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MATHEMATICAL MODEL OF LEPTOSPIROSIS IN MALAYSIA USING THE SIR APPROACH

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ABSTRACT

Leptospirosis is the most common zoonotic infection in tropical areas. Leptospirosis has become an endemic disease in Malaysia since 2010, caused by bacteria called pathogenic spirochetes of the genus leptospira. Infected animals' urine spreads the bacteria, which can enter water and soil and live for weeks or months. If you encounter soil or water where an infected animal has peed, the germ can enter your body through skin breaks such as scratches, open wounds, or dry areas. Leptospirosis is a growing public health problem, and if not adequately managed, it might have a significant health impact and burden on the country in the coming years. Numerous mathematical models of infectious diseases have been formulated. The SIR model is one of the mathematical models that has proven to be useful in analysing infectious diseases. However, there has been a minimal study on the dynamics of leptospirosis cases using the SIR model, particularly in Malaysia. Hence, this study aims to formulate a mathematical model of leptospirosis transmission in Malaysia using the SIR model. The SIR model is expressed as a set of first-order ordinary differential equations. The obtained results reveal that the basic reproduction number (R_0) for the model is lower than one, which indicates that leptospirosis is endemic in a population. In addition, the local stability analysis of the disease-free equilibrium point is also presented and discussed. The numerical analysis in this study was carried out using Matlab software. The result is graphically plotted, showing that the SIR-SI model of leptospirosis cases in Malaysia demonstrates that leptospirosis has become endemic.

Keywords: *Basic Reproduction Number, Leptospirosis, Local Stability Analysis, Malaysia, SIR Model.*

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1. Introduction

Adolf Weil, Professor of Medicine at Heidelberg University, was the first to write about Leptospirosis (Brightman, 2018). He described four cases of acute febrile illness with jaundice, abnormal signs in the central nervous system, hepatosplenomegaly, and renal malfunction in 1886 (Brightman, 2018). The patients improved. In 1887, the term "Weil's disease" was coined (Brightman, 2018). Leptospirosis is the most common zoonotic infection in tropical areas and the World Health Organization (WHO) estimates that it affects 10 or more people in every 100,000 population each year. The bacteria that cause leptospirosis, pathogenic spirochetes of the genus leptospira, are transferred by infected animals' urine, which can get into water and soil and live for weeks to months. If you encounter soil or water where an infected animal has peed, the germ can enter your body through skin breaks such as scratches, open wounds, or dry areas. It can also enter the body through the nose, mouth, or genitals. It is difficult to obtain from another human, though it can be transmitted through sex or breastfeeding (Kathri, 2021). Wild animals that might serve as reservoirs are raccoons, skunks, squirrels, rodents, etc. Leptospirosis can induce a wide range of symptoms in humans however, some infected humans may exhibit no symptoms at all. When the disease strikes, it strikes quickly. You'll develop a fever. It could reach 104 degrees Fahrenheit (Kathri, 2021).

The SIR (susceptible-infected-removed) model, developed in the early twentieth century by Ronald Ross, William Hamer, and others is a system of three coupled nonlinear ordinary differential equations with no explicit formula solution (Weiss Sir Ronald Ross, 2013). It has proven to be useful in analysing infectious diseases since it was formed in the early 20th century. It is commonly used to stimulate the spread of infectious diseases such as dengue and malaria. The basic SIR compartmental model divided a population into three classes which are susceptible, infected, and recovered in Figure 1.

