Mathematical modeling of Leptospirosis spread in Malaysia

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Leptospirosis is a zoonotic disease that is caused by the pathogen Leptospira, and it can spread indirectly or directly from infected animals to humans. According to the official statistics from the Malaysian Ministry of Health, leptospirosis outbreaks appeared to be in the most critical condition in the recent few years. The Susceptible–Infected–Recovered compartmental model and its extensions have been applied widely in disease modeling. This paper aims to present a compartmental model for leptospirosis spread in Malaysia. Using this approach, an epidemiological model is formulated for humans and vector populations. Our results indicate that the transmission rate from susceptible to infected vectors and the vector birth rate play a significant role in determining the number of infected humans. Besides, they have an impact on the duration of the outbreak as well. The simulation results have been compared with the actual data in 2017 and the analysis shows that the proposed model is able to predict the outbreak recorded in Malaysia.

1. Introduction

Leptospirosis is a zoonotic disease that spreads from infected animals to humans. Leptospirosis is not a newly discovered disease as its existence can be found in the texts of the ancient records [1,2]. However, the general cause of the disease, a bacterium called Leptospira, is only being discovered starting from the 19th century and onwards [3–6]. In general there are two specific types of Leptospira that would cause the infection of the disease, i.e. pathogenic and saprophytic. The pathogenic Leptospira provides the potential to transmit the disease in animals and humans, whereas the saprophytic one lives freely and incapable to cause disease infection [7]. The pathogenic Leptospira can survive for long periods by depending on some of the environmental living factors. For example, the alkalinity, oxygen concentration and salt concentration in the aqueous environment [8]. Leptospirosis is transmitted via direct contact with the excretions of the infected animals. Simultaneously, the infection occurs indirectly among individuals and animals by contacting directly with the pathogenic Leptospira-contaminated environment. Leptospirosis is considered an occupational disease as certain groups of people possess the unusual potential of exposure to the infection. These groups of individuals including farmers, veterinarians, underground workers, or armed personnel.

Leptospirosis occurs globally, but most of the endemic areas are subtropical or tropical places like Southeast Asia regions [9]. There are studies reviewed and newspaper reports mentioned whereby the number of leptospirosis cases is steadily increasing for many years in Malaysia (refer to Fig. 1). The number of confirmed cases for leptospirosis increased from the year 2004 with 263 reported until the

middle of 2015 with 5 370 reported [10]. The data obtained from the Malaysian Ministry of Health showed that in the year 2011, there are 2 268 reported. The cases are followed by 3 665, 4 457, 7 806, and 8 291 from the year 2012 to 2015. In 2016, the leptospirosis cases reported decreased to 5 284 [11].

The research on the mathematical modeling of the transmission of leptospirosis has been vigorously conducted in many countries, e.g. Thailand. This infectious disease is endemic and considered a significant public health issue in the country [12]. A Susceptible–Infected–Recovered–Susceptible–Infected (SIR-SI) model was developed to model the leptospirosis transmission in the juvenile and adult individuals in Thailand [13]. Triampo et al. [14] proposed a simple deterministic SIR-SI model to study the leptospirosis spread in two provinces in Thailand, i.e. Phrae and Nakhon Ratchasima for the

Fig. 1. The number of leptospirosis cases reported in Malaysia from 2004 to Dec 2017.

human and vector populations respectively. The control of leptospirosis spread realistically is a challenging public health issue. Khan et al. [15] introduced multiple control variables, such as different precautionary measures in the SIR model to control the spread of the disease.

The aim of this paper is to model the leptospirosis spread in Malaysia using a SIR-SI model. The model formulation will be presented in the following section. Section 3 is the presentation of our numerical results and analysis and followed by a conclusion in the final section.

2. Model Formulation

The models formulated by Pongsumpun [13] and Triampo et al. [14] provide some of the ideas on the interactions among the populations in the process of model formulation. Below are some assumptions made for the human and vector populations.

