

Transmission Model of *Burkholderia Pseudomallei* Infection in Thailand

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Abstract— Melioidosis is caused by burkholderia pseudomallei infection, a gram negative bacilli bacteria that is infected in soil and water. It is found in all regions of Thailand. The most infection cases in Thailand is found in the East, Northeast and South. The disease can be found in both humans and animals, and can occur rapidly and severely, sometimes fatally. We constructed the model for Melioidosis and analyze the model by using dynamical analysis. The basic reproductive number of disease is found. We found the infection rate of Melioidosis, increasing rate of Bacteria and number of total population effect to the basic reproduction number of Melioidosis. The simulations of these factors with the basic reproduction number are shown.

Keywords— Basic reproductive rate, Melioidosis, Stability, Transmisson model

I. INTRODUCTION

Melioidosis was first discovered by Whitmore and Krishnaswami in 1911 in Yangon, Myanmar. Patients are infected by prolonged contact with soil and water, such as farming, gardening. Diving without proper boots or protective equipment. When the skin touches the soil and water for a long time, the infection can enter the body directly without the need for wounds [1]. If there are wounds that can become more easily transmitted to the body or infected by drinking water or eating contaminated food, the most vulnerable groups are diabetics, schizophrenia, chronic kidney disease, as well as those with other low immunity-related diseases such as cancer [2-3]. In 2015, the Bureau of Epidemiology received a report from the surveillance system. There were 3,242 cases of Melioidosis disease, 4.96 patients per 100,000 people. The majority of patients in the Northeast died, 112 deaths, 0.17 deaths per 100,000 people. The 3.45 percent mortality rate soared, with 107 deaths, 1,165 cases of female and 2,077 male deaths, a female-to-male ratio of 1:1.8. The sick rate is 11.17 per 100,000 people, the 55-64 age group, the sickness rate of 10.41 per hundred thousand people and 45-54 years, the sick rate of 7.52 per 100,000 people. The highest occupation was agriculture, 54.63 percent, according to a study by the Melioid Research Center [4]. Sappasitthiprasong Hospital, Ubon Ratchathani Province Melioid patients were found to have confirmed the results between 1997 and 2006 every year. 200 – 300 cases, 40 percent of patients die. In 2006, 380 patients died, 154 were patients, about two-thirds were patients

in Ubon Ratchathani province, and about one-third were patients who were sent from neighboring provinces. This is because Ubon Ratchathani is the most common death toll, and melioids are considered another serious disease because of the high death rate and budget loss. Melioidosis is an infectious disease caused by a bar-shaped gram-negative bacteria called *Burkholderia pseudomallei*. Especially in patients with low immunity. The disease was first discovered by Whitmore and Krishnaswami in 1911 in Yangon, Myanmar. When the first culture was found to be *Bacillus mallei*, the infection was regrouped, with different names: *B. whitmori*, *Pfeifferellawhitmori*, *Actinobacillus pseudomallei*, *Loefflerellawhitmore*, *Malleomycespseudomallei*, *Pseudomonasmallei*, until it was eventually named as *burkholderia pseudomallei*. This infection can be detected in the soil. Laboratory studies have found that this infection can live longer in tap water. The disease is common in Southeast Asia, Madagascar and Australia. The disease has also been reported in many places around the world, including Korea, Hong Kong, Sri Lanka, India, Iran, Turkey, Britain, France, Africa, the Soviet Union and the United States. The cause of this disease is more medical attention, since the disease often causes severe symptoms, it can cause rapid death of the patient. As well as having more immigrants from Southeast Asian countries to other countries around the world, the outbreak has spread easily. Doctors in each country are not skilled or familiar with the disease. In Thailand, the cases due to Melioidosis are found both man and woman as shown in figure 1.

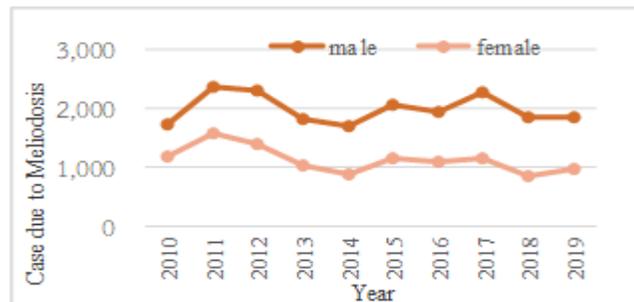


Fig 1. The number of cases of Melioidosis in Thailand [5].

