The Optimal Implementation of Chlorination, Treatment, and Education Controls in Reducing the Transmission of Cholera Disease

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Abstract. Cholera is an acute disease caused by the bacteria Vibrio Cholerae. Cholera is a contagious and deadly disease that requires immediate medical treatment. The mathematical studies are conducted to create models of cholera transmission. The cholera transmission models are carried out by implementing the optimal controls, namely the chlorination for bacteria, control treatment for quarantined individuals and education campaigns for susceptible and infected individuals. The optimal control efforts are given to minimize the spreading of cholera disease. The method used to solve this optimal control problem is Pontryagin Minimum Principle. Based on the simulation, the provision of optimal controls in forms of education and treatment in individuals and chlorination can minimize the concentration of bacteria and the number of infected humans.

1. Introduction
Cholera is an infectious disease caused by an infection bacteria Vibrio Cholerae with diarrhea symptoms accompanied by acute vomiting due to enterotoxins produced by bacteria [1]. Cholera can spread as an endemic, epidemic or pandemic disease. Since 1917, there are seven pandemics that spread across Europe. Vibrio Cholerae bacteria first appeared in Sulawesi, Indonesia and caused a cholera epidemic [2]. Cholera can kill around 95,000 people and affect 2.9 million more every year [3, 4]. In 2016, overall 54% of cases were reported from Africa, 13% from Asia and 32% from Hispaniola. Cholera is still a major public health problem and affects the developing world population, especially countries without sanitation resources [3].

Vibrio Cholerae bacteria into the body through foods or drinks that have been contaminated. The bacterium secretes enterotoxins (poisons) in the intestinal tract so that diarrhea is accompanied by acute vomiting [1]. Someone who has been infected with the Vibrio Cholerae bacterium within a few days will lose a lot of body fluids and enter dehydration [2]. Bacteria can only grow at a very high pH, which is between 8.5 - 9.5 and very good growth at pH 7.0 [5]. Cholera is currently still a concern in the medical world. Research on cholera has also been carried out by [6-8]. Various efforts were made to prevent the spread of cholera such as vaccination, clean water sanitation [9] and various other treatments [10-11]. On the other hand, treatment is the most important thing to eradicate disease [10-11]. Several alternative treatments for preventing cholera have been investigated, for example by [12-15].

These problems in the field of mathematics have been studied with mathematical modeling approaches [16]. Research on cholera has been studied by [17] through the optimum control approach of infectious diseases with its control variables namely of education and chlorination, [18] conducting research on optimal control treatment of humans infected with cholera, by providing treatment to
infected individuals and [19] conducted a study on the model of the spread of cholera by giving control in the form of medication and intervention through improved sanitation, education and quarantine. In addition, similar studies have also been studied by [20-31].

Furthermore, in this study, a mathematical model of the spread of cholera was reconstructed using a model that had been developed by [19] with optimal control variables in the form of chlorination in bacteria and control treatment in patients infected with the disease in the form of treatment and education of susceptible individuals. The purpose of giving control is to minimize the number of individuals infected cholera and reduce the concentration of Vibrio Cholerae bacteria.

2. Model Formulation
The model developed in this study using a model developed in the research of [19] for cholera, namely the SEIQRB (Susceptible-Educated-Infected-Quarantined-Recovered-Bacteria) model with the subpopulation of infected individuals divided into two, namely asymptomatic and symptomatic. The model construction divided the human subpopulation into six classes $N(t)$, namely individuals susceptible $S(t)$, educated human $E(t)$, individuals infected cholera with asymptomatic $I_a(t)$, individuals infected cholera with symptomatic $I_s(t)$, the human that is under treatment through quarantine $Q(t)$, individuals recovered $R(t)$. In addition, the bacterial concentration is expressed in $B(t)$. In this model, control variables are used in the form of chlorination ($u_1$), quarantine treatment ($u_2$) and education for susceptible individuals ($u_3$).

