[5]
η	0.005	0.005	[5]
μ	$5.48(10^{-5})$	$5.48(10^{-5})$	[5]
σ	0.1	0.1	[5]
d	0.015	0.015	[5]
γ	0.0001	0.004	Assumption
ξ	3	10	Assumption
ω	0.5	0.4	Assumption
β_{hi}	0.0075	0.0075	[14]
β_{li}	0.00012	0.00012	[14]
μ_p	0.132	0.033	[15]
K_{hi}	$2.86(10^3)$	$1.43(10^3)$	[16]

Sensitivity Analysis

Sensitivity analysis was conducted to determine the basic reproduction rate parameters. The primary reproduction rate analyzed is in the condition of $R_0 > 1$ which shows how much infection will occur in the environment. Based on this, it is necessary to conduct a sensitivity analysis on these parameters to determine what efforts must be made to suppress the spread of cholera. One way is to look at the sensitivity index of R_0 using Chitnis formula formula [17-18]. The parameter values in Table 1 are input into the sensitivity analysis for the equation $C_p^{R_0}$. Next, the value R_0 of 3.86246 and the other sensitivity index values can be seen in Table 3.

Table 3. Sensitivity Index for $R_0 > 1$

Parameter	Index value	Parameter	Index value	Parameter	Index value
A	1	σ	0.16	χ	-0.33
ξ	1	γ	-0.20	μ_p	-0.08
ϕ	-0.49	d	-0.78	K_{hi}	-0.99
η	0.49	ω	-0.66	K_{li}	-0.10
μ	-0.99	β_{hi}	0.99		

The sensitivity index in Table 3 has a sensitivity index value R_0 that has a positive and a negative values and each parameter value has a varying effect on R_0. A positive value indicates that if the parameter value is increased (decreased) while the other parameter values are constant, it will contribute to an increase (decrease) in the basic reproduction rate. For example, the value of the contribution rate parameter of each infected person to the population of Hyper infectious bacteria in an aquatic environment is denoted by ξ. It has a positive sensitivity index. This indicates that if the value of ξ is increased, the value of R_0 will also increase. On the other hand, a negative value indicates that if the parameter value is increased (decreased) while other parameters are held constant, it will contribute to a decrease (increase) in the basic reproduction number. Sensitivity analysis shows that the most sensitive parameter to changes in the value of R_0 is the birth rate and the contribution rate of each infected person to the population of V. Cholers hyper infectious bacteria in the aquatic environment. It means that an increase in the value of R_0 will increase in the bacterial population.

Population Dynamics

Population dynamics of the spread of cholera with a vaccination strategy will be observed under the following conditions: $R_0 < 1$ and $R_0 > 1$. The initial value used is $S(0) = 500,\ V(0) = 0,\ I(0) = 350,\ R(0) = 0,\ B_{hi}(0) = 200,\ B_{li} = 100$.

Equation (1) has one disease-free equilibrium point. The equilibrium point is obtained by substituting equation (1) into the parameters in Table 1 with the value of $R_0 = 0{,}293076$ and the equilibrium point is $E_0 = (612{,}701 \quad 1212{,}12 \quad 0 \quad 0 \quad 0 \quad 0)$. The population dynamics for $R_0 < 1$ can be seen in Figure 2.