Therefore, for these important reasons, it is highly appropriate to reduce the outbreak of melioidosis. Warawa studied the animal models in *burkholderia pseudomallei* [6]. In 2019, Mahikul et al [7] construct the mathematical model to examine the influences of the changing of Melioidosis incidence, and to predict the disease in Thailand. Tavaen et al.[8] constructed the model by considering hygiene care and treatment their model. They analyzed theoretically and

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numerically. They did not consider the re-infection of *Burkholderia pseudomallei*. In this paper, we study the spread of *Burkholderia pseudomallei* by mathematical modeling.

II. THE MATHEMATICAL MODEL

We consider the transmission of Melioidosis. After the person is recovered, the person can be infected again. We use the SEIRS model for the transmission of Melioidosis. S is the susceptible human, E is the exposed human, I is the infectious human, R is the recovered human. In general, this infection enters the human body through the skin. If the skin is in contact with soil and water which does not need to be scratched. Especially in cases of prolonged contact with soil and water such as farming and fishing and in patients with reduced immunity such as diabetic patients and kidney disease patients. We put S-E-I-R-S in this model because we are interested in the transmission of Melioidosis from burkholderia pseudomallei in human. All people is susceptible to this disease, if the person is infected with burkholderia pseudomallei, then that person can be infected but not infectious. After 9 days of incubation time, that person can be infectious person. If some persons have mild infections, then he/she can be infected again. We consider the mathematical model. The diagram of human population is described as follows:

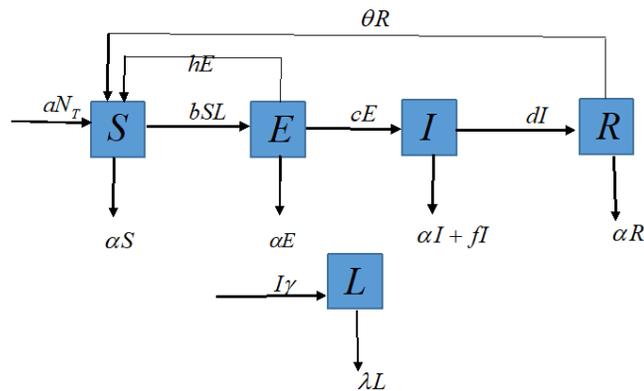


Fig 2. Diagram of human population.

In our mathematical model, the variable and parameters are defined as follows.

TABLE I. SHOW THE VARIABLE AND PARAMETERS USED IN OUR MODEL

variables/parameters	definition
S	The number of susceptible human population.
E	The number of exposed human population.
I	The number of infectious human population.
R	The number of recovered human population.
L	The number of <i>burkholderia pseudomallei</i> bacteria,
a	Natural birth rate of human population.
α	Natural death rate of human population.
b	Infection rate of Melioidosis.
c	Incubation rate of Melioidosis.
d	Recovery rate.
θ	Rate of infection again.
f	Death rate of Melioidosis.
γ	Increasing rate of Bacteria
λ	Decreasing rate of Bacteria.
h	Rate of exposed human can be susceptible human again.

From the diagram of human population in figure 2, we can write the mathematical model as follows.

$$dS/dt = aN_T + \theta R - bSL - \alpha S + hE, \tag{1}$$

$$dE/dt = bSL - cE - \alpha E - hE, \tag{2}$$

$$dI/dt = cE - dI - (\alpha + f)I, \tag{3}$$

$$dR/dt = dI - \theta R - \alpha R. \tag{4}$$

$$dL/dt = I\gamma - \lambda L. \tag{5}$$

with $N = S + E + I + R$ and L is the number of *burkholderia pseudomallei* bacteria. We assume the human population is constant. N is equivalent to the summation of susceptible, exposed, infectious and recovered human. We analyze our mathematical model in the next sections.