Mathematically, the following are the results of a dynamic system model reconstruction with optimal control

\[
\begin{align*}
\dot{S} &= \Lambda + vR + eE - \mu S - u_3\psi S - \beta \frac{B}{k+B} S, \\
\dot{E} &= u_3\psi S - eE - \mu E - \gamma E, \\
\dot{I}_a &= p\beta \frac{B}{k+B} S + \gamma E - \mu I_a - \alpha_2 I_a, \\
\dot{I}_s &= (1-p)\beta \frac{B}{k+B} S + (1-p)\gamma E - \mu I_s - \mu_s I_s - u_2\delta I_s, \\
\dot{Q} &= u_2\delta I_s - \mu Q - \mu_Q Q - \alpha_1 Q, \\
\dot{R} &= \alpha_1 Q + \alpha_2 I_a - \mu R - \nu R, \\
\dot{B} &= \eta I_s + \eta I_a - u_3 B - dB,
\end{align*}
\]

with $u_1$, $u_2$ and $u_3$ is the level of giving optimal control efforts with limits

\[0 \leq u = (u_1, u_2, u_3) \leq 1.\]

Here are some parameter used $\Lambda$ is constant human recruitment rate, $\mu$ is natural mortality rate, $\beta$ is rate consumption bacterial through contaminated sources, $k$ is half the constant saturation of the bacterial concentration, the degree of movement from subpopulation susceptible to infected cholera due contact between infected individuals and contaminated sources namely $\beta \frac{B}{k+B}$, $\psi$ is rate subpopulation susceptible $S(t)$, educated human $E(t)$, individuals infected cholera with asymptomatic $I_a(t)$, individuals infected cholera with symptomatic $I_s(t)$, the human that is under treatment through quarantine $Q(t)$, individuals recovered $R(t)$, the bacterial concentration is expressed in $B(t)$. In this model, control variables are used in the form of chlorination ($u_1$), quarantine treatment ($u_2$) and education for susceptible individuals ($u_3$).

3. Optimal Control Problems
The problem of optimal control in this study was solved using the Pontryagin Minimum Principle [32-33]. Next, the dynamic system model is as follows

\[\dot{x}(t) = f(x(t), u(t), t),\]

so that the set of state variables according to Equations (1) - (7) can be written as follows
\[ x(t) = (S(t), E(t), I_A(t), I_S(t), Q(t), R(t), B(t))^T, \]

with the initial state \( x(t_0) = x_0 \).

The purpose of this research problem is to obtain optimal control by minimizing the infected subpopulation, the number of bacteria and the costs that will be incurred on chlorine, education, and treatment. Mathematically, the purpose of optimal control can be expressed in the form of the objective function as follows

\[
J = \frac{1}{2} \int_{t_0}^{t_f} \left[ C_1 I_A^2(t) + C_2 I_S^2(t) + C_3 B^2(t) + C_4 u_1^2(t) + C_5 u_2^2(t) + C_6 u_3^2(t) \right] dt, \quad (8)
\]

where \( t_0 \) is a start time and \( t_f \) is a final time specified, as well as \( C_i > 0 \) for each \( i = 1, 2, 3, 4, 5, 6 \) is the parameter weights or price coefficient issued at each control during the day period. The type of problem optimal control of this research is fixed-final time (\( t_f \)) and free-final state (\( x(t_f) \)) with conditions \( 0 < t < t_f \). State at the start \( (x(t_0)) \) already set and state in finish \( (x(t_f)) \) not set. So, every existing system use the state boundary conditions at the initial time as follows,

\[
S(t_0) = S_0, E(t_0) = E_0, I_A(t_0) = I_{A0}, I_S(t_0) = I_{S0}, Q(t_0) = Q_0, R(t_0) = R_0, B(t_0) = B_0.
\]

The boundary condition for type fixed-final time and the free-final state as following

\[
x(t_0) = x_0, \lambda^*(t_f) = \left( \frac{\partial \phi}{\partial x} \right)_{t_f}, \quad (9)
\]

where \( x_0 = \{S_0, E_0, I_{A0}, I_{S0}, Q_0, R_0, B_0 \} \).