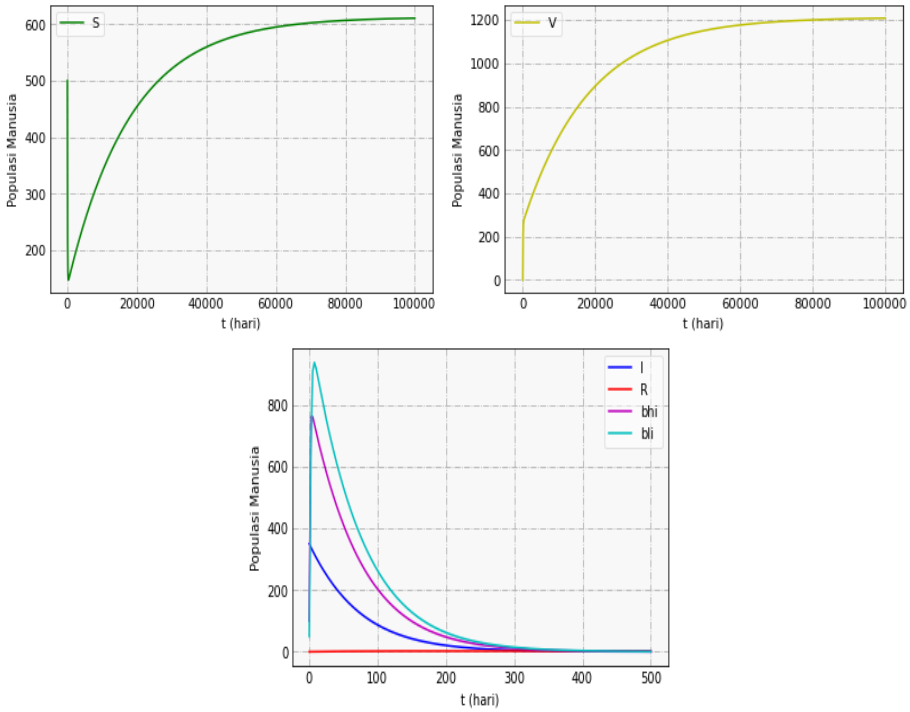
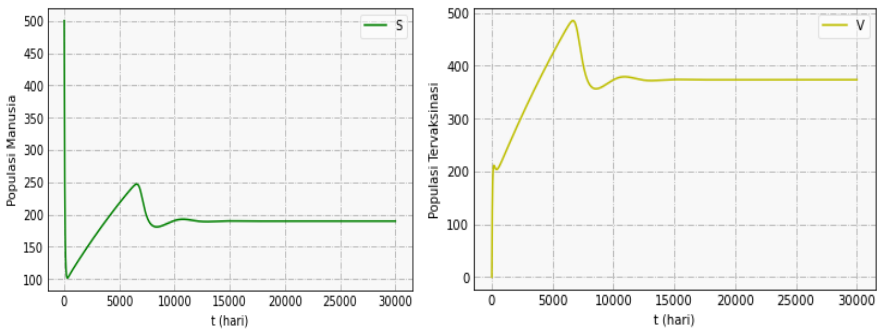


Figure 2. Population Dynamics for $R_0 < 1$

Figure 2 shows that each population is stable towards a disease-free equilibrium point. The susceptible population experienced a decrease in population from the initial value = 1000 down to a stable condition around S = 612 people. Meanwhile, for the individual population that has been vaccinated, the population has increased from the initial value to a stable point at V=1,212 people. Meanwhile, for the infected population, the population recovered, and the bacterial population decreased from the initial point until it reached a stable point $I = R = B_{hi} = B_{li} = 0$.

Then, the value of $R_0 > 1$ with the basic reproduction number $R_0 = 3;\ 36681$ was found. The followings are equilibrium points $E_1 = (189{,}866 \quad 373{,}367 \quad 3{,}62821 \quad 264{,}833 \quad 60{,}4702 \quad 27{,}9308)$. Thus, the human population for the condition $R_0 > 1$ can be seen in Figure 3.



