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Mathematical model of cholera spread based on SIR: Optimal control

Noer Hidayati [1], **Eminugroho Ratna Sari** [2*], **Nur Hadi Waryanto** [2]
[1] MTsS Arul Kumer, Mathematics, Aceh, Indonesia
[2] Department of Mathematics Education, Universitas Negeri Yogyakarta, Indonesia
* Corresponding Author. E-mail: eminugroho@uny.ac.id

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ABSTRACT

The bacterium Vibrio cholerae is the cause of cholera. Cholera is spread through the feces of an infected individual in a population. From a mathematical point of view, this problem can be brought into a mathematical model in the form of Susceptible-Infected-Recovered (SIR), which considers the birth rate. Because outbreaks that occur easily spread if not treated immediately, it is necessary to control the susceptible individual population by vaccination. The vaccine used is Oral Vibrio cholera. For this reason, the purposes of this study were to establish a model for the spread of cholera without vaccination, analyze the stability of the model around the equilibrium point, form a model for the spread of cholera with vaccination control, and describe the simulation results of numerical model completion. Based on the analysis of the stability of the equilibrium point of the model, it indicates that if the contact rate is smaller than the sum of the birth rate and the recovery rate, cholera will disappear over time. If the contact rate is greater than the sum of the birth rate and the recovery rate, then cholera is still present, or in other words, the disease can still spread. Because the spread is endemic, optimal control of the population of susceptible individuals is needed, in this case, control by vaccination, so that the population of susceptible individuals becomes minimum and the population of recovered individuals increases.

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INTRODUCTION

Feces (human waste) that are contaminated with Vibrio cholerae bacteria are mostly found on water surfaces. The bacteria can transmit through food, such as uncleaned vegetables already fertilized with infected individual's feces through consumption. Therefore, the transmission of these bacteria can be through water, food, or poor environmental sanitation because they are contaminated with infected individual's feces (Cabral, 2010). Vibrio cholerae can attack gastroenteritis, then multiply. Vibrio cholerae also causes damage to the host characterizing their virulence (Finkelstein, 1996). The disease caused by the bacteria Vibrio cholera is called cholera. Individuals infected with cholera mostly show no symptoms, but their feces are contagious (World Health Organization (WHO), 2017). Cholera is an acute diarrheal disease caused by intestinal infection due to the bacterium Vibrio cholera. The disease is easily spread if not treated soon.

Africa was the continent with the most countries contracting this disease. According to the data obtained, there are about 3-5 million cases of cholera, and 100-120 thousand of them die every year in the world (World Bank, 1994). Moreover, in the 69 cholera-endemic countries studied, there were 2,9 million cases of cholera, even 95.000 annual deaths, with the highest cases in Sub-Saharan Africa (Ali et al., 2015). Even cholera cases from December 2020 to January 2021 in Nigeria, which means that during the COVID-19 pandemic, there were 266 cases with a case fatality rate (CFR) of 12.0% (World Health Organization Africa Office Regional, 2021). Due to the many cases of cholera, it is necessary to have prevention efforts. One of the recommendations is a vaccination (World Health Organization (WHO), 2012).

Furthermore, many researchers have contributed to the health sector by analyzing the spread of disease behavior through a model. Kermack and McKendrick were the first to introduce the SIR mathematical model in 1927 (Rodrigues, 2016). The model is used to observe the spread of infectious diseases in a population. The population in the SIR model is divided into three classes, namely Susceptible (S) to describe a healthy and susceptible population, Infected (I) to declare a population infected and able to recover, and Recovered (R) to declare a recovered population and immune to the disease. One that is developed from a mathematical model of disease spread by adding a compartment exposed (E), which is used to denote a subpopulation that has been infected but has not spread the disease. The SEIR model's application is to present the spread of the flu virus (Sari, 2012). Usually, the time it takes from the first infection to the appearance of symptoms for cholera is very short, ranging from 12 hours to 5 days (Azman et al., 2013). Therefore, compartment E can be neglected, or in other words, a more suitable model for cholera is SIR.

Concern about cholera spread in mathematical sight about the analysis of the stability of the cholera epidemic model through basic reproductive numbers (Emvudu & Kokomo, 2012). Another study examined the stability analysis of cholera with bacterial growth and its movement through basic reproduction numbers (Wang & Wang, 2015). A mathematical model of a cholera spread was analyzed using monotone dynamical systems, which has its limitation; it should have dynamical system monotonicity (Tian et al., 2010). Mathematical modeling of cholera in the specific community also has been done by some researchers (Andam et al., 2015; Liao & Wang, 2011; Mukandavire et al., 2013). The model discusses both compartments to show the interaction between human and bacterial populations (Hntsa & Kahsay, 2020; Panja, 2019).

Oral Cholera Vaccine (OVC) was recommended for the cholera vaccine caused by Vibrio cholerae bacteria (World Health Organization (WHO), 2019). Meanwhile, research has been done on vaccination from mathematical sight analyzed the cholera model's endemic equilibrium point based on the SIR model and modified it with various control strategies viewed from basic reproduction numbers (Tian et al., 2013). A control strategy with a basic reproduction number has also been carried out, followed by numerical simulations for strong, weak, and no prevention (Ayoade et al., 2018).