4. Result and Discussion

Based on Section 3, it is known that the dynamic system model for the spread of cholera with optimal control, objective function, and boundary conditions. Furthermore, the problem of optimal control can be solved by several steps, namely first forming the Pontryagin function \([32-33]\). Based on Equation (8) the problems in this research can be arranged into the following equation

\[
H(x(t), u(t), \lambda(t), t) = L(x(t), u(t), t) + \lambda(t) f(x(t), u(t), t),
\]

\[
= \frac{1}{2} (C_1 I_A^2(t) + C_2 I_S^2(t) + C_3 B^2(t) + C_4 u_1^2(t) + C_5 u_2^2(t) + C_6 u_3^2(t)) + \\
+ \lambda_S (\lambda + \nu R + \epsilon E - \mu S - u_3 \psi S - \beta \frac{B}{K + B} S) + \\
+ \lambda_E (u_2 \psi S - \epsilon E - \mu E - \gamma E) + \lambda_A \left[ p \beta \frac{B}{K + B} S + \nu R - \mu I_A + \alpha_2 I_A \right] + \\
+ \lambda_{I_S} (1 - p) \beta_2 \frac{B}{K + B} S + (1 - p) \gamma E - \mu I_S - \mu_3 I_S - u_3 \delta I_S) + \\
+ \lambda_Q (u_2 \delta I_S - \mu Q - \mu_6 Q - \alpha_3 Q) + \lambda_R (\alpha_1 Q + \alpha_2 I_A - \mu R - \nu R) + \\
+ \lambda_B (\eta I_A + \eta I_S - u_1 B - dB)
\]

Next, minimize \( H \) to \( u \). The optimal control variables namely chlorination (\( u_1 \)), quarantine treatment (\( u_2 \)), and education (\( u_3 \)), so that it is obtained

\[
u_1^* = \frac{\lambda_S B}{C_4} \quad (11)
\]

\[
u_2^* = \frac{\lambda_S \delta I_S - \lambda_\phi \delta I_S}{C_5} \quad (12)
\]

\[
u_3^* = \frac{\lambda_S \phi S - \lambda_\phi \psi S}{C_6} \quad (13)
\]

The optimal control equation (11) - (13) is a proportion, so it is defined by \( 0 \leq u_1 \leq 1 \), \( 0 \leq u_2 \leq 1 \) and \( 0 \leq u_3 \leq 1 \). Then, the optimal control value can be stated as follows,

\[
u_i^* = \left\{ [0, u_i^*], 1 \right\}, \quad (14)
\]

where \( i = 1, 2, 3 \). The next step is to form a state equation. The equation of state in optimal conditions is obtained by reducing the optimal function of Pontryagin \( H \) to \( \lambda \) like the following

\[
\dot{x}^* = \frac{\partial H^*}{\partial \lambda}.
\]

(15)
Based on Equation (15) so that the state equation is obtained for each subpopulation. Next is the state equation in the susceptible subpopulation.

\[ \dot{S}^* = \Delta + vR + \epsilon E - \mu S - u^*3\psi S - \beta \frac{B}{k + B} S, \]

\[ \dot{E}^* = u^*3\psi S - \epsilon E - \mu E - \nu E, \]

\[ \dot{I}_A^* = \rho \beta \frac{B}{k + B} S + p\gamma E - \mu I_A - \alpha_2 I_A, \]

\[ \dot{I}_S^* = (1 - p)\beta \frac{B}{k + B} S + (1 - p)\gamma E - \mu I_S - \alpha S - u^*2\delta I_s, \]

\[ \dot{Q}^* = u^*2\delta I_S - \mu Q - \mu_Q Q - \alpha_1 Q, \]

\[ \dot{R}^* = \alpha_1 Q + \alpha_2 I_A - \mu R - \nu R, \]

\[ B^* = \eta I_A + \eta I_S - u^*1B - dB. \]

Next, form a costate equation by lowering the Pontryagin $H$ function negatively to the state as follows.

