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Model Simulation of Continuous Time Markov Chain Susceptible Infected Recovered-Bacterial Population for Cholera Disease

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Abstract. *Epidemic is an outbreak of an infectious disease rapidly in a population at a certain place and time. Epidemic models are used to explains the spread pattern of disease. The continuous time Markov chain susceptible infected recovered-bacterial population in the aquatic reservoir (CTMC SIR-B) model is a stochastic model, which considers the effect of bacterial population. The human population are classified into 3 groups. There are susceptible, infected, and recovered groups. Then, there are bacterial population which can infectious the cholera disease to human. CTMC SIR-B model considers treatment and water sanitation parameters. The spread of cholera disease can be modeled as CTMC SIR-B. Cholera is an acute intestinal infectious disease caused by the bacterium Vibrio cholerae. Cholera can be transmitted through the human digestive system. The symptoms of cholera disease are diarrhea, vomiting, and dehydration. The dehydration if not handled properly, may cause death. The aims of this research are to build and simulate the CTMC SIR-B model for cholera disease. The result of the model simulation shows that there is no significant difference between various values of treatment and water sanitation parameters. The pattern of the cholera disease spread describes that the transmission of cholera can occur from human to human even though there is no population of bacteria in the aquatic reservoir.*

Keywords: *cholera; ctmc sir-b; epidemic model; stochastic.*

1. INTRODUCTION

Epidemic is an outbreak of an infectious disease rapidly in a population at a certain place and time. Infectious diseases can be caused by bacteria, viruses, and fungi. Transmission of the disease from individual to other individuals can be through physical contact, the respiratory tract, and the digestive system. Epidemics can cause someone to die. Therefore, it is necessary to prevent and control the epidemic, one of which is by studying the pattern of the spread of infectious diseases. The epidemic model is a mathematical model that can analyze the pattern of the spread of a disease. Epidemic models can be viewed deterministically and stochastically. The epidemic model studied stochastically is divided into 3, namely Discrete Time Markov Chain (DTMC), Continuous Time Markov Chain (CTMC), and Stochastic Differential Equation (SDE). This research will use the CTMC stochastic epidemic model with of Susceptible Infected Recovered (SIR) pattern of disease spread which is modified into Susceptible Infected Recovered-Bacterial population in the aquatic reservoir (SIR-B).

Cholera is an acute intestinal infection caused by the bacterium Vibrio cholerae. The symptoms of cholera disease are diarrhea, vomiting, and dehydration. The dehydration if not handled properly, may cause death. According to the World Health Organization [1], during 2020

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there were 323,369 cases with the total of 857 deaths reported from 24 countries. The therapeutic treatment and vaccination can achieve recovery of individuals infected of cholera. According to Surjawidjaja, *et al*. [2] cited in Side, *et al*. [3], the treatment for cholera sufferers is to provide electrolyte fluids before or after the individual is dehydrated, the goal is to prevent dehydration (if electrolyte fluids are given before dehydration) and restore lost body fluids and avoid death (if fluid electrolytes given after dehydration). Vaccination is giving vaccines, namely biological products that contain antigens in the form of microorganisms or substances that have been processed in such a way that they are safely to be given to individuals infected of a disease. After obtaining the vaccine, the infected individuals will have an immune system against a certain disease [4]. Meanwhile, according to Anggaraditya [5], vaccination does not have a significant effect on the recovery of cholera sufferers in developing countries, especially in the Asian region because vaccine prices are not affordable for the poor and the budget in a developing country in Asia is limited to buying vaccines. Therefore, this research adopts the SIR-B stochastic model based on the research of Maisura, *et al*. [6] which was modified by eliminating the vaccination treatment.

