MATHEMATICAL MODELING AND COMPUTING, Vol. 9, No. 4, pp. 805–815 (2022)

Effects of rodents' behaviours on leptospirosis spread: an individual-based modeling approach

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(Received 11 August 2022; Accepted 3 September 2022)

Leptospirosis is a zoonotic disease common in tropical and subtropical regions. This infectious disease is endemic in Sarawak, Malaysia. In recent years, the threat of leptospirosis is on an increasing trend in Sarawak since 2010. The traditional compartmental models assume that the population is homogeneous and shares the same characteristics and behaviours. However, each individual in the population has different and unique behaviour in the real world. Thus, this paper aims to model the leptospirosis spread by adopting the individual-based modeling approach to address the heterogeneity that affects the transmission of the disease. Rodents' behaviours such as active period duration and movement range are incorporated into the model. From the sensitivity analyses, the results show that the movement range of the rodents has a significant impact on the spread of the disease compared to the active period duration. The comparison between simulation results and the actual prevalence data in Sarawak is performed to validate the model. Through regression analysis, the correlations of determination for three outbreaks in Sarawak for the year 2017 are more than 90%. In addition, the normal probability plots for three outbreaks indicate the points follow the line well and are normally distributed. This shows that the proposed individual-based model can predict leptospirosis transmission.

Keywords: *leptospirosis, individual-based, rodents' behaviour, active period duration, movement range.*

2010 MSC: 92-10, 92D30 **DOI:** 10.23939/mmc2022.04.805

1. Introduction

Leptospirosis is endemic in various places globally, particularly in tropical and subtropical regions. In recent times, the disease has approximately caused more than one million notified cases, nearly 59 000 deaths and roughly 10 000 hospitalizations of severe cases worldwide annually [1,2]. Leptospirosis is a zoonosis in which the disease is transmitted directly or indirectly from infected animals to humans. However, rare circumstances might happen with the occurrence of human-to-human transmission through sexual intercourse, pregnancy or breast milk of the infected mother, urine of infected patients, and blood transfusion [3]. The symptoms of leptospirosis are varying based on the degree of illness. The people who are asymptomatic or in mild condition have flu-like symptoms including jaundice whereas the severe condition accompanies aseptic meningitis, renal and liver failure along with other pulmonary and cardiac diseases [4].

The disease is underreported due to its similarities with other diseases such as influenza and dengue fever and causes difficulties in the clinical diagnosis of the infection [5]. Besides leptospirosis being underdiagnosed, it is also an occupational hazardous disease. Some people are highly at risk of infection, particularly the jobs that are mostly associated with animals, construction workers, agriculture, and others [6].

This project is funded by the Ministry of Higher Education, Malaysia under the Fundamental Research Grant Scheme, Grant Number FRGS/1/2020/STG06/UNIMAS/02/1.

Sarawak, one of the regions in East Malaysia is a place rich in natural resources and biodiversity. Sarawak is located near the equators and experiences a tropical climate throughout the year. Due to the weather and climatic conditions, the situation of leptospirosis in Sarawak starts to endanger the people in the region. The number of reported cases in Sarawak has risen dramatically from more than 30 cases in 2004 to nearly 300 in 2012 [7,8]. In December 2010, the Ministry of Health Malaysia highlighted leptospirosis to be a notifiable disease [9]. After the year 2010, the number of confirmed cases increases gradually and reaches nearly 700 cases from 1 January to 27 October 2018 [10]. Figure 1 shows the number of reported cases from the year 2004 to 27 October 2018.