1. Assumptions for the human population.
   — The life expectancy and natural birth rate of the human population are constant with time.
   — The life expectancy of the human is natural and same to all population sub-groups.
   — The human population is homogeneous mixing all the time as age, gender, disease status and occupations are not concerned for all the individuals.
   — The spreading of leptospirosis from the urine-contaminated environment to the human is ignored for the formation of the epidemiological model.
   — The number of immigrants is unconcerned with the population.
   — The infected human can be recovered by consuming antibiotics or medicines, and they recuperate at a constant rate.
   — The recovered human can become susceptible at a constant rate as the immunities in the human bodies decline when time passes.
   — The deaths due to leptospirosis in the human population are not considered for the model formulation.
2. Assumptions for the vector population.
   — The natural birth rate and natural life expectancy are continuous with time and the same to all vector population sub-groups.
   — The vector population is typically referring to the rats.
   — The infected vectors cannot recover as there are no vaccines or medicine are provided for them.
   — The susceptible vectors become infected instantly with no concern for the incubation period of the infectious bacteria (Leptospira) to develop.
   — The population is homogeneous mixing for each sub-group.
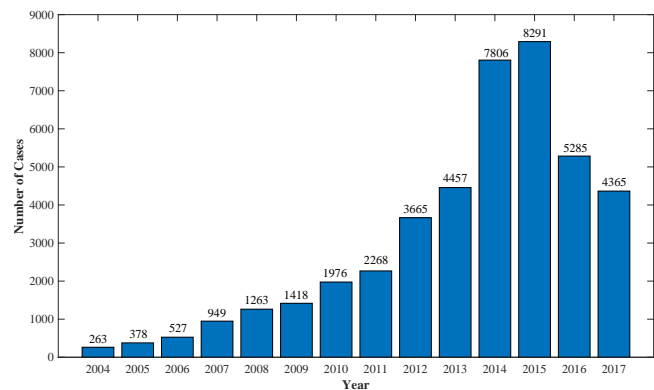
    — The death rate due to the disease among the vector population is ignored as there is insufficient data available.

3. Assumptions for the relationship between human and vector populations.
    — The infected human cannot infect the vector population.
    — Only the infected vectors can infect humans.

There are two distinct populations in our model: human and vector populations. The human population is divided into three sub-groups, which are Susceptible (S_h), Infectious (I_h) and Recovered (R_h). As for the vector, the population is divided into Susceptible (S_v) and Infectious (I_v) as the vectors do not recover from infection. The definitions of the parameters and variables used in the model are given below:

N_h: the total size of the human population,
μ_h: the natural birth rate of the human population,
λ_h: the natural life expectancy of the human population,
θ_h: the transmission rate between S_h and I_h,
γ_h: the recovery rate of infected humans from disease infection,
δ_h: the constant rate for recovered humans to become susceptible,
N_v: the total size of the vector population,
μ_v: the natural birth rate of vector population,
λ_v: the natural life expectancy of vector population,
θ_v: the transmission rate between S_v and I_v.

The compartmental diagram for the disease transmission between human and vector populations is shown in Fig. 2.
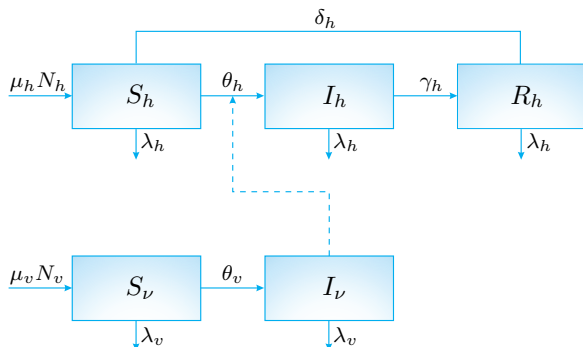

Fig. 2. Compartmental diagram of the SIRS-SI model.

where $N_h = S_h + I_h + R_h$ and $N_v = S_v + I_v$.

