

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

R. Kongnuy, and E. Naowanich

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 encouragement 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 though 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 $S_H(t)$,

$I_{Hi}(t)$, $R_{Hi}(t)$, respectively, that is,

$$S_H(t) + \sum_{i=1}^{10} I_{Hi}(t) + \sum_{i=1}^{10} R_{Hi}(t) = 1 \text{ where}$$

$i = 1$, 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,

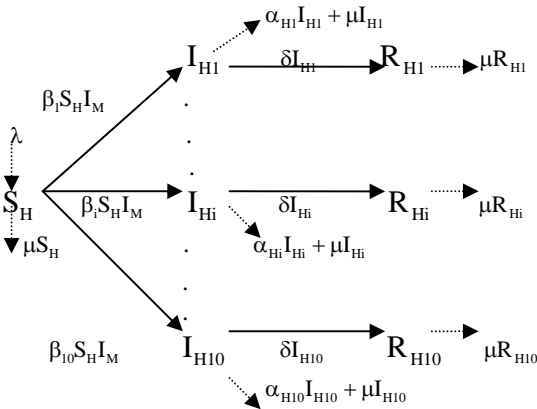
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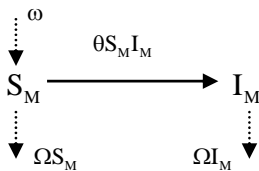
$i = 4$, it means the class of age group 15-24 year olds,
 $i = 5$, it means the class of age group 25-34 year olds,
 $i = 6$, it means the class of age group 35-44 year olds,
 $i = 7$, it means the class of age group 45-54 year olds,
 $i = 8$, it means the class of age group 55-64 year olds,
 $i = 9$, 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:



the rates populations:



when β_i is the transmission probability of leptospirosis from infected rat to human population in each i age group, the transmission of the leptospirosis infection in each age group in human populations governed by $\beta_i S_H I_M$, θ is the transmission probability of leptospirosis to rat population and the leptospirosis infection in rat populations governed by $\theta S_M I_M$, then the corresponding equations our model in human populations are:

$$\frac{dS_H}{dt} = \lambda - \mu S_H - \sum_{i=1}^{10} \beta_i S_H I_M, \quad (1)$$

$$\frac{dI_{Hi}}{dt} = \sum_{i=1}^{10} \beta_i S_H I_M - \sum_{i=1}^{10} (\alpha_{Hi} + \mu + \delta) I_{Hi}, \quad (2)$$

$$\frac{dR_{Hi}}{dt} = \sum_{i=1}^{10} \delta I_{Hi} - \sum_{i=1}^{10} \mu R_{Hi}, \quad (3)$$

when $i = 1, 2, \dots, 10$ and λ is recruitment rate into the susceptible human class, μ is the per capita natural mortality rate of human population, δ is the recovery rate, α_{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:

$$\frac{dS_H}{dt} = \lambda - \mu S_H - \sum_{i=1}^{10} \beta_i S_H I_M, \quad (4)$$

$$\frac{dI_{Hi}}{dt} = \sum_{i=1}^{10} \beta_i S_H I_M - \sum_{i=1}^{10} (\alpha_{Hi} + \mu + \delta) I_{Hi}. \quad (5)$$

In rats populations are:

$$\frac{dS_M}{dt} = \omega - \Omega S_M - \theta S_M I_M, \quad (6)$$

$$\frac{dI_M}{dt} = \theta S_M I_M - \Omega I_M, \quad (7)$$

when ω is recruitment rate into the susceptible rats class, Ω 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:

$$\lambda - \mu S_H^* - \sum_{i=1}^{10} \beta_i S_H^* I_M^* = 0, \quad (9)$$

$$\sum_{i=1}^{10} \beta_i S_H^* I_M^* - \sum_{i=1}^{10} (\alpha_{Hi} + \mu + \delta) I_{Hi}^* = 0 \quad (10)$$

$$\theta(1 - I_M^*) I_M^* - \Omega I_M^* = 0. \quad (11)$$

From (9), we have:

$$S_H^* = \frac{\lambda}{\mu + I_M^* \sum_{i=1}^{10} \beta_i}. \quad (12)$$

Substituting (12) into (10), then we obtain:

$$I_{Hi}^* = \frac{\lambda \beta_i I_M^*}{(\mu + I_M^* \sum_{i=1}^{10} \beta_i)(\alpha_{Hi} + \mu + \delta)}. \quad (13)$$