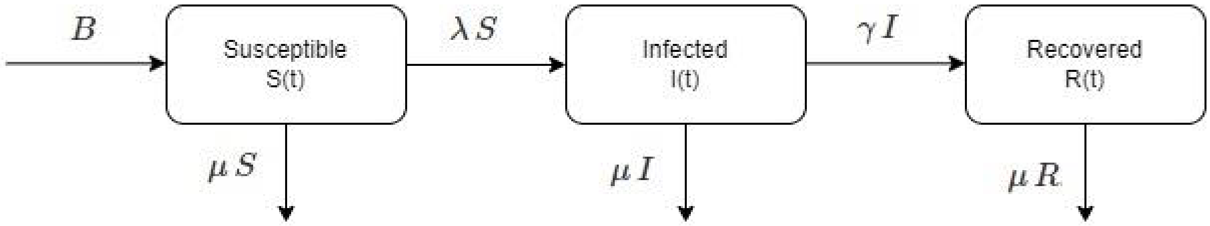

Figure 1: The schematic diagram of the SIR Model

The model illustrates how the proportion of the population falling into each of these categories evolves over time. Births are represented as flows from "elsewhere" into the susceptible class, whereas deaths are defined as flows from the S, I, or R compartment into "elsewhere." If S, I, and R represent the number of people in each compartment, then these state variables vary according to the following differential equation system:

$$\frac{dS}{dt} = B - \lambda S - \mu S$$
$$\frac{dI}{dt} = \lambda S - \gamma I - \mu I$$
$$\frac{dR}{dt} = \gamma I - \mu R.$$

From the above differential equation, B denotes the crude birth rate (number of births per unit time), μ is the death rate, γ is the recovery rate and λ is the transmission rate.

In Malaysia, leptospirosis is not an uncommon disease. Leptospirosis in Malaysia was first diagnosed in 1927 by Fletcher. Since 2010, Leptospirosis has been classified as a notifiable illness in Malaysia (Costa et al., 2015). Leptospirosis is endemic, where it may be found in both human and animal populations and the environment. Leptospirosis is a growing public health problem, and if not adequately managed, it might have a significant health impact and burden on the country in the coming years (Tan et al., 2016). Despite its considerable health and economic costs to human and livestock production, leptospirosis remains a neglected and under-reported illness (Costa et al., 2015).

With severe rainfall across the country, several places are at risk of flooding, potentially increasing incidences of water-borne infections. In the aftermath of the flood in December 2021, cases of leptospirosis, malaria, and dengue fever were reported to have almost tripled (DOC2US, 2022). In December 2014, continuous heavy rainfall hit the eastern states of Peninsular Malaysia which led to floods in these areas. There is an increase in the incidence of infectious diseases, particularly Leptospirosis, which surged dramatically after the flooding (Mohd Radi et al., 2018). According to Hayati et al. (2018), most of the leptospirosis cases were found along the flood hazard stream. Increased flood danger, inadequate sanitation, and an abundance of rats are all factors that contribute to a Leptospirosis outbreak. Figure 2 shows the Leptospirosis dynamic transmission (Victoriano et al., 2009).

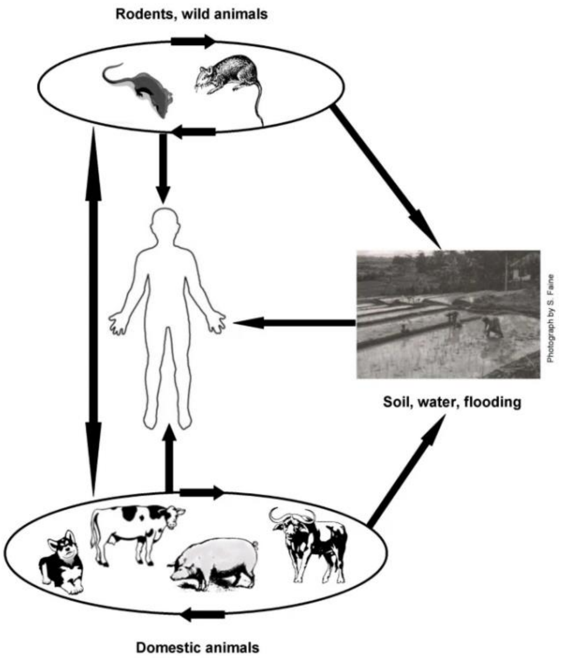

Figure 2: Leptospirosis dynamic transmission (Victoriano et al., 2009)

From Figure 2, it can be concluded that rodents, wild animals, and domestic animals can affect each other. The animals can also spread leptospirosis disease through the soil, water, and flooding. The disease can infect humans from all three sources, including domestic animals, rodents, and wildlife, as well as soil, water, and flooding.

