Research Article

Role of Tourists on Emerging of Dengue Epidemic: Model Approach

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Abstract
International travel is known as a factor that can contribute the increasing trend of dengue. It is still questioned on under what condition those travelers are able to underpin or diminish the transmission. In this study, we attempt to answer this question with the help of a mathematical model. The basic reproduction number is derived. An analysis showed that the tourists can contribute in epidemic only if the local transmission is closed to the threshold. We apply the analysis to dengue epidemic in Phuket, 2013 and showed that the tourists cannot contribute the emerging of dengue outbreak in that year.

Keywords: Dengue, Mathematical model, Basic reproduction number, Tourists

1 Introduction

Dengue fever (DF) is a mosquito-borne viral disease caused by any one of the four closely related but distinct serotypes of the dengue virus [1]. A life threatening illness called dengue hemorrhagic fever (DHF) and Dengue shock syndrome (DSS) can cause the case-fatality from <1% to 44% among hospitalized patients [2]. Although several vaccine candidates (e.g. tetravalent CYD-TDV vaccine of Sanofi Pasteur) are in the stage of clinical trials, yet no licensed dengue vaccine is available [3]. The most accepted control measure is only vector control.

International travel is known as a factor that can contribute the increasing trend of dengue, especially among the endemic area. Of particular concerns is the introduction of dengue virus by returning of travelers to the non-endemic area. In term of traveler healthcare, it should be awareness of the risk level when traveling to the endemic area. The risk factor for travelers is indicated to the length of stay.

Thailand is an endemic area of dengue where many parts are popular tourist destination. Depending on the purpose of travel, travelers may have different periods of stay in a specific location. Recently, there is a report of dengue epidemic among travelers at Koh Lanta, Krabi Province, Thailand [4]. All 55 dengue cases reported during January–May, 2012 are foreign tourists. Since the data is extracted from reviewed medical records in the hospitals where the travelers sought medical care in nearby area, the length of stay of such infected tourists becomes obscure. It may be inferred that the travel purpose of those infected tourists is recreational. For the different purpose, retrospective study shown that 19.4% of 670 German aid workers with an average overseas time of 37.7 month were detected as dengue infection after return from Thailand [5]. In general, the data on the incidence of dengue fever among travelers is rare, especially, the proportion of subclinical infections which is difficult to detect even for the people in local area.

Mathematical model is an advance method that can be used for quantifying the infection risk to travelers. The previous study [6] used a standard SIR compartmental model to predict the critical length

of stay of travelers going to dengue endemic area. Their analysis was based on the long terms of stay. However, it is still not known whether those travelers underpin the transmission under the short stay and what happens if they leave the region by the time of infectiousness.

In this study, we use a mathematical model to examine the role of tourists in terms of the length of stay together with the current number in the area on the emerging of dengue epidemic. As theoretical purpose, we aim to determine the necessary condition for which the epidemic threshold arises. This threshold will be derived through the basic reproduction number, the average secondary infection caused by an index case that introduced into the whole susceptible population. In similar analysis, the quantity is widely used in many works [7]–[9]. In addition, the results will be applied for tourists in Phuket province, the place where the dengue outbreak occurs in 2013.

2 Mathematical Model

The transmission cycle of dengue consists of a susceptible human being bit by an infected mosquito (A. aegypti or/and A. albopictus). Once in the blood, the virus undergoes an incubation period of between 3 to 14 days before the person becomes infectious (the period is called extrinsic incubation period) and enters into an acute febrile phase. Here, it is assumed that there is no differentiation in virus serotypes. So, the cross-protection is not included into the model. After the illness passes (after 2 to 10 days), the sick person gains permanent immunity to further infection. When an uninfected mosquito bites an infectious human, the virus is passed to the mosquito. The virus must again go through an incubation period before the mosquito becomes an infectious one, which is called intrinsic incubation period.

