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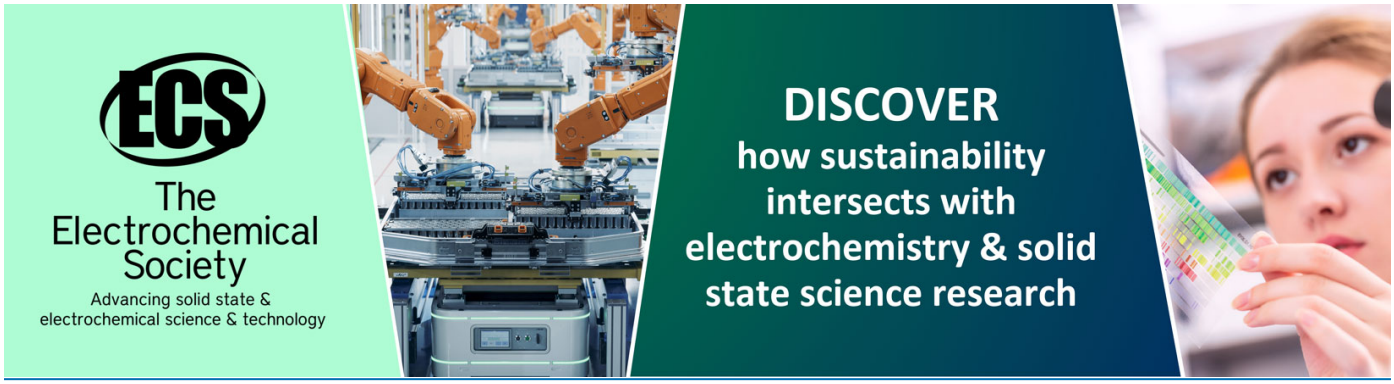

Stability analysis of mathematical model (*sirb*) in the spread of cholera with vaccination and disinfection

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Abstract. Cholera is a disease as a kind of acute diarrhea caused by bacteria *V. Cholerae*. The spread of cholera can be modeled in the form of nonlinear differential equation systems with 4 variables $SIRB$. This paper aims to research to analyze the local stability of the equilibrium point of the dynamical population in the spread of cholera by the Routh-Hurwitz stability criterion and bifurcation method. Next Generation Matrix (NGM) method is used to get the basic reproductive numbers ($\Re_0$) to find the local stability at the equilibrium point of the. The disease-free equilibrium point is locally asymptotically stable if $\Re_0 < 1$, while the endemic equilibrium point is locally asymptotically stable if $\Re_0 > 1$ the results of numerical simulations obtained $\Re_0 = 0.87$ indicated that the disease-free equilibrium point is locally asymptotically stable. In endemic condition ($\Re_0 > 1$) show that increasing the rate of vaccination and disinfection can reduce the population of susceptible, infected and bacteria of *V. Cholerae*.

1. Introduction

Vibrio Cholerae is a bacteria that causes cholera [1], which is characterized by diarrhea, vomit, and dehydration [2]. Without proper treatment, it can cause death [3]. The transmission of cholera usually through water or food that is contaminated by bacteria [4]. The emergence of cholera is often undetected, so appropriate prevention needs to be done.

Indonesia, China, and India are an endemic district of Cholera. In 1961 Cholera spread in 23 countries and the source of transmission came from Sulawesi [5], then spread to Europe and Japan in 1970 [6]. In Indonesia, there were 6882 cases from September 1994 to November/December 1999. Mathematical modeling can be used to study problems in the real world by constructing a mathematical model that according to the problems. Several papers have discussed the mathematics model in the spread of cholera, among others by looking at the effects of vaccination and demographic movements [7]. Further, Rahmi, et.al divided the population of *Vibrio Cholerae* into two types, they are *hyper infectious* bacteria and *less infectious* bacteria [8].

In this paper, discuss a mathematical model in the spread of cholera that been constructed by [9]. In previous paper analyzed the effect of the transmission rate (from human to human and from environment to human) in the dynamical population, while in this paper analyze the effect of vaccination and disinfection in the dynamical population. The population divide into two, namely the human population (*N*) and *V. Cholerae* population (*B*). The population of humans is divided into three subpopulations,

they are susceptible (*S*), infected (*I*), and recovered (*R*), then. this model considers the vaccination and disinfection to control the spread of cholera.