According to several of the studies described, different from existing research, this research will formulate cholera spread through the SIR model. We focus on the human population and describe its dynamical behavior. Through this model, stability will be analyzed around the equilibrium point of the model. In addition, this study obtains a model of the spread of cholera by vaccination given to susceptible classes so that after being controlled, the recovered class increases. Analytically the optimal control is solved by Pontryagin Minimum Principal (PMP). The completion of the model will be simulated.

METHODS

This study describes health status from the mathematical side, knowing the causes, prevention efforts, and efforts to control the disease, then this research is included in the epidemiology research (Woodward, 2013). This research was carried out with a literature study and did not treat the subject directly; this type of research is observational.

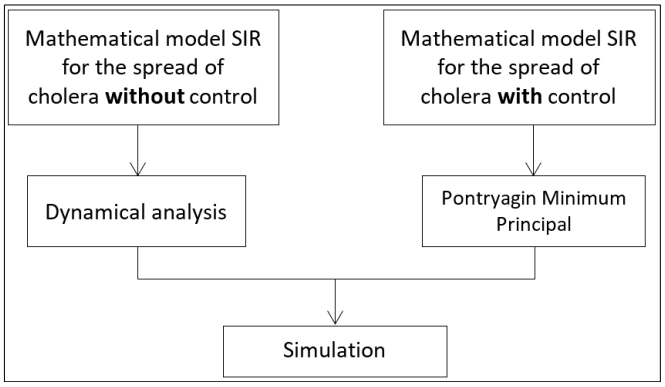


Figure 1. Flow chart of the study of the spread of cholera

In this section, we sketch the procedures for achieving the research aims. In the first part, a mathematical model of the spread of cholera without vaccination is developed. Based on the model, we determine the equili-

brium point and analyze its stability. In the other part, we developed a new model with vaccination control. Analysis of the control problem uses the Pontryagin Minimum Principal (PMP). In the last, we describe numerically to confirm the analytical results.

Figure 1 shows the flow of the studies in this article. There are two major groups discussed, namely models of cholera spread without control and models with control. Furthermore, both are illustrated numerically to strengthen the results analytically.

Assumptions of the Mathematical Model without Control

Cholera transmission occurs through contact with sufferers through food, water, and the environment contaminated with individual feces infected with Vibrio cholerae. The spread of this disease will be analyzed through the SIR model. In this case, the population is divided into three classes, namely susceptible class (S) indicating a healthy individual population and susceptible to cholera, the infected class (I) indicating the population of individuals infected with cholera and able to recover, and the recovered class (R) indicating the population of individuals recovering from cholera and immune to the disease. We define a population of susceptible individual class at time t as $S(t)$, a population of infected individual class at time t as $I(t)$, and a population of recovered individual class at time t as $R(t)$. The followings are the assumptions in our model. *First*, fixed population. *Second*, deaths that occur in each of the susceptible, infected, or recovered classes are only natural deaths. *Third*, the rate of birth and death are the same. The population that dies from each class is proportional to the population in each of the classes. If μ states the rate of death, $\mu S(t)$ states the rate of death in class S at time t, $\mu I(t)$ states the rate of death in class I at time t, and $\mu R(t)$ states the rate of death in class R at time t. *Fourth*, the susceptible individual class population is infected with cholera disease if contact occurs through feces of the infected individual class population. *Fifth*, the recovered individual population from cholera is not susceptible. *Sixth*, population born in susceptible, infected, and recovered individual classes will be susceptible to choleric disease entering the susceptible class. *Seventh*, the population of individuals infected with cholera can recover from the disease with a recovery rate γ so that the rate of the population of the infected individuals who recover during time t is $\gamma I(t)$.

Stability Analysis

In the second part, we determine its equilibrium points and analyze the stability. The equilibrium point will be determined by taking $\frac{dS}{dt}=\frac{dI}{dt}=\frac{dR}{dt}=0$. Since our model is a nonlinear system of ordinary differential equations, it is not accessible to study the stability analysis. Then linearization using the Jacobian matrix can help our discussion as long as the equilibrium points are hyperbolic – usually, consideration of stability analysis through the value of basic reproduction number. One method to determine this value is by next generating matrix.

Furthermore, we can adopt the Routh Hurwitz criterion to analyze the stability around the equilibrium point. Let

$$r(\lambda)=a_n\lambda^n+a_{n-1}\lambda^{n-1}+\ldots+a_1\lambda+a_0 \tag{1}$$

where $a_i\neq 0$ and $i=0,1,\ldots,n$. Routh Hurwitz criteria are used to analyze stability directly without determining the roots of equation (1). The coefficients of equation (1) are arranged as follows.

$$\begin{matrix} a_n & a_{n-2} & a_{n-4} & \cdots \\ a_{n-1} & a_{n-3} & a_{n-5} & \cdots \\ b_{n-2} & b_{n-4} & b_{n-6} & \cdots \\ \vdots & \vdots & \vdots & \end{matrix} \tag{2}$$

where $b_{n-2}=\frac{a_{n-1}a_{n-2}-a_na_{n-3}}{a_{n-1}}$, $b_{n-4}=\frac{a_{n-1}a_{n-4}-a_na_{n-5}}{a_{n-1}},\ldots$.

The iteration stops when the last row (2) is zero. If the first column in the arrangement (2) is all positive or all negative, then the real part of the polynomial (1) is negative (Niu & Wang, 2008; Olsder & van der Woude, 2004).