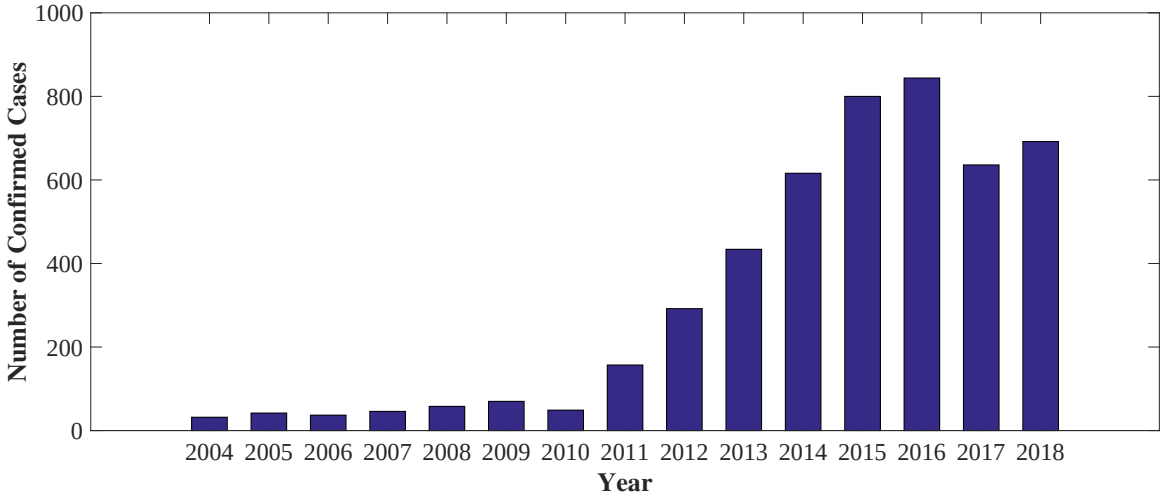

Fig. 1. Number of leptospirosis cases reported in Sarawak from 2004 to 27 October 2018.

The studies of infectious disease dynamics through mathematical models have been widely conducted. The compartmental models are the most studied ones, such as Susceptible–Infected–Recovered (SIR) [11] in the transmission of infected diseases, e.g. dengue [12], malaria [13], leptospirosis [14,15]. However, the compartmental models are not adequate for the system that considers the individuals who possess essential differences [16]. In compartmental models, the populations are assumed to be homogeneous and share the same characteristics and behaviours in model formulation. However, each individual possesses distinct and unique behaviours in real-world circumstances, which means heterogeneity exists within the population. For zoonotic disease or vector-borne disease, the heterogeneity of the vectors or hosts can bring significant impacts on the disease transmission [17]. Hence, individual-based models (IBM), also known as agent-based models (ABM) are more suitable models to capture the heterogeneity of the population.

IBM simulates the dynamic systems that are depending on stochasticity including heterogeneity, and numerous works have been conducted to model infectious disease by using IBM [18]. Jindal and Rao [19] modeled the transmission of mosquito-borne diseases by using ABM. The study deduced that ABM overcame the limitations in determining the factors of interactions between hosts and vectors that drive the disease transmission such as mobility, and distributions of the host and the vector populations, geographical and weather conditions. Mahmood et al. [20] formulated an ABM to study the dengue fever transmission among the people in Pakistan. The model considered the behaviour of mosquitoes such as biting rate and environmental factors including temperature for the spread of dengue fever. Their study deduced that the temperature rise increased the biting rate of mosquitoes and caused the dengue cases to multiply. Alvarez Castro and Ford [21] studied the spread of coronavirus among university students by implementing the ABM. The model focused on the relationships between locations including the activities of the students and their influences on the transmission of the disease. Their results deduced the implementation of preventive measures such as wearing face masks, early lockdown and self-isolation approach could reduce the infection and keep students safe.

To the best of our knowledge, there is very little research on the modeling of the leptospirosis transmission by using IBM. Therefore, the purpose of this paper is to propose an IBM for the spread of leptospirosis. In Section 2, the assumptions for both populations and the model will be presented. The results of IBM simulations, model validation, and sensitivity analyses are covered in Section 3. The last section is the conclusion of the paper.

2. Model formulation

In the formulation of a model, the assumptions or rules are essential as the rules act as the behaviours of the agents in the model simulation. In our work, there will be two agents, humans and vectors (rodents). The assumptions for both populations are as follows:

1. Assumptions for the human population
   - The humans are stationary in their housing area.
   - There are principally three states of human health conditions: Susceptible, Infected and Recovered.
   - The incubation period of the leptospirosis is assumed negligible.
   - The death of infected humans due to disease is not considered.
   - The spreading of leptospirosis typically involves humans and vectors only.
   - The indirect transmission of leptospirosis from the bacteria-contaminated environment is not in the consideration.
2. Assumptions for the vector population
   - The vectors are referring to the rodents.
   - The vectors are active at certain periods. Other than the active period, the rodents will stay at their nests.
   - The vectors are wandering around outside their nests and approach the humans' housing areas during the active period.
   - The transmission of leptospirosis occurs when the vectors are active and moving around.
   - There are two states of vector health conditions: Susceptible and Infected.
   - The death of vectors due to leptospirosis infection is not considered.
   - The lifespan of a vector is between 26–40 months.