We apply the standard compartmental epidemic model for dengue transmission. The model consists of transmission in human and in vector population. In addition, the human population is separated into two groups such as local people subscripted by L and tourists subscripted by T. Since we are focusing on short term dynamic the total human population is assumed to be constant. Here, birth and death are not included in the model. The change in number of tourists staying in focused area is described by

$$\frac{dN_T}{dt} = B - cN_T \qquad (1)$$

where B and c are the rate at which the tourist move in and move out, respectively. The standard SEIR compartmental model is applied for dengue transmission in human population. The system of differential equations of full model is expressed in Appendix. We noted that the exposed class for tourists cannot transmit the virus but may affect the dynamics due to the temporal stay.

The transmission model for vector population is SEI model where the mosquitoes in class E are infected and being in the period of extrinsic incubation (see Appendix). The total number of mosquitoes in equilibrium is the recruitment rate times the average life expectancy and we assume that the mosquito infects for lifelong. A set of essential parameters are summarized in Table 1.

Table 1: Summary of model parameters

Parameter	Definition	Estimated Value	Reference
β	Transmission coefficients from vector to human	0.1-0.3	[10]
β_V	Transmission coefficients from human to vector	0.1-0.3	[10]
μ_V	Mosquitoes death rate	0.07	[11]
A	Recruitment rate of mosquitoes	See Text	-
σ^{-1}	Average extrinsic incubation period	4	[12]
γ^{-1}	Average infectious period	7	[13]
α^{-1}	Average intrinsic incubation period	4	[13]

3 Analysis

3.1 *The basic reproduction number*

The basic reproduction number, denoted by R_0 is a threshold quantity fundamentally relevant in the emerging of a disease in a whole susceptible area. For the model that includes more than one type of host, the contact process is heterogeneity. In this case, R_0 can be derived by using the next generation method [14]. For the present model, we have

$$R_0 = \sqrt{\left(\frac{A\beta_V\beta\sigma}{\mu_V^2 N\gamma(\mu_V+\sigma)}\right)\left(\frac{N_L}{N}+\frac{N_T\alpha\gamma}{N(c+\alpha)(c+\gamma)}\right)}. \quad (2)$$

In the absence of tourists the quantity reduces to the form that has been derived for closed population [15]. The second factor in the square root reflects the influence of tourists on this parameter. It is described by means of the proportion of tourists in local area and the average time spent by an individual in the infected state (both exposed and infectious) during the period of stay. In our model, there is no distinguish in disease progression between tourists and local people, so the latter factor clearly depends on the rate of moving out c.

It should be remarked that the number of tourists in disease-free state is B/c. Variation of parameter c implies tuning both the number of tourists and the average duration of stay. In fact, these two factors may not be directly reciprocal. As possible extension, the number of tourists may be driven by economic factor or by season rather than constant. For our model, however, the average time spent by visitor is assumed to be exponentially distributed and, the number of tourists could be altered also by changing the rate of arrivals. To concentrate on the role of tourists that can either contribute or diminish the epidemic, the variation on this factor should not be affect the number of tourists in consideration. Thus, we assume that $N_T = \theta N_L$ where $0 < \theta < 1$ is the fraction of tourists per local people that can be known from data. The fraction is assumed to be independent of the period of stay. As a result, Equation (2) can be rewritten as

$$R_0 = \frac{R_{in}}{1+\theta}\sqrt{1+\frac{\theta\alpha\gamma}{(c+\alpha)(c+\gamma)}}, \quad (3)$$

where

$$R_{in} = \sqrt{\frac{A\beta_V\beta\sigma}{\mu_V^2 N_L\gamma(\mu_V+\sigma)}}$$

is defined as an intrinsic reproduction number, the basic reproduction number in the absence of tourists.

3.2 *Threshold of epidemic induced by tourists*

The threshold condition arises in such a way that if $R_0 < 1$, then the disease will die out otherwise, there is a

chance of epidemic. We are now interested in whether or not the threshold can be achieved by the parameter c which is an inverse of the length of stay and, to see on what condition.