III. ANALYTICAL RESULTS

We use standard dynamical modeling method to find the equilibrium points. We set the right hand side of equations (1)-(5) to zero. Then we get the equilibrium points as follows.

i) The disease free equilibrium point;

$$E_0(S^*, E^*, I^*, R^*, L^*) = E_0\left(\frac{aN_T}{\alpha}, 0, 0, 0, 0\right)$$

ii) The endemic equilibrium point

$$E_1(\bar{S}^*, \bar{E}^*, \bar{I}^*, \bar{R}^*, \bar{L}^*) \quad \text{where} \\ \bar{S}^* = \frac{(\alpha + c + h)(\varphi + d + f)\lambda}{b(\alpha + c + d + f)\gamma},$$

$$\begin{aligned} \overline{E}^* &= \frac{(\alpha+d+f)(\alpha(\alpha+c+h)(\alpha+d+f)\lambda - ab(\alpha+c+d+f)\gamma N_T)(\alpha+\theta)}{b(\alpha+c+d+f)\gamma(\alpha(\alpha+c)(\alpha+d+f) + (\alpha(\alpha+c+d) + (\alpha+c)f)\theta)} \\ \overline{I}^* &= \frac{c(\alpha(\alpha+c+h)(\alpha+d+f)\lambda - ab(\alpha+c+d+f)\gamma N_T)(\alpha+\theta)}{b(\alpha+c+d+f)\gamma(\alpha(\alpha+c)(\alpha+d+f) + (\alpha(\alpha+c+d) + (\alpha+c)f)\theta)} \\ \overline{R}^* &= \frac{cd(\alpha(\alpha+c+h)(\alpha+d+f)\lambda + ab(\alpha+c+d+f)\gamma N_T)}{b(\alpha+c+d+f)\gamma(\alpha(\alpha+c)(\alpha+d+f) + (\alpha(\alpha+c+d) + (\alpha+c)f)\theta)} \\ \overline{L}^* &= \frac{(\alpha(\alpha+c+h)(\alpha+d+f)\lambda + ab(\alpha+c+d+f)\gamma N_T)(\alpha+\theta)}{b\lambda(\alpha(\alpha+c)(\alpha+d+f) + (\alpha(\alpha+c+d) + (\alpha+c)f)\theta)} \end{aligned}$$

Local stability of each equilibrium point can be determined from the sign of eigenvalues for each equilibrium state. If there are the negative signs for all eigenvalues, then that equilibrium point will be local stability. The eigenvalues (λ) can be found from setting $\det(J - \lambda I) = 0$ where J is the Jacobian matrix of the equilibrium point and I is the identity matrix. Jacobian matrix of our equation can be found from

$$J = \begin{pmatrix} -\alpha - bL & h & 0 & \theta & -bS_h \\ bL & -\alpha - c - h & 0 & 0 & bS_h \\ 0 & c & -\alpha - d - f & 0 & 0 \\ 0 & 0 & d & -\alpha - \theta & 0 \\ 0 & \gamma & \gamma & 0 & -\lambda \end{pmatrix}$$

For the disease free equilibrium point;

$$\det(J - \lambda I) = \begin{vmatrix} -\alpha & h & 0 & \theta & -(ab/\alpha)N_T \\ 0 & -\alpha - c - h & 0 & 0 & (ab/\alpha)N_T \\ 0 & c & -\alpha - d - f & 0 & 0 \\ 0 & 0 & d & -\alpha - \theta & 0 \\ 0 & \gamma & \gamma & 0 & -\lambda \end{vmatrix}$$

The eigenvalues for the disease Free State can be found from

$$(\lambda + \varphi)(\lambda + \varphi + \theta)(\lambda^3 + c_2\lambda^2 + c_1\lambda + c_0) = 0 \quad \text{where} \quad (6)$$

$$c_2 = 2\alpha + c + d + f + h + \lambda, \quad (6)$$

$$c_1 = \frac{\alpha(\alpha+d+f)(\alpha+c+h) + \alpha(2\alpha+c+d+f+h)\lambda - ab\gamma N_T}{\alpha} \quad (7)$$

$$c_0 = (\alpha+d+f)(\alpha+c+h)\lambda(1 - R_0) \quad (8)$$

where $R_0 = \frac{ab(\alpha+c+d+f)\gamma N_T}{\alpha(\alpha+d+f)(\alpha+c+h)\lambda}$

From the Routh-Hurwitz criteria [9], the eigenvalues will have negative signs when the following conditions are satisfied.