It is necessary to keep researching this topic as this infectious disease has never stopped attacking humans worldwide until today. Therefore, it is important to continue to find critical models so can increase the potential to stop the spread of leptospirosis. Several mathematical models have been developed to study and evaluate the rapid spread of infectious diseases to limit and prevent transmission through using protective equipment when working with potentially infected animals, washing after contact, and others. In this study, the Susceptible-Infected-Removed (SIR) model, which is commonly used to stimulate the spread of infectious diseases will be used.

As for this study, a mathematical model of leptospirosis transmission in Malaysia will be constructed using the SIR model. Then, analysing the disease-free equilibrium state and basic reproduction number. By examining the basic reproduction number, $R0$, the dynamic of leptospirosis transmission can be verified.

2. Methodology/Implementation

2.1 Source of Data and Calculation Method

The main source of data used in this project is obtained from the Malaysian Ministry of Health, which is the number of leptospirosis cases reported in Malaysia from 2004 to Dec 2019 (Fig. 3). Furthermore, all numerical analysis and calculations will be performed using the Matlab.

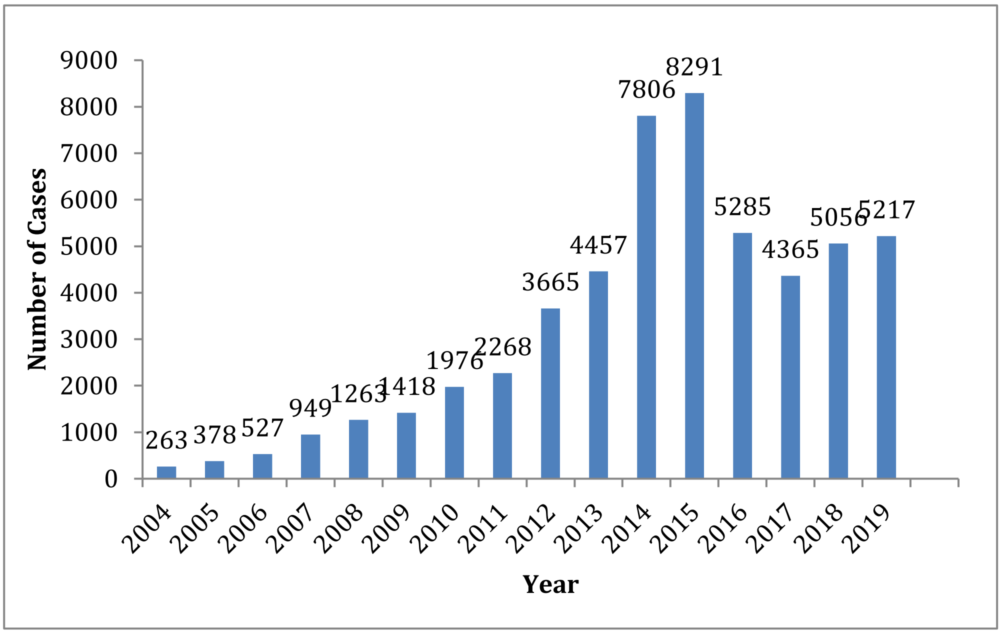

Figure 3: The number of leptospirosis cases reported in Malaysia from 2004 to Dec 2019 (Chong et al., 2022)

2.2 The Proposed Model

The models formulated have some assumptions made for the human and rat populations.

1. The human population.
   - The human life expectancy is normal.
   - The human life expectancy and natural birth rate remain constant over time.
   - The infected human can be recovered, and they recover at a constant rate.
   - The recovered human might become susceptible at a constant rate.
   - The model does not consider the deaths in the human population.

