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Sensitivity Analysis for the Dynamics of Leptospirosis Disease

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ABSTRACT

Leptospirosis is a bacterial disease caused by bacteria called Leptospira and it is spread in human when the open wounds in contact with water or soil containing infected animals' urine. In this paper, we consider a mathematical model of transmission of Leptospirosis with the aim to control the disease in future. The objective is to investigate the impact of parameters in Leptospirosis model by using sensitivity analysis. Our result shows that transmission rate between the susceptible and infected human gives major impact on disease transmission and spreading.Thus, the number of Leptospirosis patients could be reduced if the transmission factors decrease.

Keywords: Leptospirosis, dynamical systems, mathematical model and sensitivity analysis.

1. Introduction

In 1883, Landouzy (1883) discovered Leptospirosis is a disease of sewer worker, caused by spirochetes belonging to Leptospira. Rodents is the most common animals that spread the disease. This bacterium can be spread to human when a broken skin or open wound in contact with water or soil containing animal urine. This disease can lead to liver failure, kidney damage, respiratory distress, and even death depending on exposure rate between contaminated source and infected within 2 days to 4 weeks. This illness usually begins abruptly with fever and other symptoms. Leptospirosis occurs in two phases - first the infected person become ill after recovered for the first time and the second phase (more severe), the infected person suffers from kidney or liver failure. Previous studies reported that the transmission of Leptospirosis disease have become interest by many researchers including Zaman (2010),Pongsumpun (2012), Muhammad et al. (2013), Pimpunchat et al. (2013) and Kazeem et al. (2016).

In order to control the transmission rate of Leptospirosis disease, it is essential to investigate each parameter that contribute to the transmission rate. One of the methods to determine this character is called the *sensitivity analysis*. We consider the Leptosirosis model by Khan et al. (2016). In this previous paper by Khan et al. (2016), the authors did not used the sensitivity analysis method to determine the most effective parameter that contribute to the increment of infected peopl with this disease. Therefore, the objective of this paper is to extend the work by Khan et al. (2016) by applying the sensitivity analysis method to determine the most effective parameter for this Leptospirosis model in Khan et al. (2016). This method is very important to show the robustness of model prediction to parameter value. We will calculate the sensitivity indices for all the parameters involved in the model. By using this method, we may control the most influential parameter in order to reduce the spreading of Leptospirosis disease among human population.

2. Leptospirosis model in Khan et al. (2016)

In this paper, we consider a Leptospirosis transmission model proposed by Khan et al. (2016). The mathematical model is divided into two populations which are human population and vector population. The human population denoted by N_h, is subdivided into three compartments; susceptible individuals (S_h), infected individuals (I_h) and recovered individuals (R_h). Therefore $N_h = S_h + I_h + R_h$. Whereas, vector population denoted by N_v is subdivided into two classes; susceptible vector (S_v) and infected vector (I_v). Therefore the total vector population is $N_v = S_v + I_v$. A flow diagram of the model is as depicted in Figure 1.

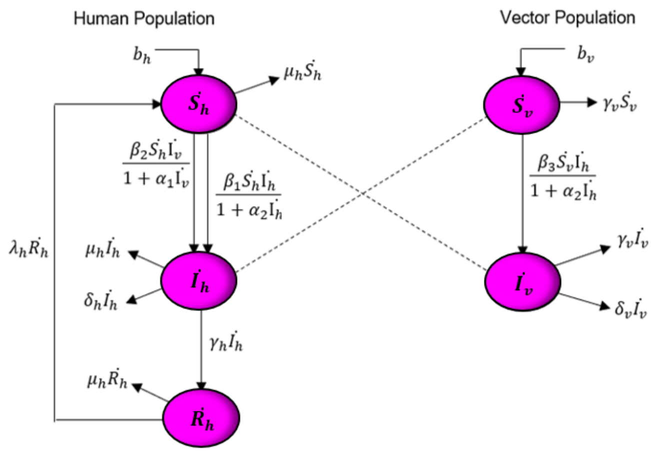

Figure 1: The flow diagram of human and vector interaction in Leptospirosis model (Khan et al. (2016))