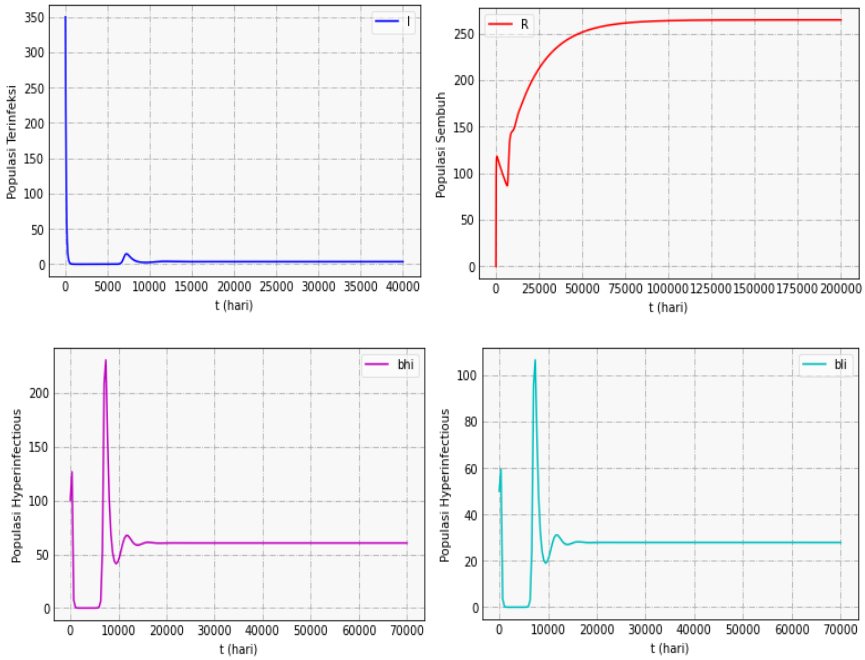
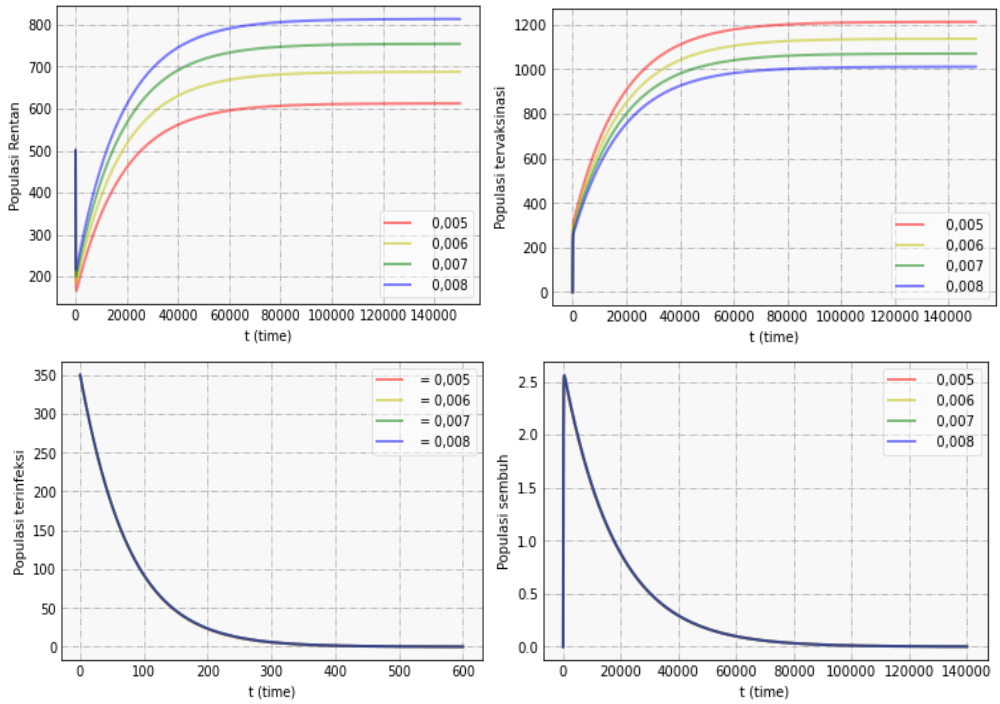


Figure 3. Population Dynamics for $R_0 > 1$

Figure 3 shows that each population at one time is not immediately stable but still fluctuates. At a particular time, the population will experience an increase or decrease depending on the factors that influence it. Until a specific time (t), it will be stable. It shows that each population is approaching the endemic equilibrium point. The population susceptible to the spread of cholera has decreased until it reaches a stable point when S = 189,866 or about 190 people and (vaccinated population) V = 373,367 or about 373 people. The population recovered from cholera was stable at R=264,833 or about 265 people, for infected pollutant I = 3.62821 or about 4 people, for the population of bacteria B_{hi} = 60.4702 and the population of less infectious bacteria B_{li} = 27.9308.

Based on the sensitivity analysis, the value of η = 0.49367 is obtained. This value shows that 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. It can be a consideration in making vaccines. Vaccines that can last a long time in the human body are needed. Figure 4 shows the shrinkage rate of vaccination.



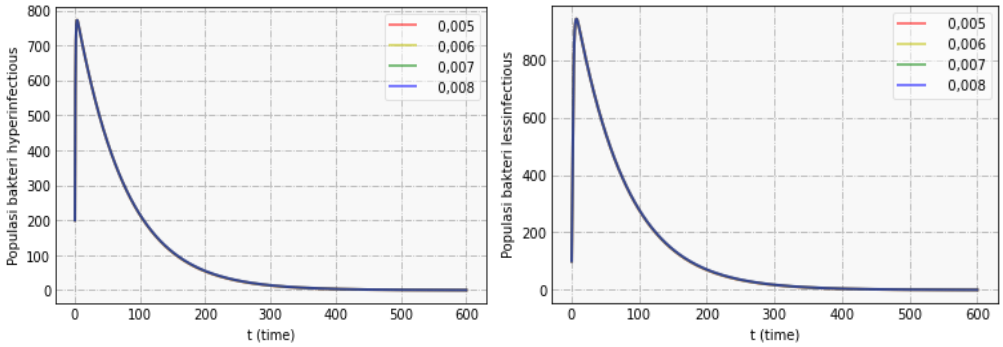


Figure 4. Simulation of Vaccine Depreciation Rate on Population Dynamics $R_0 < 1$

In Figure 4, it can be seen that the value of the vaccine shrinkage parameter causes the population of susceptible individuals to increase and causes the population of infected individuals to decrease. It shows that vaccine shrinkage can increase the occurrence of disease transmission so that the disease is difficult to control. In addition, vaccine shrinkage can also accelerate the increase in the number of susceptible, infected, and hyper infectious bacteria and less infectious bacteria.