- i) $c_2 > 0$
- ii) $c_0 > 0$
- iii) $c_1c_2 - c_0 > 0$.

$$\begin{aligned} c_1c_2 - c_0 &= (1/\alpha)((2\alpha+c+d+f+h+\lambda)(\alpha(\alpha+d+f)(\alpha+c+h) \\ &+ ab\gamma N_T) + \alpha\lambda(3\alpha^2 + 3ac + c^2 + 3ad + cd + d^2 + 3af + cf \\ &+ 2df + f^2 + 3ah + 2ch + dh + fh + h^2 + 2\alpha\lambda + (c+d+f+h)\lambda \\ &+ (\alpha+d+f)(\alpha+c+h)R_0)) \end{aligned}$$

We can see that i)-iii) are satisfied when $R_0 < 1$.

For the endemic equilibrium point;

The eigenvalues can be found from

$$\lambda^5 + d_4\lambda^4 + d_3\lambda^3 + d_2\lambda^2 + d_1\lambda + d_0 = 0$$

where

$$\begin{aligned} d_4 &= 4\alpha + c + d + f + h + bL + \lambda + \theta, \\ d_3 &= 6\alpha^2 + (d+f)h + bL(d+f) + \lambda(d+f+h+bl) \\ &+ (d+f+h+bL^* + \lambda)\theta + c(d+f+bL^* + \lambda + \theta) \\ &+ \alpha(3(c+d+f+h+bL^*) + 4\lambda + 3\theta), \\ d_2 &= 4\alpha^2 + (d+f)(c+h)\lambda + ((d+f)(c+h) + (c+d+f+h)\lambda)\theta \\ &+ 3\alpha^2(c+d+f+h+bL^* + 2\lambda + \theta)\theta + \alpha(2cd + 2cf + 2dh + 2fh \\ &+ 2bcl + 2bdl + 2bfl + 3c\lambda + 3d\lambda + 3f\lambda + 3h\lambda + 3bl\lambda - 3b\gamma S^*) \\ &+ (2(c+d+f+h+bl) + 3\lambda)\theta + b((d+f)(L\lambda - \gamma S^*) \\ &+ (L(d+f+\lambda) - \gamma S^* + (L(d+f+\lambda) - \gamma S^* \\ &+ c(\gamma S^* + L(d+f+\lambda+\theta))), \\ d_1 &= \alpha^4 + bc(d+f)L^*\lambda + (d+f)(c+h)\lambda\theta \\ &+ b(cfL^* + (c+d+f)L^*\lambda + (c+d+f)\gamma S^*)\theta + \alpha^3(c+d+f+h+bl \\ &+ 4\lambda + \theta) + \alpha^2(fh + bfL^* + 3f\lambda + 3h\lambda + 3b\gamma S^* + (f+h+bL^* + 3\lambda)\theta \\ &+ d(h+bL^* + 3\lambda + \theta)\alpha(2(d+f)(c+h)\lambda + ((d+f)(c+h) \\ &+ 2(c+d+f+h)\lambda + \alpha(2(d+f)(c+h)\lambda + ((d+f)(c+h)), \\ d_0 &= \alpha((\alpha+d+f)(\alpha(\alpha+c+b) + b(\alpha+c)L)\lambda - ab(\alpha+c+d+f)\gamma S^*) \\ &+ ((\alpha(\alpha+d+f)(\alpha+c+h) + b(\alpha(\alpha+b+d) + (\alpha+c)f)L)\lambda \\ &+ ab(\alpha+c+d+f)\gamma S^*). \end{aligned}$$

From the Routh-Hurwitz criteria [9], the eigenvalues will have negative signs when the following conditions are satisfied.

i) $d_i > 0 (i = 0,1,2,3,4), \quad (9)$

ii) $d_2d_3d_4 > d_2^2 + d_4^2d_1, \quad (10)$

iii) $(d_1d_4 - d_0)(d_2d_3d_4 - d_3^2 - d_4^2d_1) - d_0(d_3d_4 - d_2)^2 - d_4d_0^2 > 0. \quad (11)$

By using Mathematica, we can say that (9)-(11) will satisfied when $R_0 > 1$.