2. Construction of model

The assumptions used in the process of modeling the spread of cholera are as follows, the values of birth rate and death rate are the same, equal to μ. There are two ways of transmission, from human to human and environment to human. Vaccination and disinfection are used to control cholera. A recovered individual becomes invulnerable.

Susceptible individuals increase due to the natural birth rate μ. It reduced due to interactions between the susceptible individual and *V. Cholaerae* with a concentration in the environment k, the transmission rate is β_e, and the interactions with an infected individual, the transmission rate is β_h. It also reduced due to the natural death rate μ and vaccination rate ν.

Infected individuals increase due to interactions between susceptible individuals and *V. Cholaerae* with a concentration in the environment k, the transmission rate is β_e, and the interactions with infected individuals, the transmission rate is β_h. Infected individuals reduced due to the recovered rate from its self as γ and natural death rate μ. It influences the population of *V. Cholerae* ξI but does not affect the number of it.

Recovered individual increase due to recovered rate from infected individuals as γ and vaccination rate from susceptible individuals as ν. Then it reduces due to the natural death rate μ. The population of *V. Cholerae* increase due to contribution rate of human that infected as ξ. It reduces due to the death rate from its self (δ)and disinfection rate (c).

Obtained the system of differential equation [9],

$$\frac{dS}{dt} = \mu N - \beta_e S\frac{B}{k+B} - \beta_h SI - \mu S - \nu S, \quad (1)$$

$$\frac{dI}{dt} = \beta_e S\frac{B}{k+B} + \beta_h SI - \gamma I - \mu I, \quad (2)$$

$$\frac{dR}{dt} = \gamma I - \mu R + \nu S, \quad (3)$$

$$\frac{dB}{dt} = \xi I - \delta B - cB, \quad (4)$$

where S, I, R, and B are susceptible, infected, recovery, and bacteria *V.* Cholerae, because variable R only appears in equation (4), so the system can be reduced to:

$$\left.\begin{aligned}\frac{dS}{dt} &= \mu N - \beta_e S\frac{B}{k+B} - \beta_h SI - \mu S - \nu S = f_1\\ \frac{dI}{dt} &= \beta_e S\frac{B}{k+B} + \beta_h SI - \gamma I - \mu I = f_2\\ \frac{dB}{dt} &= \xi I - \delta B - cB = f_3\end{aligned}\right\} \quad (5)$$

3. Equilibrium point of the model

The equilibrium point is a condition where there are no changes in each population over time. System (5) can be written :

$$\mu N - (\beta_e S \frac{B}{k+B} + \beta_h SI) - \mu S - vS = 0, \quad (6)$$

$$\beta_e S \frac{B}{k+B} + \beta_h SI - (\gamma + \mu)I = 0, \quad (7)$$

$$\xi I - \delta B - cB = 0. \quad (8)$$

Disease-free equilibrium (DFE) point $E_0 = (S_0, I_0, B_0)$ is a condition when there is no disease and bacteria in populations $(I_0 = B_0 = 0)$, by substituting $I_0 = B_0 = 0$ into equation (6) was obtained E_0 as follows:

$$E_0 = (S_0, I_0, B_0) = (\frac{\mu N}{(\mu + v)}, 0, 0).$$

To look for basic reproductive number ($\Re_0$) is used NGM method, $\Re_0$ is a parameter used to know the effect of the spread of cholera in population, it was obtained

$$\Re_0 = \frac{\beta_h \mu N}{(\mu + v)(\gamma + \mu)} + \frac{\beta_e \mu N \xi}{(\mu + v)(\gamma + \mu)(\delta + c)k}.$$

The endemic equilibrium point $E^* = (S^*, I^*, B^*)$ is a condition where there are diseases and bacteria in populations. By solving the equations (3.6) – (3.8) was obtained E^* as follows:

$E^* = (S^*, I^*, B^*)$, where

$$S^* = \frac{(k(\delta + c) + \xi I^*)(\gamma + \mu)}{\beta_e \xi + \beta_h (k(\delta + c) + \xi I^*)},$$

$$B^* = \frac{\xi I^*}{(\delta + c)}, \text{ and}$$

$m_1 I^{*2} + m_2 I^* + m_3 = 0$, where

$$m_1 = [\beta_h (\gamma + \mu)\xi]$$

$$m_2 = \left[(\beta_h (\gamma + \mu)k(\delta + c)) + ((\mu + v)(\gamma + \mu)\xi) + (\beta_e (\gamma + \mu)\xi) - (\beta_h \mu N \xi) \right]$$

$$m_3 = [((\mu + v)(\gamma + \mu)k(\delta + c)) - (\beta_h \mu N k(\delta + c)) - (\beta_e \mu N \xi)]$$

To state the population of I^* having at least one positive root, so $I_1^* I_2^* < 0$ if and only if $D = m_2^{\,2} - 4m_1 m_3 > 0$ and $\frac{m_3}{m_1} < 0$ by inequality analysis $m_3 < 0$ and $m_1 > 0$.

$m_1 = [\beta_h (\gamma + \mu)\xi]$ so $m_1 > 0$

$$m_3 = ((\mu + v)(\gamma + \mu)k(\delta + c)) - (\beta_h \mu N k(\delta + c)) - (\beta_e \mu N \xi) < 0$$

$$\Leftrightarrow ((\mu + v)(\gamma + \mu)k(\delta + c)) < (\beta_h \mu N k(\delta + c)) + (\beta_e \mu N \xi)$$

$$\Leftrightarrow 1 < \frac{\beta_h \mu N}{(\mu + v)(\gamma + \mu)} + \frac{\beta_e \mu N \xi}{(\mu + v)(\gamma + \mu)k(\delta + c)}$$

$$\Leftrightarrow \Re_0 > 1$$

So the existence $I^* \geq 0$ is guaranteed by $\Re_0 > 1$.

4. Stability analysis

Stability analysis is carried out to obtain the behavior of the equilibrium points. Stability of the DFE point can be stated by theorem;

Theorem 1. *Point* E_0 *is locally asymptotically stable if* $\Re_0 < 1$.

Proof:

System (3.5) is a nonlinear system, so it must first be linearized by forming Jacobian Matrix around E_0 , was obtained:

$$J(E_0) = \begin{bmatrix} -(\mu+\nu) & -\dfrac{\mu N \beta_h}{\mu+\nu} & -\dfrac{\beta_e \mu N}{(\mu+\nu)k} \\ 0 & \dfrac{\mu N \beta_h}{\mu+\nu} - \gamma - \mu & \dfrac{\beta_e \mu N}{(\mu+\nu)k} \\ 0 & \xi & -(\delta + c) \end{bmatrix}$$

The characteristic equation of the Jacobian $J(E_0)$ is

$$(\lambda+\mu+\nu)\left[\lambda^2 + \lambda(\delta + c - p + \gamma + \mu) + (\gamma+\mu)(\delta+c) - p(\delta+c) - \xi q\right] = 0 \qquad (9)$$

where $p = \dfrac{\mu N \beta_h}{\mu+\nu}$ and $q = \dfrac{\beta_e \mu N}{(\mu+\nu)k}$. From equation (9) we obtain eigenvalue are $\lambda_1 = -(\mu+\nu)$ and polynomial equation $\mathrm{P}(\lambda) = a_0\lambda^2 + a_1\lambda + a_2 = 0$, where

$a_0 = 1$

$a_1 = \delta + c - p + \gamma + \mu$

$a_2 = (\gamma+\mu)(\delta+c) - p(\delta+c) - \xi q$

Based on *Routh-Hurwitz* criteria, E_0 locally asymptotically stable if $a_1 > 0, a_2 > 0$, and $a_1 a_2 > 0$, these conditions are met if $\Re_0 < 1$.□

Further, the stability of the E^* point can be state by theorem;

Theorem 2. *Point* E^* *is locally asymptotically stable if* $\Re_0 > 1$.