Thus, we have the following system of differential equations to describe the dynamics of disease transmission,

$$\frac{dS_h}{dt} = \mu_h N_h - \lambda_h S_h - \theta_h I_v S_h + \delta_h R_h, \quad (1)$$

$$\frac{dI_h}{dt} = \theta_h I_v S_h - \lambda_h I_h - \gamma_h I_h, \quad (2)$$

$$\frac{dR_h}{dt} = \gamma_h I_h - \lambda_h R_h - \delta_h R_h, \quad (3)$$

$$\frac{dS_v}{dt} = \mu_v N_v - \lambda_v S_v - \theta_v I_v S_v, \quad (4)$$

$$\frac{dI_v}{dt} = \theta_v I_v S_v - \lambda_v I_v, \quad (5)$$

3. Results and Discussion

The parameter values that have been used in the model simulations are summarised in Table 1. Three parameters, θ_h, μ_v and θ_v are taken to be arbitrary constants as there is insufficient data available.

Fig. 3 and Fig. 4 illustrate the results for the human subgroups whereby Fig. 5 and Fig. 6 are the outcomes for the vector subgroups. The results show the population behavior among human and vector subgroups reaching steady states. For susceptible humans, the numbers increase initially and are followed by a stable trend. The subgroup does not experience any decline in numbers due to the recovered individuals becoming susceptible as their immunities lose when time passes. As for the infected and recovered humans, the numbers increase to a limiting point. The population behaviors among the vector subgroups are different from humans. The trends for both subgroups are opposite to each other and most of the vectors are infected which indicate the disease can spread very fast among the vector population.

Table 1. Parameter values.

| Parameter	Value	Description	References
N_h	32022600	total Malaysian human population	[16]
μ_h	0.04356	per capita, the birth rate in days corresponds to 15.9 per capita birth	[17]
λ_h	0.03673	per capita, the mortality rate per day corresponds to 74.6 years of life expectancy of Malaysian	[18]
θ_h	$5.0 \cdot 10^{-14}$	transmission rate from susceptible humans to infected humans	arbitrary constant
γ_h	0.01587	recover within 6 to 12 weeks from the disease infection	[19]
δ_h	$3.0 \cdot 10^{-4}$	the rate of loss immunity for 9 years	[20]
N_v	256180800	estimated total vector population with scale of 1 person associates with 8 rats	[10]
μ_v	1.13	estimated per capita birth rate of rats	arbitrary constant
λ_v	1.09589	estimated per capita death rate with corresponds to 2–3 years lifespan of rats	[21]
θ_v	$4.5 \cdot 10^{-9}$	transmission rate from susceptible vectors to infected vectors	arbitrary constant
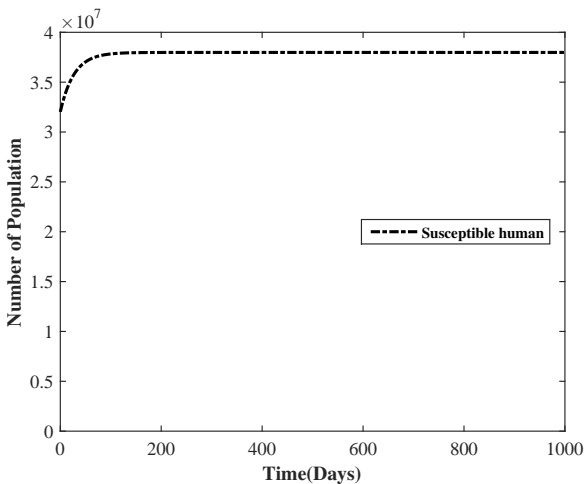
Fig. 3. Simulation results of the susceptible human subgroup.
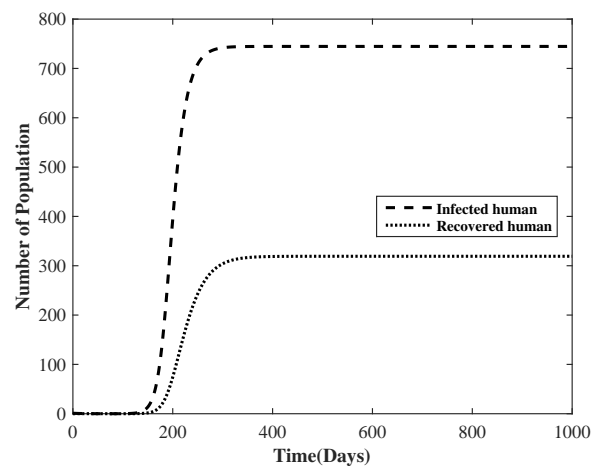

