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Mathematical Model on the Effect of Disinfection and Treatment on the Transmission of Melioidosis

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Abstract: **Melioidosis is an infectious disease caused by *Burkoldera pseudomallei* bacteria. In this study, we have developed a Mathematical model on the effects of disinfection and treatment on the transmission of Melioidosis. From analyzing how disinfection and treatment affect different compartments, we have demonstrated that varying the rate of these two control measures will vary the rate of transmission of melioidosis disease. The R_0 was developed and the model stability and the existence of equilibrium points determined. From the quantitative analysis of the study, it was found that the local stability existed when $R_0 < 1$. The D.F.E is also globally stable when $R_0 < 1$. The numerical analysis determined that disinfecting the environment and treating the infected reduces the rate of infection of the disease.**

Keywords: **Melioidosis, Modelling, disinfection, treatment, stability, transmission, contamination, stability, equilibrium.**

I. INTRODUCTION

Melioidosis is a bacterial infectious disease which is caused by a bacteria called *Burkholderia pseudomallei.* It is also called Pseudomonas *pseudomallei* or Whitmore's bacillus [1].

It mainly affects humans and several species of animals. Since Melioidosis can affect any organ, it can imitate many other diseases; thus, it's other name "the great imitator." Infections can hibernate for months or years without being noticed, and later emerge to cause disease [2]. *Burkholderia pseudomallei* or *B. pseudomallei* as its commonly known, is susceptible to a few antibiotics.

Transmission

Earlier research has shown that melioidosis is an opportunistic disease that mostly spreads through the environment than it does from one animal to another [9]. Melioidosis is usually transmitted when a person gets in contact with contaminated soil or contaminated water through unconcealed wounds or in apparent skin wounds, inhalation of dust particles from contaminated soil and drinking/swallowing of contaminated water. Transmission from one human to another is extremely rare but has occurred through direct contact or through sexual contact in three reported cases [4].

A study done by Merck showed that, infections in the placenta of some animals like goats have led to abortions. It's more likely that sexual transmission can cause the disease. (Merck, 2012) [11]. Because rodents have a long course of the disease and infected animals transmit the organism in their feces, rodents are significant reservoirs of infection (Radostitis et al., 2006) [10].

A new born child can also get the disease from the mother through vertical transmission. Milk and meat products have been found to be the cause of infections in some cases (CFSPH, 2007; CDC, 2012) [12,13]

Several other animal species are also susceptible to melioidosis, these animals include but not limited to: monkeys, pigs, goats, dogs, horses, cattle, cats, sheep and many others [6]. Direct transmission from animals to humans and vice versa is not known to occur but these animals can act as carriers of the disease.

Diagnosis

Diagnosis of Melioidosis is done by isolating *B. pseudomallei* from urine, sputum, blood, throat swabs, skin lesions or through observation of antibody response to the *B. pseudomallei* bacteria. The incubation period for Melioidosis ranges from one day to three weeks with an average of nine days. However, in some cases, several years may elapse between exposure and appearance of the symptoms of clinical disease [7].

Treatment

After diagnosis, Melioidosis can be treated with the use of appropriate medication. Generally, the treatment commences with an antimicrobial therapy for between ten to 15 days, followed by three to seven months of administering oral antimicrobial therapy. Some of the antimicrobial agents that have been used and yield positive results includes: Intravenous therapy of Ceftazidime administered every seven hours or Meropenem which is taken after every seven hours [8][5].

Control

In endemic regions, *B. pseudomallei* is mainly found in infected soil and water bodies. Therefore, these water bodies should be chlorinated to reduce the risk of infection from these sources. Open wounds on the surface of the skin should be covered to protect them from being exposed to contamination and infection. In case the wounds are exposed to infection, they should be well cleaned. Any agricultural worker in contaminated areas is encouraged to use gloves and gum boots to reduce the risk of exposure to *B. pseudomallei.*

Generally, disinfecting, the contaminated soil and water bodies will drastically reduce the rate of transmission of Melioidosis by a bigger percentage. Open wounds should also be disinfected to kill the bacteria that might find their way into the body through open skin. Milk and from dairy animals should be pasteurized to eliminate infections.

The Need for this study

Mahikul et al., 2019. [14] studied a mathematical model of Melioidosis with eight compartments. They analyzed and solved the model numerically to find the structure and the future behavior of Melioidosis in Thailand. Their main focus was on the demographic behavior of the disease. However, their model did not perform the analysis of stability and reproductive number.