Previous researches on the dynamics of the spread of cholera include Codeço [7] which introduced a model of the spread of cholera using the SI-B (Susceptible Infected-Bacterial population in the aquatic reservoir) model with the role of water sanitation considered to inhibit the growth of bacteria. Furthermore, Wang & Modnak [8] refined the Codeco model by taking into account the presence of cured human conditions, namely the SIR-B (Susceptible Infected Recovered-Bacterial population in the aquatic reservoir) model. The SI-B and SIR-B models are studied using a deterministic epidemic model. Meanwhile, the deterministic model cannot explain the uncertainty factor contained in the epidemic model, so it requires a stochastic model. This research will discuss the application of the CTMC SIR-B stochastic model simulation on the spread of cholera. This research uses parameter values according to research by Maisura, *et al*. [6]. Next, a numerical simulation will be carried out to find out the spread pattern of cholera without any vaccination treatment. So, the purpose of this research are to build and simulate the CTMC SIR-B model for cholera disease.

2. MATERIALS

2.1 Stochastic Process

Based on Parzen [9], stochastic process is the set of random variables X_t denoted as $\{X_t | t \in T, X_t \in S\}$; T is the set of time indices, where t is the parameter that runs according to the set of time indices T and S is the state space, namely all possible values that can occur in the random variable X_t. The stochastic process has continuous parameters when the $T = [0, \infty)$, then denoted as $\{X_t\}$.

2.2 Markov Process

The Markov process is a stochastic process which explains that the future events of a system depend only on the present time and do not depend on the past. The Continuous Time Markov Chain (CTMC) is a Markov process with continuous time parameters expressed as $\{X(t), t \geq 0\}$ for n integers in the time sequence $t_1, t_2, \dots, t_n, t_{n+1}$ with $t_1 < t_2 < \cdots < t_n < t_{n+1}$ at any real number $x_1, \dots, x_{n+1}$. Therefore, according to Parzen [9], the CTMC is expressed as $P[X(t_n) \leq x_n \,|X(t_1) = x_1, \dots, X(t_{n-1}) = x_{n-1}] = P[X(t_n) \leq x_n \mid X(t_{n-1}) = x_{n-1}]$.

2.3 SIR Model

According to Allen [10], the SIR (Susceptible-Infected-Recovered) model is a mathematical model that describes the pattern of disease spread with the characteristic that every individual who has recovered will have a permanent immune system. The SIR model is divided into 3 groups. There are susceptible (S) group as a group of population of individuals who are healthy but susceptible to infection, infected (I) group as a group of infected individuals population, and recovered (R) group as a group of population of individuals who have recovered from infection and have permanent immunity to the same disease. The rate of disease transmission is denoted as β and the cure rate is denoted as γ. The diagram of the SIR model is shown on the Figure 1.

Figure 1. Diagram of the SIR Model

Maisura, *et al.* [6] created a SIR-B model group diagram that combines the SIR model group with an additional group B (Vibrio cholerae bacteria in the environment). The bacteria in group B can be a medium for transmitting cholera to susceptible individuals. The rate of disease transmission is denoted as $(\beta_e \frac{B}{k+B} + \beta_h I)S$, k is the saturated concentration of bacteria in the water that causes a 50% chance of contracting cholera. The cure rate is denoted as $(\gamma + a)I$, a is the therapeutic treatment parameter. The bacteria's growth rate is denoted as ξI. The death rate of bacteria is denoted as $(\delta + w)B$, w is the water sanitation parameter. The diagram of the SIR-B model for cholera disease with the therapeutic treatment and water sanitation parameters is shown on the Figure 2.

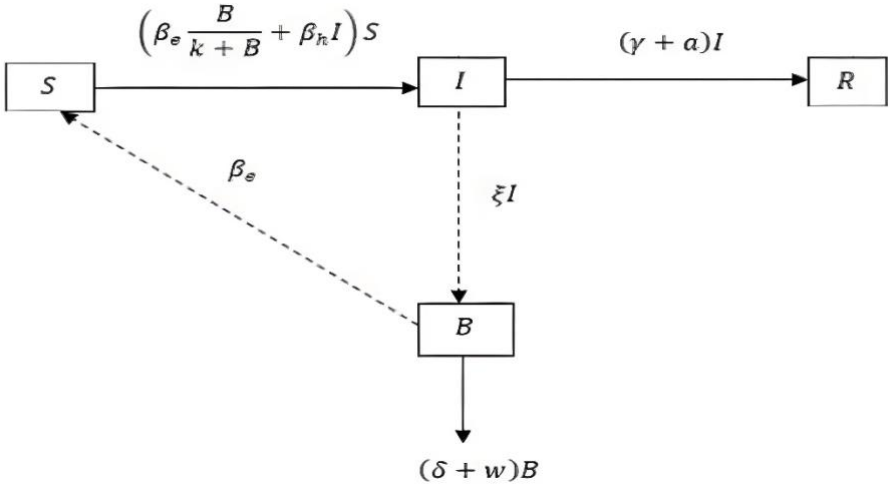

Figure 2. Diagram of the SIR-B Model for Cholera Disease with the Therapeutic Treatment and Water Sanitation