Proof:

Theory of *Manifold Center* [10] used to carry out the stability of E^* in $\Re_0 > 1$. The parameter bifurcation from $\Re_0 = 1$ is β_h, where $\beta_h = \beta_h^*$, was obtained:

$$\beta_h = \frac{(\mu+\nu)(\gamma+\mu)(\delta+c)k - \beta_e \mu N \xi}{\mu N(\delta+c)k}$$

Matrix Jacobian around DFE point when $\beta_h = \beta_h^*$ is :

$$J(E_0, \beta_h^*) = \begin{bmatrix} -(\mu+\nu) & -\dfrac{(\mu+\nu)(\gamma+\mu)(\delta+c)k - \beta_e \mu N \xi}{(\mu+\nu)(\delta+c)k} & -\dfrac{\beta_e \mu N}{(\mu+\nu)k} \\ 0 & \dfrac{(\mu+\nu)(\gamma+\mu)(\delta+c)k - \beta_e \mu N \xi}{(\mu+\nu)(\delta+c)k} - \gamma - \mu & \dfrac{\beta_e \mu N}{(\mu+\nu)k} \\ 0 & \xi & -(\delta+c) \end{bmatrix}$$

It has simple eigenvalue as $\lambda_2 = 0$. Then obtain right eigen vector as ***w*** and left eigen vector as ***v*** that corresponding to the eigenvalue $\lambda_2 = 0$.

The right eigenvector denoted by $\mathbf{w}=\begin{bmatrix} w_1 & w_2 & w_3 \end{bmatrix}^T$ satisfied $J(E_0,\beta_h^*)\mathbf{w}=0$

$$\begin{bmatrix} (-\mu-\nu)w_1 & \left(-\dfrac{(\mu+\nu)(\gamma+\mu)(\delta+c)k-\beta_e\mu N\xi}{(\mu+\nu)(\delta+c)k}\right)w_2 & \left(-\dfrac{\beta_e\mu N}{(\mu+\nu)k}\right)w_3 \\ 0 & \left(\dfrac{(\mu+\nu)(\gamma+\mu)(\delta+c)k-\beta_e\mu N\xi}{(\mu+\nu)(\delta+c)k}-\gamma-\mu\right)w_2 & \left(\dfrac{\beta_e\mu N}{(\mu+\nu)k}\right)w_3 \\ 0 & \xi w_2 & (-\delta-c)w_3 \end{bmatrix}=0$$

taken $w_2=1$, so obtained $w_3=\dfrac{\xi}{(\delta+c)}$ and $w_1=-\dfrac{(\gamma+\mu)}{(\mu+\nu)}$. The right eigen vector is

$$\mathbf{w}=\begin{bmatrix} -\dfrac{(\gamma+\mu)}{(\mu+\nu)} \\ 1 \\ \dfrac{\xi}{(\delta+c)} \end{bmatrix}$$

While the left eigen vector denotes by $\mathbf{v}=\begin{bmatrix} \mathrm{v}_1 & \mathrm{v}_2 & \mathrm{v}_3 \end{bmatrix}$ satisfied $\mathbf{v}J(E_0,\beta_h^*)=0$

$$\begin{bmatrix} -(\mu+\nu)\mathrm{v}_1 \\ \left(-\dfrac{(\mu+\nu)(\gamma+\mu)(\delta+c)k-\beta_e\mu N\xi}{(\mu+\nu)(\delta+c)k}\right)\mathrm{v}_1+\left(\dfrac{(\mu+\nu)(\gamma+\mu)(\delta+c)k-\beta_e\mu N\xi}{(\mu+\nu)(\delta+c)k}-\gamma-\mu\right)\mathrm{v}_2+\xi\mathrm{v}_3 \\ \left(-\dfrac{\beta_e\mu N}{(\mu+\nu)k}\right)\mathrm{v}_1+\left(\dfrac{\beta_e\mu N}{(\mu+\nu)k}\right)\mathrm{v}_2-(\delta+c)\mathrm{v}_3 \end{bmatrix}^T=0$$

obtained $\mathrm{v}_1=0$, $\mathrm{v}_2=\dfrac{(\mu+\nu)(\delta+c)k}{\beta_e\mu N}\mathrm{v}_3$, and $\mathrm{v}_3=\mathrm{v}_3$, then look for $\mathbf{v}$ that satisfy $\mathbf{v}\cdot\mathbf{w}=1$

$$\begin{bmatrix} 0 & \dfrac{(\mu+\nu)(\delta+c)k}{\beta_e\mu N}\mathrm{v}_3 & \mathrm{v}_3 \end{bmatrix}\begin{bmatrix} -\dfrac{(\gamma+\mu)}{(\mu+\nu)} \\ 1 \\ \dfrac{\xi}{(\delta+c)} \end{bmatrix}=1$$