From Figure 1, a nonlinear differential equation can be constructed as follows:

$$
\begin{array}{lllll}
\frac{dS_h}{dt} & = & \dot{S}_h & = & b_h - \mu_h S_h - \left(\frac{\beta_2 I_v}{1+\alpha_1 I_v} + \frac{\beta_1 I_h}{1+\alpha_2 I_h}\right) S_h + \lambda_h R_h, \\
\frac{dI_h}{dt} & = & \dot{I}_h & = & \left(\frac{\beta_2 I_v}{1+\alpha_1 I_v} + \frac{\beta_1 I_h}{1+\alpha_2 I_h}\right) S_h - (\mu_h + \delta_h + \gamma_h) I_h, \\
\frac{dR_h}{dt} & = & \dot{R}_h & = & \gamma_h I_h - (\mu_h + \lambda_h) R_h, \\
\frac{dS_v}{dt} & = & \dot{S}_v & = & b_v - \gamma_v S_v - \left(\frac{\beta_3 I_v}{1+\alpha_2 I_v}\right) S_v, \\
\frac{dI_v}{dt} & = & \dot{I}_v & = & \left(\frac{\beta_3 I_v}{1+\alpha_2 I_v}\right) S_v - \gamma_v I_v - \delta_v I_v,
\end{array}
\tag{1}
$$

where the variables and parameters in (1) are described as in Table 1. The set of equations for $\frac{dS_h}{dt}, \frac{dI_h}{dt}, \frac{dR_h}{dt}, \frac{dS_v}{dt}, \frac{dI_v}{dt}$ denote the rates of change of populations S_h, I_h, R_h, S_v, I_v respectively.

Table 1: Description of variables and parameters for model (1)

Symbol	Description	Value
S_h	The number of susceptible human in the population	unknown
I_h	The number of infected human in the population	unknown
R_h	The number of recovered human in the population	unknown
S_v	The number of susceptible vector	unknown
I_v	The number of infectious vector	unknown
b_h	Recruitment rate for human	1.2
b_v	Recruitment rate for vector	1.3
γ_h	Recovery rate of the infected human	2.7×10^{-3}
γ_v	Natural mortality rate of vector population	1.8×10^{-3}
α_1	Saturation factor that measure inhibitory effect I_v	0.83
α_2	Saturation factor that measure inhibitory effect I_h	0.83
β_1	Transmission rate for human population	0.04
β_2	Transmission rate for vector population	0.04
β_3	Transmission rate S_v and I_h	0.04
δ_h	Disease death rate for human population	1.0×10^{-3}
δ_v	Disease death rate for vector population	0.04
μ_h	Natural mortality rate of human population	4.6×10^{-5}
λ_h	Rate of infected human become susceptible again	2.85×10^{-3}

3. Sensitivity Analysis

Sensitivity analysis is used to investigate the impact of model parameters on Leptospirosis transmission rate. This analysis has been widely used for examples for Malaria model (Chitnis et al. (2008)) and for dengue model (Perez and Loaiza (2016)). We use next generation method to derive the reproduction number, R_0. In this section, the sensitivity analysis is used for all the parameters involved in model (1). For example, the normalized forward sensitivity index of a variable R_0, that depends on a parameter β_1, which is denoted as $\gamma_{\beta_1}^{R_0}$ can be defined as:

$$\gamma_{\beta_1}^{R_0} := \frac{\partial R_0}{\partial \beta_1} \times \frac{\beta_1}{R_0}, \tag{2}$$

where,

$$R_0 = \frac{\frac{1}{2}\left(\beta_1 b_h \delta_v \gamma_v + \beta_1 b_h \gamma_v^2 + \sqrt{a_1 + a_2 + a_3 + a_4 + a_5 + a_6 + a_7 + a_8 + a_9}\right)}{\mu_h \gamma_v (\mu_h \delta_v + \mu_h \gamma_v + \delta_h \delta_v + \delta_h \gamma_v + \delta_v \gamma_h + \gamma_v \gamma_h)},$$

and where,

$$
\begin{aligned}
a_1 &= 4\mu_h^2\beta_2\beta_3 b_h b_v \delta_v \gamma_v,\\
a_2 &= 4\mu_h^2\beta_2\beta_3 b_h b_v \gamma_v^2,\\
a_3 &= 4\mu_h\beta_2\beta_3 b_h b_v \delta_h \delta_v \gamma_v,\\
a_4 &= 4\mu_h\beta_2\beta_3 b_h b_v \delta_h \gamma_v^2,\\
a_5 &= 4\mu_h\beta_2\beta_3 b_h b_v \delta_v \gamma_h \gamma_v,\\
a_6 &= 4\mu_h\beta_2\beta_3 b_h b_v \gamma_h \gamma_v^2,\\
a_7 &= \beta_1^2 b_h^2 \delta_v^2 \gamma_v^2,\\
a_8 &= 2\beta_1^2 b_h^2 \delta_v \gamma_v^3,\\
a_9 &= \beta_1^2 b_h^2 \gamma_v^4.
\end{aligned}
$$