\[ \dot{\lambda}^* = -\frac{\partial H^*}{\partial x}. \]  

Equation (23) is used to form the costate equation in each subpopulation. The following is the costate equation of the susceptible subpopulation.

\[ \dot{\lambda}_S^* = \mu \lambda_S + u^*3\psi \lambda_S + \beta \frac{B}{k + B} \lambda_S - u^*3\psi \lambda_E - \lambda_A \rho \beta \frac{B}{k + B} - \lambda_I S (1 - p) \frac{B}{k + B}, \]  

\[ \dot{\lambda}_E^* = -\epsilon \lambda_S + \epsilon \lambda_E + \mu \lambda_E + \gamma \lambda_E - p\lambda I_A - (1 - p)\gamma \lambda_I S, \]  

\[ \dot{\lambda}_{I_A}^* = -C_1 \lambda_A + \mu \lambda_A + \alpha_2 \lambda_A + \alpha_2 \lambda_R - \eta \lambda_B, \]  

\[ \dot{\lambda}_{I_S}^* = -C_2 \lambda_S + \mu \lambda I_S + \mu_2 \lambda I_S + u^*2\delta \lambda_s - (1 - p)\gamma \lambda_I S, \]  

\[ \dot{\lambda}_Q^* = \mu_0 \lambda_Q + \mu \lambda_Q + \alpha_1 \lambda Q - \alpha_1 \lambda_R, \]  

\[ \dot{\lambda}_R^* = \mu \lambda_R - \nu \lambda_S + \nu \lambda_R, \]  

\[ \dot{\lambda}_B^* = -C_3 \lambda_S + \frac{S B k \lambda_S}{(k + B)^2} - \frac{S p \beta k \lambda I_A}{(k + B)^2} - \frac{S (1 - p)\beta k \lambda I_S}{(k + B)^2} + u^*1 \lambda_B + dB. \]

In the next step, numerical simulation is carried out on the model of spreading cholera with optimal control [34-35]. In this section, the results of the simulation have been explained. The following are the parameter values shown in Table 1. The parameter values in Table 1 are used to obtain numerical simulation results. Simulations with optimal control using the Forward-Backward method Sweep Runge-Kutta Order 4. The purpose of the numerical simulation is to determine the effect of the effectiveness of giving optimal control in each subpopulation.

| Parameter | Value | Reference | Parameter | Value | Reference |
|-----------|-------|-----------|-----------|-------|-----------|
| $\Lambda$ | $24.4N(0)$ | [9] | $d$ | $1/30$ | [9] |
| $\mu$ | $2.2493.10^{-5}$ | [9] | $S(0)$ | $5750$ | [9] |
| $\beta$ | $0.08$ | [9] | $E(0)$ | $0$ | [15] |
| $k$ | $10^6$ | [9] | $I_A(0)$ | $1000$ | [15] |
| $\nu$ | $0.4/365$ | [9] | $I_S(0)$ | $700$ | [15] |
| $\delta$ | $0.05$ | [9] | $Q(0)$ | $0$ | [9] |
| $\epsilon$ | $0.003$ | [15] | $R(0)$ | $0$ | [9] |
| $\psi$ | $0.008$ | [15] | $B(0)$ | $275000$ | [9] |
| $\gamma$ | $0.005$ | [15] | $t_f$ | $100$ days | [15] |
| $\rho$ | $0.78$ | [15] | $\alpha_2$ | $0.15$ | [15] |
| $\alpha_1$ | $0.2$ | [9] | $\mu_3$ | $0.00127$ | [15] |
| $\mu_Q$ | $0.0001$ | [9] | $\eta$ | $50$ | [15] |
It is reviewed from the comparison of the number of individuals at the beginning time with the number of individuals at the end or at certain times through comparison before and after giving optimal control in each subpopulation. The following are the simulation results of each subpopulation.