We first observe that for any value of parameter c and for $0 < \theta < 1$, the value of R_0 lies in an interval

$$\left[\frac{R_{in}}{\sqrt{1+\theta}}, \frac{R_{in}}{1+\theta}\right).$$

Thus, if $R_{in} < 1$, then $R_0 < 1$. This is clear that under the low transmission potential inside the area, the disease could not be spread by introducing from outside. Beyond that trivial situation, we restrict ourselves to the case $R_{in} > 1$. It is easy to see that the necessary and sufficient condition for which the threshold induced by tourists arises is given by

$$R_{in} < \theta+1 < R_{in}^2. \quad (4)$$

Specifically, there exists a critical value $c* \in (0, \infty)$ such that the epidemic occurs if $c < c*$ and the epidemic dies out if $c > c*$ for $c \in (0, \infty)$. As a consequence, the associated critical length of stay can be determined so that there is a risk of infection as the period of stay is longer than the critical value.

From the theoretical point of view, one can also determine the critical number of tourists, i.e., $\theta* \in (R_{in} - 1, R_{in}^2 - 1)$ staying in the local epidemic area given the average length of stay. In this case, the epidemic occurs if $\theta < \theta*$ and dies out otherwise. As opposed to the case of length of stay, increasing the faction of tourists means increasing the susceptibility and hence infectivity, meanwhile the basic reproduction number is discounted by decreasing the ratio between number of mosquitoes and human. For our case, R_0 is reduced by increasing of θ which is in fact, can be vary in a small range. In summary, the threshold line can be drawn from the set of point $(c*, \theta*)$ which separates the case $R_0 < 1$ and $R_0 > 1$ in the parametric plan (see Figure 1).

4 Numerical Simulation

In this section, we apply the model and our analysis to examine the role of tourists on dengue transmission in Phuket province. The island is one of the most popular tourist's attractions located in the Southern
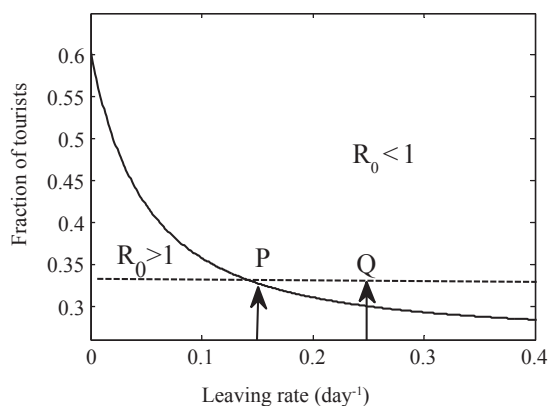
Figure 1: The epidemic threshold induced by the fraction of tourists and the leaving rate parameter. Solid line shows the set of critical points ($c*$, $\theta*$) separating the region for which epidemic occurs (below) and dies out (above). By fixing the fraction of tourists at 33.8%, the critical point P is calculated for leaving rate at 0.13 per day, whereas the leaving rate at point Q is given by 0.25.

part of Thailand. According to the Provincial statistical report [16], the number of tourists has been increasing in recent years.

Phuket is an endemic area for DF and DHF. We focus on the statistical data for year 2013 since the dengue incidence is remarkable [17]. The population size is 369,522. The number of tourists (only tourist foreigners) is 11,339,885 with the average length of stay at 4.02 days. Using these data we can estimate the proportion of tourists per local people at 33.8%. For epidemiological data, the number of cases report is 2,263 and the incidence per 100,000 is 639.54. However, the data of cases report for tourists is not available. We then use the parameters values in Table 1 to simulate the tourist incidence. Throughout, we will set the number of female adult mosquitoes to be equal to the number of local population in Phuket.

We will first restrict to the condition that the critical length of stay for tourists exists based on the above data. From the condition (4), the bound of intrinsic reproduction number is 1.338. So, this is somewhat restrictive for searching of parameters. Nevertheless, by using the parameter values in Table 1, and choosing $\beta = \beta_V = 0.145$, we obtain $R_{in} = 1.266$. Thus, we can calculate the critical value of leaving rate as $c* = 0.13$, which is equivalent to the average length of stay about

7.7 days. From this prediction, if a tourist spends longer than 8 days in the risk area, there will be a chance to contact with dengue. However, the chance seems to be very small since the value of R_0 in that case will be close to the threshold. For example, for the length of stay at 10 days, we have $R_0 = 1.011$.