3. RESEARCH METHODS

The steps taken in this research are:

1. Derive the CTMC SIR-B stochastic epidemic model consisting of,
   a) Determine the assumptions of the CTMC SIR-B stochastic epidemic model.
   b) Determine the transition probability of individuals between groups.

2. Determine the parameter values in the model obtained based on the research of Maisura, *et al*. [6].
3. Perform a numerical simulation of the model, then make interpretations of the results.

4. RESULTS AND DISCUSSION

4.1 CTMC SIR-B Model

The Continuous Time Markov Chain Susceptible Infected Recovered-Bacterial Population in the Aquatic Reservoir (CTMC SIR-B) model was reproduced based on research by Maisura, *et al*. [6]. The CTMC SIR-B model is a function of the probability of the independent random variables. There are three independent random variables, namely $S(t), I(t), B(t)$. $S(t)$ is the number of individuals susceptible at time t, $I(t)$ is the number of infected individuals at time t, and $B(t)$ is the number of bacteria in the environment at time *t*. The random variables S, I, and B are expressed in random samples s, i, and b, respectively. The number of individuals who have recovered from infection is denoted by $R(t)$ and can be expressed as $R(t) = N - S(t) - I(t)$, where N is the constant population size of human. The joint probability function is written on Equation (1).

$$p_{(s,i,b)} = P[S(t) = s, I(t) = i, B(t) = b] \tag{1}$$

with $t = [0, T]$, $s = 1, 2, \ldots, N$, $i = 1, 2, \ldots, N$, and $b = 1, 2, \ldots, N$.

The process of moving individuals between groups is called transition. Based on the nature of the transition probability in a constant population, this research assumes that there is only one individual transits at a very small time interval (Δt) in the interval $t = [0, T]$ and can be expressed in a probability. $S(t)$, $I(t)$, and $B(t)$ can change any time in the time interval $t = [0, T]$. The transition probability of an individual in group S denoted by s becomes $s + j$, an individual in group I denoted by i becomes $i + k$, and an individual in group B denoted by b becomes $b + l$ at a certain time interval is written on Equation (2).

$$p_{(s+j,i+k,b+l),(s,i,b)}(\Delta t) = P\{(\Delta S, \Delta I, \Delta B) = (j, k, l \mid S(t), I(t), B(t) = (s, i, b)\} \tag{2}$$

The derivation of the CTMC SIR-B epidemic model uses the following assumptions:

1. The spread of disease occurs in a constant population, so there is no individual enters and leaves the population.
2. The population mixes homogeneously.
3. Human birth and death factors are not considered in the model, so that the transition to groups S, I, R, and B only involves transmission rates, recovery rates, bacterial growth rates, and bacterial death rates.
4. There is only one individual transits from s to $s + j$, i to $i + k$, and b to $b + l$ at a very small Δt.
5. There is only one disease that spreads in a population.

Based on the fourth assumption, the transition occurs at a very small time interval (Δt), so the possibility that will occur is that there is only one individual transits, from state (s, i, b) to state $(s - 1, i + 1, b)$, from state (s, i, b) to state $(s, i - 1, b)$, from state (s, i, b) to state $(s, i, b + 1)$, from state (s, i, b) to state $(s, i, b - 1)$, and from state (s, i, b) to state (s, i, b) in a very small

time interval (Δt). The value of the transition probability with the number of individuals moving more than or equal to two (≥ 2) in a very small-time interval (Δt) is written on Equation (3).