Figure 2 shows the interactions and leptospirosis transmission between human and vector agents. Based on the figure, the interactions of two parties are formed according to the established rules earlier. The natural birth rates, μ_1 and μ_2, allow the agents to enter both human and vector populations. As for the natural death rates, λ_1 and λ_2, both parameters ensure that individuals must leave when they experience death. Otherwise, they would remain in the populations. Both humans and vectors possess several epidemiological states. Initially, humans are in a susceptible state. Once the individuals contact the infected vectors, they become infected by interacting with the bacteria at a transmission rate of θ_1. If the humans are not in contact with the infected vectors or the bacteria, then the humans remain as susceptible status. When the infected humans undergo proper treatment and receive medicine, they would recover from the disease at a recovery rate of γ. However, if the humans do not show any signs of recovery, then they remain in the infected stage. Meanwhile, the recovered human may become a susceptible again with an immunity loss rate of δ. As for the vectors or the rodents, they are active within an active period (α_s to α_e) with active periods duration α_d. The rats are wandering around from their nests with a movement range of η when they are active. Other than the active period, they remain in their nests. When the rodents are active, they interact with the bacteria or pathogenic Leptospira and become infectious at a transmission rate, θ_2. However, the rodents remain susceptible if they do not interact with the bacteria.

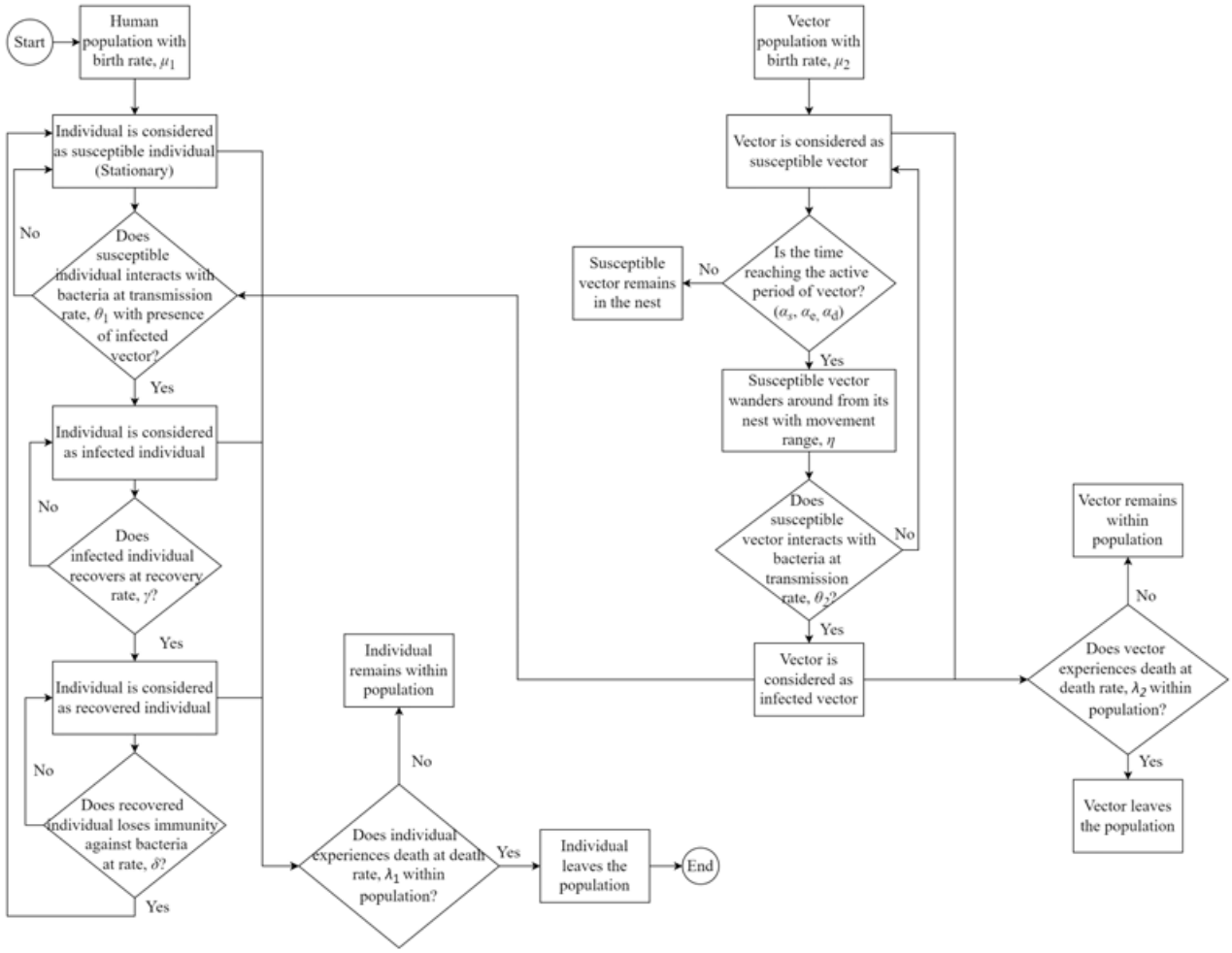

Fig. 2. Flowchart of IBM for leptospirosis transmission.

3. Results and discussion

For the IBM simulation, the NetLogo [22] is chosen as the working mechanism as the software is simple for academicians or researchers to understand and easy to implement [23]. IBM is a stochastic model, which means the results are varying for each simulation. The coefficient of variation, C_v can be used to determine the number of runs required [24]. In our work, it is determined that 20 runs are sufficient and the average is taken as the results.

3.1. Initial conditions and parameter listing

For the simulation of leptospirosis transmission in Sarawak, the initial value for the susceptible human is set as 100 as the leptospirosis cases reported during 2017 did not exceed 50 cases throughout the 52 epidemiological weeks [8]. In addition, NetLogo cannot afford to conduct the model simulation with a significantly massive scale of numbers of agents. For the infected and recovered humans, the initial values are set as one and zero respectively. In terms of vector population, the initial value for the susceptible vector is set as 800 with one person living associatively with eight rats [25] whereas the infected vector is set as one. Table 1 shows the parameter values and references for the simulation of leptospirosis transmission.

Table 1. Parameter values and descriptions.

Parameter	Value	Description	References
μ_1	0.03726	the birth rate of the Sarawak human population in days corresponds to 13.6 per capita birth	[26]