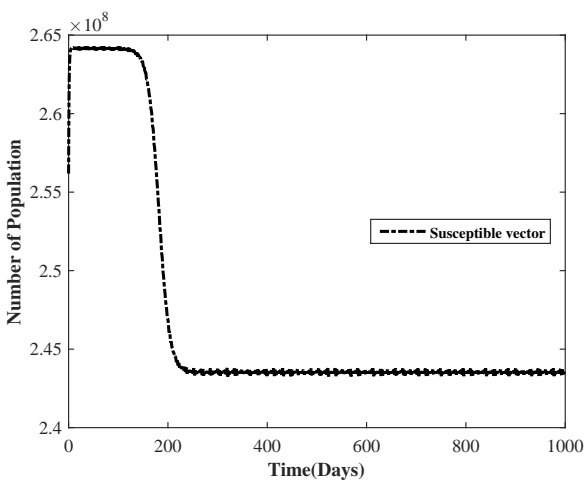**Fig. 4.** Simulation results of the infected and recovered human subgroup.

Fig. 5. Simulation results of the susceptible vector subgroup.
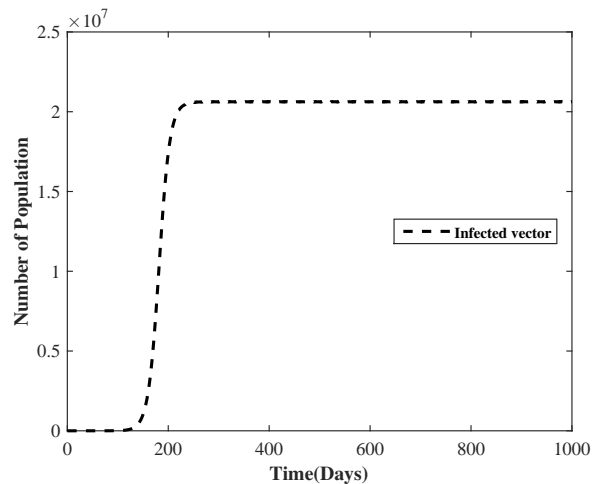

Fig. 6. Simulation results of the infected vector subgroups.

Next, the comparison between the simulation result from the model and the actual data of the Leptospirosis spread in Malaysia were performed. The data obtained from the Malaysian Ministry of Health is processed by considering the average of the recovery period to be 9 weeks so that the data reflects the prevalence data as illustrated in Fig. 7.
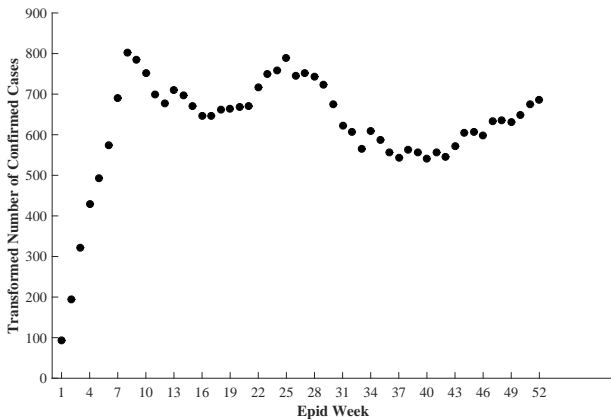

Fig. 7. The prevalence data of leptospirosis cases in Malaysia for the year 2017.

