ssue 1 [1551N 2475-2258]

Publication Date : 30 October, 2015

Near Endemic Coexistence in a Model of Dengue and Chikungunya

[Bilvy Fadhlil Khaliq, Edwin Setiawan Nugraha, Nuning Nuraini, Janson Naiborhu, Edy Soewono]

Chikungunya and dengue are re-emerging diseases which are transmitted by Aedes spp. mosquitoes. Although originated from a different location, as the human mobility increases a concurrent outbreak may happen in other places. A mathematical model of chikungunya and dengue transmission with a control is constructed in the framework of SEIR-SEI model. The model is expressed in the form of a 13-dimensional system of ordinary differential equations to describe the dynamics of compartments within human and mosquito populations. We find three equilibrium points and discuss its stability. By using the next generation matrix, we obtain two thresholds represent the basic reproduction number that related to chikungunya and dengue. We show that although there is no coexistence equilibrium, the two diseases could coexist for a relatively long period of time. In terms of control, we investigate the effect of fumigation treatment as a constant parameter in the model. Our analysis and simulation results show that with a proper selection of treatment we can reduce the intensity of transmission of both diseases

Keywords—Chikungunya, Dengue, Endemic Equilibrium, Basic Reproduction Number

I. Introduction

Until now, dengue fever is still a serious vector-born disease that become threat for global public health. From year to year the number of infection cases grow rapidly. Currently more than 3.5 billion people are living in tropical and subtropical region that high risk to the disease. It is estimated that annually 50 to 200 million people get infected, 500 thousand are in severe situation and then 20 thousand died related the disease [1].

Dengue fever is caused by virus DEN-V and usually transmitted by mosquito of *Aedes Aegypti* as primary vector and *Aedes Albopictus* as secondary vector [23]. This virus is the *Flaviviridae* family and genus *Flavivirus* that has four serotype such as DEN-1, DEN-2, DEN-3, and DEN-4. A person infected by one of them will have long term immunity to this serotype but will loss immunity to another serotype after recovering around 12 weeks [2]. Secondary infection is potential to cause Dengue Hemorrhagic Fever (DHF) [3].

One other similar disease which is caused by virus and spread by the same mosquitoes is chikungunya. Nowadays, it is also become serious problem for global public health. The outbreak of chikungunya disease has been hit several countries in Africa, Asia, around Indian Ocean and Europe [9, 10]. Although rarely causing death, many patients who are recovering still experienced pain joints for weeks even years [11] that reduced productivity and disturb activity of their lives so that it is become problem in social and economic. Chikungunya is caused by virus CHIK-V that transmitted to human via bites of infected mosquito. This virus is family of *Togaviridae* and genus of Alphavirus. The vectors are *Aedes Aegypti* and *Aedes Albopictus* [23, 25]. The vectors of this virus is the same with vectors of DEN-V virus. Therefore both mosquitoes are responsible for chikungunya and dengue fever.

In recent years there were several cases that chikungunya and dengue has simultaneously occurred in the same location and at the same times. Some researchers have reported such incidents in India [4, 5, 6], in Gabon [7], and in Yamen [8].

The problem of dengue fever has attracted attention of mathematicians. Since 1990s, research activities in modelling of dengue fever is increasing. Many papers in literature about model of dengue fever from simple model to more complex model that include factors such as control, mobility population, immigration, age structure, climate change [12, 13, 14, 15, 16, 17, 18, 22] and so on, while modelling of chikungunya is only several papers founded in literature [19, 20, 21].

In this paper we propose and develop a model of chikungunya and dengue that describe dynamics within human and mosquito populations. The model is expressed in the form of system of ordinary differential equations. We will explore the model to study the case where chikungunya and dengue fever coexist at the same time and in the location. The paper is organized as follows. Second section formulation model, third section is analysis model, fourth section is numerical simulation and the last section is discussion.

п. Model Formulation

Model Description

The model consists two populations, human as host and mosquito as vector, respectively. Each population is identified into two parts which is infected by dengue or chikungunya. The human populations is divided into four compartments such as susceptible, exposed, infectious, and recovery. Especially, we add a chronic state to the chikungunya compartment in order to check its effect to the dynamic. The mosquito population is divided into three compartments i.e. susceptible, exposed, and infectious.