λ_1	0.03581	the natural mortality rate of the Sarawak human population in days corresponds to 76.5 years of life expectancy for Sarawakian	[27]
θ_1	0.10	transmission rate from susceptible human to infected human with the presence of infected vector	[28]
γ	0.01587	recovery rate in days corresponds to 6–12 weeks for recovering from leptospirosis infection	[29]
δ	0.00030	the rate of immunity loss against leptospirosis in days for 9 years (immunity lasts not more than 10 years)	[30]
μ_2	1.10	per capita birth rate of vector population in days	assumed
λ_2	0.99626	the natural death rate of the vector population in days corresponds to 26–40 months of the lifespan of the vectors	[31]
θ_2	0.20	transmission rate from susceptible vector to infected vector	assumed
α_s	18:00	active period start time of vector population	assumed
α_e	06:00	active period end time of vector population	assumed
α_d	12	active period duration of the vector population	difference between α_s and α_e
η	20	the movement range of the vector population	assumed

Among the parameters, the vector birth rate, μ_2 and the transmission rate from susceptible to infected vectors, θ_2 are assumed as there is not enough available information to determine the values. As for the active periods of the vector and the vector movement range, η, the assumed values are based on the consideration of the rats being nocturnal animals and the movement range of 10 to 20 m for Norway rats [32]. However, this study does not consider the species of the rats.

3.2. Result simulations

Figures 3 and 4 represent the averaged population behaviours of the human population whereas Figs. 5 and 6 are for the averaged population behaviours for the vectors. It can be observed that the number of susceptible humans decreases over time as more humans become infected, and in the end, reaches a stable trend. As for the infected humans, the number escalates initially and reduces after reaching a peak between Day 21 to Day 24. Inversely, the recovered individuals increase at the beginning and stabilised throughout the simulation. For the vectors, the behaviours of both susceptible and infected groups are very similar to the human population. However, the number of both groups reaches nearly zero as most of the vectors die naturally.

3.3. Model validation

To validate the proposed IBM, a comparison between simulation results and the actual prevalence data is performed. As the obtained data from the Malaysia Ministry of Health contains only the number of leptospirosis confirmed cases, the raw data requires processing with the consideration of the average recovery period of 9 weeks. Figure 7 shows the processed data.

Based on Fig. 7, there are three waves of leptospirosis outbreaks in 2017. The first wave of outbreaks starts from epidemiological week 1 to 16 (red line). As for the second and third waves, the outbreaks begin from week 17 to 39 (blue line) and from week 40 to 52 (green line) respectively. For model validation, the regression analysis is performed to compare the data for the three outbreaks. Figures 8–10 illustrate the outcomes of the comparisons whereby Figs. 11–13 are the normal probability plots of the comparisons.