Assumptions of the Mathematical Model using Control

After the spread of the disease becomes endemic, it is necessary to control cholera by vaccination in case of cholera. Furthermore, it is assumed that the vaccine $u(t)$ is given after an outbreak, meaning immediate control by vaccination. Vaccines $u(t)$ are only given to the individual class S. We used the Pontryagin Minimum Principal (PMP) to analyze the optimal control following some articles (e.g., Mahmudah et al., 2013; Njagarah & Nyabadza, 2015; Sari et al., 2017).

RESULTS

This section discussed the SIR model formulation to cholera without control, analyzed the stability to its equilibrium points, developed a model with control, and described the results numerically.

SIR Model Formulation without Control

As previously explained, based on the problem of the cholera spread and the assumptions given, a transfer diagram can be drawn in Figure 2.

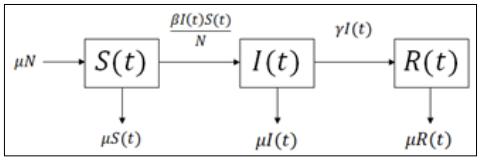


Figure 2. Transfer diagram to spread of cholera

Based on Figure 2, the SIR model obtained is shown in the following nonlinear system of ordinary differential equations.

$$\begin{aligned}\frac{dS(t)}{dt} &= \mu N - \mu S(t) - \frac{\beta I(t)S(t)}{N}\\ \frac{dI(t)}{dt} &= \frac{\beta S(t)I(t)}{N} - \gamma I(t) - \mu I(t)\\ \frac{dR(t)}{dt} &= \gamma I(t) - \mu R(t)\end{aligned} \tag{3}$$

where $S(0) = S_0 \geq 0$, $I(0) = I_0 \geq 0$, $R(0) = R_0 \geq 0$, and $S(t) + I(t) + R(t) = N$. System of ordinary differential equation (3) is a mathematical model of spreading cholera. The following section will be discussed the equilibrium points of the model (3).

Equilibrium Points

There are two kinds of equilibrium points, namely disease-free and endemic equilibrium point, which are expressed in Lemma 1 and Lemma 2.

Lemma 1. If $I(t) = 0$, then system (3) has equilibrium point $E_0 = (S_0, I_0, R_0) = (N, 0, 0)$ called disease-free equilibrium point.

Proof. For each equation in system (3) which taking in the right-hand side is zero, we obtain from the second equation

$$\frac{\beta S(t)I(t)}{N} - \gamma I(t) - \mu I(t) = 0$$

or

$$\left[\frac{\beta S(t)}{N} - (\gamma + \mu)\right] I(t) = 0. \tag{4}$$

From equation (4), we have $I(t) = 0$ or

$$S(t) = \frac{N}{\beta}(\gamma + \mu). \tag{5}$$

If $I(t)=0$ is substituted to the third equation in system (3) which has zero in the right-hand side, then we obtain $R(t)=0$. If $I(t)=0$ is substituted to the first equation in system (3) which has zero in the right-hand side, then we obtain $S(t)=N$. In other word, we have an equilibrium point $(N,0,0)$. □

Lemma 2. If $I(t)\neq 0$, then system (3) has equilibrium point

$$E_1=(S_1,I_1,R_1)=\left(\frac{(\gamma+\mu)N}{\beta},\mu N\left[\frac{1}{(\gamma+\mu)}-\frac{1}{\beta}\right],\gamma N\left[\frac{1}{(\gamma+\mu)}-\frac{1}{\beta}\right]\right), \quad (6)$$

which is called an endemic equilibrium point.

Proof. Notice for equation (4) in this case. If this equation is substituted with the first and third equation in system (3), we have an endemic equilibrium point (6). □

Basic Reproduction Number

Basic reproduction numbers, $\hat{R}_0$, represent the number of cases of secondary infection in the population, then it sees the presence or reduction of infection at the disease-free equilibrium point (van den Driessche, 2017). Next $\hat{R}_0$ from system (3) will be sought using the infected class equation, and the following is defined

$$M(I,S)=\frac{\beta S(t)I(t)}{N}$$

and

$$V(I,S)=(\gamma+\mu)I(t).$$

So, linearization result for $M(I,S)$ and $V(I,S)$ in E_0 is β and $(\gamma+\mu)$, respectively. Then, what is obtained is $\frac{\beta}{\gamma+\mu}$, as next generation matrix, so that the basic reproduction number is obtained from the largest eigenvalue of the matrix. Furthermore, it is obtained

$$\hat{R}_0=\frac{\beta}{(\gamma+\mu)}. \quad (7)$$

Local Stability of Disease-Free Equilibrium Point

From Lemma 1, we have a disease-free equilibrium point. Now, analysis of stability around the disease-free equilibrium point E_0 is stated in the Theorem 1.

Theorem 1. If $\hat{R}_0<1$, then E_0 is stable asymptotic local. If $\hat{R}_0>1$, then E_0 is not stable.