2. The rat population.
   - The rat life expectancy and natural birth rate are both continuous over time.
   - The infected rats cannot be recovered.
   - The susceptible rats become infected promptly.
   - The death rate of rats among the rat population is negligible.

3. The relationship between human and rat populations.
   - The rat population cannot be infected by an infected human.
   - The infected rats can infect humans.

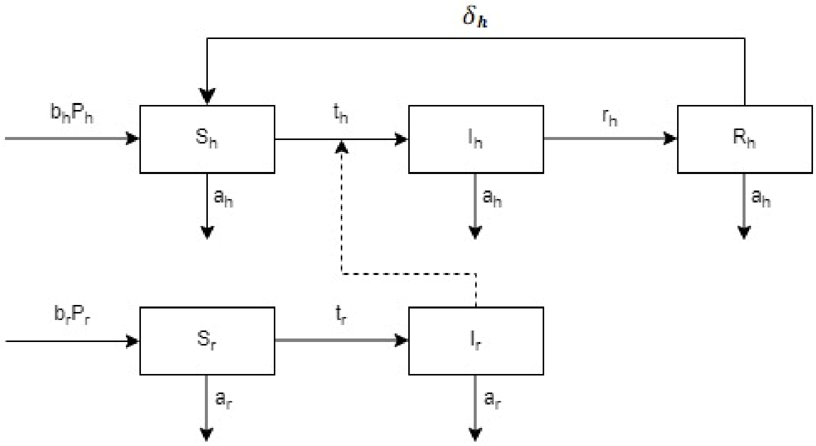

Figure 4: The SIR-SI Model

The system of differential equations involved in this SIR model for leptospirosis transmission are as below:

$$\begin{aligned}
\frac{dS_h}{dt} &= b_hP_h - a_hS_h - t_hI_rS_h + \delta_hR_h \\
\frac{dI_h}{dt} &= t_hI_rS_h - a_hI_h - r_hI_h \\
\frac{dR_h}{dt} &= r_hI_h - a_hR_h - \delta_hR_h \\
\frac{dS_r}{dt} &= b_rP_r - a_rS_r - t_rI_rS_r \\
\frac{dI_r}{dt} &= t_rI_rS_r - a_rI_r
\end{aligned} \tag{1}$$

where $P_h = S_h + I_h + R_h$ and $P_r = S_r + I_r$

The parameters description and value are given in Table 1 while the variables description is given in Table 2.

Table 1: Descriptions and Value of Parameter (Chong et al., 2022)

Parameter	Descriptions	Value
P_h	Size human population	30 807 769
P_r	Size rats' population	246 462 152
b_r	Birth rate of rats	1.13
b_h	Birth rate of humans	0.04356
t_r	Infection rate of rats	4.5×10^{-9}
t_h	Infection rate of humans	5.0×10^{-14}
r_h	Recovery rate of humans	0.01587
a_h	Natural life expectancy of the human population	0.03673
a_r	Natural life expectancy of the rat's population	1.09589
δ_h	The constant rate for recovered humans to become susceptible	3.0×10^{-4}

Table 2: Descriptions of Variable

Variable	Descriptions
S_r	The population number of susceptible rats at time t
S_h	The population number of susceptible humans at time t
I_r	The population number of infected rats at time t
I_h	The population number of infected humans at time t
R_h	The population number of recovery humans at time t

This project is begun by conducting a literature review on leptospirosis cases in Malaysia and around the world. All the possible factors are reviewed and there are few article that is read in order to gain knowledge about leptospirosis diseases.

Next, the variables and parameters that will be used in this study are identified. After doing the data collection, the study is then continues with the formulation of the mathematical model of the fractional-order differential equations for leptospirosis transmission. Then, using the formulated mathematical model, the analytical analysis which is the disease free equilibrium point, the basic reproduction number and the stability analysis is calculated. Then, determine the numerical analysis is determine using the Matlab software.

3. Results and Discussion

3.1 Analysing the results

In this section, analytical and numerical analysis are presented. The analytical analysis involves the finding of disease-free equilibrium points and its stability, as well as the computation of basic reproduction number and, R_0.

