The Integrated Studies of Infectious Disease Using Mathematical Modeling and Computer Simulation

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Abstract—In this paper we develop and analyze the model for the spread of Leptospirosis by age group in Thailand, between 1997 and 2010 by using mathematical modeling and computer simulation. Leptospirosis is caused by pathogenic spirochetes of the genus Leptospira. It is a zoonotic disease of global importance and an emerging health problem in Thailand. In Thailand, leptospirosis is a reportable disease, the top three age groups are 23.31% in 35-44 years olds group, 22.76% in 25-34 year olds group, 17.60% in 45-54 year olds group from reported leptospirosis between 1997 and 2010, with a peak in 35-44 year olds group. Our paper, the Leptospirosis transmission by age group in Thailand is studied on the mathematical model. Some analytical and simulation results are presented.

Keywords—Age Group, Equilibrium State, Leptospirosis, Mathematical Modeling.

I. INTRODUCTION

The mathematical modeling has become a valuable equipment in the analysis of the infectious disease dynamics. It can encourage the development of the control plans. Leptospirosis is an infectious disease caused by a type of bacteria called a spirochete. Leptospirosis can be transmitted by many animals such as rats, opossums, raccoons, and foxes. It is transmitted through contact with infected soil or water. The soil or water is polluted with the waste products of an infected animal. Human get the disease by either ingesting contaminated food or water or by broken skin and mucous membrane catch with the infected water or soil.

The symptoms of the disease can range from headaches and fever, to jaundice, severe myalgia and conjunctival suffusion [1-2], kidney failure, and internal bleeding. People who are seriously ill with leptospirosis often need to be hospitalized.

For beginning the mathematical modeling to study the Leptospirosis transmission, in 2006 J. Holt and et al [3], they present a basic model for the dynamics of leptospirosis infection in a common African rodent, the multimammate mouse. In 2007, W. Triampo and et al [4], they considered a deterministic model for the transmission of Leptospirosis which is spreading in Thai population. They using the Susceptible-Infectious-Recovered (SIR) model to described the transmission dynamics of the disease.

Reported Leptospirosis case in Thailand between 1997 and 2010 by age group are investigated by the Division of Epidemiology, Ministry of Public Health. The number of leptospirosis cases occurs peak in 35-44 year olds class (the average mean between 1997 and 2010). We model the spread of the leptospirosis in Thailand that there are ten age groups for infectious and recovered classes.

Our study, the local dynamics of the three-dementional model of leptospirosis transmission model by ten age groups of Thai people is resolved through the use of the standard dynamic analysis the mathematical model. We use the real data from the Division of Epidemiology, Ministry of Public Health to analysis with our model. The purpose of this paper is to use the mathematical model to study the behavior of the transmission of leptospirosis by ten age groups in Thai people for understanding and controlling the leptospirosis transmission in Thai population. We prove the local asymptotic stability of the equilibrium states. Our discussion and conclusion are contained in the last section.

II. THE MODEL

A. A Model

A model for Leptospirosis transmission in Thailand by ten age groups. We divide the age group into ten age groups by using real data from Division of Epidemiology, Ministry of Public Health. We denote the fractions of the susceptible human individuals, the infectious human individuals that belong to ten different subclasses by age group and the recovered human individuals in the population by $S_{ii}(t)$, $I_{ii}(t)$, $R_{ii}(t)$, respectively, that is,

$$S_{ii}(t) + \sum_{i=1}^{10} I_{ii}(t) + \sum_{i=1}^{10} R_{ii}(t) = 1$$

i = 1, it means the class of age group which less than or equal 6 year olds,

i = 2, it means the class of age group 7-9 year olds,

i = 3, it means the class of age group 10-14 year olds,
i = 4, it means the class of age group 15-24 year olds, 
i = 5, it means the class of age group 25-34 year olds, 
i = 6, it means the class of age group 35-44 year olds, 
i = 7, it means the class of age group 45-54 year olds, 
i = 8, it means the class of age group 55-64 year olds, 
i = 9, it means the class of age group which more than or equal 65 year olds and 
i = 10, it means the unknown age group from reported.