Proof. The Jacobian matrix of E_0 from system (3) is notated by $J(E_0)$. The eigenvalue λ can be obtained if $|J(E_0)-\lambda I|=0$. Then we have

$$\left\|\begin{bmatrix}-\mu & -\beta & 0\\ 0 & \beta-\gamma-\mu & 0\\ 0 & \gamma & -\mu\end{bmatrix}-\begin{bmatrix}\lambda & 0 & 0\\ 0 & \lambda & 0\\ 0 & 0 & \lambda\end{bmatrix}\right\|=0 \text{ or } \begin{vmatrix}-\mu-\lambda & -\beta & 0\\ 0 & \beta-\gamma-\mu-\lambda & 0\\ 0 & \gamma & -\mu-\lambda\end{vmatrix}=0$$

and we have

$$(-\mu-\lambda)(\beta-\gamma-\mu-\lambda)(-\mu-\lambda)=0$$

or $\lambda_1=\lambda_2=-\mu$, meanwhile we can be modified for the third λ as

$$\begin{aligned}\lambda_3&=\beta-\gamma-\mu\\&=(\gamma+\mu)\left[\frac{\beta}{(\gamma+\mu)}-1\right]\\&=(\gamma+\mu)\left(\hat{R}_0-1\right)\end{aligned}$$

Two possibilities for λ_3. *First*, if $\hat{R}_0 < 1$, then λ_3 is negative. Because $\lambda_1, \lambda_2 < 0$ is obtained, then all eigenvalues are negative. Therefore, it can be concluded $E_0 = (S_0, I_0, R_0) = (N, 0, 0)$ is stable asymptotic local. *Second*, if $\hat{R}_0 > 1$, then λ_3 is positive, so there is a positive eigenvalue. Therefore, E_0 is not stable. □

Local Stability of Endemic Equilibrium Point

The endemic equilibrium point is obtained based on Lemma 2 that is $E_1 = (S_1, I_1, R_1)$. The following is the Theorem 2 about the local stability of this endemic equilibrium point.

Theorem 2. If $\hat{R}_0 > 1$, then E_1 is stable asymptotic local.

Proof. Jacobian matrix in E_1 is denotated by $J(E_1)$. To obtain the eigenvalue, λ, then it should be solved by $|J(E_1) - \lambda I| = 0$. Then

$$\left| \begin{bmatrix} -\mu - \frac{\beta I(t)}{N} & -\frac{\beta S(t)}{N} & 0 \\ \frac{\beta I(t)}{N} & \frac{\beta S(t)}{N} - \gamma - \mu & 0 \\ 0 & \gamma & -\mu \end{bmatrix} - \begin{bmatrix} \lambda & 0 & 0 \\ 0 & \lambda & 0 \\ 0 & 0 & \lambda \end{bmatrix} \right| = 0$$

or

$$\begin{vmatrix} -\mu - \frac{\beta I(t)}{N} - \lambda & -\frac{\beta S(t)}{N} & 0 \\ \frac{\beta I(t)}{N} & \frac{\beta S(t)}{N} - \gamma - \mu - \lambda & 0 \\ 0 & \gamma & -\mu - \lambda \end{vmatrix} = 0.$$

We obtained the characteristic equation

$$\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0,$$

where

$a_1 = \gamma\mu^2\left(\hat{R}_0 - 1\right) + \mu^3\left(\hat{R}_0 - 1\right)$

$a_2 = \mu^2(2\hat{R}_0 - 1) + \gamma\mu(\hat{R}_0 - 1)$, and

$a_3 = \mu + \frac{\beta\mu}{(\gamma + \mu)}$.

Furthermore, the stability analysis of the equilibrium point can be conducted by using the Routh Hurwitz criteria (Niu & Wang, 2008) through the coefficient of the characteristic equation. Routh Hurwitz table is obtained as follows.

$$\begin{matrix} 1 & a_2 \\ a_3 & a_1 \\ b_1 & 0 \\ c_1 & 0 \end{matrix}$$

According to Routh Hurwitz's table, the first column must be all positive or all negative. Meanwhile, a_3 is positive, so b_1 and c_1 must be positive, where $b_1 = \frac{a_3a_2 - a_1}{a_3}$ and $c_1 = \frac{b_1a_1}{b_1} = a_1$. In order that b_1 is positive, then $a_3a_2 > a_1$ should be satisfied due to $a_3 > 0$. Notice that if $\hat{R}_0 > 1$, then what is obtained is

$$
\begin{aligned}
a_2a_3 &= \mu\left[1+\frac{\beta}{(\gamma+\mu)}\right]\left[-\mu^2\left[1-\frac{2\beta}{(\gamma+\mu)}\right]+\gamma\mu\left[\frac{\beta}{(\gamma+\mu)}-1\right]\right] \\
&= \mu^3\left[1+\frac{\beta}{\mu+\gamma}\right]\left[\frac{2\beta}{(\gamma+\mu)}-1\right]+\gamma\mu^2\left[\frac{\beta}{(\gamma+\mu)}-1\right]\left[1+\frac{\beta}{\mu+\gamma}\right] \\
&> \gamma\mu^2\left[\frac{\beta}{\gamma+\mu}-1\right]+\mu^3\left[\frac{\beta}{\gamma+\mu}-1\right] \\
&= \gamma\mu^2\left(\hat{R}_0-1\right)+\mu^3\left(\hat{R}_0-1\right) \\
&= a_1
\end{aligned}
$$

Thus, the first column is marked the same. Based on the Routh Hurwitz criteria, the eigenvalues in the real part are negative. Furthermore, E_1 is locally stable asymptotic. □