**Figure 1. Infectious Individuals Asymptomatic**

Based on Figure 1, it is known that the number of individuals $I_A$ with optimal control, every day decreases compared to without optimal control. Decreasing the graph with optimal control significantly at $t = 10$ days. The graph decreases rapidly compared to without optimal control. It is assumed that the number of subpopulations at the beginning is 1000 individuals. The number of individuals without optimal control when $t = 10$ days has increased, which is to 850 individuals while the number of individuals with optimal control decreases to 330 individuals. Therefore, education of cholera for susceptible and educated subpopulations is very important. So, in this case, the level of effectiveness of giving optimal control in the Infected Asymptomatic subpopulation in the form of education is 22%.

Individuals symptomatic (can see Figure 2) if not treated immediately will increase contamination of the environment. Thus, the number of individuals affected by cholera has increased, given the rapid spread of bacteria. However, if the Infected Symptomatic subpopulation is given optimal control in the form of treatment during quarantine, then the number of individuals infected with the disease will decrease significantly. At the end of the number of subpopulations with optimal control as many as 50 individuals. This means that the level of effectiveness in providing optimal control in the form of treatment has an effect of 97.27%. So, in this case, the goal is to minimize the number of individuals infected with symptomatic can be fulfilled. Next, we can see the rate of change in the number of bacterial concentration in Figures 4.

**Figure 2. Infectious Individuals Symptomatic**

**Figure 3. Individuals Susceptible**

**Figure 4. Bacteria Concentration**
Based on Figure 3 it is known that susceptible individuals decrease when given optimal control. The number of individuals susceptible to optimal control at the end time is 2733.28 or around 2733 individuals while without optimal control the number of individuals at the end is 134 individuals. Therefore, susceptible individuals need to be given control in the form of education. So, if the educated individual increases, the number of individuals infected with the disease will decrease. When given control in the form of education, the susceptible subpopulation will decrease until the end time. This means that the effectiveness of providing education to individuals susceptible has an effect of 95%. Furthermore, it can be seen the rate of change in the number of individuals infected with asymptomatic and symptomatic.

The concentration level at the initial time was 275000 cell/ml. Figure 4 shows a graph of the ratio of changes in the number of bacterial concentrations with and without optimal control. Without optimal control, the rate of development of bacterial concentrations increases significantly from day 10 to $9.5 \times 10^5$, whereas when given optimal control the level of bacterial concentration decreases on day 10 to $4 \times 10^4$ and continues to decline to 5144 at the end. The level of bacterial concentration without control at the end time is $2.8 \times 10^6$. So, in this case, the goal is to minimize bacterial concentration can be attained. In more detail, the optimal control value is shown in Figure 5.

5. **Conclusion**
Based on the results and discussion in this study, it can be concluded that after reconstructing the model by adding optimal control variables in the form of education and treatment in individuals and chlorination can minimize the concentration of bacteria and the number of infected humans.
References