In this study a mathematical model is designed. The model examines the effect of disinfection and treatment on the transmission of the *B. pseudomallia* bacteria. We performed a theoretical analysis and numerical analysis of the model and obtained a basic reproductive number. We also established the equilibrium points of the model and the stability of the model.

II. MODEL FORMULATION

We have developed a model that deals with the effect of disinfection and treatment on the transmission of Melioidosis. Our model has five compartments i.e., Susceptible (S) which is the number of susceptible individuals, exposed (E) which is the number of exposed individuals, Infected (I) which the number of individuals infected with Melioidosis and Recovered (R) which is the number of recovered individuals. Finally, we have B which is the concentration of *Burkholderia pseudomallei* bacteria.

The following list contain definitions of parameters used in the model:

Λ= Recruitment rate

ω = Transmission Rate

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$\boldsymbol{\mu}$ = Ratre of Natural death

$\boldsymbol{\kappa}$ =Rate at which exposed are infected

$\boldsymbol{\delta}$ = rate of death as a result of the disease

$\boldsymbol{\tau}$ = Increase rate of bacteria by E and I

$\boldsymbol{\varphi}$ = Rate of death of the bacteria

$\boldsymbol{\lambda_1}$ = Efficiency of disinfection control on Susceptible individuals

$\boldsymbol{\lambda_2}$ = Rate of treatment control on infected individuals

Figure 1 Below shows the illustration of our developed model.

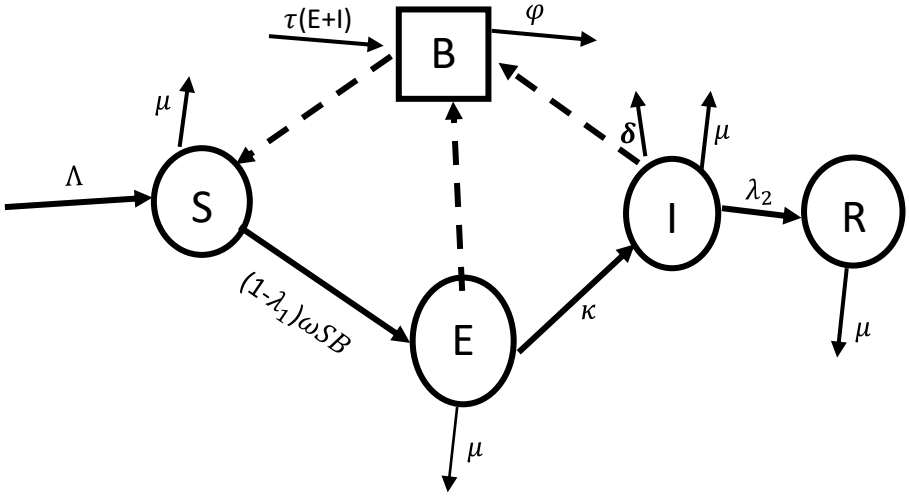

Figure 1: The Model

The following systems of differential equations were developed to help us find the solution to our model;

$\frac{dS}{dt} = \Lambda - (1-\lambda_1)\omega SB - \mu S$

$\frac{dE}{dt} = (1-\lambda_1)\omega SB - (\kappa+\mu)E$

$\frac{dI}{dt} = \kappa E - (\lambda_2 + \delta\_\mu)I$

$\frac{dR}{dt} = (\lambda_2)I - \mu R$

$\frac{dB}{dt} = \tau(E+I) - \varphi B$

The initial condition is given by $N_t = S_t + E_t + I_t + B_t + R_t$ with the initial conditions given by; $S_0 \geq 0, E_0 \geq 0, I_0 \geq 0, R_0 \geq 0, B_0 \geq 0$

Disease Free Equilibrium Point ($\boldsymbol{E_0}$)

There is absolute absence of the disease at the disease-free equilibrium. The compartments that depend on the existence of the disease have zero individuals in them. (Obuya, 2020) [15]. The compartments that ware set at zero are; Exposed (E), Infected(I), Recovered (R) and the one that contain the bacteria (B). We therefore set $\frac{d}{dt} = 0$, such that

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$$E_0 = (S_0, E_0, I_0, R_O, B_0) = \left(\frac{\Lambda}{\mu}, 0,0,0,0\right)$$

Endemic Equilibrium (E^*)