Susceptible human will be infected after bitten by an infectious mosquito. The virus will enter incubation period and the human will be in exposed state. After this period, then the human enter infectious state where the symptoms of the



Publication Date : 30 October, 2015

disease appear and is capable to infect mosquito. Then the human moves to the recovered state. Especially, for the case of chikungunya, after recovered from infectious state, humans will enter to chronic state where the human undergoes a long pain persist due to infection. The susceptible mosquitoes will be infected after biting an infectious human. Then the mosquito will enter to the exposed state and after incubation period of the virus, the mosquito will be in infectious compartment for the rest if their life. All processes of flow between state is shown in Figure 1

Our model will be restricted by the following assumptions

- 1. There is no human or mosquito that is infected with two different viruses in the same time.
- 2. We assume there only one type of mosquito as a vector ad each disease has only one serotype.
- 3. A total cross-immunity, therefore either host or vector is infected by one of viruses, then they will be immune to both viruses.
- 4. There is no death of population caused by disease, except natural death.
- 5. Recruitment of each populations enters susceptible compartment.
- 6. Each populations is perfectly mixed so interaction between host and vector occurs randomly.
- 7. We assume that population is in relatively stable condition, so the total population remains constant.

The model is expressed in the following 13-dimensional system of differential equations

$$\frac{dS_{h}}{dt} = A_{h} - \frac{bp_{hc}Inc_{v}S_{h}}{N_{h}} - \frac{bp_{hd}Ind_{v}S_{h}}{N_{h}} - \mu_{h}S_{h}$$

$$\frac{dEc_{h}}{dt} = \frac{bp_{hc}Inc_{v}S_{h}}{N_{h}} - \alpha_{c}Ec_{h} - \mu_{h}Ec_{h}$$

$$\frac{dInc_{h}}{dt} = \alpha_{c}Ec_{h} - \beta_{c}Inc_{h} - \mu_{h}Inc_{h}$$

$$\frac{dCc_{h}}{dt} = \beta_{c}Inc_{h} - \gamma_{c}Cc_{h} - \mu_{h}Cc_{h}$$

$$\frac{dRc_{h}}{dt} = \gamma_{c}Cc_{h} - \mu_{h}Rc_{h}$$

$$\frac{dInd_{h}}{dt} = \alpha_{d}Ed_{h} - \beta_{d}Ind_{h} - \mu_{h}Ed_{h}$$

$$\frac{dInd_{h}}{dt} = \alpha_{d}Ed_{h} - \beta_{d}Ind_{h} - \mu_{h}Ind_{h}$$

$$\frac{dRd_{h}}{dt} = \beta_{d}Ind_{h} - \mu_{h}Rd_{h}$$

$$\frac{dS_{v}}{dt} = A_{v} - \frac{bp_{vc}Inc_{h}S_{v}}{N_{h}} - \frac{bp_{vd}Ind_{h}S_{v}}{N_{h}} - (\mu_{v} + \delta)S_{v}$$

$$\frac{dEc_v}{dt} = \frac{bp_{vc}Inc_h S_v}{N_h} - \theta_c Ec_v - (\mu_v + \delta)Ec_v$$

$$\frac{dInc_v}{dt} = \theta_c Ec_v - (\mu_v + \delta)Inc_v$$

$$\frac{dEd_v}{dt} = \frac{bp_{vd}Ind_h S_v}{N_h} - \theta_d Ed_v - (\mu_v + \delta)Ed_v$$

$$\frac{dInd_v}{dt} = \theta_d Ed_v - (\mu_v + \delta)Ind_v$$

with total of population

$$S_h + Ec_h + Inc_h + Cc_h + Rc_h + Ed_h + Ind_h + Rd_h = N_h$$

 $S_v + Ec_v + Inc_v + Ed_v + Ind_v = N_v.$

The model is biologically and mathematically well posed in the domain

$$\begin{aligned} \Omega &= \{ \left(S_h, Ed_h, Ind_h, Rd_h, Ec_h, Inc_h, Cc_h, Rc_h, S_v, Ed_v, Ind_v, Ec_v, Inc_v \right) \in \Box_+^{13} \mid \\ S_h &+ Ec_h + Inc_h + Cc_h + Rc_h + Ed_h + Ind_h + Rd_h = N_{h_v}, \\ S_v &+ Ec_v + Inc_v + Ed_v + Ind_v = N_v \}, \end{aligned}$$