SIR Model Formulation with Control

The goal to be achieved is to minimize the class population S and I. Individual class population S and I become optimum by minimizing the objective function (Zaman et al., 2008) as follows

$$K(u)=\int_0^{t_f}\left(C_1S(t)+C_2I(t)+\frac{1}{2}\tau u^2(t)\right)dt \tag{8}$$

where C_1 is the positive constant of the weight of $S(t)$, C_2 is the positive constant of the weight of $I(t)$, $u(t)$ is proportion of susceptible population given vaccine, τ is a positive parameter corresponding with $u(t)$. Furthermore, it is assumed $0<\tau<N$ and t_f is maximal time to infection. We defined the boundary condition of $u(t)$ as $U=\left\{u\middle|u(t),0\le u(t)\le 0.9,t\in\left[0,t_f\right]\right\}$.

The population given vaccines is the susceptible individual class population, so system (3) is obtained by substituting $u(t)$ into the system. After the vaccine is given, the individual class S is included in the individual class R to prevent transmission of cholera in that class, while the class I is given antibodies. Figure 3 is a transfer diagram to this model.

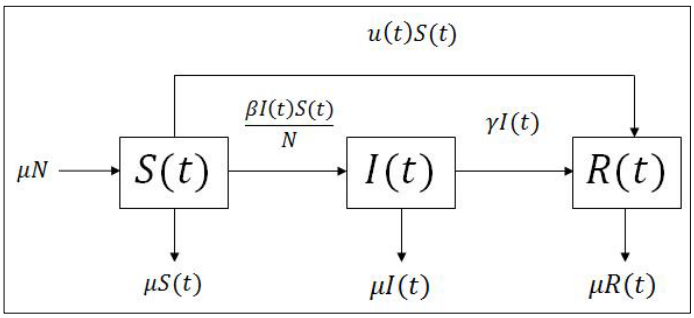


Figure 3. Transfer diagram of SIR model of cholera with vaccination

Based on Figure 3, we formulate a mathematical model of cholera spread with vaccination as follows.

$$
\begin{aligned}
\frac{dS(t)}{dt} &= \mu N-\left(\mu+u(t)\right)S(t)-\frac{\beta I(t)S(t)}{N} \\
\frac{dI(t)}{dt} &= \frac{\beta S(t)I(t)}{N}-\gamma I(t)-\mu I(t) \\
\frac{dR(t)}{dt} &= \gamma I(t)-\mu R(t)+u(t)S(t)
\end{aligned} \tag{9}
$$

where $S(0)=S_0\ge 0$, $I(0)=I_0\ge 0$, $R(0)=R_0\ge 0$, and $0\le u(t)\le 0.9$. The Theorem 3 is the optimal control to model (9).

Theorem 3. If $S^*(t)$, $I^*(t)$, and $R^*(t)$ are the constraint variables of system (9), then the optimal control for system (9) is

$$u^*(t) = \max\left\{\min\left[\frac{l_1 S^*(t) - l_3 S^*(t)}{\tau}, 0.9\right], 0\right\}.$$

Proof. We define Lagrangian function $L(S,I,u) = C_1 S(t) + C_2 I(t) + \frac{1}{2}\tau u^2(t)$ and Hamiltonian function that corresponds to system (9) is

$$\begin{aligned} H(S,I,R,u,l_1,l_2,l_3,t) = {} & C_1 S(t) + C_2 I(t) + \frac{1}{2}\tau u^2 + \\ & l_1\left[\mu N - (\mu + u(t))S(t) - \frac{\beta I(t) S(t)}{N}\right] + \\ & l_2\left[\frac{\beta S(t) I(t)}{N} - (\gamma + \mu) I(t)\right] + \\ & l_3\left[\gamma I(t) - \mu R(t) + u(t) S(t)\right] \end{aligned}$$

where $l_{i=1,2,3}$ is Lagrange multiplier. State equations are determined using

$$\frac{\partial H}{\partial l_1} = \mu N - (\mu + u(t))S(t) - \frac{\beta I(t) S(t)}{N}$$

$$\frac{\partial H}{\partial l_2} = \frac{\beta I(t) S(t)}{N} - (\gamma + \mu) I(t)$$

$$\frac{\partial H}{\partial l_3} = \gamma I(t) - \mu R(t) + u(t) S(t)$$

Co-state equations are determined by

$$\begin{aligned} i_1(t) &= -\frac{\partial H}{\partial S} \\ &= -\left[C_1 - l_1(\mu + u(t)) - l_1\frac{\beta I(t)}{N} + l_2\frac{\beta I(t)}{N} + l_3 u(t)\right] \\ &= l_1\frac{\beta I(t)}{N} - l_2\frac{\beta I(t)}{N} + l_1(\mu + u(t)) - l_3 u(t) - C_1 \end{aligned}$$

$$\begin{aligned} i_2(t) &= -\frac{\partial H}{\partial I} \\ &= -\left[C_2 - l_1\frac{\beta S(t)}{N} + l_2\frac{\beta S(t)}{N} - l_2(\gamma + \mu) + l_3\gamma\right] \\ &= l_1\frac{\beta S(t)}{N} - l_2\frac{\beta S(t)}{N} + l_2(\gamma + \mu) - l_3\gamma - C_2 \end{aligned}$$

$$i_3(t) = -\frac{\partial H}{\partial R} = -[-l_3 u] = l_3 u$$

The optimal control at the solutions $S^*(t), I^*(t), R^*(t)$ of the corresponding state of system (9) is derived by

$$\begin{aligned} \frac{\partial H}{\partial u} = 0 &\Leftrightarrow \tau u(t) - l_1 S(t) + l_3 S(t) = 0 \\ &\Leftrightarrow u(t) = \frac{l_1 S(t) - l_3 S(t)}{\tau} \end{aligned}$$