3.1.1 Disease-Free Equilibrium (DFE)

At the disease-free equilibrium (DFE) state, the population have no infection. As a result, all infected individuals will be zero, and only susceptible individuals will exist in the population. The disease-free equilibrium points of the SIR model (1) are determined by equated the derivatives to zero. From that, the equation for S_h, I_h, R_h, S_r, I_r is:

$$S_h = \frac{b_h P_h}{a_h}$$

$$I_h = \frac{t_h I_r S_h}{a_h + r_h}$$

$$R_h = \frac{r_h I_h}{a_h \delta_h}$$

$$S_r = \frac{b_r P_r}{a_r}$$

$$I_r = 0$$

Consequently, for $\mathrm{I} = 0$, a disease-free equilibrium of the model (1) exists at:

$$x_0 = (S_h, I_h, R_h, S_r, I_r) = \left(\frac{b_h P_h}{a_h}, 0, 0, \frac{b_r P_r}{a_r}, 0\right) \tag{2}$$

3.1.2 Basic Reproduction Number (R_0)

The basic reproduction number, R_0 is a mathematical term that explains the dynamic of disease transmission. It denotes the average number of humans who are most likely to get infected by from a single infected human. In this study, the basic reproduction number will be find using the next generation matrix.

From two compartments that spread the infection which are I_h and I_r, the matrices F and V are obtained.

$$F(x) = \begin{bmatrix} 0 & t_h S_h \\ 0 & t_r S_r \end{bmatrix}$$

$$V(x) = \begin{bmatrix} a_h + r_h & 0 \\ 0 & a_r \end{bmatrix}$$

Then, the matrices F and V are evaluated at the equilibrium point $x_0 = \left(\frac{b_h P_h}{a_h}, 0, 0, \frac{b_r P_r}{a_r}, 0\right)$

$$F(x_0) = \begin{bmatrix} 0 & t_h(\frac{b_h P_h}{a_h}) \\ 0 & t_r(\frac{b_r P_r}{a_r}) \end{bmatrix}$$

and

$$V(x_0) = \begin{bmatrix} a_h + r_h & 0 \\ 0 & a_r \end{bmatrix}$$

The inverse of matrix V is given by:

$$V^{-1} = \begin{bmatrix} \frac{1}{a_h + r_h} & 0 \\ 0 & \frac{1}{a_r} \end{bmatrix}$$

So, the product of FV^{-1} is obtained as:

$$FV^{-1} = \begin{bmatrix} 0 & (\frac{t_h b_h P_h}{a_h a_r}) \\ 0 & (\frac{t_r b_r P_r}{(a_r)^2}) \end{bmatrix}$$

The R_0 is defined by the spectral radius ρ, which is the dominant eigenvalue in magnitude of the matrix FV^{-1}

$$\rho(FV^{-1}) = \begin{bmatrix} 0 - \lambda & (\frac{t_h b_h P_h}{a_h a_r}) \\ 0 & \left(\frac{t_r b_r P_r}{(a_r)^2}\right) - \lambda \end{bmatrix}$$

This implies that either $\lambda = 0$ or $\lambda = \frac{t_r b_r P_r}{(a_r)^2}$. Therefore, R_0 can be written as

$$R_0 = \frac{t_r b_r P_r}{(a_r)^2} \tag{3}$$

3.1.3 Stability Analysis

The stability analysis of the disease-free equilibrium state will be proved in this study by using the calculated disease-free equilibrium point, $(S_h, I_h, R_h, S_r, I_r) = (\frac{b_h P_h}{a_h}, 0, 0, \frac{b_r P_r}{a_r}, 0)$ through Jacobian matrix.