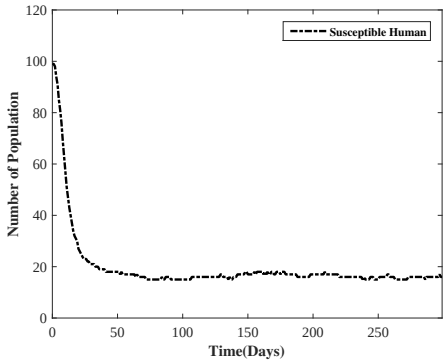

Fig. 3. The averaged population behaviour of susceptible humans for 300 days.

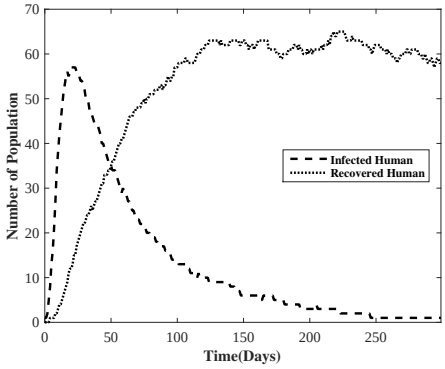

Fig. 4. The averaged population behaviours of infected and recovered humans for 300 days.

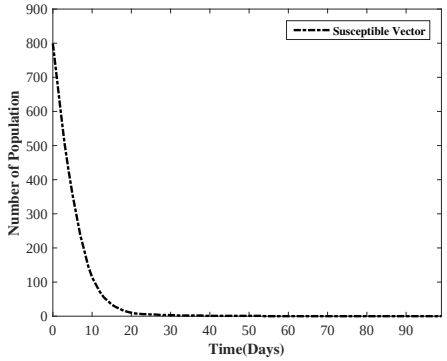

Fig. 5. The averaged population behaviours of susceptible vectors for 100 days.

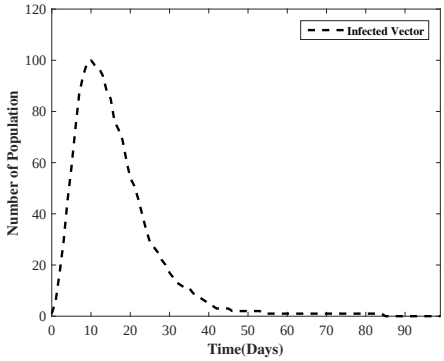

Fig. 6. The averaged population behaviour of infected vectors for 100 days.

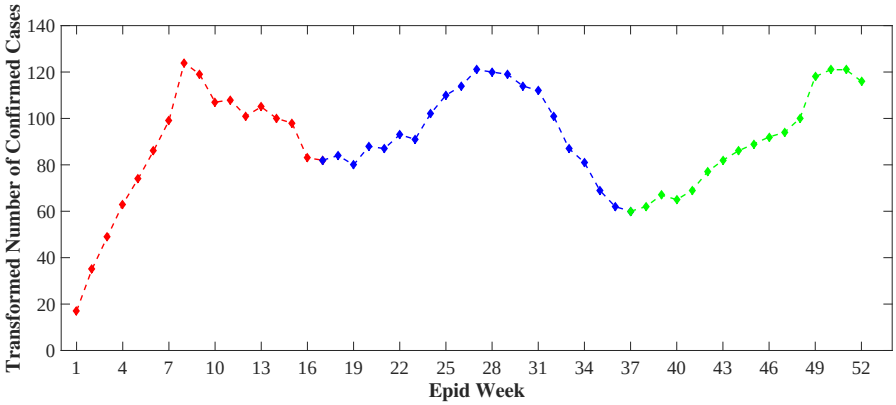

Fig. 7. The prevalence data of leptospirosis confirmed cases in 2017.

From Figs. 8–10, the r-squares (r^2) or the correlations of determination for three outbreaks are 96.08%, 91.01% and 94.68% respectively. As for the normality plots (see Figs. 11–13), three plots indicate the residuals follow the line well. By performing regression analysis, high r^2 and the patterns of residuals reflect that IBM is an adequate model. Fundamentally, high r^2 indicates a better response to the variability of the actual and predicted data around the mean of the data. The residuals follow the line well showing the simulated results are normally distributed and the model is a good fit for the actual prevalence data.