We focus on the contagion of leptospirosis transmission is rats by dividing the rats group into two groups. We denote the fractions of the susceptible rats individuals and the infectious rats individuals in the rats population by \( S_M(t) \) and \( I_M(t) \) that is, \( S_M(t) + I_M(t) = 1 \).

Then our diagram for human populations and rats populations are human populations:

\[
\begin{align*}
\text{rates populations:} \\
\begin{array}{c}
\beta S_H I_M \\
\omega S_M I_M \\
\omega S_M I_M \\
\end{array}
\end{align*}
\]

the rates populations:

\[
\begin{align*}
\frac{dS_H}{dt} &= \lambda - \mu S_H - \sum_{i=1}^{10} \beta_i S_H I_M, \\
\frac{dI_H}{dt} &= \sum_{i=1}^{10} \beta_i S_H I_M - \sum_{i=1}^{10} (\alpha_{HI} + \mu + \delta)I_H, \\
\frac{dR_H}{dt} &= \sum_{i=1}^{10} \delta I_H - \sum_{i=1}^{10} \mu R_H,
\end{align*}
\]

when \( i = 1, 2, \ldots, 10 \) and \( \lambda \) is recruitment rate into the susceptible human class, \( \mu \) is the per capita natural mortality rate of human population, \( \delta \) is the recovery rate, \( \alpha_{HI} \) is the per capita death rate in each age group. Then (3) for the recovered class can be exempted. The most common reason for these assumptions is when the population size is constant or when the variation of the population is either negligibly small or slow compared to the time scale of the epidemic process.

The corresponding equations are:

\[
\begin{align*}
\frac{dS_H}{dt} &= \lambda - \mu S_H - \sum_{i=1}^{10} \beta_i S_H I_M, \quad (4) \\
\frac{dI_H}{dt} &= \sum_{i=1}^{10} \beta_i S_H I_M - \sum_{i=1}^{10} (\alpha_{HI} + \mu + \delta)I_H, \quad (5) \\
\frac{dR_H}{dt} &= \sum_{i=1}^{10} \delta I_H - \sum_{i=1}^{10} \mu R_H,
\end{align*}
\]

In rats populations are:

\[
\begin{align*}
\frac{dS_M}{dt} &= \omega - \Omega S_M - \theta S_M I_M, \quad (6) \\
\frac{dI_M}{dt} &= \theta S_M I_M - \Omega I_M, \quad (7) \\
\end{align*}
\]

when \( \omega \) is recruitment rate into the susceptible rats class, \( \Omega \) is the per capita natural mortality rate of rats population, Then (6) for the susceptible rats class can be exempted. The corresponding equations for rat populations are:

\[
\frac{dI_M}{dt} = \theta(1 - I_M) I_M - \Omega I_M. \quad (8)
\]

B. Properties of the Models

Next, we will show (4), (5) and (8) has an infection equilibrium state. Let the right hand side of (4), (5) and (8) to zero and then we obtain:

\[
\lambda - \mu S^* - \sum_{i=1}^{10} \beta_i S^*_H I^*_M = 0, \quad (9)
\]
\[
\sum_{i=1}^{10} \beta_i S^*_H I^*_M - \sum_{i=1}^{10} (\alpha_{Hi} + \mu + \delta) I^*_H = 0 \tag{10}
\]
\[
\theta(1 - I^*_M) I^*_M - \Omega^*_M = 0. \tag{11}
\]
From (9), we have:
\[
S^*_H = \frac{\lambda}{\mu + \sum_{i=1}^{10} \beta_i}. \tag{12}
\]
Substituting (12) into (10), then we obtain:
\[
I^*_H = \frac{\lambda \beta_i I^*_M}{(\mu + \sum_{i=1}^{10} \beta_i)(\alpha_{Hi} + \mu + \delta)} \tag{13}
\]
From (11), we have two solutions, the first one solution is
\[
I^*_M = 0 \quad \text{and the second solution is:}
\]
\[
I^*_M = 1 - \frac{\Omega}{\theta}. \tag{14}
\]
From our calculate, we have two equilibrium states, the first is the disease-free equilibrium state
\[
E_0 = (S^*_H, I^*_H, I^*_M) = \left(\frac{\lambda}{\mu}, 0, 0\right). \tag{15}
\]
The second equilibrium state is the endemic equilibrium state:
\[
E_1 = (S^*_H, I^*_H, I^*_M)
\]
\[
\frac{\lambda \beta_i I^*_M}{(\mu + \sum_{i=1}^{10} \beta_i)(\alpha_{Hi} + \mu + \delta)} \tag{15}
\]
If the endemic equilibrium state exists and is stable, then the infection will persist endemically at this state. If the disease-free equilibrium state occurs and is stable, then the population can remain disease-free indefinitely.