From equilibrium point, the Jacobian matrix result are as follows:

$$J(x) = \begin{bmatrix} -a_h - t_h I_r & 0 & \delta_h & 0 & -t_h S_h \\ t_h I_r & -a_h - r_h & 0 & 0 & t_h S_h \\ 0 & r_h & -a_h - \delta_h & 0 & 0 \\ 0 & 0 & 0 & -a_r - t_r I_r & -t_r S_r \\ 0 & 0 & 0 & t_r I_r & t_r S_r - a_r \end{bmatrix}$$

Substitute $x_0 = (\frac{b_h P_h}{a_h}, 0, 0, \frac{b_r P_r}{a_r}, 0)$ into $J(x)$, the Jacobian matrix $J(x_0)$ is:

$$J(x_0) = \begin{bmatrix} -a_h & 0 & \delta_h & 0 & -t_h[\frac{b_h P_h}{a_h}] \\ 0 & -a_h - r_h & 0 & 0 & t_h[\frac{b_h P_h}{a_h}] \\ 0 & r_h & -a_h - \delta_h & 0 & 0 \\ 0 & 0 & 0 & -a_r & -t_r[\frac{b_r P_r}{a_r}] \\ 0 & 0 & 0 & 0 & t_r[\frac{b_r P_r}{a_r}] - a_r \end{bmatrix}$$

with eigenvalue λ, $|J(x_0) - \lambda I| = 0$

$$\begin{bmatrix} -a_h - \lambda & 0 & \delta_h & 0 & -t_h[\frac{b_h P_h}{a_h}] \\ 0 & (-a_h - r_h) - \lambda & 0 & 0 & t_h[\frac{b_h P_h}{a_h}] \\ 0 & r_h & (-a_h - \delta_h) - \lambda & 0 & 0 \\ 0 & 0 & 0 & -a_r - \lambda & -t_r[\frac{b_r P_r}{a_r}] \\ 0 & 0 & 0 & 0 & \left(t_r\left[\frac{b_r P_r}{a_r}\right] - a_r\right) - \lambda \end{bmatrix} = 0$$

$$(-a_h - \lambda)\left[(-a_r - \lambda)\left[\left(\frac{t_r b_r P_r}{a_r} - a_r\right) - \lambda\right][((-a_h - r_h) - \lambda)((-a_h - \delta_h) - \lambda)]\right] = 0$$

The eigenvalues of the Jacobian matrix are:

$$\lambda_1 = -a_h,$$

$$\lambda_2 = -a_r,$$

$$\lambda_3 = a_r(R_0 - 1),$$

$$\lambda_4 = -a_h - r_h,$$

$$\lambda_5 = -a_h - \delta_h$$

The basic reproduction number is:

$$R_0 = \frac{t_r b_r P_r}{(a_r)^2}$$

$$= 0.002859$$

The local stability of the equilibrium x_0 can be determined by using the eigenvalues and the value of R_0. Hence, x_0 is stable since $R_0 < 1$.

3.1.4 Numerical Analysis

In this part, we use the Matlab software in order to generate the graphs for the ordinary differential equations from (1). The parameter value used in this analysis is shown in Table 1. For the initial conditions of the human population, P_h we calculate the average of the 10-year period from 2010 to 2019, which is 30 807 769.

Otherwise, we multiply the number of humans by 8 to estimate the total vector population on a scale of 1 person to 8 rats, where we get the $P_r = 246\ 462\ 152$.