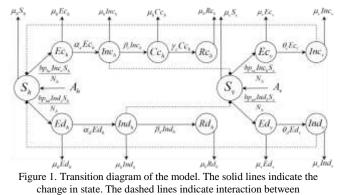
which is a positively invariant for system (2.1). The description of state variables are presented in Table 1 and description of parameters in Table 2.

The rate of average infection from mosquito to human is product of average of mosquito bites, probability of infectious mosquito bit susceptible human and probability of success transmission for every single bite. Meanwhile, the rate of average infection from human to mosquito product of average of mosquito bites, probability of susceptible mosquito bit infectious human and probability of success transmission for every single bite.

In this paper, we also involve the model with a simple fumigation control. The aim of the control is to increase the death rate of mosquitoes. The control parameters is denoted by δ .

Stability Analysis of Equilibria

From our model, we get three equilibrium points, which is belong to boundary of Ω :



populations.



Publication Date : 30 October, 2015

State variables of model		
S_h	Number of susceptible humans	
$Ed_h(Ec_h)$	Number of exposed humans with dengue (or chikungunya)	
$Ind_h(Inc_h)$	Number of infectious humans with dengue virus (or chikungunya)	
$Rd_h(Rc_h)$	Number of fully recovered humans from dengue virus (or chikungunya)	
Cc_h	Number of chronic humans after recovered from chikungunya virus	
S _v	Number of susceptible mosquitoes	
$Ed_{v}(Ec_{v})$	Number of exposed mosquitoes with dengue virus (or chikungunya)	
$Ind_{v}(Inc_{v})$	Number of infectious mosquitoes with dengue virus (or chikungunya)	
N_h	Total human population size	
N _v	Total mosquito population size	

$$\begin{split} X_{dfe} &= \left(N_h, 0, 0, 0, 0, 0, 0, 0, N_v, 0, 0, 0, 0\right), \\ X_{dee} &= \left(S_h^*, Ed_h^*, Ind_h^*, Rd_h^*, 0, 0, 0, 0, S_v^*, Ed_v^*, Ind_v^*, 0, 0\right), \\ X_{cee} &= \left(S_h^*, 0, 0, 0, Ec_h^*, Inc_h^*, Cc_h^*, Rc_h^*, S_v^*, 0, 0, Ec_v^*, Inc_v^*\right). \end{split}$$

Thus, X_{dfe} is disease-free equilibrium where there are no viruses inside both human and mosquito populations. X_{dee} and X_{cee} are endemic equilibriums for dengue and chikungunya, respectively, where only one of them can exist.

In order to analyze the stability of equilibrium points, we introduce two basic reproduction numbers:

$$R_{0}^{c} = \sqrt[4]{\frac{\theta_{c}b^{2}p_{vc}A_{v}\mu_{h}\alpha_{c}p_{hc}}{(\mu_{v}+\theta_{c})\mu_{v}^{2}A_{h}(\beta_{c}+\mu_{h})(\alpha_{c}+\mu_{h})}},$$

$$R_{0}^{d} = \sqrt[4]{\frac{\theta_{d}b^{2}p_{vd}A_{v}\mu_{h}\alpha_{d}p_{hd}}{(\mu_{v}+\theta_{d})\mu_{v}^{2}A_{h}(\beta_{d}+\mu_{h})(\alpha_{d}+\mu_{h})}}.$$
(2.2)

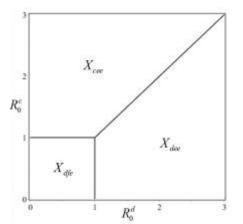


Figure 2. Bifurcation diagram of equilibrium points. Stability of equilibrium points change as both R_0 value change.