Hence, we obtain

$$u^*(t) = \max\left\{\min\left[\frac{l_1 S^*(t) - l_3 S^*(t)}{\tau}, 0.9\right], 0\right\}. \square$$

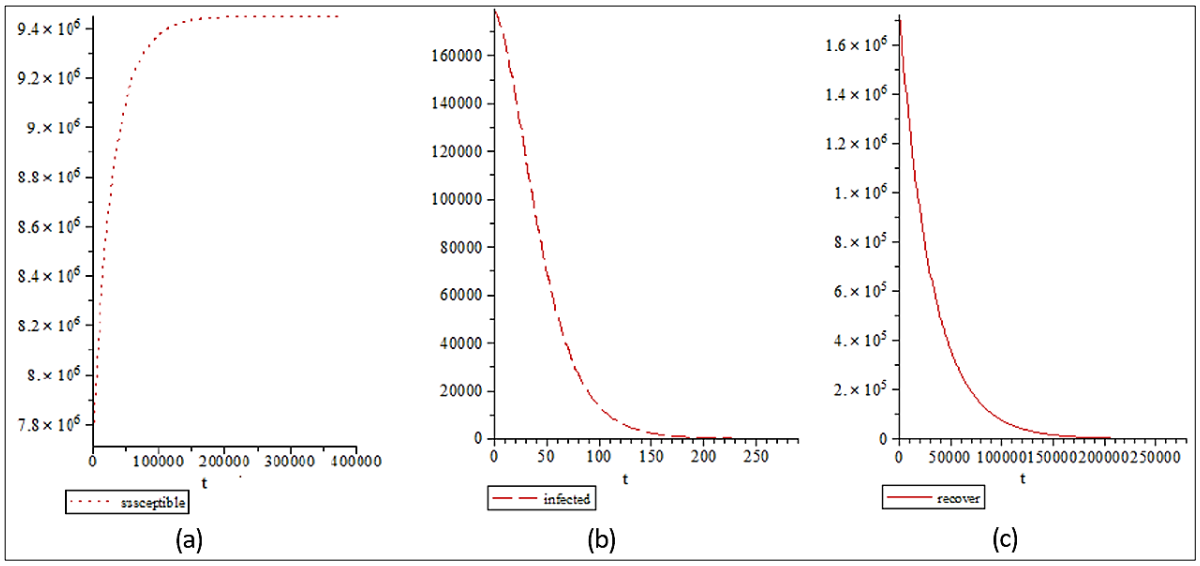
Simulation

In line with the analytical discussion, this section discusses numerically as an illustration to support the analytical results. In this section, we present the numerical simulation to describe the optimal solution of cholera spread. The parameter value is shown in Table 1.

Table 1. Parameter value

Parameter	Value (day)	References
β	0.6 or 0.2	Assumed
γ	0.2	Hendrix (1984)
μ	0.14285714285	Chiang (1979)

If $\beta = 0.2$ means $\hat{R}_0 < 1$, then S toward to 9446001. Apparently, with enlarged *t*, the individual class of subpopulation S is always constant towards 9446001 while the individual class population I and R for enlarged *t*, the value goes to 0. It means the subpopulation I decreases, and the transmission of disease will gradually disappear. Figure 4 (a), (b), dan (c) show us the illustration of this condition. If $\beta = 0.6$ means $\hat{R}_0 > 1$, then infected class will reach the highest number before decreasing slowly (see Figure 5). It can be interpreted that the disease will exist. This is in line with the analysis result described in Theorem 1 and Theorem 2.



(a) (b) (c)

Figure 4. The illustration of numerical simulation of the optimal solution of cholera spread: (a) susceptible subpopulation towards 9446001 if $\beta = 0.2; \hat{R}_0 < 1$; (b) infected subpopulation goes to 0 if $\beta = 0.2; \hat{R}_0 < 1$; and (c) the recovered subpopulation goes to 0 if $\beta = 0.2; \hat{R}_0 < 1$

Figure 6 (a) concludes that the smaller the value is given, the reduction in the population of individual class I will be longer. As a result, at a certain time *t*, the individual class population is still sufficient, so the opportunity to transmit cholera to the population the individual class S is larger than before. Figure 6 (b) provides the conclusion that the population of individual class I without control increased dramatically at time $t = 13$. Meanwhile, the population of individual class I with control tends to decrease at time $t = 13$. Figure 7 (a) shows that the optimal u is 0.9; there is a decrease at time $t = 40$. The vaccine production function value in the current dose $t = 40$ based on equation (8) is K (0.9) = 12335.850. If we do simulation for three months which is approximately 100 days, then we can see from Figure 7 (b) that the graph decreases significantly.