From our theory, if $c > c* = 0.13$, the epidemic will not occur. But, from the real data in 2013, we can estimate that $c = 0.248$ (see Figure 1). This discrepancy indicates that the epidemic in Phuket is indeed dominated by the intrinsic process and the contribution of tourists becomes irrelevant. More precisely, the transmission potential should transcend the bound 1.338 so that the condition (4) is failed.

To do this, we choose $\beta = 0.2$ and $\beta_V = 0.2$, and set the average length of stay to be 4.02 days. We thus have $R_{in} = 1.75$ and $R_0 = 1.34$.

The simulation results are shown in Figure 2(a). Notice that the weekly incidence and cumulative incidence of dengue are rescaled by 10%. This is because we assume 90% of dengue infections are the inapparent cases those were not been clinically diagnosed. The new cases among tourists shown have the highest about 37 cases while the peak for local incidence is about 61 cases. The curve just slightly follows the curve of local incidence since we assume that all arrival visitors are susceptible. As opposed to local people, we speculate that there is about 20% of population that have prior immunity. Since the infection by one serotype produces lifelong immunity to that serotype. While our model considers only one infection, the interaction between serotypes such as the antibody enhancement and the effects of cross-protection will not be included. Thus, all individuals who have the prior immunity are passed into the recovery class. The cumulative incidences present all individuals who have been infected with dengue through the courses of epidemic [see Figure 2(b)]. The total number of cases for local people is about 2,434 cases, while the total number of cases for tourists is about 1,520, which is about 62.45%, and is 12.17% of total number of tourists.

5 Discussion

The model in this study is modified from the previous study [6] by adding the exposed class, since the short stay of tourists is presumed to alter the possibility
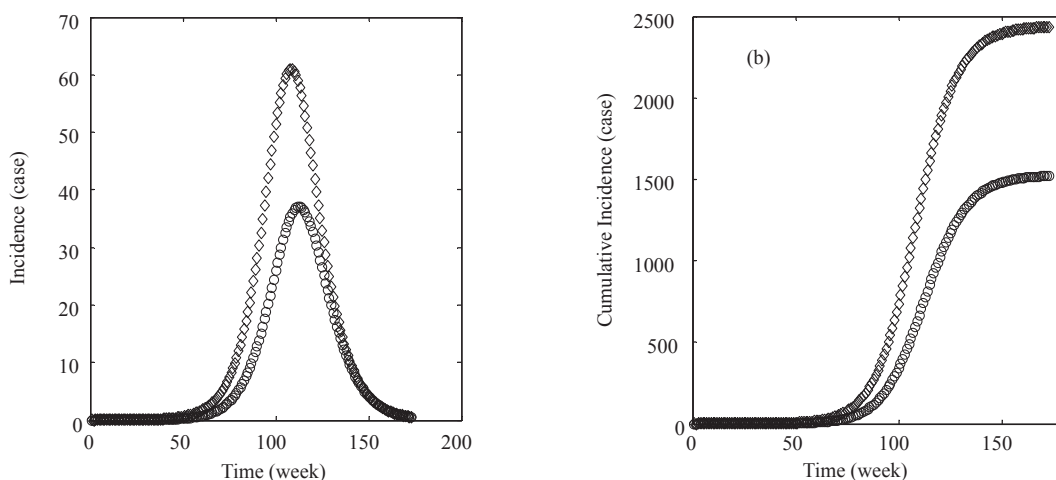
Figure 2: Simulated dengue epidemic in Phuket, 2013. (a) weekly dengue incidences and (b) cumulative incidence. Diamonds represent local people and circles represent tourists. The average length of stay is 4.02 days and the basic reproduction number is 1.34. The results are rescaled by 10%.

of epidemic. The closed form of basic reproduction number is derived. It is a decreasing function of the fraction of tourists per local and the leaving rate.