TABLE II. PARAMETERS DESCRIPTION

Parameters for model with their values for dengue (or chikungunya)		
Parameter	Meaning	
b	bites per mosquito per day	
$p_{hd}(p_{hc})$	Success probability of virus transmission from mosquito to human	
$p_{vd} (p_{vc})$	Success probability of virus transmission from human to mosquito	
$1/\mu_h$	Human life span	
$1/\mu_{v}$	Mosquito life span	
$\frac{1}{\alpha_d} \left(\frac{1}{\alpha_c} \right)$	Human latent duration	
$\frac{1}{\beta_d} \left(\frac{1}{\beta_c} \right)$	Human Infectious duration	
$\frac{1}{\gamma_c}$	Chronic period of human	
$\frac{1}{\theta_d} \left(\frac{1}{\theta_c} \right)$	Mosquito latent duration	
δ	Constant control parameter	

which are obtained by using the next generation matrix method [24] and take $\delta = 0$. The basic reproduction number which is usually denoted by R_0 , is biologically defined as the effective number of secondary infections caused by an infected individual during his entire period of infectiousness. [24]. R_0^c and R_0^d related to the basic reproduction number of chikungunya and dengue, respectively.

The general form of the equilibrium points is too complicated to be fully expressed. However we have shown that X_{dfe} always in Ω , and conditional for existence in Ω of X_{cee} and X_{dee} points are $R_0^c > 1$ and $R_0^d > 1$, respectively.

Stability of disease-free equilibrium

Stability properties of X_{dfe} can be determined from its eigen values from the following polynomial

$$P_{dfe} = \left(\lambda + \mu_h\right)^3 \left(\lambda + \mu_v\right) \left(\lambda + \gamma_c + \mu_h\right) P_c P_d$$

where P_c and P_d are fourth-ordered polynomial that has form

 $K1\lambda^4 + K2\lambda^3 + K3\lambda^2 + K4\lambda + K5$ for K1 > 0, K2 > 0, K3 > 0, K4 > 0, $K5 = K1(A_h\mu_v^2(\theta_i + \mu_v)(\beta_i + \mu_h)(\mu_h + \alpha_i) - b^2A_v\mu_h\theta_ip_{hi}p_{vi}\alpha_i)$ with i = c for P_c and i = d for P_d .

The positive real roots values of P_{dfe} may be given by polynomial of P_c and P_d . In order to get all negative real roots of P_c and P_d , according to the Routh–Hurwitz criteria, the criteria is K5 > 0 (we have shown that other criteria is



Publication Date : 30 October, 2015

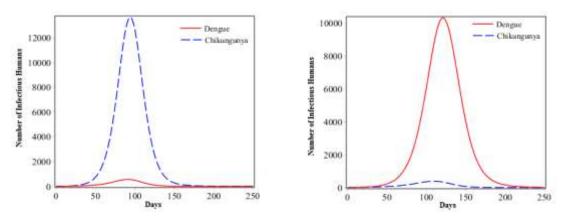


Figure 3. Dynamics of infectious human. Simulation run with initial condition $N_h = 100.000$ and $N_v = 110.000$ and the values of needed parameter is taken from [23] for different type of mosquito. Left figure shows when $R_0^c > R_0^d$ chikungunya dominates the infection while the right figure shows when $R_0^d > R_0^c$ dengue is dominant.

satisfied). With a little manipulation we get the X_{dfe} is locally asymptotically stable if and only if $R_0^c < 1$ and $R_0^d < 1$.

Stability of endemic equilibrium

The stability properties of X_{dee} dan X_{cee} are too complicated to be determined analytically. Therefore, we numerically check their stability with change in R_0 values. The stability region of these points is shown in Figure 2.

III. Numerical Results

In this paper we simulate the dynamic of both infections for several variations of parameters..

Figure 3 shows the number of infectious humans with different values of parameters It can be seen from the figure, the disease with larger value of R_0 is dominant in infecting more population than the smaller one.