Based on the sensitivity analysis, the value of ϕ = -0.49908 is obtained. This value shows that the change in the parameter value is inversely proportional to the change in the value of R_0. It means that if the parameter value is enlarged, it will contribute to a decrease in the value of R_0. This means that giving the vaccine is right to suppress the spread of cholera.

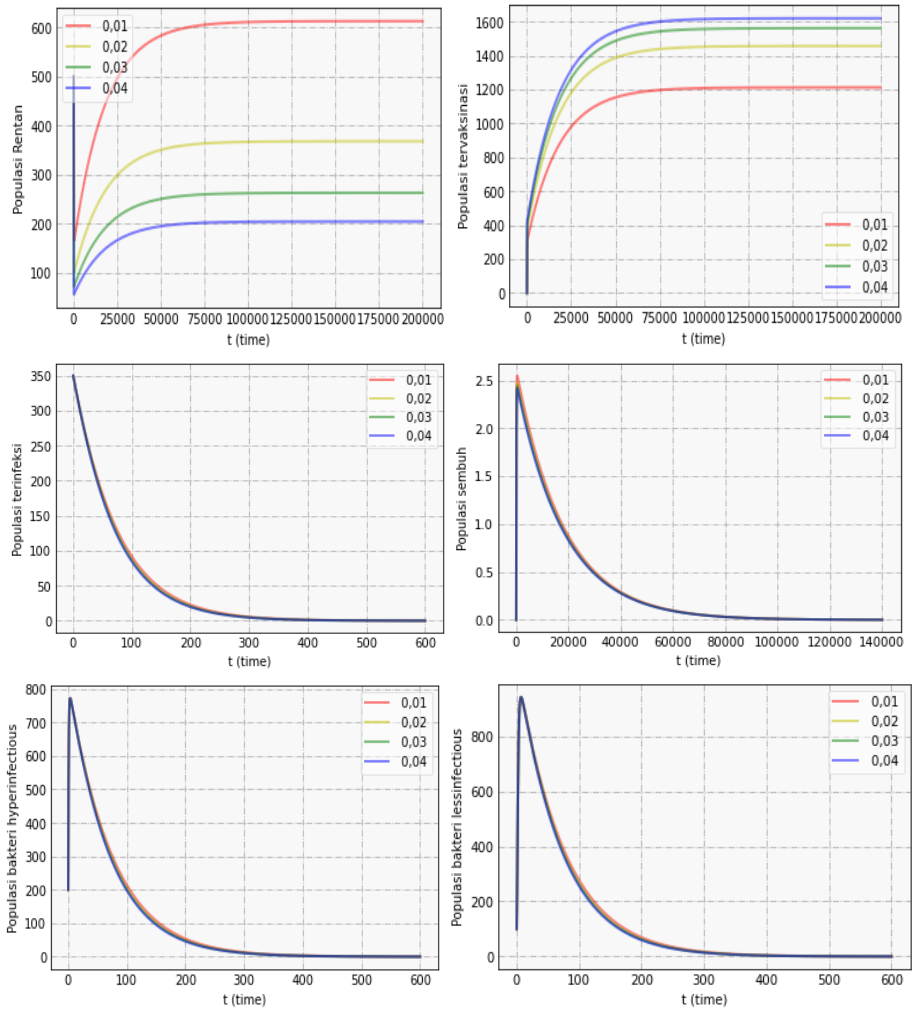


Figure 5. Vaccination rates on population dynamics $R_0 < 1$

Figure 5 shows that increasing vaccination can reduce the number of ranged individuals and increase the infected and cured individual's population. In addition, vaccination also slows the increase in the number of infected populations, populations of hyper infectious bacteria, and populations of less infectious bacteria.

Thus, it can be stated that increasing vaccine administration is a way that can be done to reduce the spread of cholera disease.

4. CONCLUSIONS

The cholera spread model has two equilibrium points, namely the disease-free equilibrium point and the endemic equilibrium point. The disease-free equilibrium point is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$. The endemic equilibrium point is locally asymptotically stable if $R_0 > 1$ and unstable if $R_0 < 1$. Sensitivity analysis showed that the most sensitive parameter affecting the transmission of cholera was the contribution rate of each infected person to the population of *V. Cholers* hyper infectious bacteria in the aquatic environment. Furthermore, the numerical simulation results show that an increase in the vaccination rate can reduce the basic reproduction number, which means that an increase in vaccination can reduce the spread of cholera.

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