We showed in principle that the tourists group may contribute the epidemic if the intrinsic reproduction number is closed to the threshold. Although this condition depends also on the fraction of tourists, its variation may not significantly alter the conclusion since the fraction is usually small. It can be seen that if the condition (4) is satisfied, then the value of R_0 is too restrictive (close to one) since the small fraction of tourist is predominated. The exception for this is only that the fraction of tourists is high which may be unrealistic. Nevertheless, the result of putting higher fraction of tourist is vividly the same. In that case, it may not be clear if the epidemic can occur since the value of R_0 is still close to one. However, we show theoretically that the epidemic is possible just in average sense and eventually dies out quickly. On the other hand, if the condition (4) is unsatisfied, then the intrinsic reproduction number becomes the dominating factor to determine the bursting out of the disease. In this case, the role of tourists becomes meaningless.

We apply our theory to dengue epidemic in Phuket focusing on year 2013. The data shows that Phuket is very attractive destination for tourist foreigners since the number was estimated about one third of the local population. Yet, we showed by contradiction that the tourists cannot be contributed in the emerging of

dengue outbreak in that year. Based on the available data, we predicted that the critical length of stay is 8 days. Beyond this period, tourists may have a small risk of exposure to dengue. It is remarkable that the predicted critical period is concurrent with the average time spent in the disease stage. So, if the tourist leaves the area before that then he has a few chances to transmit the virus to mosquitoes. For the actual period that is four days, it is speculated that the infected tourist leaves the area before he becomes infectious as well. Therefore, the actual transmission potential must be higher than the prediction in the first scenario. In our theory, if this is the case, then there is no epidemic threshold induced by tourists at all.

The numerical simulation for dengue epidemic in Phuket is based on the data in 2013 and re-selected value of intrinsic reproduction number. Comparison shows that the predicted cumulative incidence is overestimated (~90% higher than the case report). The reason behind this may be the discounting the subclinical infections and some fractions of prior immunity. While clinically diagnosed cases of DF or DHF are regularly reported to the Provincial Health Offices, the actual number of infected individuals remains unknown [18]. If this is the case, the predicted total cases should be reduced by 10% of the present results. The model predicts that there is about 12% of tourists may be infected with dengue in which the cases report is not available.

There are a number of possible extensions motivated by this study. In terms of model, one can take into account the seasonal effects on the mosquito population and also the rate of arrival of tourists. The first one has been extensively studied [19] whereas the latter is still not known. These further outlooks, in addition to be more realistic in modeling, could increase the potential to fit the model with the observed data.

Appendix

The differential equations for dengue transmission model in human are given by

$$\frac{dS_L}{dt} = -\frac{\beta}{N} S_L I_v \qquad \frac{dS_T}{dt} = B - \frac{\beta}{N} S_T I_v - cS_T$$

$$\frac{dE_L}{dt} = \frac{\beta}{N} S_L I_v - \alpha E_L \qquad \frac{dE_T}{dt} = \frac{\beta}{N} S_T I_v - (\alpha + c)E_T$$

$$\frac{dI_L}{dt} = \alpha E_L - \gamma I_L \qquad \frac{dI_T}{dt} = \alpha E_T - (\gamma + c)I_T$$

with $S_L + E_L + I_L + R_L = N_L$, $S_T + E_T + I_T + R_T = N_T$. The differential equations for mosquitoes are

$$\frac{dS_v}{dt} = A - \frac{\beta}{N} S_v (I_L + I_T) - \mu_v S_v$$

$$\frac{dE_v}{dt} = \frac{\beta_v}{N} S_v (I_L + I_T) - (\sigma + \mu_v)E_v$$

$$\frac{dI_v}{dt} = \sigma E_v - \mu_v I_v$$

where $S_v + E_v + I_v = N_v = \dfrac{A}{\mu_v}$.

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