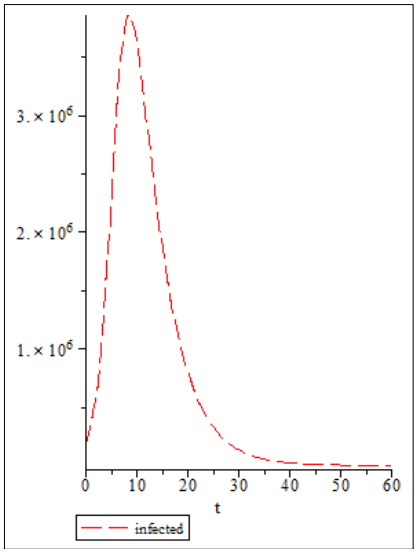


Figure 5. Infected subpopulations reach a high position if $\beta = 0.6; \hat{R}_0 > 1$

DISCUSSION

The classical mathematical model related to the spread of disease is in the form of SIR (Rodrigues, 2016). Because in general, the human population is divided into susceptible subpopulations, infected subpopulations, and recovered subpopulations. Through this classic model, it was developed into SEIR. In this case, E stands for "exposed" meaning someone who is in the incubation period. The emergence of compartment E can be used to describe the spread of Singapore flu (Sari, 2012) and the COVID-19 (Feng et al., 2021). In the case of cholera, the suitable model to apply is SIR. Based on other researchers, the model can be divided into the human and bacteria populations (Emvudu & Kokomo, 2012; Hntsa & Kahsay, 2020; Liao & Wang, 2011; Panja, 2019).

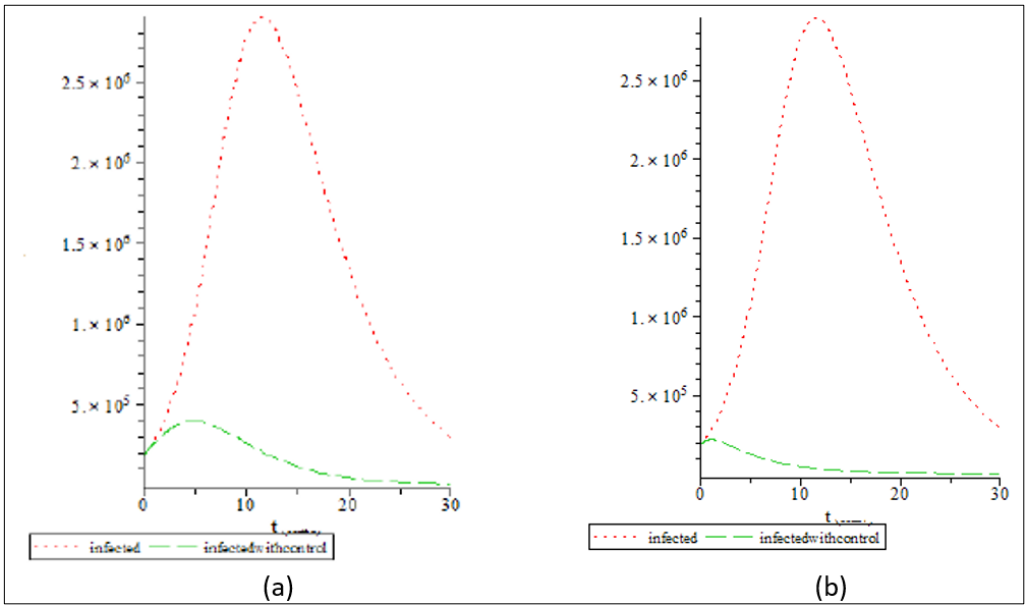


Figure 6. Infected subpopulation with and without control if (a) $\beta = 0.6; u = 0.2$ and (b) $\beta = 0.6; u = 0.9$

In our model, we focus on the human population to spread cholera disease. We interest in studying the dynamical behavior of the human population caused by bacteria infection. We have presented the mathematical model of cholera with and without control. The discussion of stability analysis based on basic reproduction number can be interpreted as an effort and prevention to reduce the value below one, so the cholera spread can be controlled. Based on Theorem 2, cholera spread becomes endemic if the value of basic reproduction number is above one. On the other hand, based on Theorem 1, if the value of basic reproduction number is below one,

then there is a unique disease-free which is locally asymptotically stable. It is essential to know the behavior of the solution if the value of basic reproduction number is equal to one. In the dynamical analysis, the possibility of the emergence of bifurcation is huge when the value of basic reproduction number is one. The existence of bifurcation will help to interpret the prognosis of cholera in more detail. Nevertheless, we leave this concern to the subsequent research.