[1] Merrell D S, Butler S M, Qadri F, Dolganov, N A, Alam A, Cohen M B, Calderwood S B, Schoolnik G K, Camili A 2002 Nature 417 (6889) 642-645
[2] Setiati S, Idrus A, et al 2014 Ilmu Penyakit Dalam (Jakarta: InternaPublishing)
[3] World Health Organization 2017 Cholera annual report 2016, [online]: https://www.who.int/wer/2017/wer9236/en/
[4] World Health Organization 2018 Cholera, [online]: http://www.who.int/news-room/fact-sheets/detail/cholera
[5] Amelia S 2005 Vibrio Cholerae (Medan: Universitas Sumatera Utara)
[6] Guli M M 2016 J. Biocelebes 10 (2) 18-24
[7] Guntina R K and Sri A F K 2017 J. Farmaka Suplemen 15 (1) 92-104
[8] I Wayan Y W, Retno K and Anak A G R D 2015 J. Metamorfosa, 11 (1) 16-22
[9] Unicef Indonesia 2012 Ringkasan Kajian Air Bersih, Sanitasi, dan Kebersihan, [online]: http://www.unicef.org
[10] World Health Organization 2018 Prevention of Cholerae, [online] tersedia di: http://www.who.int/en/news-room/feature-stories/detail/prevention-for-a-cholera-free-world
[11] World Health Organization 2017 Prevention for a cholera free world. [online] tersedia di: https://www.who.int/en/news-room/feature-stories/detail/prevention-for-a-cholera-free-world
[12] Christy A S 2012 J. Ilmu Kesehatan dan Kedokteran Keluarga 8 (2) 97-102
[13] Karmila 2016 Skripsi Daya Hambat Ekstrak Daun Mengkudu (Morinda Citrifolia L.) terhadap Pertumbuhan Bakteri Penyebab Diare (Makassar: Universitas Alauddin Makassar)
[14] Sugianti L, Dwi S and Sofiyatul N J 2019 J. Pengabdian Kesehatan 2 (1) 63-77
[15] Utami P R and Don A R 2018 Seminar Nasional Penelitian Lingkungan (SENPLING) (Riau: Universitas Riau) 586
[16] Cahyono 2013 Pemodelan Matematika Edisi Pertama (Yogyakarta: Graha Ilmu)
[17] Bakhtiar T 2015 Peran Edukasi dan Klorinasi dalam Pengendalian Penyakit Menular: Sebuah Pendekatan Kontrol Optimum Proc Seminar dan Rapat Tahunan Bidang MIPA BKS-PTN Barat (Pontianak: Universitas Tanjungpura) 430-440
[18] Lemos-Paiao A P, Christina J S and Delfim F M T 2016 J. of Computational and App Math 318 168-180
[19] Syafi’I A M, Irma F, et al 2018 Conf. Nasional Matematika XIX (Malang: Universitas Brawijaya)
[20] Adaniyah A 2016 Skripsi Analisis Kestabilan dan Kontrol Optimal pada Model Matematika Epidemi Kolera (Surabaya: Universitas Airlangga)
[21] Asfarina G T, Syafruddin S and Sukarna 2016 Skripsi Analisis Kestabilan Penyebaran Penyakit Kolera Menggunakan Model SEIRS dengan Vaksinasi dan Faktor Treatment (Makassar: Universitas Negeri Makassar)
[22] Dany A R 2016 Skripsi Model Matematika Penyebaran Kolera dengan Mempertimbangkan Intervensi Kesehatan Masyarakat (Surabaya: Universitas Airlangga)
[23] Fitriannah A 2015 Skripsi Analisis Dinamika Model Penyebaran Penyakit Kolera (Bogor: Institut Pertanian Bogor)
[24] Fitriyah A 2015 Thesis Suatu Analisis dari Model Matematika Penyakit Kolera (Yogyakarta: Universitas Gadjah Mada)
[25] Maisura H and Sumarno P S 2018 J. of Math and Its App 17 (1) 33-46
[26] Mahmudah Y, Fatmawati and Yayuk W 2013 J. Matematika 2 (1) 73-80
[27] Nirwani N, V H Badshah and R Khandelwal 2015 Advances in Applied Science Research, 6 (6) 181-186
[28] Renny 2009 Proc. Seminar Nasional Matematika dan Pendidikan Matematika, Jurusan Pendidikan Matematika
[29] Stephen E and Nkuba N 2015 Applied and Computational Math 4 (2) 53-63
[30] Wang J and Chairat M 2011 Canadian Applied Mathematics Quartely 19 (3)
[31] Zulaikha T and Intan F 2017 *Proc. Seminar Nasional Integrasi Matematika dan Nilai Islami* I (1) 41-51
[32] Naidu D S 2002 *Optimal Control System* (New York: Idaho State University)
[33] Subchan and Zbikowski R 2009 *Computational Optimal Control Tools and Practice* (United Kingdom: John Wiley & Sons Ltd)
[34] Burden R L and Faires J D 2011 *Numerical Analysis Ninth Edition* (Camden: Brooks/Cole Cengage Learning)
[35] Lenhart S and John T W 2007 *Optimal Control Applied to Biological Models* (New York: Chapman & Hall/CRC Taylor and Francis Group)