According to Obuya (2020), a system of differential equations has an endemic equilibrium if and only if R0 > 1, and it is globally asymptotically stable [16].

$$\boldsymbol{E^* = (S^*, E^*, I^*, R^*, B^*)}$$

Such that

$$S^* = \frac{(\kappa+\mu)(\lambda_2+\delta+\mu)}{(1-\lambda_1)\omega\tau(\lambda_2+\delta+\mu+\kappa)}$$

$$E^* = \frac{(\lambda_2+\delta+\mu)I^*}{\kappa}$$

$$I^* = \frac{(\kappa+\mu)(\lambda_1+\delta+\mu)\kappa\mu\varphi + \Lambda\kappa(1-\lambda_1)\omega\tau(\lambda_2+\delta+\mu+\kappa)}{(1-\lambda_1)(\kappa+\mu)(\lambda_2+\delta+\mu)\omega\tau(\lambda_2+\delta+2\mu)}$$

$$R^* = \frac{\lambda_2 I^*}{\mu}$$

$$B^* = \frac{\tau(\lambda_2+\delta+\mu+k)I^*}{\kappa\varphi}$$

Basic Reproduction Number (R_0)

We used the next generation matrix to get the basic reproduction number. The basic reproduction is the average number of new cases of infection that is caused by one person among the susceptible individuals [15]. For us to use the next generation matrix, we only considered compartments with the presence of the infection.

The R_0 was obtained using the following formulae;

$$R_0 = \frac{(1-\lambda_1)\omega\tau\lambda(\lambda_2+\delta+\mu+\kappa)}{(\kappa+\mu)(\lambda_2+\delta+\mu)\varphi\mu}$$

Stability of the system

A system is considered to be stable if and only the eigenvalues of the Jacobian matrix lie within the stability region of the said system.[16]

Local Stability

The DFE equilibrium is asymptotically locally stable of the $R_0 < 1$. At the DFE the Jacobian matrix (J) is given by:

$$J(S, E, I, R, B) = \begin{bmatrix} -(1-\lambda_1)\omega B^* & 0 & 0 & 0 & -(1-\lambda_1)\omega S^* \\ (1-\lambda_1)\omega B^* & -(\kappa+\mu) & 0 & 0 & (1-\lambda_1)\omega S^* \\ 0 & \kappa & -(\lambda_2+\delta+\mu) & 0 & 0 \\ 0 & 0 & \lambda_2 & -\mu & 0 \\ 0 & \tau & \tau & 0 & \varphi \end{bmatrix}$$

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At the DFE (E_0) the Jacobian Matrix is given by:

$$J\left(\frac{\Lambda}{\mu},0,0,0,0\right)=\begin{bmatrix} -\mu & 0 & 0 & 0 & -(1-\lambda_1)\omega\dfrac{\Lambda}{\mu} \\ 0 & -(\kappa+\mu) & 0 & 0 & (1-\lambda_1)\omega\dfrac{\Lambda}{\mu} \\ 0 & \kappa & (\lambda_2+\delta+\mu) & 0 & 0 \\ 0 & 0 & \lambda_2 & -\mu & 0 \\ 0 & \tau & \tau & 0 & \varphi \end{bmatrix}$$

From our Jacobian matrix above, we set the determinant of $\det(J(E_0)-\gamma I)=0$ to obtain the eigenvalues.

From the Jacobian matrix above, we work out to obtain the eigenvalues as follows:

$$(-\mu-\gamma)(-\mu-\gamma)(\gamma^3+(\kappa+2\mu+\lambda_2+\delta+\varphi)\gamma^3+(\varphi\big((\kappa+2\mu+\lambda_2+\delta)\big)+$$

$$(\kappa+\mu)(\lambda_2+\delta+\mu)-\left(\frac{(1-\lambda_1)\omega\Lambda\tau}{\mu}\right)\gamma+\varphi(\kappa+\mu)(\lambda_2+\delta+\mu)-\left(\frac{(1-\lambda_1)\omega\Lambda\tau(\kappa+\lambda_2+\delta)}{\mu}\right)=0$$