$$\frac{(\mu+\nu)(\delta+c)k}{\beta_e\mu N}\mathrm{v}_3+\frac{\xi}{(\delta+c)}\mathrm{v}_3=1$$

obtained $\mathrm{v}_3=\dfrac{\beta_e\mu N(\delta+c)}{(\mu+\nu)(\delta+c)^2k+\beta_e\mu N\xi}$, so the left eigen vector is

$$\mathbf{v}=\begin{bmatrix} 0 \\ \dfrac{(\mu+\nu)k}{(\mu+\nu)k+\beta_e\mu N\xi} \\ \dfrac{\beta_e\mu N(\delta+c)}{(\mu+\nu)(\delta+c)^2k+\beta_e\mu N\xi} \end{bmatrix}^T$$

Suppose that $S = y_1$, $I = y_2$, and $B = y_3$. Derivative partial levels two of the system equation (3.5) in free equilibrium disease case are :

$$\frac{\partial^2 f_2}{\partial y_1 \partial y_2} = \frac{\partial^2 f_2}{\partial y_2 \partial y_1} = \beta_h,\ \frac{\partial^2 f_2}{\partial y_1 \partial y_3} = \frac{\partial^2 f_2}{\partial y_3 \partial y_1} = \frac{\beta_e k}{(k+y_3)^2},\ \frac{\partial^2 f_2}{\partial y_3 \partial y_3} = -\frac{2\beta_e y_1 k}{(k+y_3)^3},\ \frac{\partial^2 f_2}{\partial y_1 \partial \beta_h^*} = y_2,$$

and $\frac{\partial^2 f_2}{\partial y_2 \partial \beta_h^*} = y_1$

Then find the parameter a and b , where:

$$a = \sum_{k,i,j=1}^{n} v_k w_i w_j \frac{\partial^2 f_k}{\partial y_i \partial y_j}(0,0) \text{ and } b = \sum_{k,i=1}^{n} v_k w_i \frac{\partial^2 f_k}{\partial y_i \partial \beta_h^*}(0,0)$$

obtained

$$a = -\frac{k\left[\beta_h(\gamma+\mu)(\delta+c)^2(k+y_3)^3 + \beta_e(\gamma+\mu)(\delta+c)(k+y_3)\xi k^2 + 2\beta_e(\mu+v)\xi^2 k y_1\right]}{\left[(\mu+v)k + \beta_e \mu N \xi\right](\delta+c)^2(k+y_3)^3} < 0$$

and $b = \frac{(\mu+v)ky_1}{(\mu+v)k+\beta_e \mu N \xi} > 0$. Based on the theory of *Manifold Center* [10] if $a < 0$ and $b > 0$, then case 4 applies to the system (3.5) and E^* the point is locally asymptotically stable if $\Re_0 > 1$.□

5. Numerical simulation

Parameters used for numerical simulation based on the parameter from Rahmi, et al [8] and Sun, et al [9] are as follows, natural birth (μ) = $\frac{0.0066}{356}$ /day and death rate (μ) = $\frac{0.0066}{356}$ /day, concentration of *Vibrio Cholerae* in environment (k)= 500 cell/ml, human population (N)=1.36×10^9 individuals, transmission rate from environment to human (β_e) = $\frac{2669}{365}\times10^{-6}$/day, transmission rate from human to human (β_h) = $\frac{53508}{365}\times10^{-9}$/day, recovered rate (γ) = 0.2 /day, Rate of human contribution to *Vibrio Cholerae* (ξ) = 10 cell/ml/day, death rate of *V. Cholerae* (δ) = 0.033/day.

In disease-free conditions $v = 0.5$ and $c = 0.01$ are taken [8], obtained $\Re_0 = 0.8723273720$, and $E_0 = (49181,0,0)$. It shows that the stability DFE point of cholera is reached when the susceptible individuals are 49181. the graphic is:

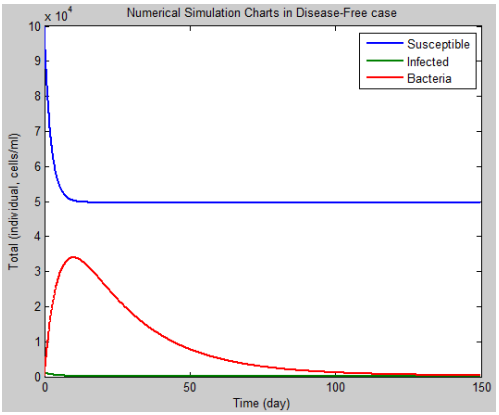

Figure 1. Numerical Simulation Charts in Disease-Free Case

In the initial situation, the number of susceptible individuals was 100000 people and then decline until at t> 30 stable approaching 49181 people. In an infected individual with an initial number of 1000 people decline until at> 30 stable approaching 0 people. Whereas in bacteria *V. Cholera* the initial amount of 100 cells/ml has fluctuated until t> 130 is stable close to 0.

In endemic conditions, variations in the value of *v* are taken, they are 0.09, 0.3, and 0.4, then variations values of *c* are 0.5, 0.7, and 0.9. these values result $\Re_0 > 1$, then it is used to see the effect of the vaccination and disinfection rate on dynamical populations of cholera spread. Obtained the graphics are:

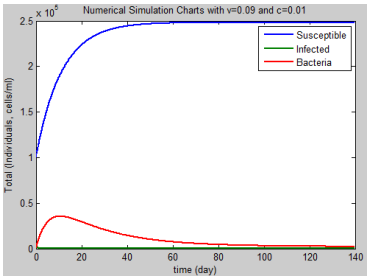

Figure 2. *v*=0.09 and *c*=0.001

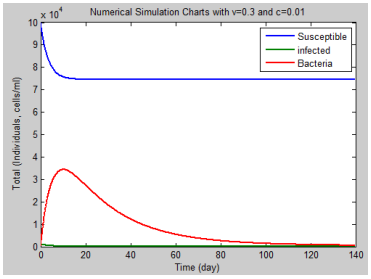

Figure 3. *v*=0.3 and *c*=0.001

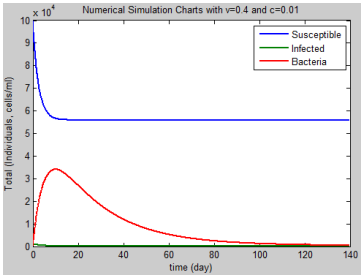

Figure. 4 *v*=0.4 and *c*=0.001

From Figure 2 – Figure 4, In the initial situation the number of susceptible individuals is 100000, in the infected individual are 1000 people, and in bacteria *V. Cholera* the initial are100 cells/ml. From figure 2 the susceptible individual is increased until t >70 is stable approaching 248.340 people. In infected individual decline until t > 30 stable approaching 10 people. while in bacteria *V. Cholera* has fluctuated until t > 130 is stable close to 2.280 cells/ml.

From figure 3 the susceptible individual is decline until t >10 is stable approaching 7.452 people. In infected individual decline until at> 10 stable approaching 0 people. while in bacteria *V. Cholera* has fluctuated until t > 130 is stable close to 57 cells/ml.

From figure 4 the susceptible individual is decline until t >10 is stable approaching 5.589 people. In infected individual decline until at> 10 stable approaching 0 people. while in bacteria *V. Cholera* has fluctuated until t > 130 is stable close to 44 cells/ml.

Table 1. Total populations in 140th day with various values of *v*

Simulations	*v*	Susceptible Individuals (person)	Infected Individuals (person)	*V. Cholerae* (cells/ml)	$\Re_0$
1	0,09	248.340	10	2.280	4,86
2	0,3	7.452	0	57	1,46
3	0,4	5.589	0	44	1,09

From table 1 appears that increase of vaccination and disinfection rate can reduce the population