Meanwhile, the occurrences of a few leptospirosis outbreaks might be related to various factors. For instance, the climate within the region might affect the spreading of infectious diseases. The region has frequent flooding frequently results in a higher number of individuals suffering from the zoonotic disease [14]. In addition, the rise of temperature in the middle of the year may encourage more humans and animals to involve in water-based activities and simultaneous exposure to the Leptospira-

contaminated environment [33]. Apart from climate, misdiagnosis of leptospirosis might influence the exact situation of the disease as well. In Malaysia, leptospirosis is frequently diagnosed as tropical fever as the clinical symptoms of leptospirosis are very alike to other diseases [34].

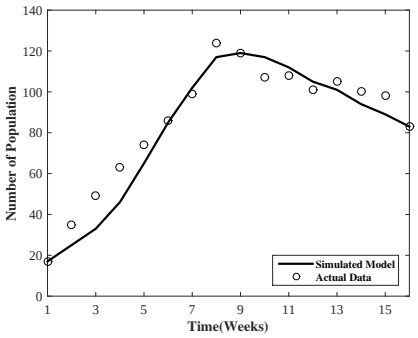

Fig. 8. The comparison from Epid Week 1 to Epid Week 16 with $\mu_v = 7.15$, $\theta_v = 0.35$, $\alpha_d = 12$ hours, $\eta = 22$ m.

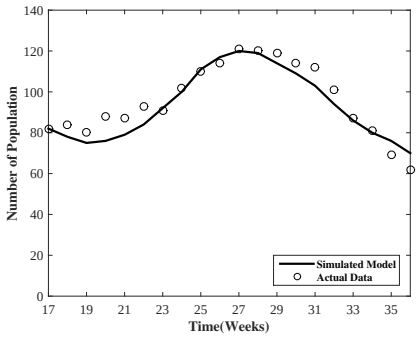

Fig. 9. The comparison from Epid Week 17 to Epid Week 36 with $\mu_v = 7.15$, $\theta_v = 0.35$, $\alpha_d = 12$ hours, $\eta = 19$ m.

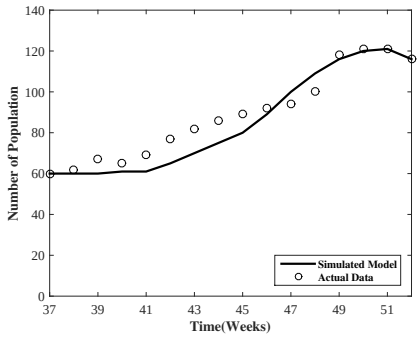

Fig. 10. The comparison from Epid Week 37 to Epid Week 52 with $\mu_v = 7.15$, $\theta_v = 0.35$, $\alpha_d = 12$ hours, $\eta = 16$ m.

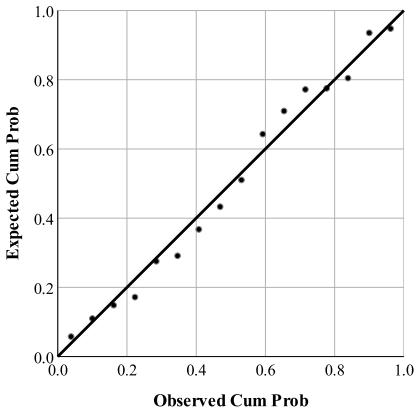

Fig. 11. Normal probability plot of the comparison for Epid Week 1 to Epid Week 16.

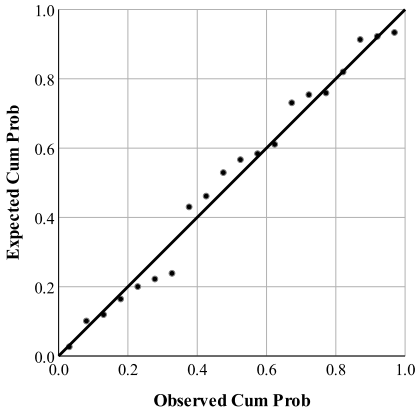

Fig. 12. Normal probability plot of the comparison for Epid Week 17 to Epid Week 36.

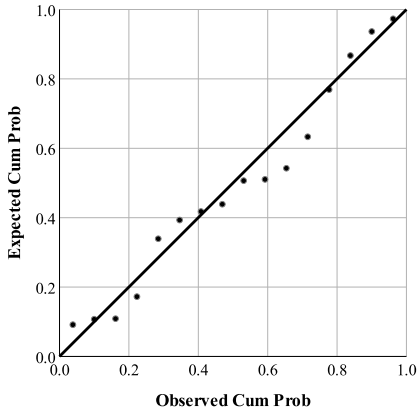

Fig. 13. Normal probability plot of the comparison for Epid Week 37 to Epid Week 52.