IV. NUMERICAL SIMULATIONS

The total populations are supposed as $N = 1,000$ populations. The initial variables are $S(0)=100$ populations, $E(0) = 200$ populations, $I(0) = 500$ populations, $R(0) = 200$ populations. The natural birth and death rates are supposed equal to $\alpha = \mu = 1/(365 \times 74.18)$, $h = 1/5$ because the period of exposed human changed to be the susceptible human equal to 5 days, $c = 1/9$ because the period of melioidosis infection begins to change until the onset of symptoms which takes approximately 9 days.

$d = 1/60$ because the time that Melioidosis is treated which takes approximately 60 days, $\theta = 1/90$ is the rate of recurrence per 1 person can return to Melioidosis as 90 days, $f = 1/2$ is the death rate of Melioidosis 2 days. ; Increasing rate of bacteria $\gamma = 0.0001$; Decreasing rate of bacteria $\lambda = 0.00001$.

Case 1. We suppose $b = 0.00001$.

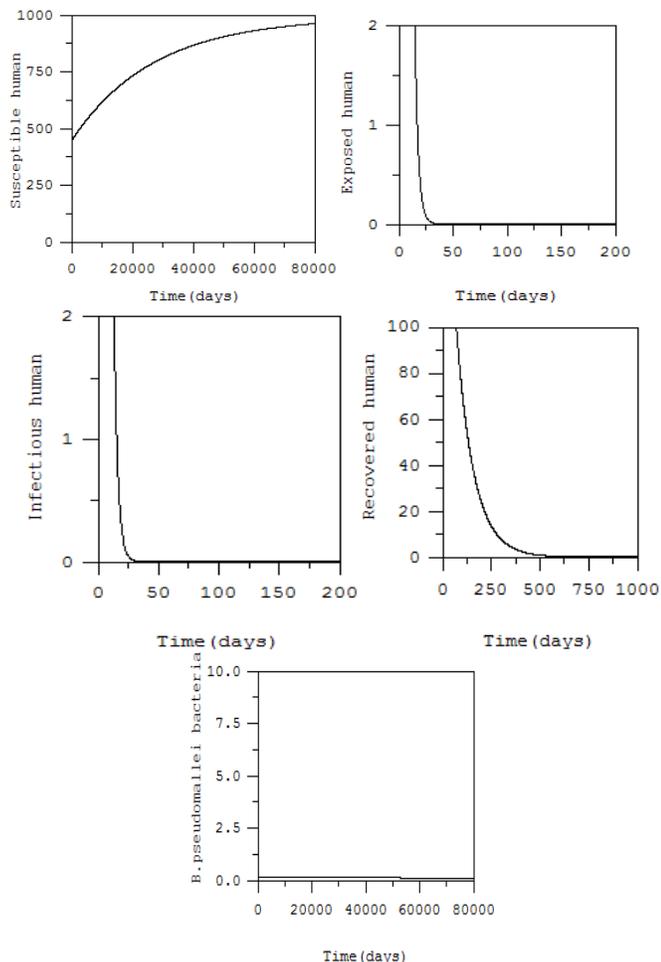


Fig 3. Time series solutions of our mathematical model.

We will see that the solutions converge to the disease free equilibrium point $(1000, 0, 0, 0, 0)$ and $R_0 = 0.39$.

Case 2. We suppose $b = 0.001$.