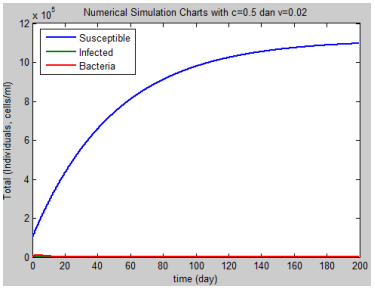

Figure 5. *c*=0.5 and *v*=0.02

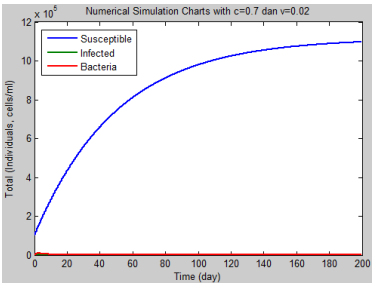

Figure 6. *c*=0.7 and *v*=0.02

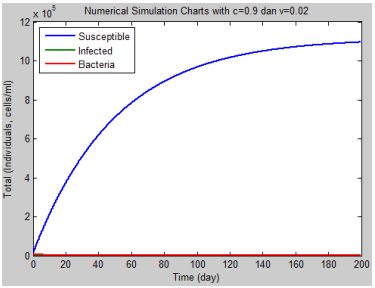

Figure 7. *c*=0.9 and *v*=0.02

From Figure 5 – Figure 7, In the initial situation the number of susceptible individuals is 100000, in the infected individual are 1000 people, and in bacteria *V. Cholera* the initial are100 cells/ml. From figure 5 the susceptible individual increases until t >180 is stable approaching 105.450 people. In infected individual decline until t > 10 stable approaching 10 people. while in bacteria *V. Cholera* has fluctuated until t > 10 is stable close to 210 cells/ml.

From figure 6 the susceptible individual increases until t >180 is stable approaching 105.270 people. In infected individual decline until at> 10 stable approaching 10 people. while in bacteria *V. Cholera* has fluctuated until t > 10 is stable close to 130 cells/ml.

From figure 7 the susceptible individual increases until t >180 is stable approaching 104.930 people. In infected individual decline until at> 10 stable approaching 10 people. while in bacteria *V. Cholera* has fluctuated until t > 130 is stable close to 80 cells/ml.

Tabel 2. Total populations in 140th day with various values of *c*

Simulations	*c*	Susceptible Individuals (person)	Infected Individuals (person)	*V. Cholerae* (cell/ml)	$\Re_0$
1	0,5	105.450	10	210	2,65
2	0,7	105.270	10	130	2,17
3	0,9	104.930	10	80	1,91

From table 2, it appears that the increase of the disinfection rate can reduce the populations.

6. Conclusion

This paper has proposed a mathematical model in the form of first-order non-linear differential equation systems with 4 variables $SIRB$. The disease-free equilibrium point is locally asymptotically stable if $\Re_0 < 1$, while the endemic equilibrium point is locally asymptotically stable if $\Re_0 > 1$. The results of the numerical simulations obtained $\Re_0 = 0.87$ indicated that the DFE point is locally asymptotically stable. In endemic conditions ($\Re_0 > 1$) show that increasing the rate of vaccination and disinfection can reduce the population of susceptible, infected, and bacteria of *V. Cholerae*.

References

[1] Misra A K, Gupta A, and Venturino E 2016 *Chaos, Solitons and Fractals* Vol **9** pp. 610-621

[2] Triyono E A 2015 *Buku Ajar Ilmu Penyakit Dalam* (Jakarta, Airlangga University Press) pp. 691-694

[3] Berge T, Bowong S and Lubuma J M S 2015 Mathematics and Computers in Simulation vol. **133** pp. 142-146

[4] Zhou X Y and Cui J A 2012 Vol **37** pp. 3093-3101

[5] Soedarto 2009 *Penyakit Menular di Indonesia* (Jakarta: CV Sagung)

[6] Tian J P and Wang J 2011 *Mathematical Biosciences* vol. 232 pp. 31-41

[7] Kokomo E and Emvudu Y 2018 *Nonlinear Analysis: Real World Applications,* vol. **45** pp. 142-156

[8] Rahmi N, J and N 2016 *Global Journal of Pure and Applied Mathematics* vol. 12, pp. 3105-3121.

[9] Sun G Q, Xie J H, Huang S H, Jin Z, Li M T, and Liu L 2016 *Commun Nonlinear Sci Numer Simulat,* vol. 40, pp. 235-244

[10] Castillo C 2004 *Math. Biosci. Eng,* vol. 1 p. 361 – 404

[11] P P B d F B L Depkes 2010 *Identifikasi Penyebab Kejadian Luar Biasa Kolera di Papua Terkait Kontak Jenazah dan Sanitasi* (Jakarta: Departemen Kesehatan).

[12] Manda E H, 2014 *Within Host Dynamics for Treatment of R5 HIV Infection in The Langerhans Cell*, (Thesis African Institute for Mathematical Sciences (AIMS).