3.4. Sensitivity analyses

In this section, the results of the sensitivity analyses are presented to investigate the effects of the parameters on leptospirosis transmission. Univariate sensitivity analysis is one of the techniques that can analyse the outcomes of simulation concerning a parameter at one time [19]. Through univariate sensitivity analysis, the outcomes indicate 7.1 is the best value for vector birth rate, μ_2. The best outcome for the transmission rate from susceptible to infected vectors, θ_2 is 0.35 and the movement ranges of the vectors, η are 22 m, 19 m and 16 m for the three outbreaks respectively. However, the univariate sensitivity analysis does not apply to the vector active period durations, α_d as the parameter can show the influence sufficiently by ± 1 hour or ± 2 hours.

Figures 14–21 show the effects of four parameters, μ_2, θ_2, α_d and η on infected humans and infected vectors. The results show that a higher vector birth rate, μ_2 and higher transmission rate from susceptible to infected vectors, θ_2 would result in more humans and vectors being infected. As for the vector active period durations, α_d, there are no clear influences on both subgroups (see Figs. 18 and 19). In terms of vector movement range, η, the bigger range could cause more numbers of infected humans and infected vectors (see Figs. 20 and 21).

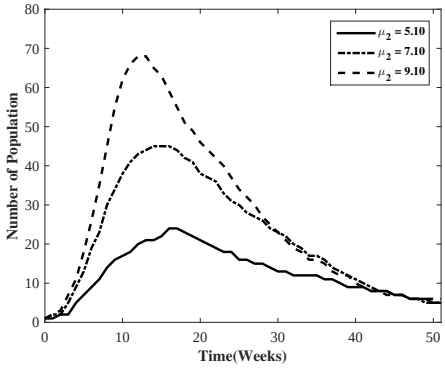

Fig. 14. Effects of various vector birth rates, μ_2 on infected humans.

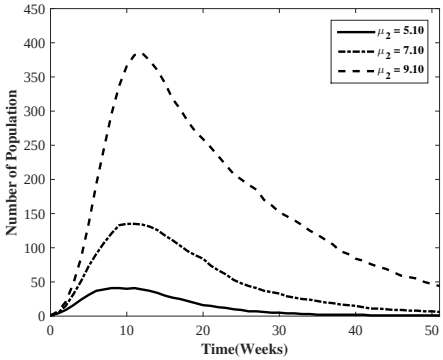

Fig. 15. Effects of various vector birth rates, μ_2 on infected vectors.

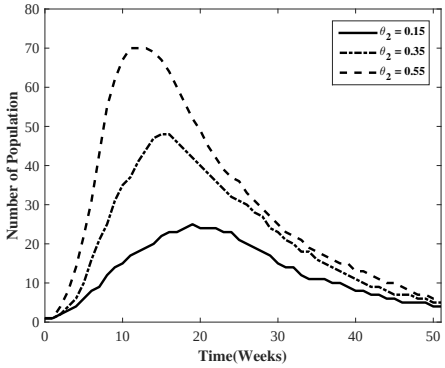

Fig. 16. Effects of various transmission rates from susceptible to infected vectors, θ_2 on infected humans.

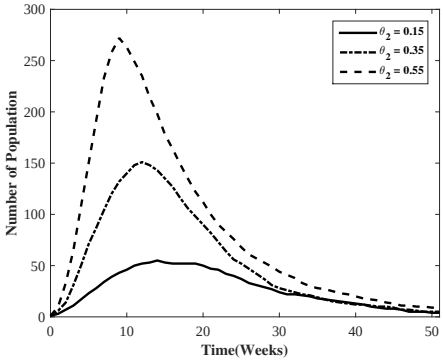

Fig. 17. Effects of various transmission rates from susceptible to infected vectors, θ_2 on infected vectors.

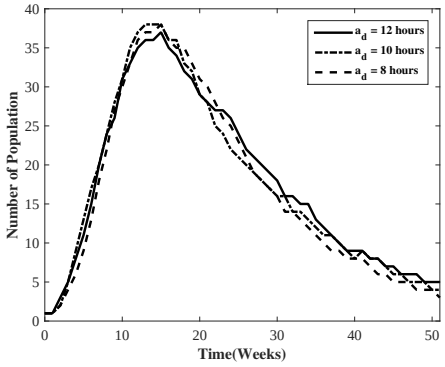

Fig. 18. Effects of various vector active period durations, α_d on infected humans.