From (11), we have two solutions, the first one solution is $I_M^* = 0$ and the second solution is:

$$I_M^* = 1 - \frac{\Omega}{\theta}. \quad (14)$$

From our calculate, we have two equilibrium states, the first is the disease-free equilibrium state $E_0 = (S_{H0}, I_{H0i}, I_{M0}) = (\frac{\lambda}{\mu}, 0, 0)$. The second equilibrium state is the endemic equilibrium state:

$$E_1 = (S_H^*, I_{Hi}^*, I_M^*) = \left(\frac{\lambda}{\mu + I_M^* \sum_{i=1}^{10} \beta_i}, \frac{\lambda \beta_i I_M^*}{(\mu + I_M^* \sum_{j=1}^{10} \beta_j)(\alpha_{Hi} + \mu + \delta)}, 1 - \frac{\Omega}{\theta} \right). \quad (15)$$

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) $E_0 = (\frac{\lambda}{\mu}, 0, 0)$ is the disease free equilibrium state and
- ii) $E_1 = (S_H^*, I_{Hi}^*, I_M^*)$ is the endemic disease equilibrium

state where S_H^*, I_{Hi}^*, I_M^* are defined in (12),(3) and (14), respectively.

Let:

$$X_H = \lambda - \mu S_H^* - \sum_{i=1}^{10} \beta_i S_H^* I_M^*, \quad (16)$$

$$X_i = \sum_{i=1}^{10} \beta_i S_H^* I_M^* - \sum_{i=1}^{10} (\alpha_{Hi} + \mu + \delta) I_{Hi}^*, \quad (17)$$

$$Y_M = \theta(1 - I_M^*) I_M^* - \Omega I_M^* \quad (18)$$

then we have:

$$\begin{aligned} \frac{\partial X_H}{\partial S_H^*} &= -\mu - I_M^* \sum_{i=1}^{10} \beta_i, & \frac{\partial X_H}{\partial I_{Hi}^*} &= 0, & \frac{\partial X_H}{\partial I_M^*} &= -S_H^* \sum_{j=1}^{10} \beta_j, \\ \frac{\partial X_i}{\partial S_H^*} &= \beta_i I_M^*, & \frac{\partial X_i}{\partial I_{Hi}^*} &= -(\alpha_{Hi} + \mu + \delta), & \frac{\partial X_i}{\partial I_{Hj,j \neq i}^*} &= 0, \\ \frac{\partial X_i}{\partial I_M^*} &= \beta_i S_H^* & \text{and} & & \frac{\partial Y_M}{\partial I_M^*} &= \theta - 2\theta I_M^* - \Omega \end{aligned}$$

for $i, j = 1, 2, \dots, 10$.

The Jacobian matrix is 12×12 matrix:

$$\begin{bmatrix} -\mu - I_M^* \sum_{i=1}^{10} \beta_i & 0 & 0 & \dots & -S_H^* \sum_{j=1}^{10} \beta_j \\ \beta_1 I_M^* & -(\alpha_{H1} + \mu + \delta) & 0 & \dots & \beta_1 S_H^* \\ \beta_2 I_M^* & 0 & -(\alpha_{H2} + \mu + \delta) & 0 & \beta_2 S_H^* \\ \vdots & \vdots & \vdots & \vdots & \vdots \\ \vdots & \vdots & 0 & \vdots & \vdots \\ \beta_{10} I_M^* & \vdots & \vdots & -(\alpha_{H10} + \mu + \delta) & \beta_{10} S_H^* \\ 0 & 0 & 0 & \dots & \theta - 2\theta I_M^* - \Omega \end{bmatrix}. \quad (19)$$