III. MODAL ANALYSIS

A. Analytical Results

From our model and analytic, the equilibrium solutions we have two equilibrium states:

i) \( E_0 = \left(\frac{\lambda}{\mu}, 0, 0\right) \) is the disease free equilibrium state and

ii) \( E_1 = (S^*_H, I^*_H, I^*_M) \) is the endemic disease equilibrium state where \( S^*_H, I^*_H, I^*_M \) are defined in (12), (3) and (14), respectively.

Let:
\[
X_H = \lambda - \mu S^*_H - \sum_{i=1}^{10} \beta_i S^*_H I^*_M, \tag{16}
\]
\[
X_i = \sum_{i=1}^{10} \beta_i S^*_H I^*_M - \sum_{i=1}^{10} (\alpha_{Hi} + \mu + \delta) I^*_H, \tag{17}
\]
\[
Y_M = \theta(1 - I^*_M) I^*_M - \Omega^*_M. \tag{18}
\]
then we have:
\[
\frac{\partial X_H}{\partial S_H} = -\mu - \sum_{j=1}^{10} \beta_j (\alpha_{Hi} + \mu + \delta), \quad \frac{\partial X_H}{\partial X^*_H} = 0, \quad \frac{\partial X_H}{\partial Y^*_M} = 0; \tag{20}
\]
\[
\frac{\partial X_i}{\partial S^*_H} = \beta_i \frac{\partial X^*_H}{\partial S^*_H} = (\alpha_{Hi} + \mu + \delta), \quad \frac{\partial X_i}{\partial X^*_H} = 0, \quad \frac{\partial X_i}{\partial Y^*_M} = \beta_i S^*_H; \tag{21}
\]
\[
\frac{\partial X_i}{\partial Y^*_M} = -\alpha_{Hi} + \mu + \delta, \quad \frac{\partial Y^*_M}{\partial X^*_H} = \beta_i S^*_H; \tag{22}
\]
\[
\frac{\partial Y^*_M}{\partial Y^*_M} = \theta(1 - I^*_M) I^*_M - \Omega^*_M = -2\beta_i S^*_H - \Omega^*_M \tag{23}
\]
for i, j = 1, 2, ..., 10.

The Jacobian matrix is 12×12 matrix:
\[
\begin{bmatrix}
-\mu - \sum_{j=1}^{10} \beta_j & 0 & 0 & ... & -S^*_H \sum_{j=1}^{10} \beta_j \\
\beta_i S^*_H & -\alpha_{Hi} + \mu + \delta & 0 & ... & \beta_i S^*_H \\
\beta_i S^*_H & 0 & -\alpha_{Hi} + \mu + \delta & 0 & \beta_i S^*_H \\
\vdots & \vdots & \vdots & \ddots & \vdots \\
0 & \beta_i S^*_H & 0 & ... & -\alpha_{Hi} + \mu + \delta & \beta_i S^*_H \\
0 & 0 & 0 & ... & \theta(1 - I^*_M) I^*_M - \Omega^*_M
\end{bmatrix} \tag{19}
\]

