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An Optimal Integrated Vector Control for Prevention the Transmission of Dengue

Kasbawati[1], Surya Ningsih[1], Agustinus Ribal[1], Fatmawati[2]

[1]Department of Mathematics, Faculty of Mathematics and Natural Sciences, Hasanuddin University, Jl. Perintis Kemerdekaan Km. 10 Makassar 90245, Indonesia
[2]Department of Mathematics, Faculty of Science and Technology, Universitas Airlangga, Surabaya 60115, Indonesia

[2]E-mail: fatma47unair@gmail.com

Abstract. Dengue is a tropical infectious disease caused by dengue virus which is transmitted by mosquitos such as *Aedes Aegypti* and *Aedes Albopictus*. The spread of this disease could be controlled by applying some optimal strategies. In this research, we study optimal strategy in controlling the spread of dengue by taking into consideration an integrated vector control strategy. The strategy combines chemical and non-chemical vector control methods to prevent the transmission of vector-borne disease. If we assume that the control functions are constant functions then numerically we obtain a critical chemical control which leads to the non-endemic condition. When the chemical and non-chemical controls are varying in time, we obtain the analytical form of the both control functions by using Pontryagin Maximum Principle. The numerical simulations are performed using the Steepest Descent method and the results show that the peak of the non-chemical control effect occurs at the end of the observation time. Conversely, the chemical control reaches the maximum effect at the early of the observation time. It indicates that the integrated vector control strategy is a continuous prevention method that succefully ensures the system free from dengue infection.

1. Introduction

One of the most common problems in the community is the emergence of various infectious diseases that threaten people's lives. One type of infectious disease that becomes endemic in Indonesia is dengue haemorrhagic fever (DHF). Dengue haemorrhagic disease in Indonesia was first discovered in Surabaya and Jakarta in 1968 [1]. The disease then spread to various regions throughout the country, except areas that have a height of more than 1000 meters above the sea level. The spread of dengue haemorrhagic fever in Indonesia is heavily influenced by population mobility, population density, and environmental conditions such as the presence of artificial or natural containers in landfills or other waste bins [1].

The incidence of dengue has grown dramatically around the world in the last few decades. According to WHO (2017) [2] data, there are estimated to be 390 million dengue infections per year (95% between 284-528 million), of which 96 million (67-136 million) are clinically manifested (with disease severity). Another study on the prevalence of dengue fever estimated that 3.9 billion people in 128 countries were at risk of being infected with dengue virus [2].

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The phenomenon of dengue hemorrhagic fever spread is interesting to be studied through mathematical modeling approach. Mathematical modeling is one of applied field of mathematics that aims to represent and explain a physical system or problem in the real world into a mathematical expression such as dynamics of malaria [3,4], tuberculosis [5,6], and TB-HIV co-infection [7,8]. Through mathematical modeling, information about how basic mechanisms affect disease spread and control strategies can be assessed. The study of mathematical modeling of dengue hemorrhagic disease is continuously studied and developed. The models could be used to identify main factors of endemic diseases. Some researchers examined modeling of the DHF [9,10]. Some models partially applied various mathematical theories such as the application of optimal control theory [10-13]. Development of DHF vaccine was also mathematically studied to determine effect of vaccinations on human associated with complex human immune systems [14]. The study will provide theoretical results on the DHF endemic.

In this paper, a modeling study on DHF spread was also conducted to complement mathematical analysis presented by previous researchers. The model was constructed by taking into account a control strategy that was recently introduced by WHO namely Integrated Vector Management (IVM) [15]. This method promotes multi-sectoral approaches to human health. There are five key elements for the successful implementation of IVM. One of them is integrating chemical and non-chemical vector control methods to minimize the transmission of vector-borne disease such as dengue [15]. The chemical control includes space spraying using a suitable insecticide for rapid destruction of the adult vector (mosquito) population. While the non-chemical control performs an environmental management strategy that prevents the transmission of disease by changing human habitat or behavior i.e. an action needed for restriction the human-vector contact. In this study, effects of the chemical and non-chemical controls are modeled as control functions. Optimal control theory is applied on the epidemiological models to obtain the optimal strategies that can suppress the spread of the virus both in human and mosquito populations. The dynamic of mosquito larvae is also considered by taking into consideration reduction of mosquito larvae caused by cleaning activities carried out by humans.

We organize the paper as follows. In Section 2, we formulate the mathematical model by involving the integrated vector control strategy. In Section 3, analytical results are presented to study the steady state condition of the system. Optimal control study is presented in Section 4 and numerical simulation and some discussions are presented in Section 5. Conclusions are then presented in the last section.