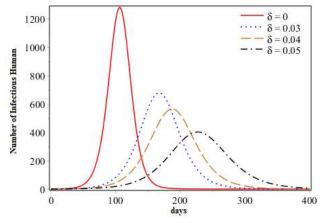


Figure 4. The intensity of infection is reduced when a constant parameter is given.

We also show the effect of fumigation control to the intensity of infection. The form of basic reproduction number with a control (i.e. $0 < \delta < 1$) is expressed as following

$$\begin{split} R_{0f}^{c} &= \sqrt[4]{\frac{\theta_{c}b^{2}p_{vc}A_{v}\mu_{h}\alpha_{c}p_{hc}}{\left(\left(\mu_{v}+\delta\right)+\theta_{c}\right)\left(\mu_{v}+\delta\right)^{2}A_{h}\left(\beta_{c}+\mu_{h}\right)\left(\alpha_{c}+\mu_{h}\right)}}\\ R_{0f}^{d} &= \sqrt[4]{\frac{\theta_{d}b^{2}p_{vd}A_{v}\mu_{h}\alpha_{d}p_{hd}}{\left(\left(\mu_{v}+\delta\right)+\theta_{d}\right)\left(\mu_{v}+\delta\right)^{2}A_{h}\left(\beta_{d}+\mu_{h}\right)\left(\alpha_{d}+\mu_{h}\right)}}. \end{split}$$

It can be seen from Figure 4 the number of infectious humans is reduced as higher values of control parameter. When properly selected, it can reduce the value of both R_0 to be less than one and eradicate both disease.

IV. Discussion and Conclusion

We have shown a mathematical model for the spread of dengue and chikungunya virus within human and mosquito population. The simulation results show the spread of a disease with larger R_0 is much faster than the smaller one. Due to the assumption of total cross-immunity, the slower disease will lose compete in infecting the susceptible population because more humans is getting immune to both disease. Simulations show that after an outbreak occurred and there is a lack of susceptible humans, the number of infections of both diseases are decreasing and tend to zero. There is also no coexistence equilibrium from the model. However, for a relatively long time period both diseases still exist in population. This situation we called near endemic coexistence of both disease. If there is another susceptible humans get into population, another outbreaks may occur.

Yet, the model in this paper is strict to the given assumptions. In the real world the spread would be more complex because more factors must be involved. This model can be elaborated by removing the total cross-immunity assumption which will having different analysis and results.



Publication Date : 30 October, 2015

We also have shown several effects of control with fumigation treatment. The control is much effective to reduce the intensity of transmission and with a proper selection can eradicate both disease.

Acknowledgment (Heading 5)

This research is funded by Hibah Unggulan DIKTI-ITB 2015.