B. The Local Stability

To determine the local stability of two equilibrium states, we calculate from the Jacobian matrix. If all eigenvalues which can be obtained by diagonalizing the Jacobian matrix have negative real parts then the equilibrium solution is local stability. Diagonalizing the Jacobian for the equilibrium states, the characteristic equation is given by setting:
\[
\det (J - \eta I_{12}) = 0 \tag{20}
\]
where \( J \) is the Jacobian matrix for the equilibrium states, \( \eta \) is the eigenvalue and \( I_{12} \) is the identity matrix. At the disease free equilibrium state \( E_0 = \left(\frac{\lambda}{\mu}, 0, 0\right) \), thus we have:
\[
\eta_1 = -\mu, \quad \eta_2 = -(\alpha_{Hi} + \mu + \delta), \quad \eta_3 = -(\alpha_{Hi} + \mu + \delta),
\]
\[ \eta_1 = -(\alpha_{H3} + \mu + \delta), \eta_2 = -(\alpha_{H4} + \mu + \delta), \eta_3 = -(\alpha_{H5} + \mu + \delta), \eta_4 = -(\alpha_{H6} + \mu + \delta), \eta_5 = -(\alpha_{H7} + \mu + \delta), \eta_6 = -(\alpha_{H8} + \mu + \delta), \eta_7 = -(\alpha_{H9} + \mu + \delta), \eta_8 = -(\alpha_{H10} + \mu + \delta). \]  

For the other two eigenvalues are obtained by solving:

\[ \eta^2 + a_1 \eta + a_0 = 0 \]  

when

\[ a_1 = (-\theta + \Omega + \delta + \mu + \alpha_{H11}), \quad a_0 = (-\theta + \Omega)(\delta + \mu + \alpha_{H10}). \]

So \( \eta_{11} = \frac{-a_1 + \sqrt{a_1^2 - 4a_0}}{2} \) and \( \eta_{12} = \frac{-a_1 - \sqrt{a_1^2 - 4a_0}}{2} \).

It can be seen easily \( \eta_{11} \) is always negative. Next we consider \( \frac{a_1^2 - 4a_0}{\Omega} \) is always positive. Then we consider \( \eta_{12} \) is negative when \( a_0 \geq 0 \) or \( \frac{\theta}{\Omega} \leq 1 \).

For checking the local stability of the endemic equilibrium state at \( E_1 = (S_{i1}, I_{i1}^*, I_{M}^*) \), we use the same method of the disease free equilibrium state. Then we obtain ten eigenvalues are \( \eta_1 = -(\alpha_{H1} + \mu + \delta), \eta_2 = -(\alpha_{H2} + \mu + \delta), \eta_3 = -(\alpha_{H3} + \mu + \delta), \eta_4 = -(\alpha_{H4} + \mu + \delta), \eta_5 = -(\alpha_{H5} + \mu + \delta), \eta_6 = -(\alpha_{H6} + \mu + \delta), \eta_7 = -(\alpha_{H7} + \mu + \delta), \eta_8 = -(\alpha_{H8} + \mu + \delta), \eta_9 = -(\alpha_{H9} + \mu + \delta), \eta_{10} = -(\alpha_{H10} + \mu + \delta). \)

The remaining two eigenvalues are obtained by solving

\[ \eta^2 + b_1 \eta + b_0 = 0 \]

where

\[ b_0 = (\Omega - \theta)(\mu + I_M \sum_{i=1}^{10} \beta_i), \]

\[ b_1 = (\mu + \Omega - \theta) + I_M \sum_{i=1}^{10} \beta_i. \]

We have

\[ \eta_{11} = \frac{-b_1 - \sqrt{b_1^2 - 4b_0}}{2} \quad \text{and} \quad \eta_{12} = \frac{-b_1 + \sqrt{b_1^2 - 4b_0}}{2}. \]

Then we consider \( \eta_{12} \) is negative when \( b_0 < 0 \).

\[ b_1^2 - 4b_0 = ((\mu + \Omega + \theta)I_{M}^{10} \sum_{i=1}^{10} \beta_i)^2 \]

is always positive.

**IV. Numerical Results**

Numerical solutions are shown to compare the leptospirosis transmission by ten age groups in Thailand. The values of the parameters used are corresponding to real data from the Division of Epidemiology, Ministry of Public Health between 1997 and 2010 which are shown in Table I.