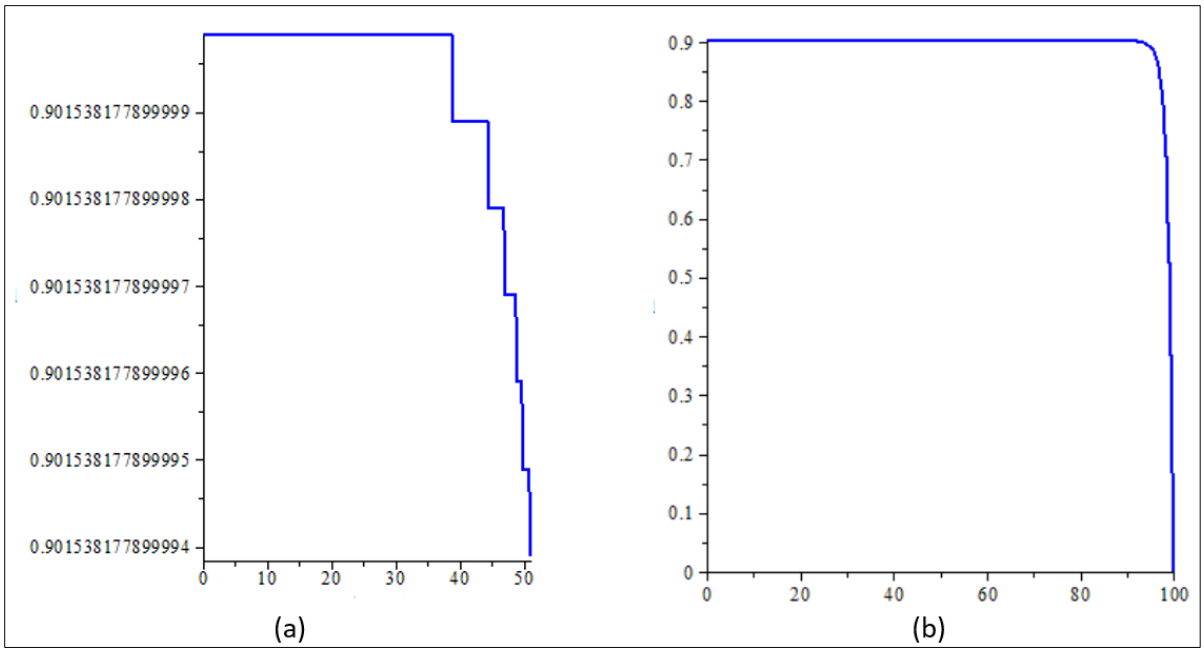


Figure 7. Optimal control u when (a) $t = 50$ days and (b) $t = 100$ days

Since Vibrio cholerae contaminated water, then water treatment is one of the effective ways to control the concentration of bacteria (Andam et al., 2015). In the susceptible and infectious individuals population, strong control, weak control, and no control can be done by looking at the value of basic reproduction number (Ayoade et al., 2018). If the value of basic reproduction number is less than one, the population has carried out strong control of the spread. If basic reproduction number is more than one, it means that the disease-free equilibrium point is unstable. In line with this, the endemic equilibrium point is globally asymptotically stable, which means that the control is weak. Meanwhile, when the value of basic reproduction number is increased from before, the infected population is greater than the susceptible, which means a significant cholera tragedy occurs (Ayoade et al., 2018). The other measurements of control are treatment, vaccination, water sanitation, and education campaign. All the parameter is included in the model as constant control (Edward & Nyerere, 2015). Generally, the control parameter is better as time-dependent since it may change all the time. Time-dependent characterization of control can be attained from several interventions, such as mobilization, drug administration, and sanitation improvement. The optimal control strategy is obtained by combining the three controls (Bakare & Hoskova-Mayerova, 2021).

In our model, the control parameter is a function of time. We concentrate on the vaccination control of the susceptible individual. Therefore, our goal is to minimize the objective function (8). The population given vaccines is the susceptible individual class population. After the vaccine is given, the susceptible population is included in the recovered population to prevent transmission of cholera in the susceptible class, while the infected population is given antibodies. To analyze the control problem, we use the Pontryagin Minimum Principle (PMP). The optimal value of this control is used in anticipation to resist disease (Njagarah & Nyabadza, 2015).

The vaccine dose is given to the individual class S with the minimum, and the individual class I is also the minimum so that the class individual R becomes increased. However, to enlarge t resulted in the vaccine is no longer effective, it is shown in Figure 9. It can be seen from Figure 9 concluded that at t = 100, the population of the individual class S who were given the vaccine has decreased, as well as when t = 100 vaccine given is no longer used effectively. This result is consistent with the reports that there was a decrease of 80% of approximately three months in the population of individual class I, after the class S individual population was given the vaccine (CDC,

2018). Our results also align with the other paper that although infection can still occur even after controls have been administered, it may be up to 8 times less damaging than cases in the absence of controls (Njagarah & Nyabadza, 2015).

CONCLUSION

This paper has discussed the formulation of a mathematical model for the cholera spread based on SIR. Initially, a model of the spread of cholera without vaccination is presented in system (3). Based on model (3), we presented in Lemma 1 and Lemma 2 that two types of equilibrium points are obtained, i.e., disease-free and endemic. The stability of the model around the equilibrium point has been shown in Theorem 1 and Theorem 2. If the contact rate is lower than the sum of the birth rate and the recovery rate, then the cholera disease disappears over time. If the contact rate is greater than the sum of the birth rate and the recovery rate, then cholera is still present, meaning that the disease can still spread.

Due to the emergence of disease endemicity, it is necessary to form a model of the spread of cholera with vaccination control, as shown in system (9). Using the Pontryagin Minimum Principle (PMP) analytically, there is an optimal control as described in Theorem 3. We also proved numerically that with a control strategy, we could decrease the population of infectious class. For future research can discuss global stability to find out the solution behavior in infinite time. Study about the value of basic reproduction number if equal with one is out of our concern. So, it is more interesting to discuss further. Moreover, since vaccine doses need to be repeated, it is necessary to divide class S according to age in administering the vaccine.

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