References

- Murray, N.E Anne, M.B Quam & A. Wilder-Smith. Epidemiology of dengue: past, present, and future prospect. Clinical epidemiology, 5(2013):299.
- [2] dengue fact sheet, http://www.who.int/mediacentre/factsheet/fs1117/en, accessed in May 2, 2015
- [3] World Health Organization, Dengue Haemorrhagic Fever: Diagnosis, Treatment, Prevention and Control, Geneva, 1997.
- [4] B.S Arora, S. Chugh, B. Gupta & K.C. Agrawal. Dengue & Chikungunya Virus Fever Outbreaks In Delhi, Ig-M Serology Status-A Recent Experience. National Journal of Basic Medical Sciences, (2011):336-40
- [5] P.V. Barde, M.K Shukla, P.K. Bharti, B.K. Kori, J.K Jatav, & N. Singh. Co-circulation of dengue virus serotypes with chikungunya virus in Madhya Pradesh, central India. WHO South-East Asia Journal of Public Health ;3.1(2014): 36-40.
- [6] H. S. Chahar, P. Bharaj, L. Dar, R. Guleria, S.K. Kabra, & S. Broor. Coinfections with chikungunya virus and dengue virus in Delhi, India. Emerging infectious diseases, 15.7 (2009):1077.
- [7] E. M. Leroy, D. Nkoghe, B. Ollomo, C. Nze-Nkogue, P. Becquart, G. Grard & X. De Lamballerie. Concurrent chikungunya and dengue virus infections during simultaneous outbreaks, Gabon, 2007. Emerging infectious diseases, 15.4(2009):591.
- [8] G. Rezza, G. El-Sawaf, G. Faggioni, F. Vescio, R. Al Ameri, R.De Santis & F. Lista. Co-circulation of dengue and chikungunya viruses, Al Hudaydah, Yemen, 2012. Emerging infectious diseases, 20.8 (2014):1351.
- [9] J. E. Staples, R. F. Breiman, and A.M. Powers. "Chikungunya fever: an epidemiological review of a re-emerging infectious disease." Clinical Infectious Diseases 49.6 (2009): 942-948.
- [10] http://www.cdc.gov/chikungunya/index.html accessed on July 2, 2015.
- [11] chikungunya fact sheet, http://www.who.int/mediacentre/factsheets/fs327/en/ accessed on May 2, 2015
- [12] A.Dipo, T. Götz, and E. Soewono. "An optimal control problem arising from a dengue disease transmission model." Mathematical biosciences 242.1 (2013): 9-16.
- [13] L. Esteva and C. Vargas. "Analysis of a dengue disease transmission model." Mathematical biosciences 150.2 (1998): 131-151.
- [14] T.A McLennan-Smith and G. N. Mercer. "Complex behaviour in a dengue model with a seasonally varying vector population." Mathematical biosciences 248 (2014): 22-30.
- [15] N. Nuraini, E. Soewono, & K.A. Sidarto. Mathematical model of dengue disease transmission with severe DHF compartment. Bulletin of the Malaysian Mathematical Sciences Society, 30.2 (2007): 143-157.
- [16] H. S. Rodrigues, M.T. Monteiro, & D.F. Torres. Dynamics of dengue epidemics when using optimal control. Mathematical and Computer Modelling, 52.9 (2010):1667-1673
- [17] A.K. Supriatna, E. Soewono, & S.A Van Gils. A two-age-classes dengue transmission model. Mathematical biosciences, 216.1 (2008):114-121.
- [18] H. Tasman, A.K Supriatna, N. Nuraini, & E. Soewono. A dengue vaccination model for immigrants in a two-age-class population. International Journal of Mathematics and Mathematical Sciences, (2012)
- [19] M. Robinson, A. Conan, V. Duong, S. Ly, C. Ngan, P. Buchy, & X. Rodo. A Model for a Chikungunya Outbreak in a Rural Cambodian Setting: Implications for Disease Control in Uninfected Areas. PLoS neglected tropical diseases, 8.9(2014): e3120.

- [20] D. Ruiz-Moreno, I.S. Vargas, K.E. Olson, & L.C. Harrington. Modeling dynamic introduction of chikungunya virus in the United States. PLoS neglected tropical diseases, 6.11 (2012):e1918.
- [21] L. Yakob, & A.C. Clements. A mathematical model of Chikungunya dynamics and control: the major epidemic on Reunion Island. PloS one, 8.3 (2013):e57448.
- [22] M. Bouzid, F.J. Colón-González, T. Lung, I.R Lake, & P.R. Hunter. Climate change and the emergence of vector-borne diseases in Europe: case study of dengue fever. BMC public health, 14.1 (2014): 781.
- [23] C A.Manore, K S.Hickmann, SenXu, H J.Wearing, J M.Hyman, Comparing dengue and chikungunya emergence and endemic transmission in A.aegypti and A.albopictus, Journal of Theoretical Biology, doi:10.1016/j.jtbi.2014.04.033 0022-5193,2014
- [24] O. Diekmann, J. A. P. Heesterbeek, dan M. G. Roberts The construction of next-generation matrices for compartmental epidemic models, J. R. Soc. Interface, doi:10.1098/rsif.2009.0386, 2009
- [25] A. M. Power, and C. H. Logue. "Changing patterns of chikungunya virus: re-emergence of a zoonotic arbovirus." Journal of General Virology 88.9 (2007): 2363-2377.

About Author (s):



Bilvy Fadhlil Khaliq Students of Mathematic Institut Teknologi Bandung