$$o(\Delta t) \tag{3}$$

When an individual experience a transition from state (s, i, b) to state $(s-1, i+1, b)$, it means that the number of susceptible individuals (S) decreases by one, while the number of infected individuals (I) increases by one, and the number of bacteria in the environment is constant. Therefore, there is a transition of one individual from group S to group I which causes disease transmission from individuals in group I to individuals in group S through an interaction expressed in the transmission rate ($\left(\beta_e \frac{B}{k+B} + \beta_h I\right) S$). The transition probability value from state (s, i, b) to state $(s-1, i+1, b)$ in a very small Δt is written on Equation (4).

$$\left(\beta_e \frac{B}{k+B} + \beta_h I\right) s\Delta t + o(\Delta t) \tag{4}$$

When individuals experience a transition from state (s, i, b) to state $(s, i-1, b)$, it means that the number of susceptible individuals (S) remains constant, while the number of individuals infected (I) decreases by one. So that there was a transition of one individual from group I to group R which caused the recovery of infected individuals through therapeutic treatment which was expressed in the recovery rate $(\gamma + \alpha)$. Thus, the probability value of the transition from state (s, i, b) to state $(s, i-1, b)$ in a very small Δt is written on Equation (5).

$$(\gamma + \alpha) i\Delta t + o(\Delta t) \tag{5}$$

Then, when an individual experiences a transition from state (s, i, b) to state $(s, i, b+1)$, it means that the number of infected individuals (I) remains constant, while the number of bacteria in the environment (B) increases by one. This causes an increase in the number of bacteria in the environment from the feces of infected individuals through the rate of bacteria addition (ξ). The probability value from state (s, i, b) to state $(s, i, b+1)$ in a very small Δt is written on Equation (6).

$$\xi i\Delta t + o(\Delta t) \tag{6}$$

When an individual experiences a transition from state (s, i, b) to state $(s, i, b-1)$ it means that the number of infected individuals (I) remains constant, while the number of bacteria in the environment (B) decreases by one. This causes a reduction in the number of bacteria in the environment due to good water sanitation through the bacterial death rate $(\delta + w)$. Thus, the transition probability value from state (s, i, b) to state $(s, i, b-1)$ in a very small Δt is written on Equation (7).

$$(\delta + w) b\Delta t + o(\Delta t) \tag{7}$$

The transition from state (s, i, b) to state (s, i, b) means that there is no change in the number of individuals in groups S, I, and B. The transition probability value of state (s, i, b) to state (s, i, b) is written on Equation (8).

$$1 - (\left(\beta_e \frac{B}{k+B} + \beta_h I\right) s + (\gamma + \alpha) i + \xi i + (\delta + w) b) \Delta t + o(\Delta t) \tag{8}$$

The equations (3), (4), (5), (6), (7), and (8) can be written in a transition probability system, written on Equation (9).

$$p_{(s+j,i+k,b+l),(s,i,b)}(\Delta t) = \begin{cases} \left(\beta_e \frac{B}{k+B} + \beta_h I\right) s\Delta t + o(\Delta t), (j,k,l) = (-1,1,0); \\ (\gamma+\alpha) i\Delta t + o(\Delta t), (j,k,l) = (0,-1,0); \\ \xi i\Delta t + o(\Delta t), (j,k,l) = (0,0,1); \\ (\delta + w) b\Delta t + o(\Delta t), (j,k,l) = (0,0,-1); \\ 1 - \left(\left(\beta_e \frac{B}{k+B} + \beta_h I\right) s + (\gamma+\alpha) i + \xi i + (\delta+w) b\right) \Delta t + o(\Delta t), (j,k,l) = (0,0,0); \\ o(\Delta t), \text{others.} \end{cases} \quad (9)$$

4.2 CTMC SIR-B Model Simulation

Based on the CTMC SIR-B model that has been obtained, a simulation of this model is carried out on the spread of cholera with parameter values referring to the research of Maisura, *et al*. [6], some of which were obtained from research by Wang & Modnak [8]. The research assumes the parameter values as follows on the Table 1.