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:

$$\det (J - \eta I_{12}) = 0 \quad (20)$$

where J is the Jacobian matrix for the equilibrium states, η is the eigenvalue and I_{12} is the identity matrix. At the disease

free equilibrium state $E_0 = (\frac{\lambda}{\mu}, 0, 0)$, thus we have:

$$\eta_1 = -\mu, \quad \eta_2 = -(\alpha_{H1} + \mu + \delta), \quad \eta_3 = -(\alpha_{H2} + \mu + \delta),$$

$\eta_4 = -(\alpha_{H3} + \mu + \delta)$, $\eta_5 = -(\alpha_{H4} + \mu + \delta)$,
 $\eta_6 = -(\alpha_{H5} + \mu + \delta)$, $\eta_7 = -(\alpha_{H6} + \mu + \delta)$,
 $\eta_8 = -(\alpha_{H7} + \mu + \delta)$, $\eta_9 = -(\alpha_{H8} + \mu + \delta)$,
 $\eta_{10} = -(\alpha_{H9} + \mu + \delta)$. For the other two eigenvalues are
 obtained by solving:

$$\eta^2 + a_1\eta + a_0 = 0 \quad (21)$$

when

$$a_1 = (-\theta + \Omega) + (\delta + \mu + \alpha_{H10}), \quad (22)$$

$$a_0 = (-\theta + \Omega)(\delta + \mu + \alpha_{H10}). \quad (23)$$

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

It can be seen easily η_{11} is always negative. Next we consider
 $a_1^2 - 4a_0 = ((-\theta + \Omega) - (\delta + \mu + \alpha_{H10}))^2$ is always
 positive. Then we consider η_{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 $E_1 = (S_H^*, I_{Hi}^*, I_M^*)$, 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

$$\eta^2 + b_1\eta + b_0 = 0 \quad (24)$$

where

$$b_0 = (\Omega - \theta)(\mu + I_M \sum_{i=1}^{10} \beta_i), \quad (25)$$

$$b_1 = (\mu + \Omega - \theta) + I_M \sum_{i=1}^{10} \beta_i. \quad (26)$$

We have

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

So η_{11} is always negative. Next we consider

$$b_1^2 - 4b_0 = ((\mu - \Omega + \theta)I_M^* \sum_{i=1}^{10} \beta_i)^2 \text{ is always positive.}$$