This will give us the eigenvalues as,

$$\gamma_1=\gamma_2=-\mu<0$$

$$\gamma^3+(\kappa+2\mu+\lambda_2+\delta+\varphi)\gamma^2+\big(\varphi(\kappa+2\mu+\lambda_2+\delta)\big)+(\kappa+\mu)((\mu+\lambda_2+\delta)-\left(\frac{(1-\lambda_1)\omega\Lambda\tau}{\mu}\right)\gamma$$

$$+\varphi(\kappa+\mu)(\mu+\lambda_2+\delta)-(1-\lambda_1)\omega\Lambda\tau\frac{(\kappa+\mu+\lambda_2+\delta)}{\mu}=0$$

This equation can simply be taken in the form;

$$\gamma^3+b_1\gamma^2+b_2\gamma^1+b_3=0$$

Thus

$$b_1=(\kappa+2\mu+\lambda_2+\delta+\varphi)$$

$$b_2=\varphi(\kappa+2\mu+\lambda_2+\delta)+(\kappa+\mu)(\lambda_2+\delta+\mu)-\frac{(1-\lambda_1)\omega\Lambda\tau}{\mu}$$

$$b_3=(\kappa+\mu)(\mu+\lambda_2+\delta)\varphi(1-R_0)$$

From the work above, it is evidence that $b_1>0$ and $b_1>0$ when $R_0<1$ and also $b_1,b_2>b_3$ when $R_0<1$. Hence, by using Routh – Hurwitz criterion the D.F.E point is asymptotically stable when $R_0<1$.

From the Jacobian matrix of endemic equilibrium point we obtain

$$\text{J(S*, E*, I*, R*, B*)} = \begin{bmatrix} -(1-\lambda_1)\omega B^* & 0 & 0 & 0 & -(1-\lambda_1)\omega S^* \\ (1-\lambda_1)\omega B^* & -(\kappa+\mu) & 0 & 0 & (1-\lambda_1)\omega S^* \\ 0 & \kappa & -(\lambda_2+\delta+\mu) & 0 & 0 \\ 0 & 0 & \lambda_2 & -\mu & 0 \\ 0 & \tau & \tau & 0 & \varphi \end{bmatrix}$$

We then set the $\det(J(E_0)-\gamma I)=0$

From this the first eigenvalue is $\gamma=-\mu<0$

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We then consider the Characteristics equation as

$$\gamma^4 + b_1\gamma^3 + b_2\gamma^2 + b_3\gamma + b_4 = 0$$

Such that

$$b_1 = (\kappa + \mu) + (\lambda_2 + \delta + \mu) + \varphi + \mu + (1 - \lambda_1)\omega B^*$$

$$b_2 = (\kappa + \mu)\varphi - \tau(1 - \lambda_1)\omega S^* + (\lambda_2 + \delta + \mu)(\kappa + \mu - \varphi) + ((1 - \lambda_1)\omega B^* + \mu)(\lambda_2 + \delta + 3\mu + \kappa)$$

$$b_3 = (\kappa + \mu)(\lambda_2 + \mu + \delta)\varphi - \tau(1 - \lambda_1)(\lambda_2 + \delta + \mu)\omega S^* + \left((1 - \lambda_1)\omega B^* + \mu\right)\left((\kappa + \mu)\mu - \tau(1 - \lambda_1)\omega S^* + (\lambda_2 + \delta + \mu)(\kappa + \mu + \varphi)(1 - \lambda_2)\omega S^*\tau(1 - \lambda_1)\omega B^* - \kappa\right)$$

$$b_4 = ((1 - \lambda_1)\omega B^* + \mu)((\kappa + \mu)(\lambda_2 + \delta + \mu)\varphi - \tau(1 - \lambda_1)(\lambda_1 + \delta + \mu)\omega S^* + (1 - \lambda_1)\omega S^*\tau((1 - \lambda_1)(\lambda_2 + \delta + \mu)\omega B^* - \kappa\mu)$$

By Using the Routh- Hurwitz method the equilibrium point is only stable if

$b_3, b_4 > 0$ and $b_1, b_{2,} b_3 > b_3^2 + b_1^2 b_4$.