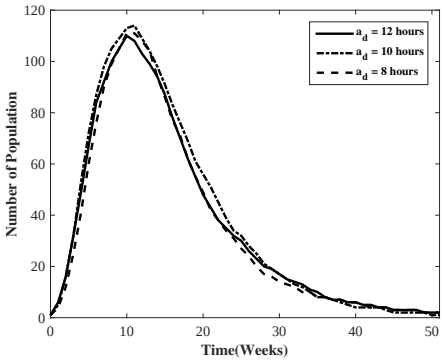

Fig. 19. Effects of various vector active period durations, α_d on infected vectors.

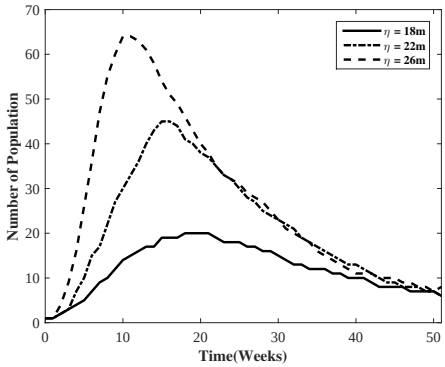

Fig. 20. Effects of various vector movement ranges, η on infected humans.

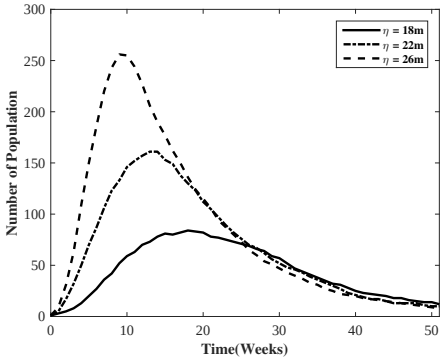

Fig. 21. Effects of various vector movement ranges, η on infected vectors.

4. Conclusions

In this paper, we have proposed an IBM for leptospirosis spread. The results of regression analysis and normal probability plots reflect that the proposed IBM is an adequate model when compared with the actual prevalence data. Based on the analysis, a higher vector birth rate and higher transmission rate from susceptible to infected vectors can influence the disease transmission among human and vector populations. From the perspective of behaviours of vectors (rodents), the active period durations do not show any influence on leptospirosis transmission. This means the disease can spread anywhere where the rodents are actively wandering around the places regardless of the duration of the active period. However, the bigger movement range of vectors can cause more people and vectors to be infected. Based on the comparison made between the model simulation and the actual prevalence data suggest that the vector (rodents) movement range in Sarawak is between 16 m to 22 m. This information is significant for the public health authorities and institutions to control the spread of leptospirosis.

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Вплив поведінки гризунів на поширення лептоспірозу: індивідуальний підхід до моделювання

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Лептоспіроз — зоонозне захворювання, поширене в тропічних і субтропічних регіонах. Це інфекційне захворювання є ендемічним у Сараваку, Малайзія. Останніми роками загроза лептоспірозу в Сараваку зростає з 2010 року. Традиційні компартментальні моделі припускають, що популяція є однорідною та має однакові характеристики та поведінку. Проте кожна особина в популяції має різну та унікальну поведінку в реальному світі. Тому ця стаття має на меті змоделювати поширення лептоспірозу шляхом застосування індивідуального підходу до моделювання для усунення гетерогенності, яка впливає на передачу захворювання. Поведінка гризунів, така як тривалість активного періоду та діапазон руху, включена в модель. Результати аналізу чутливості показують, що діапазон руху гризунів має значний вплив на поширення хвороби порівняно з тривалістю активного періоду. Порівняння між результатами моделювання та фактичними даними поширеності в Сараваку виконується для перевірки моделі. Завдяки регресійному аналізу кореляція визначення для трьох спалахів у Сараваку за 2017 рік становить понад 90%. Крім того, графіки нормальної ймовірності для трьох спалахів вказують на те, що точки добре лягають на лінію та розподіляються нормально. Це показує, що запропонована індивідуальна модель може передбачити передачу лептоспірозу.

Ключові слова: *лептоспіроз, індивідуальний підхід, поведінка гризунів, тривалість активного періоду, ареал руху.*