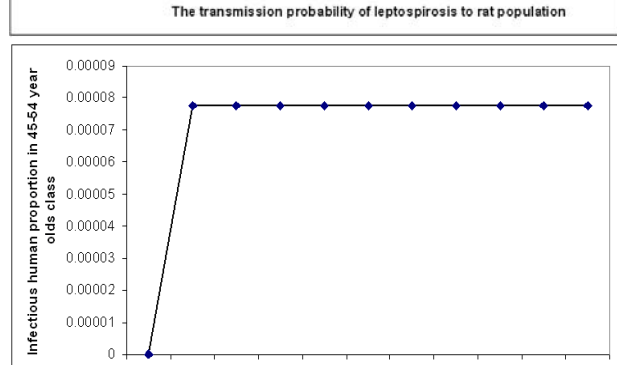
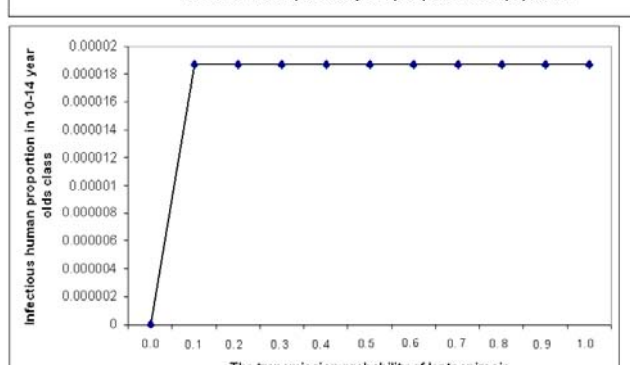
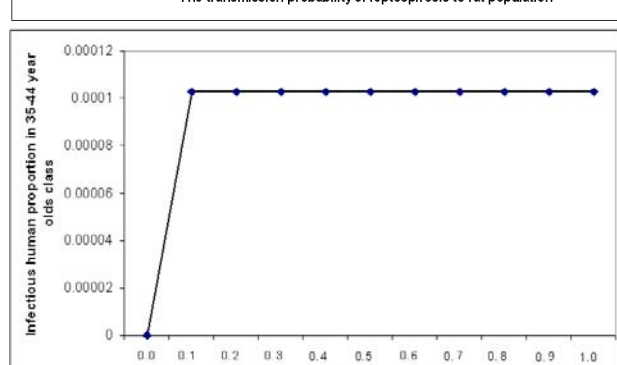
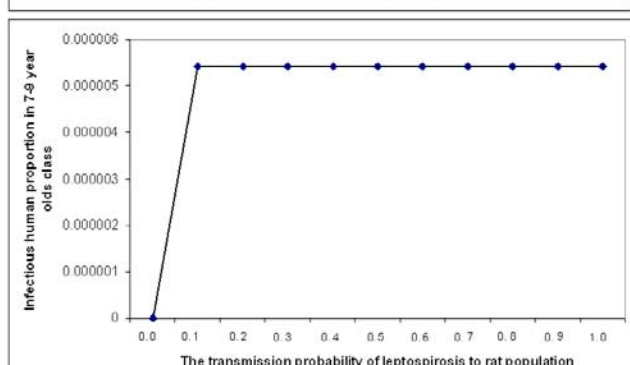
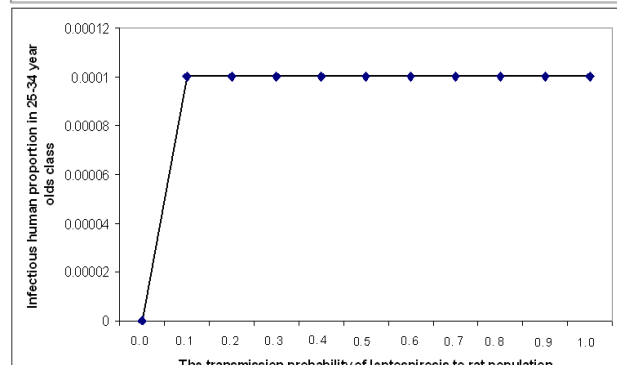
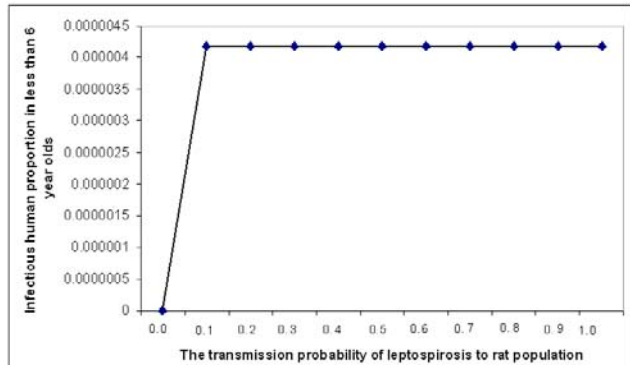
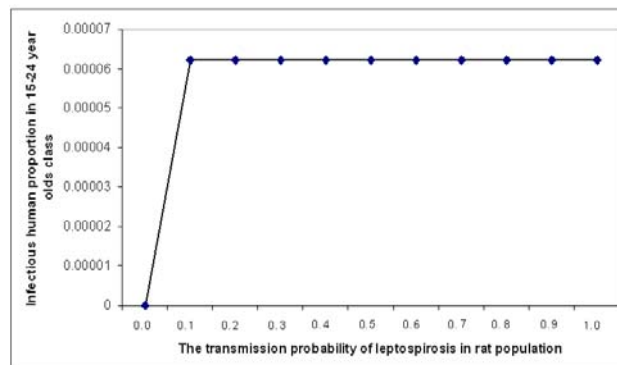
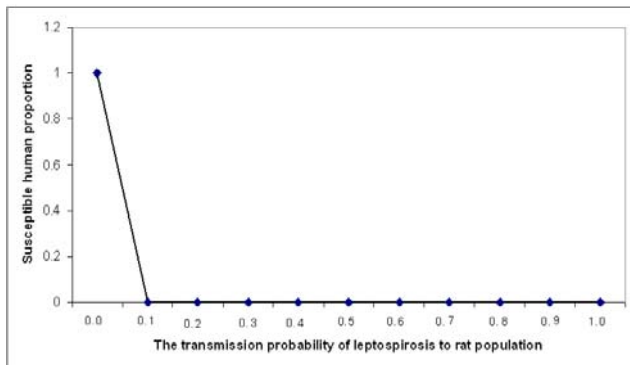
Then we consider η_{12} is negative when $b_0 < 0$.