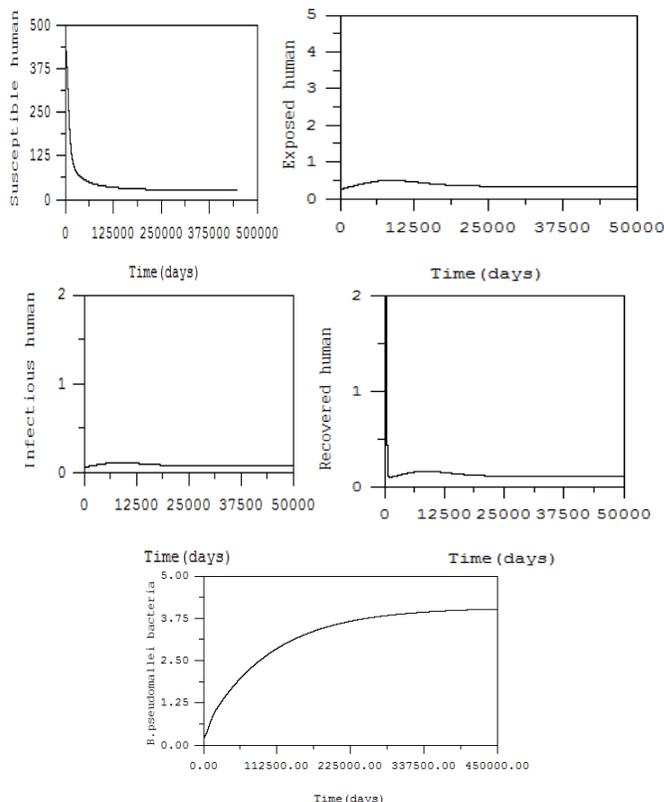
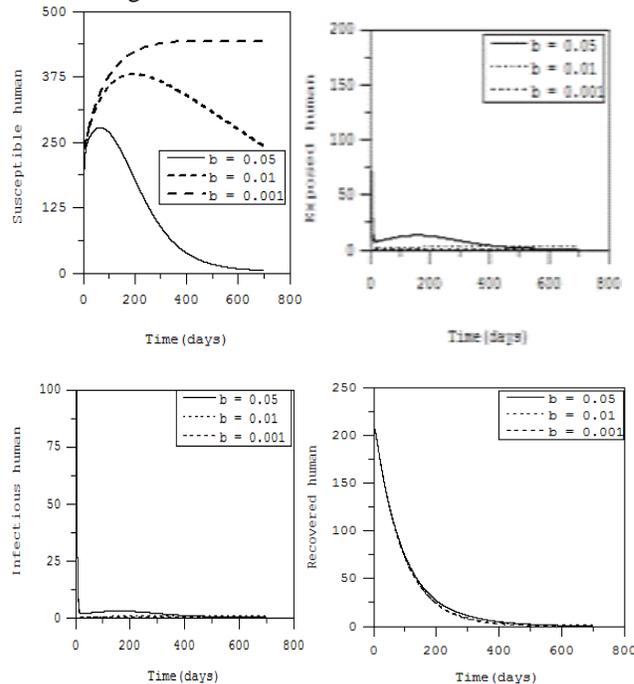


Fig 4. Time series solutions of our mathematical model.

We will see that the solutions converge to the endemic equilibrium point $(26, 0.33, 0.072, 0.11, 4)$ and $R_0 = 39$. Therefore the solutions converge to the disease free equilibrium for $R_0 < 1$ as shown in figure 3. The solutions converge to the endemic equilibrium point for $R_0 > 1$ as shown in figure 4.



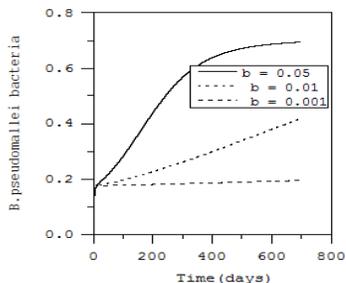


Fig 5. Time series solutions of our mathematical model for the difference infection rates.

From figure 5, when there is the higher infection rate, the lower number of susceptible human and the higher number of exposed, infectious, recovered human and number of *Burkholderia pseudomallei* bacteria.

V. DISCUSSION AND CONCLUSIONS

We consider the transmission model of Melioidosis. Basic reproductive number is the number of secondary cases directly generated by primary case in a population where all individuals are susceptible to infection [10-11]. The basic reproductive number of this disease is defined by

$$R_0 = \frac{ab(\alpha + c + d + f)\gamma N_t}{\alpha(\alpha + d + f)(\alpha + c + h)\lambda}$$

Basic reproductive number is the division of $ab(\alpha + c + d + f)\gamma N_t$ and $\alpha(\alpha + d + f)(\alpha + c + h)\lambda$. The higher rate of infection rate of Melioidosis, increasing rate of Bacteria and number of total population increase the basic reproductive number of the disease as shown in figure 6-8.

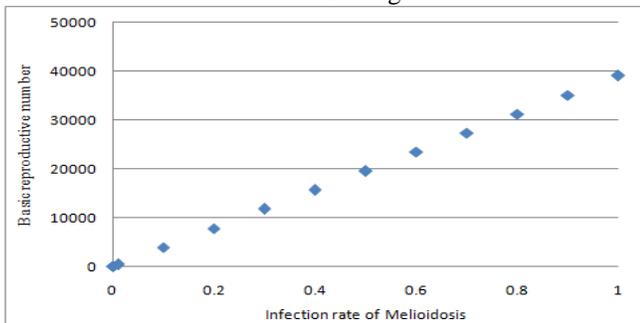


Fig 6. Basic reproductive number of our mathematical model for the difference infection rates.