Fig. 7 shows there are three waves of leptospirosis outbreak in 2017. The occurrence of leptospirosis outbreaks is influenced by other dynamic factors like rainfall and the geographical distribution of the human population [22]. Therefore, these dynamic factors result in different waves of disease spreading. The first wave of outbreak spends 16 weeks, which start from epidemiological week 1 to week 16. The duration of the second wave is from week 17 to week 39, which is 23 weeks. As for the third wave, the outbreak is from week 40 to week 52. Hence, the model simulations are conducted based on three outbreaks and the parameter values are converted into weekly basis. Three arbitrary constants, θ_h, μ_v, θ_v are calibrated for the simulation on weekly basis. The comparisons are illustrated from Fig. 8 to Fig. 10.
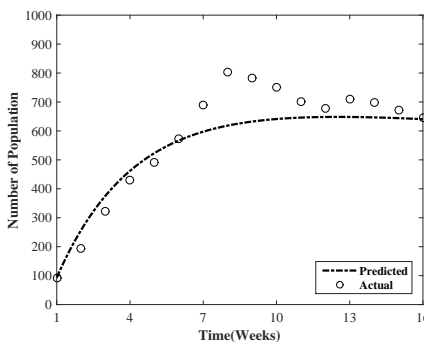

Fig. 8. The comparison for Epid Week 1 to Epid Week 16 where $\theta_h = 6.1 \cdot 10^{-6}$, $\mu_v = 7.82$, $\theta_v = 2.95 \cdot 10^{-8}$.
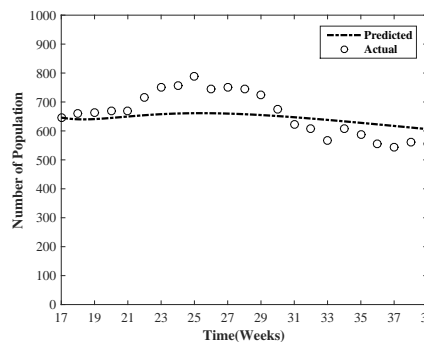
Fig. 9. The comparison for Epid Week 17 to Epid Week 39 where $\theta_h = 7.2 \cdot 10^{-6}$, $\mu_v = 7.82$, $\theta_v = 2.95 \cdot 10^{-8}$.
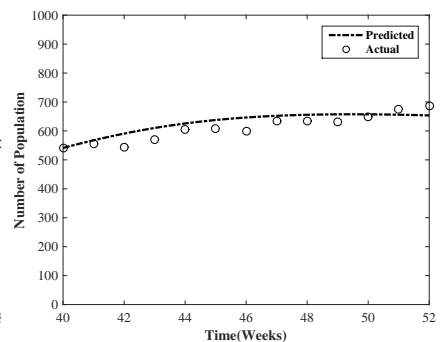
Fig. 10. The comparison for Epid Week 40 to Epid Week 52 where $\theta_h = 6.9 \cdot 10^{-6}$, $\mu_v = 7.82$, $\theta_v = 2.95 \cdot 10^{-8}$.

The normality of the residuals are shown from Fig. 11 to Fig. 13. The regression analysis for each wave of the outbreak is conducted. The r-square (r^2) or the correlation of determination for the three waves are 92.22%, 79.06% and 77.33% respectively. Fundamentally, high r^2 results in a better response to the variability of the actual and predicted data around the mean of the data. At the same time, the points in the normal probability plots follow the line quite well indicating that the points are normally distributed. In other words, the high r^2 and the normally distributed points in the plots indicate that the model is an adequate model.