We will calculate the sensitivity indices for all the parameters involved by using the formula above. Then we will arrange all the parameter from most sensitive to the least sensitive. Then most sensitive parameter will change the system if its value changed. Therefore, this parameter will help us to control the transmission of Leptospirosis.

4. Results and Discussion

In order to reduce the rate of Leptospirosis disease transmission, it is very important to know the character of each of the parameters that involved in the transmission. Since the basic reproduction number influence the initial disease transmission, therefore, we have to find the sensitivity indices of all the parameters that involved in basic reproduction number. If we substitute the values of all parameters in Table 1 to the R_0 in Khan et al. (2016), we have that $R_0 = 27925$. Next, we calculate the sensitivity index. For example, by using the formula in (2) the calculation for the transmission rate for human population, β_1 is as follows:

$$\gamma_{\beta_1}^{R_0} := 6946799 \cdot \frac{0.04}{27925} = 0.993.$$

Other sensitivity indices for different parameters (Table 2) are also determined. b_h showed the largest sensitivity index, however the parameter is uncontrolled. Therefore, β_1 is considered. Whereas, the least sensitive parameter is δ_h.

Table 2: Sensitivity indices for model parameters of R_0. b_h is the most sensitivity index, δ_h is the least sensitivity index.

Parameter	Sensitivity Indices
b_h	173241481
β_1	0.993
β_3	3.544×10^{-4}
μ_h	5.025×10^{-11}
β_2	1.425×10^{-11}
b_v	2.193×10^{-9}
λ_h	0
δ_v	0
γ_h	-4.716×10^{-47}
γ_v	-2.18×10^{-19}
δ_h	-1.554×10^{21}

A small value changes for the most sensitive parameter leads to a large quantitative changes. A simulation for the transmission rate, β_1 is illustrated in Figure 2. The infected individual with initial parameter value $\beta_1 = 0.04$ (middle line), increases 10% (upper line) and decreases 10% from the initial parameter value (lowest line). Figure 2 shows that when the transmission rate,β_1 increases 10% which is 0.044, the number of infected human also increases, whereas when the transmission rate decreases 10% which is 0.036, the number of infected human also decreases.

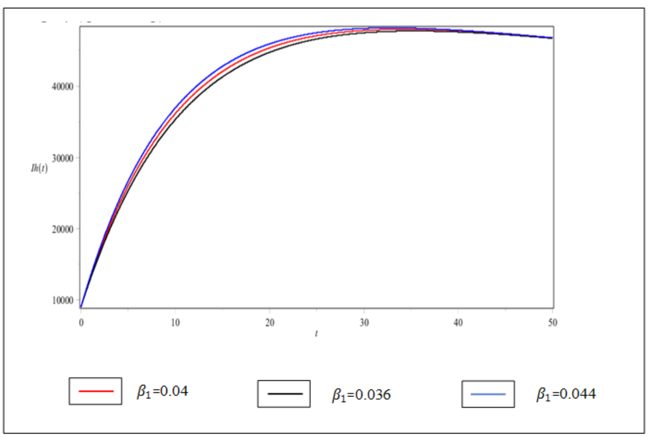

Figure 2: The changes in infected human when the transmission rate is either increase or decrease by 10%

5. Conclusions

We conclude that the Leptospirosis transmission rate is proportional to susceptible and infected human. Therefore, a few preventions should be taken in order to reduce the transmission rate of human such as avoid swallowing the contaminated water at river side, the people working in agricultural areas wear protective clothes, wash the surface of the can food or drinks before open it and people should avoid playing with water during the flood (Zamir et al. (2017)). Our future work will focus on adding other variables such as vaccination or treatment for the model considered in this paper which more useful in helping to determine effective ways of controlling the spread of Leptospirosis disease.

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