Global stability

The system of differential equations is said to have a unique endemic equilibrium if $R_0 > 1$, and it is globally asymptotically stable [17]

We used the Lyapunov function to demonstrate this as follows;

$$L = \left(\frac{\tau\kappa + \tau(\lambda_2 + \delta + \mu)}{(\kappa + \mu)(\lambda_2 + \delta + \mu)\varphi}\right)E + \left(\frac{\tau}{(\lambda_2 + \delta + \mu)}\right)I + \left(\frac{1}{\varphi}\right)B$$

We then find the derivative of L and use boundary solutions to get

$$L' = \left(\frac{(1 - \lambda_1)\omega S\tau(\kappa + \lambda_2 + \delta + \mu)}{(\kappa + \mu)(\lambda_2 + \delta + \mu)\varphi} - 1\right)B \leq \left(\frac{(1 - \lambda_1)\omega\Lambda\tau(\kappa + \lambda_2 + \delta + \mu)}{(\lambda_2 + \delta + \mu)\varphi} - 1\right) = B(R_0 - 1)$$

We then manipulate the above equation to find that

$L' < 0$ when $R_0 < 1$ and $L' = 0$ when $E = I = B = 0$

Therefore, we ascertain that E_0 is globally asymptotically stable when $R_0 < 1$

NUMERICAL SOLUTIONS

In this section we looked at the quantitative analysis of the system of differential equations of the model using the Runge-Kutta fourth order method. The analysis was done using the Maple 8.2 software. We estimated the parameters used in our computations based on the existing literature.

Table 1: Parameter Estimations

Symbol	Description	Value (per week)	Source
Λ	Recruitment rate	1	Estimate
ω	Rate of transmission	0.004	[7]
μ	Rate of Natural death	0.0003	[10]
κ	Rate at which the exposed are infected	0.6	[10]
δ	Rate of death as a result of the disease	0.035	[7]
τ	Increase rate of bacteria by E and I	0.8	Estimate
φ	Rate of death of bacteria	0.5	Estimate
λ_1	Efficiency of disinfection control on susceptible individuals	0.5	Variable
λ_2	Rate of treatment control for infected individuals	0.5	Variable

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Dynamics of Increasing disinfection