Different values of three parameters μ_v, θ_h and θ_v are observed to have impact on the number of infected humans and the duration of the outbreak. Fig. 14 and Fig. 15 show that elevated μ_v and θ_v cause more people to be infected. Conversely, the number of infected humans reduced with declined μ_v and θ_v. As for θ_h, although the values affect the infection, the influence of θ_h is less significant compared to μ_v and θ_v (see Fig. 16). Although both μ_v and θ_v affect the transmission of the disease, yet small changes of θ_v cause more influences when compared with μ_v.

Additionally, the higher values of μ_v and θ_v cause longer outbreak durations. It takes longer time to reach the epidemic peak (see Fig. 17 and Fig. 18). However, the value of θ_h does not influent the outbreak duration. Fig. 19 shows that the time taken to reach epidemic peak is the same.
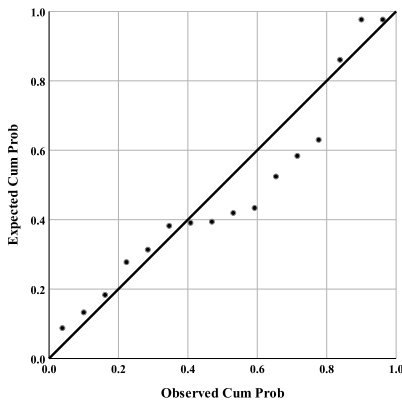
Fig. 11. Normal probability plot of the comparison for Epid Week 1 to Epid Week 16.
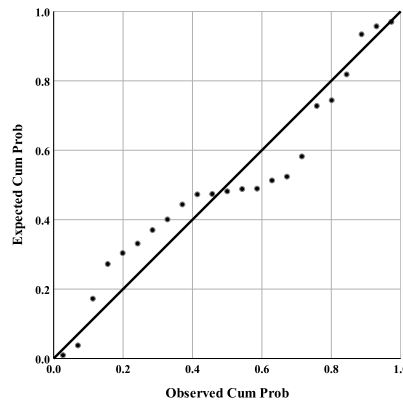

Fig. 12. Normal probability plot of the comparison for Epid Week 17 to Epid Week 39.
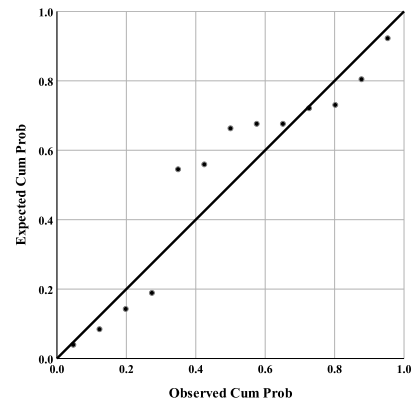

Fig. 13. Normal probability plot of the comparison for Epid Week 40 to Epid Week 52.
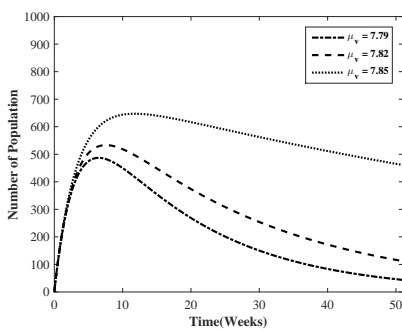

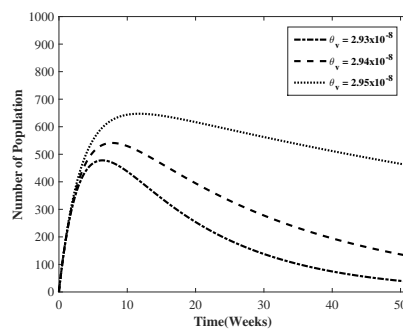**Fig. 14.** Simulation results of various transmission rates, μ_v for infected humans with constant θ_h and θ_v.