Table 1. Parameters of the Cholera Spread Model

Parameter	Description	Value	Unit
β_e	The digestion rate of Vibrio cholerae bacteria from contaminated water	$(0.075)^a$	day^{-1}
β_h	The digestion rate of Vibrio cholerae bacteria from human-to-human interactions	$(0.00011)^a$	day^{-1}
k	Saturated concentration of bacteria in water	$(10^6)^a$	$\frac{\text{cell}}{\text{ml}}$
γ	Rate of recovery	$(5^{-1})^a$	day^{-1}
ξ	The growth rate of bacteria in the environment from the feces of an infected individual	$(10)^a$	$\frac{\text{cell}}{\text{ml}}.\text{day}^{-1}$
δ	The natural death rate of Vibrio cholerae bacteria	$(30^{-1})^a$	day^{-1}
N	Total of human population	$(10000)^a$	individual
$S(0)$	Initial number of susceptible individuals	$(9997)^b$	individual
$I(0)$	Initial number of infected individuals	$(2)^a$	individual
$B(0)$	Initial numbers of Vibrio cholerae bacteria in the environment	1	individual

Note: [a)] Parameter values were obtained from Wang & Modnak (2011), [b)] Parameter values were obtained from Maisura, *et al*. (2018)

The parameter values that will be changed are the rate of therapeutic treatment (α) and the rate of water sanitation (w). There are two events that will be simulated using Python, event 1 is given a non-zero value in the parameters referring to the research of Maisura, *et al*. [6] and event 2 were given 4/3 parameter value of event 1. Those two events and the parameter values are written on the Table 2.

Table 2. Therapeutic Treatment and Water Sanitation Parameter Values [6]

Parameter	Event 1	Event 2
Therapeutic treatment (α)	0.0002	0.00027
Water sanitation (w)	0.001	0.0013

The results of CTMC SIR-B stochastic model simulation on the spread of cholera disease are shown on the Figure 3 and Figure 4.