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 I
 PARAMETERS VALUES USED IN THE SIMULATIONS

| Symbol | Parameter | Value for Fig. 1. | Value for Fig. 2. |
|---------------|---|---|--|
| λ | The recruitment rate into the susceptible human class | $1/(365 \times 70)$ per day | $1/(365 \times 70)$ per day |
| μ | The per capita natural mortality rate of human population | $1/(365 \times 70)$ per day | $1/(365 \times 70)$ per day |
| β_i | The transmission probability of leptospirosis from infected rat to human population in each age group | $\beta_1 = 0.0095$, $\beta_2 = 0.0123$, $\beta_3 = 0.0425$, $\beta_4 = 0.1410$, $\beta_5 = 0.2276$, $\beta_6 = 0.2331$, $\beta_7 = 0.1760$, $\beta_8 = 0.1029$, $\beta_9 = 0.0550$, $\beta_{10} = 0.0004$ | $\beta_1 = 0.0095$, $\beta_2 = 0.0123$, $\beta_3 = 0.0425$, $\beta_4 = 0.1410$, $0 \leq \beta_5 \leq 1$, $\beta_6 = 0.2331$, $\beta_7 = 0.1760$, $\beta_8 = 0.1029$, $\beta_9 = 0.0550$, $\beta_{10} = 0.0004$ |
| α_{Hi} | The per capita death rate from infected | $\alpha_{H1} = \alpha_{H2}, \dots$ $= \alpha_{H10} = 0.0222$ | $\alpha_{H1} = \alpha_{H2}, \dots$ $= \alpha_{H10} = 0.0222$ |
| δ | The recovery rate of human population | $1/15$ per day | $1/15$ per day |
| Ω | The per capita natural mortality rate of rats population | $1/(365 \times 1.5)$ per day | $1/(365 \times 1.5)$ per day |
| θ | The transmission probability of leptospirosis to rat population | $0 \leq \theta \leq 1$ $0, 0.1, 0.2, \dots, 1$ | 0.2 |