Fig. 15. Simulation results of various transmission rates, θ_v for infected humans with constant θ_h and μ_v.
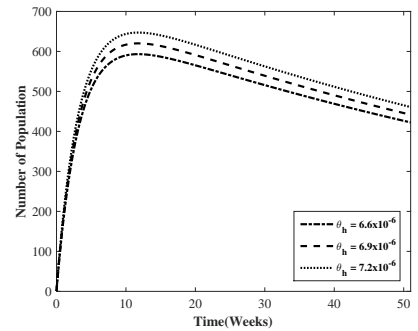
Fig. 16. Simulation results of various transmission rates, θ_h for infected humans with constant μ_v and θ_v.
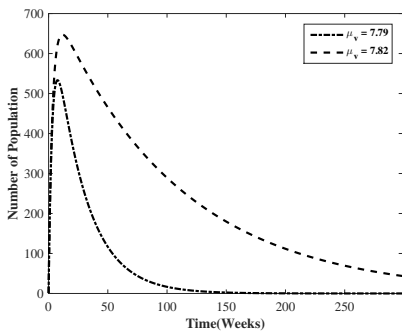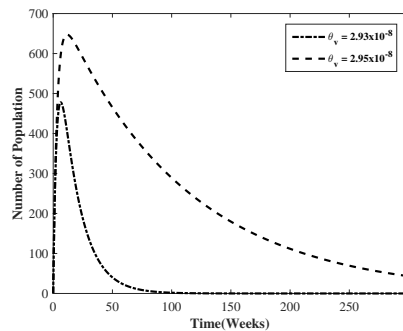

Fig. 17. Impact of various transmission rates, μ_v on the outbreak duration.

Fig. 18. Impact of various transmission rates, θ_v on the outbreak duration.
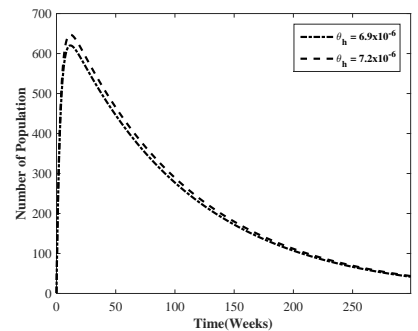

Fig. 19. Impact of various transmission rates, θ_h on the outbreak duration.

4. Conclusion

A deterministic epidemiological model is developed to describe the leptospirosis spread in Malaysia. The regression analysis proves that the model is an adequate one and is capable to predict the disease outbreak. Our results show that both the transmission rate from susceptible to infected vectors, θ_v and the vector birth rate μ_v influence the number of infected humans. However, the impact of θ_v is more significant than μ_v. At the same time, the duration of the outbreak is prolonged when the values of θ_v and the vector birth rate μ_v increase. Therefore, controlling the number of vectors is an important intervention to control the spread of the disease.

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Математичне моделювання поширення лептоспірозу в Малайзії

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Лептоспіроз — це зоонозне захворювання, що викликається збудником Leptospira, яке може опосередковано або безпосередньо поширюватися від інфікованих тварин до людей. Згідно з офіційною статистикою Міністерства охорони здоров'я Малайзії, за останні декілька років спалахи лептоспірозу виявилися найкритичнішими. Компартментальна модель "сприйнятливі–інфіковані–одужані" та її розширення широко застосовуються для моделювання захворювань. Ця стаття має на меті подати компартментальну модель поширення лептоспірозу в Малайзії. Використовуючи цей підхід, формується епідеміологічна модель для людей та популяцій переносників. Наші результати вказують на те, що швидкість передавання від сприйнятливих до інфікованих переносників та рівень народжуваності відіграє значну роль у визначенні кількості інфікованих людей. Крім того, вони впливають і на тривалість спалаху. Результати моделювання було порівняно з фактичними даними 2017 року, аналіз показує, що запропонована модель здатна передбачити спалах, який був зафіксований в Малайзії.

Ключові слова: *лептоспіроз, передавання, математичне моделювання, модель SIR.*