<table>
<thead>
<tr>
<th>Symbol</th>
<th>The parameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \lambda )</td>
<td>The recruitment rate into the susceptible human class</td>
</tr>
<tr>
<td>( \mu )</td>
<td>The per capita natural mortality rate of human population</td>
</tr>
<tr>
<td>( \beta_i )</td>
<td>The transmission probability of leptospirosis from infected rat to human population in each age group</td>
</tr>
<tr>
<td>( \alpha_{H11} )</td>
<td>The per capita death rate from infected</td>
</tr>
<tr>
<td>( \delta )</td>
<td>The recovery rate of human population</td>
</tr>
<tr>
<td>( \Omega )</td>
<td>The per capita natural mortality rate of rats population</td>
</tr>
<tr>
<td>( \theta )</td>
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</tr>
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**TABLE I**

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</tr>
<tr>
<td>( \mu )</td>
<td>( \mu = \mu_{11}, \ldots, \mu_{10} = \mu_{H1}, \ldots, \mu_{H10} )</td>
</tr>
<tr>
<td>( \beta_i )</td>
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</tr>
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</tr>
<tr>
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For checking the local stability of the endemic equilibrium state at \( E_1 = (S_{i1}, I_{i1}^*, I_{M}^*) \), we use the same method of the disease free equilibrium state. Then we obtain ten eigenvalues are \( \eta_1 = -(\alpha_{H1} + \mu + \delta), \eta_2 = -(\alpha_{H2} + \mu + \delta), \eta_3 = -(\alpha_{H3} + \mu + \delta), \eta_4 = -(\alpha_{H4} + \mu + \delta), \eta_5 = -(\alpha_{H5} + \mu + \delta), \eta_6 = -(\alpha_{H6} + \mu + \delta), \eta_7 = -(\alpha_{H7} + \mu + \delta), \eta_8 = -(\alpha_{H8} + \mu + \delta), \eta_9 = -(\alpha_{H9} + \mu + \delta), \eta_{10} = -(\alpha_{H10} + \mu + \delta). \)

The remaining two eigenvalues are obtained by solving

\[ \eta^2 + b_1 \eta + b_0 = 0 \]

where

\[ b_0 = (\Omega - \theta)(\mu + I_M \sum_{i=1}^{10} \beta_i), \]

\[ b_1 = (\mu + \Omega - \theta) + I_M \sum_{i=1}^{10} \beta_i. \]

We have

\[ \eta_{11} = \frac{-b_1 - \sqrt{b_1^2 - 4b_0}}{2} \quad \text{and} \quad \eta_{12} = \frac{-b_1 + \sqrt{b_1^2 - 4b_0}}{2}. \]
Fig. 1 Bifurcation diagrams of the solutions (4), (5) and (8) for different values of $\Theta$. The value of parameters in the model are shown in Table 1.
Fig. 2 Bifurcation diagrams of the solutions (4), (5) and (8) for different values of $\beta_2$. The value of parameters in the model are shown in Table I.
V. CONCLUSION

In this paper, we consider the local properties of the mathematical model of the leptospirosis transmission in Thailand by incorporate ten age groups in our model. Because of Thailand is an agricultural country. The main occupation of Thai population is the farmers. Then the epidemic of leptospirosis disease in Thai population corresponding the occupations and the ages of the populations. An important development in the study of the leptospirosis diseases has used the application of the mathematical model to understand the interplay between the factors, the hosts and the transmission dynamics. The highest incidence was found in 35-44 age group.

In Fig. 1, all parameters proportions approach to the equilibrium state when the transmission probability of leptospirosis to rat population (θ) are difference (0 ≤ θ ≤ 1). It almost no effect to the proportion of parameters. But the transmission probability of leptospirosis from infected rat to human population in the second peak reported cases in Thailand (in 25-34 years olds group (β5)) are difference. It has an impact to the proportions of all parameters. When β5 is higher, we can see the infectious human proportion in 25-34 years olds class increase. The infectious rat proportions are constant while the other parameters proportions decrease which are shown in Fig. 2.

After that, we try to check the changes of transmission probability in human populations in each age class. We found that the results as same as Fig. 2. So the control of leptospirosis transmission in Thailand will be successful when the transmission probability of leptospirosis from infected rat to human in each age group decrease.

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REFERENCES