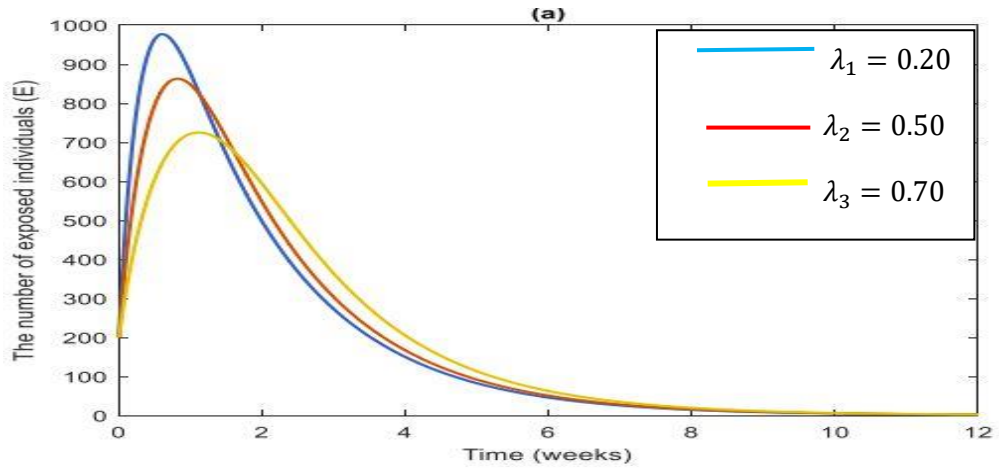

Figure 2: Increasing Disinfection vs Exposed Population

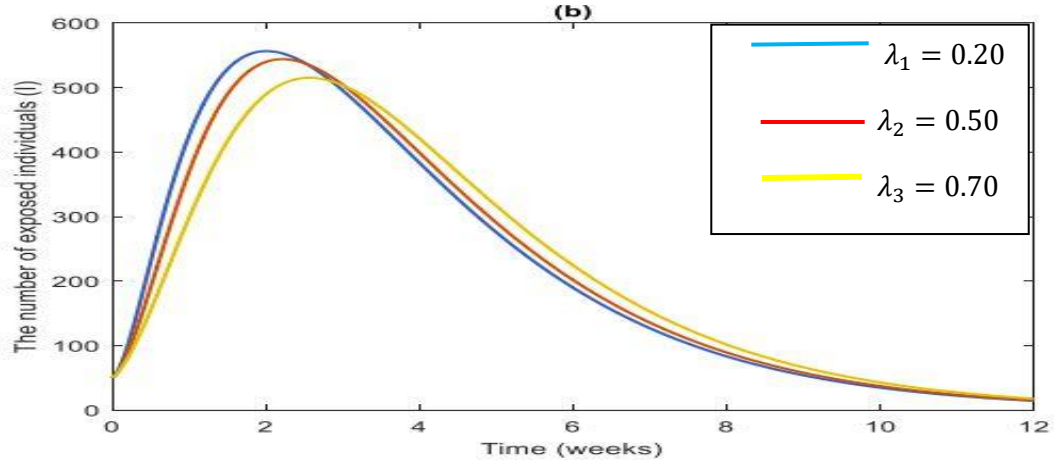

Figure 3: Increasing Disinfection Vs Infected Population

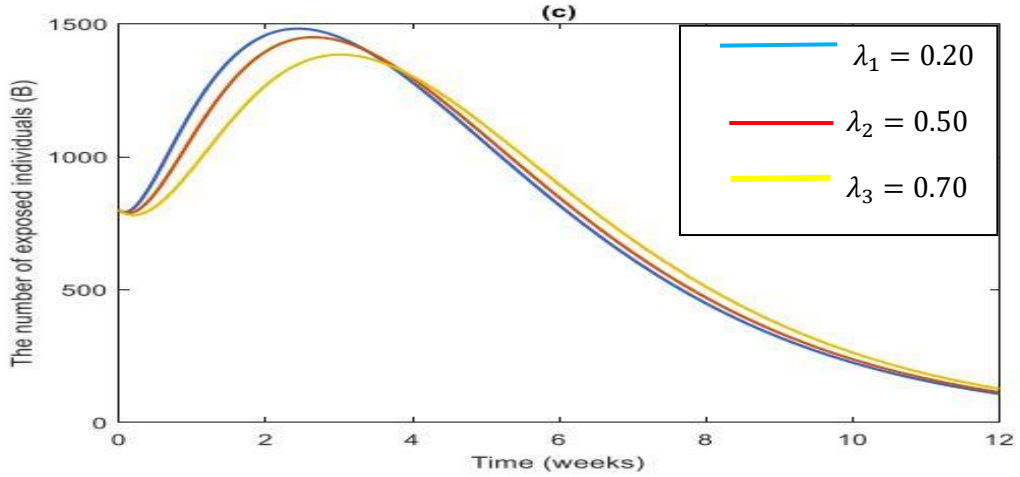

Figure 4: Increase in Disinfection vs Concentration of Bacteria

Figure 2 shows the dynamics of the exposed population when the disinfection of the surrounding is increased. Figure 3 shows the dynamics of the infected population when the disinfection of the surrounding is increased. Finally, figure 4 shows the dynamics of the concentration of the bacteria when the disinfection is increased.

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As shown in the figures 2 ,3 and 4, an increase in disinfection of the environment results into a decrease in the number of exposed individuals, infected individuals and also to a decrease in the concentration of the bacteria.

This shows that there is a positive result when we use disinfectants as a means of reducing the transmission of melioidosis. Therefore, we recommend the use of disinfectants as one of the means of reducing the transmission of the melioidosis disease.