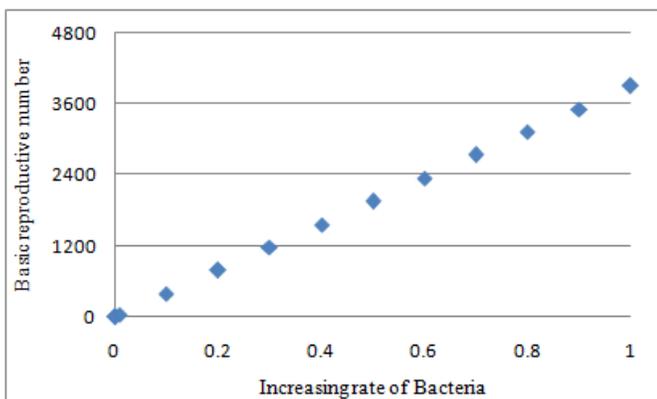


Fig 7. Basic reproductive number of our mathematical model for the difference increasing rate of bacteria.

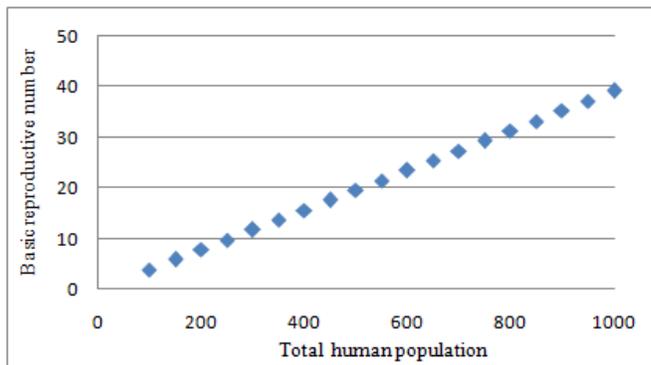


Fig 8. Basic reproductive number of our mathematical model for the difference total human population.

We use sensitivity analysis to our solutions. We used difference initial values of $(E(0), I(0))$. The solutions are shown robust. We obtained the trajectories as shown in figure 9.

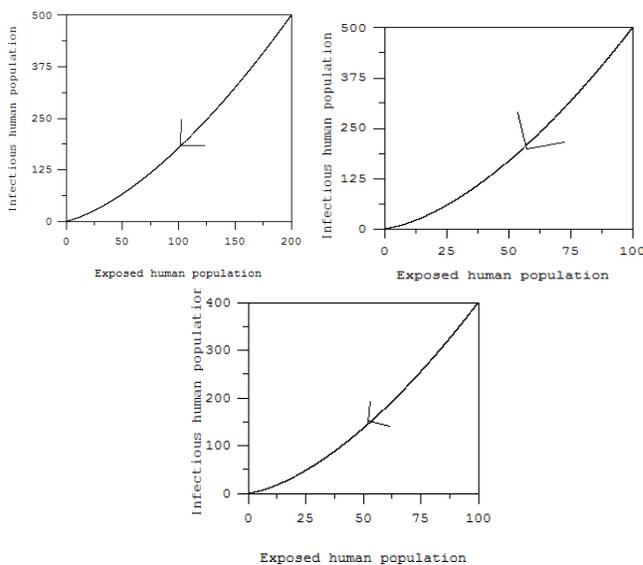


Fig 9. The trajectories of the solutions E-I space for the initial conditions (200,500), (100,500) and (100,400)

We can see that all the new trajectories converge to the same endemic equilibrium point (0.27,0.06). We can see that the infection rate of Melioidosis, increasing rate of Bacteria and number of total population effects to the transmission of Melioidosis. The basic reproductive number influence to the number of infectious Melioidosis. If the less basic reproductive number of Melioidosis, the less infectious number of Melioidosis. Melioidosis cases will be reduced. In the future, we may consider the dynamical model of the age and the gender of human population for the transmission of Melioidosis. There are many researches about construction and analyzing the dynamical model for the transmission of disease [12-14].

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