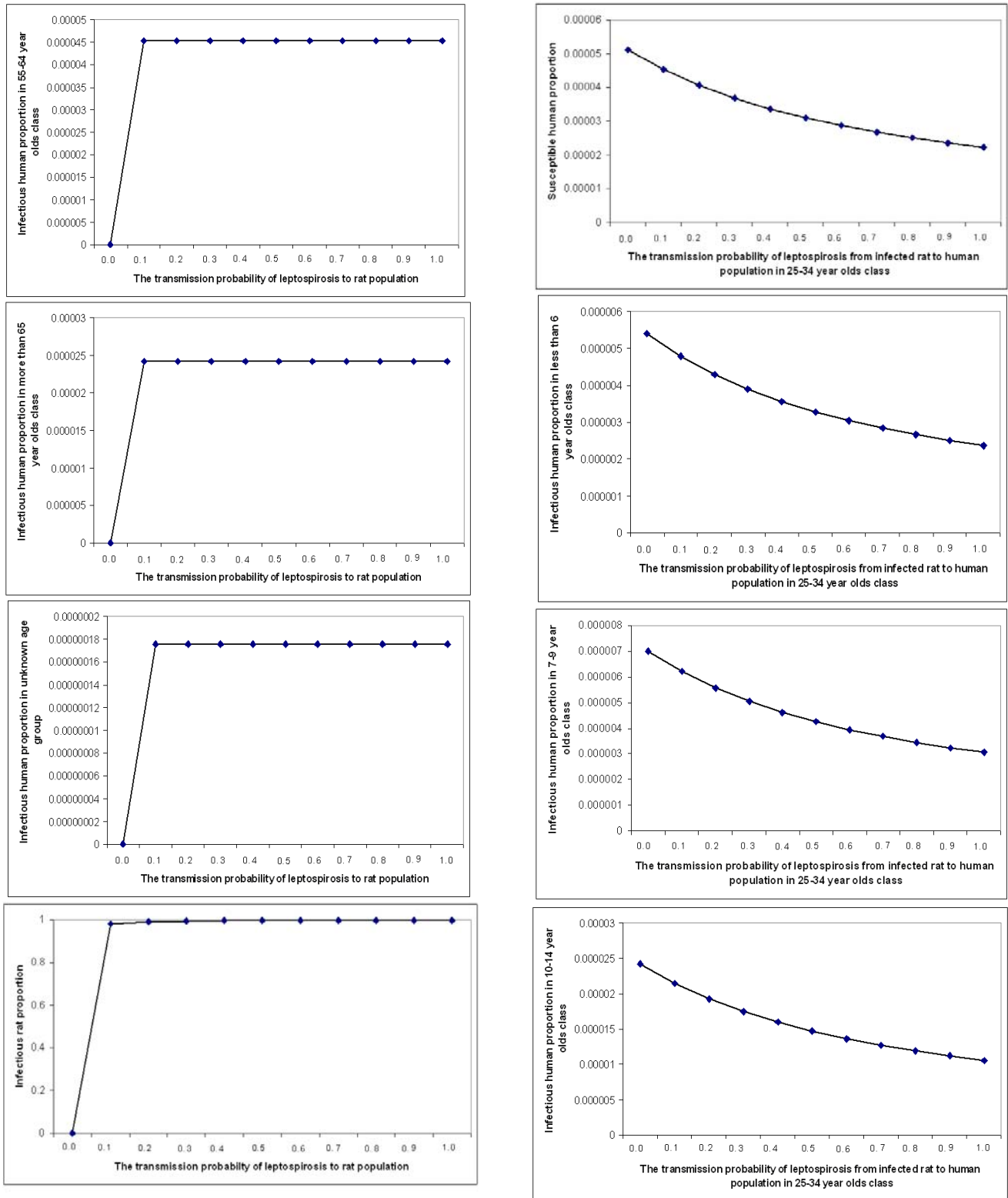


Fig. 1 Bifurcation diagrams of the solutions (4), (5) and (8) for different values of θ . The value of parameters in the model are shown in Table I