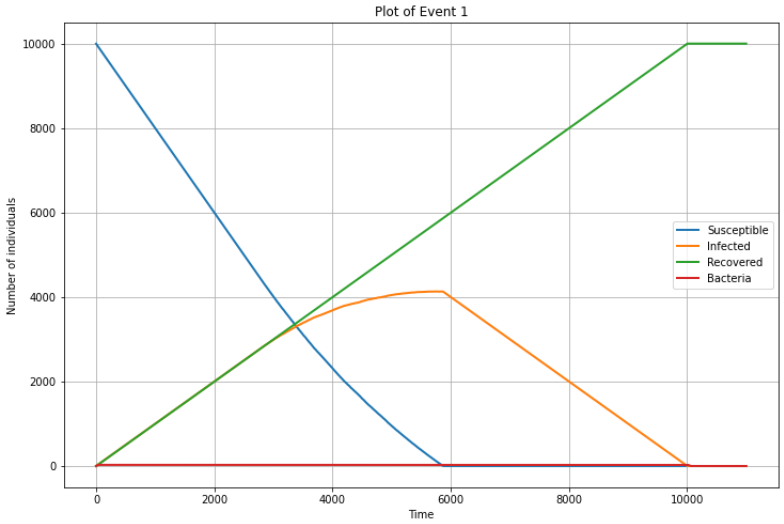

Figure 3. Spread Pattern of Cholera Disease Based on Event 1

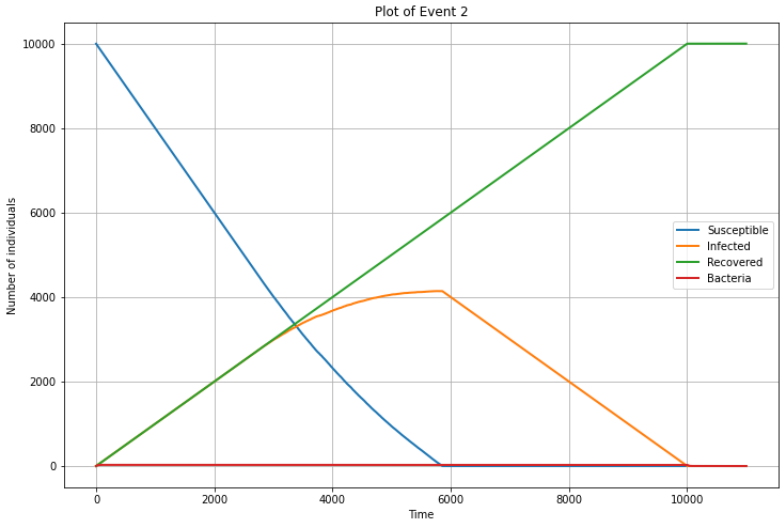

Figure 4. Spread Pattern of Cholera Disease Based on Event 2

Based on the Figure 3 and Figure 4, visually can be seen that the numerical simulation of the CTMC SIR-B stochastic model on the spread of cholera has a similar pattern between event 1 and event 2. This is due to the difference values of the therapeutic treatment and water sanitation between event 1 and event 2 were only a few. So, this research also carried out numerical simulations using random values from Python to obtain therapeutic treatment and water sanitation values with the aim of knowing how the spread pattern of cholera in the CTMC SIR-B stochastic model using the more varied values of those parameters as follows on the Table 3.

However, the numerical simulation results of the CTMC SIR-B stochastic model on the spread of cholera with therapeutic treatment and water sanitation parameters generated randomly

using Python show that there is no significant difference between one random event and another random event, the graph as same as Figure 3 and Figure 4.

Table 3. Therapeutic Treatment and Water Sanitation Parameter Random Values

Generation	Parameters	Random Value
1	Therapeutic treatment (α)	0.6105
	Water sanitation (w)	0.1280
2	Therapeutic treatment (α)	0.2048
	Water sanitation (w)	0.1318
3	Therapeutic treatment (α)	0.0681
	Water sanitation (w)	0.5526

The graph of the simulation results shows that in the continuous time span (0; 11,000), the number of individuals who were susceptible to infection initially was 9997, while the initial number of infected individuals was 2, and the initial number of bacteria in the environment was 1 [6]. Based on that, the number of individuals who have recovered initially was 1, which is obtained from the total human population minus the number of susceptible individuals and the number of infected individuals. Then, over time, the number of individuals who are susceptible to infection has decreased along with the increase in the number of infected and recovered individuals. The number of susceptible individuals reaches zero at around the $5{,}700^{\text{th}}$ time, together with the number of infected individuals reaching a peak of around 4,100 at that time, then the number of infected individuals decreases to zero at the $1{,}000^{\text{th}}$ time at the same time as the number of recovered individuals reached a peak of 10,000 at that time. The number of bacteria in the environment, which was initially 1, decreased to zero around the 2^{nd} time. The pattern of the cholera disease spread describes that the transmission of cholera can occur from human to human even though there is no population of bacteria in the aquatic reservoir. The therapeutic treatment and water sanitation did not significantly influence the spread pattern of cholera disease. This was indicated by the results of numerical simulations that did not differ between the values of various therapeutic treatment and water sanitation parameters.

5. CONCLUSION

Based on the discussion that has been described, the conclusions in this research are:

1. The CTMC SIR-B model of cholera disease is

$$p_{(s+j,i+k,b+l),(s,i,b)}(\Delta t) = \begin{cases} \left(\beta_e \dfrac{B}{k+B} + \beta_h I\right) s\Delta t + o(\Delta t), (j,k,l) = (-1,1,0); \\ (\gamma+\alpha) i\Delta t + o(\Delta t), (j,k,l) = (0,-1,0); \\ \xi i\Delta t + o(\Delta t), (j,k,l) = (0,0,1); \\ (\delta + w) b\Delta t + o(\Delta t), (j,k,l) = (0,0,-1); \\ 1 - \left(\left(\beta_e \dfrac{B}{k+B} + \beta_h I\right) s + (\gamma+\alpha) i + \xi i + (\delta+w) b\right)\Delta t + o(\Delta t), (j,k,l) = (0,0,0); \\ o(\Delta t), \text{others.} \end{cases}$$

2. The result of the model simulation shows that there is no significant difference between various values of therapeutic treatment and water sanitation parameters.
3. The pattern of the cholera disease spread describes that the transmission of cholera can occur from human to human even though there is no population of bacteria in the environment (aquatic reservoir).

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