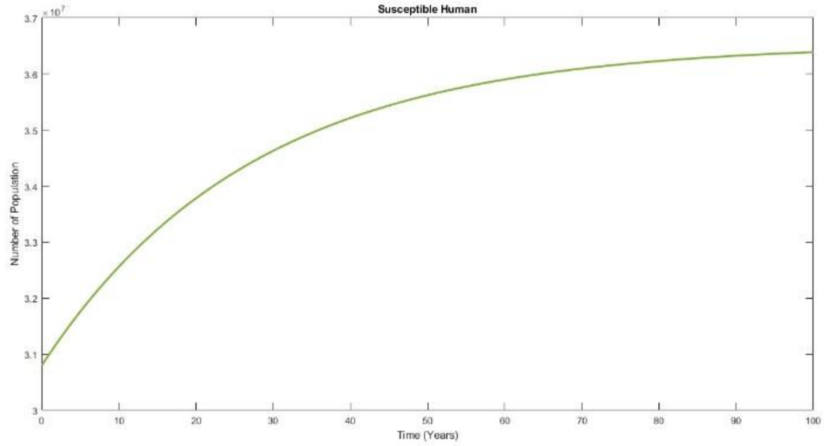

Figure 5: Simulations result of the susceptible human

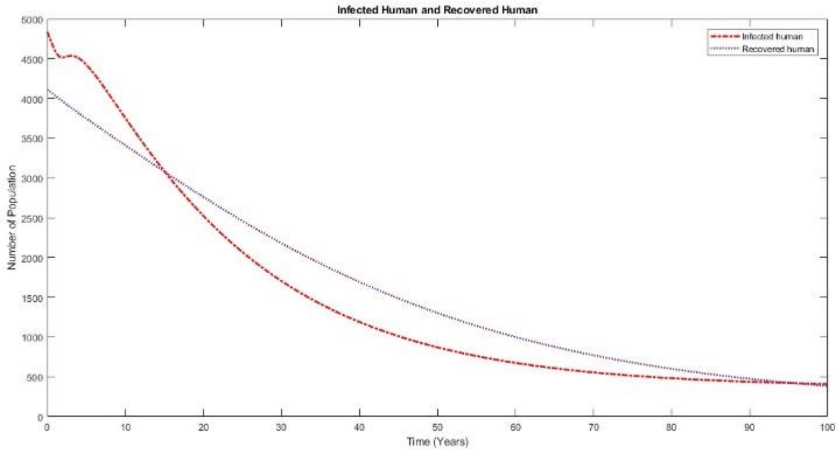

Figure 6: Simulation result of infected human and recovered human

Figure 5 shows the simulation of susceptible versus time in years. To evaluate the graph in Figure 5, we extracted the number of human populations in Malaysia from the World Bank website (The World Bank Group, 2023). We use the 10-year average of the human population from 2010 to 2019 as the initial condition. Next, we calculate the number of infected humans, $I_h = 4839$ which we get by adding the number of infected humans from 2010 to 2019 and dividing it by 10 years. According to Leong et al. (2016), the age standardized death rate for the overall population was 0.45 per 100,000 individuals, hence the expected number of recovered humans, R_h is taken to be 4113. From the graph, we can conclude that the susceptible population is increasing over time as the number of humans in Malaysia increases year by year.

From Figure 6, we can see the graph of infected humans is gradually decreasing towards the end. The graph is approaching the steady state when $R_0 < 1$. So, the graph verified the local stability of disease-free equilibrium point means the disease has become endemic which explain the research question. In the same graph, the recovered human decline from the first year towards the final year. The number of recovered humans is influenced by the number of infected humans but for some years, the number of infected human and recovered human are different as we should consider the number of infected humans that die from the disease and also during the infection.