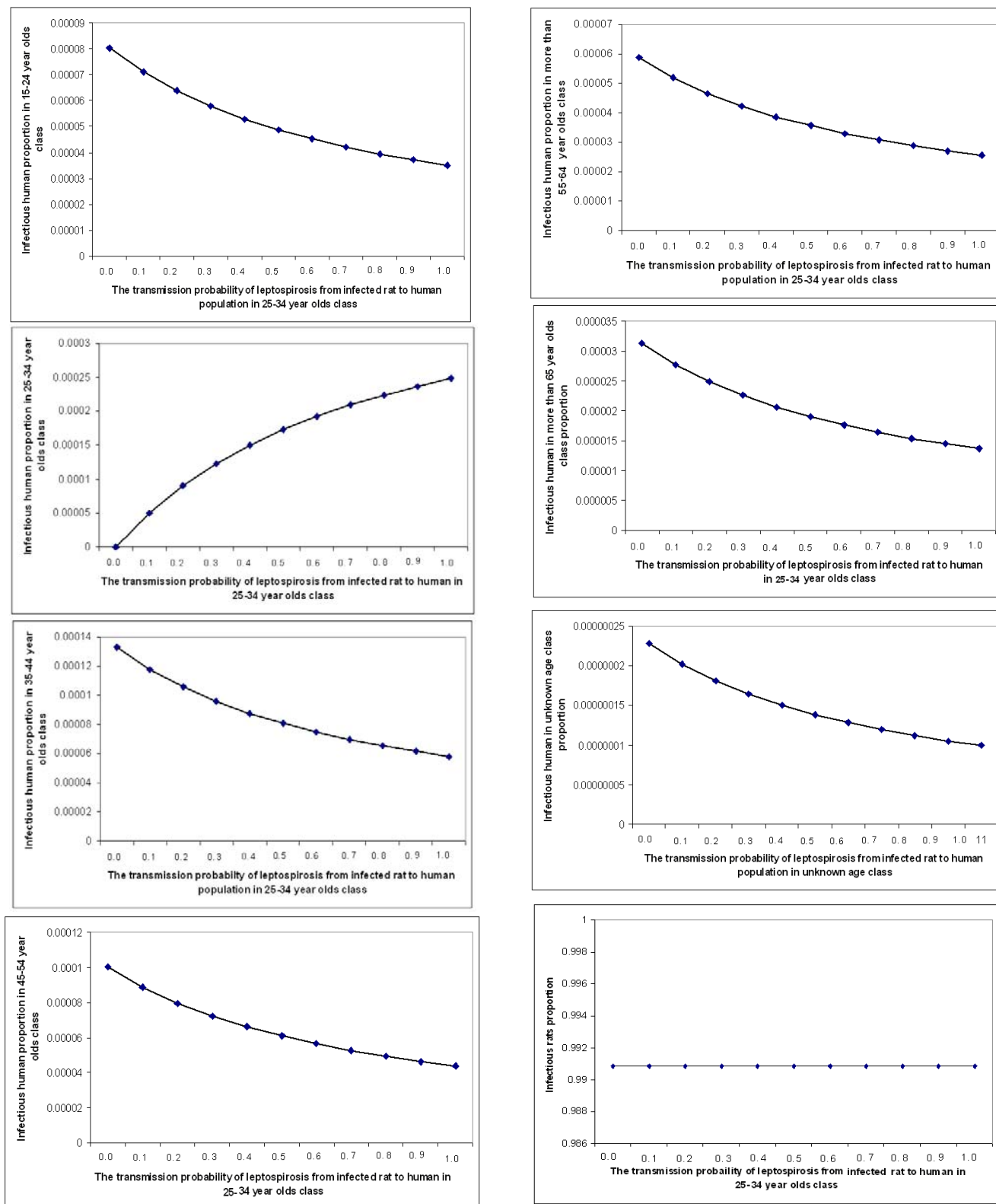


Fig. 2 Bifurcation diagrams of the solutions (4), (5) and (8) for different values of β_5 . The value of parameters in the model are shown in Table I

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 ($0 \leq \theta \leq 1$). 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 (β_5)) are difference. It has an impact to the proportions of all parameters. When β_5 is higher, we can see the infectious human proportion in 25-34 year 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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