Dynamics of treatment

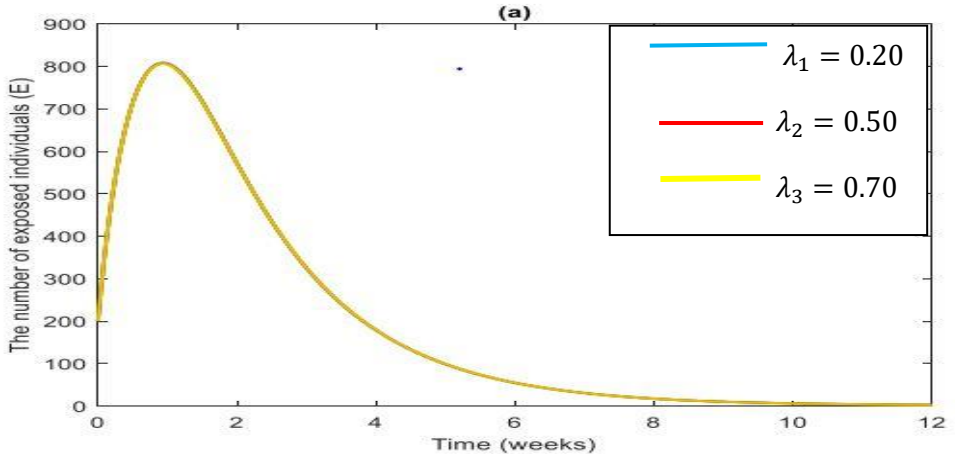

Figure 5: Increasing Treatment vs Exposed Population

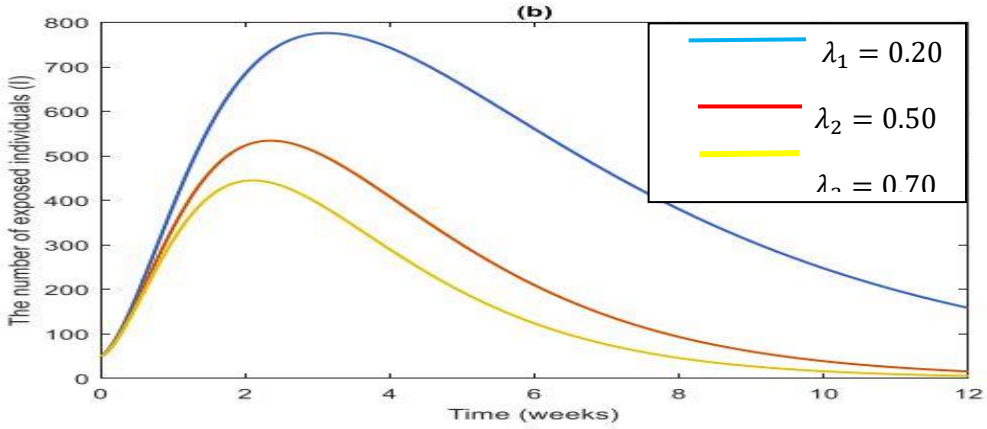

Figure 6: Increasing Treatment Vs Infected Population

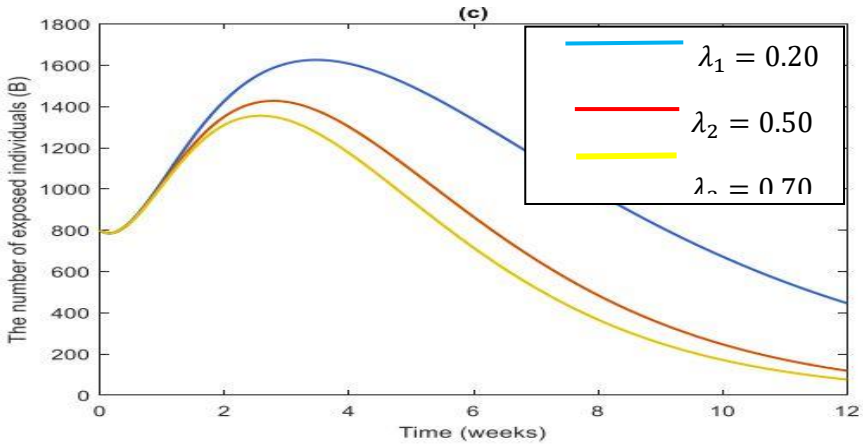

Figure 7: Increase in Disinfection vs Concentration of Bacteria

Figure 5 shows the dynamics of the exposed individuals when the rate of treatment is increased while figure 6 shows the dynamics of the infected individuals when the rate of treatment is increased. Finally, figure 7 shows the dynamics of the concentrations of the bacteria when the rate of treatment is increased.

From figure 5, 6 and 7 we can deduce that when the rate of treatment is increased, there is no change in the number of the exposed individuals. It also shows that when the rate of treatment is increased, there is a notable decrease in the number of infected individuals and also in the concentration of the bacteria.

Therefore, this is a demonstration that treatment reduces the number of people who are infected and also the concentration of the bacteria. Thus, the infected need to be treated as a means of reducing the transmission of the disease.

III. CONCLUSION

In this study, we have developed a Mathematical model on the effects of disinfection and treatment on the transmission of Melioidosis. From analyzing how disinfection and treatment affect different compartments, we have demonstrated that varying the rate of these two control measures will vary the rate of transmission of melioidosis disease.

Through this developed model we have studied its dynamics and came to a conclusion that increasing the rate of disinfection and treatment reduces the rate of transmission and help in reducing the disease.

We have established that the points of equilibrium exists and that the D.E.F is globally stable when $R_0 < 1$. With these findings, we can conclude that there is need for different stakeholders to come on board to promote and improve sanitation by disinfecting both contaminated and uncontaminated surroundings and also to champion for treatment of the infected individuals to help reduce the rate of transmission of melioidosis.

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