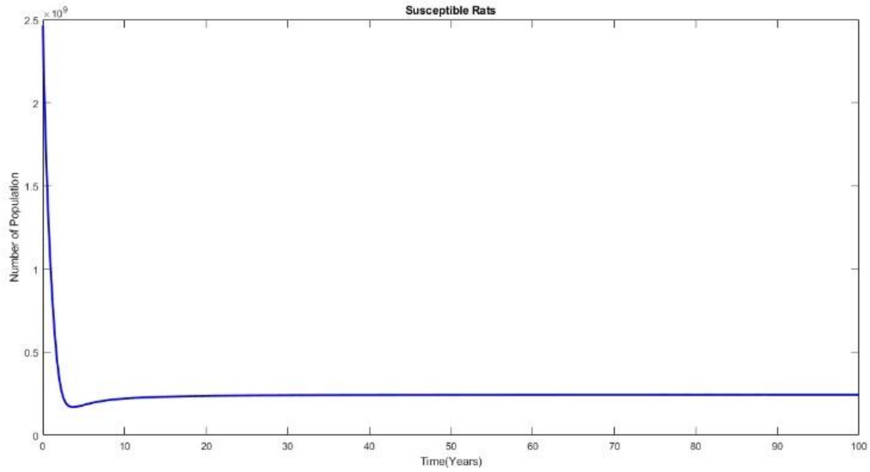

Figure 7: Simulation result of the susceptible rats

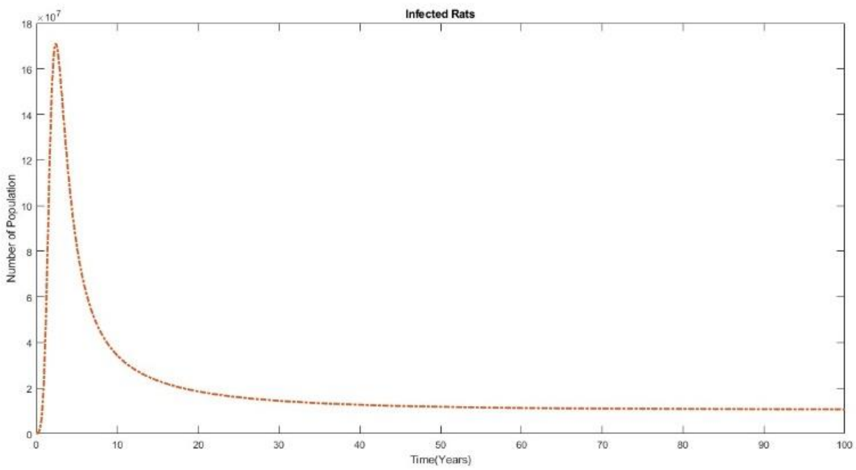

Figure 8: Simulation result of infected rats

Figure 7 indicates the results of the susceptible rats. The initial conditions that we use to simulate the graphs are the total population of vectors, $P_r = 246\ 462\ 152$. The number of infected vectors, I_r which we assume to be $72\ 579$ is an increment of 50% from the number of infected humans. From the graph, we can see that the number of susceptible rats decreasing at the early year and then increase a little bit and remain a flattening path across time.

From Figure 8, we can see the number of infected rats. The number of infected rats is increasing at the early year and then decreasing approaching 0, but it will never reach that value. Based on Figure 7 and Figure 8, we can conclude that susceptible rats and infected rats remained constant over time. This result is also related to the graph of infected humans. This is because when the number of infected rats is constant, it affects the number of infected humans because leptospirosis is transmitted from rats to humans, while rats cannot be infected by humans. This reinforces the statement that the number of infected humans is approaching a steady state and has become endemic in Malaysia.

4. Conclusion and Recommendation

In this study, a mathematical model is developed to describe the leptospirosis spread in Malaysia using the existing SIR model by Kermack and McKendrick. The disease-free equilibrium and the significance of the basic reproduction number, R_0 have been discussed as they are vital in categorising the dynamics of the model. Hence, from the calculation, the basic reproduction number for the SIR-SI model is smaller than one ($R_0 < 1$). It indicates that the disease is stable showing that the leptospirosis cases in Malaysia have reached endemic levels.

Based on the Matlab graph, we can conclude that the number of susceptible humans is increasing as the human population in Malaysia grows, whereas the number of infected and recovered humans is decreasing initially and then remaining constant. The proportion of susceptible and infected vectors is decreasing over time. This result agrees with the basic reproduction number determined by the calculation. Thus, the hypothesis that leptospirosis has become endemic in Malaysia is true. Therefore, we suggest that all people who work with potentially infected animals keep their hands sanitised to decrease the possibility of the virus spreading. In addition, people who live in places that are at risk of flooding should prepare themselves with protective equipment since flooding will potentially increase incidences of water-borne infections. Last but not least, public awareness and the necessary precautions must be taken seriously because the disease in Malaysia has not yet been eradicated and there is still no vaccine.

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