2. Model Formulation

In this section, we present the modeling formulation of dengue hemorrhagic fever spread. The built model is in line with the model from Rodrigues et al. (2014) [13]. The model development is carried out by taking into account the integrated vector control for reducing the transmission of dengue. Here, the integrated vector control is defined as a combination of chemical and non-chemical control strategies.

Suppose the human population is divided into three compartments, namely $S_h(t)$ represents number of susceptible humans at time t, $I_h(t)$ represents number of infected humans with dengue virus at time t, and $R_h(t)$ represents number of humans recovered from dengue hemorrhagic fever at time t. The mosquito population is divided into three compartments, i.e. number of mosquitoes in the water phase including eggs, larvae, and pupae at time t $(A_m(t))$, number of susceptible mosquitoes that do not carry dengue virus at time t ($S_m(t)$), and number of dengue virus-infected mosquitoes that can spread the virus to human at time t ($I_m(t)$). In general the interactions between human populations and the mosquitoes are illustrated in the schematic diagram given in Figure 1. It is assumed that individual displacements occur only from one compartment to another. It is assumed that no migration factor exits and into the system so that the total population is constant.

Number of susceptible human (S_h) could naturally increase through birth process with the rate $\mu_h S_h$ individual/time unit. Number of susceptible human could decrease through naturally death with constant rate μ_h per time unit. It is assumed that mosquitoes could produce larvae with the constant rate

φ per time unit. Number of larvae (A_m) produced by mosquitoes is influenced by number of eggs from susceptible mosquitoes and dengue virus-infected mosquitoes. The mosquito population could naturally decrease through naturally death with constant rate μ_m per time unit. Larvae of the mosquito population will naturally decrease with constant rate of μ_A per time unit. In addition, larvae population could change into adult mosquito population with constant rate η_A per time unit. It is also assumed that the larvae population will be reduced by the direct action carried out by humans with a proportion of $\frac{A_m}{kN_h}$, so that the average number of surviving larvae is $\varphi\left(1-\frac{A_m}{kN_h}\right)$ per time unit.

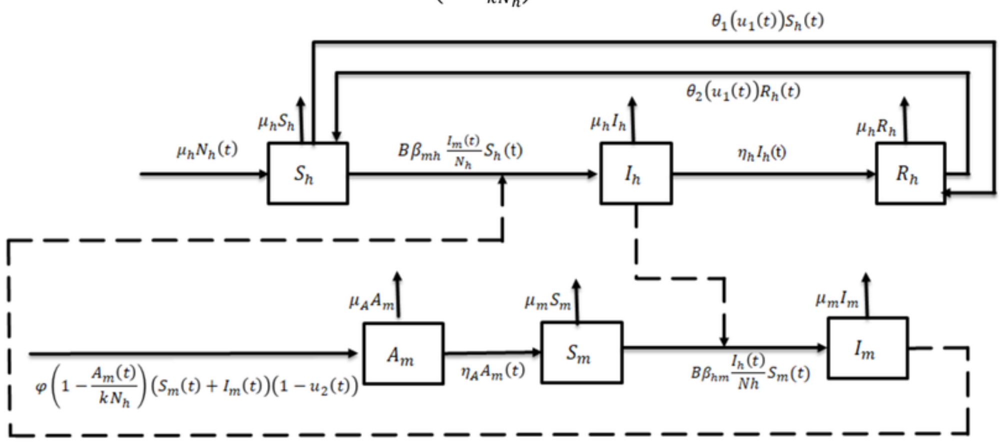

Figure 1. Schematic diagram of the interaction between human population and the mosquito on the spread of dengue hemorrhagic fever. The solid line represents interaction between humans or between mosquitoes, while the dashed lines represents interaction between mosquitoes and humans.

The transmission rate of susceptible human to infected humans is influenced by the interaction between infected mosquitoes with susceptible humans. The interaction is influenced by the probability of dengue virus transmitting from mosquito to human (β_{mh}). Similarly, the transmission rate of susceptible mosquitoes to infected mosquitoes is influenced by the interaction between susceptible mosquitoes with infected humans. The interaction is a multiplication of probability of dengue virus transmitting from human to mosquito (β_{hm}) and number of mosquito biting per time unit (B). It is assumed that the viremic amount (virus contained in the human body) decreases with the rate of $\eta_h I_h$ individual per time unit. The decrease rate resulted in the infected human population moved into recovered human population from dengue hemorrhagic fever (R_h).

Furthermore, as we have stated before that recently WHO has promoting Integrated Vector Management (IVM) as a control strategy to prevent the transmission of vector-borne disease such as dengue. Chemical control strategy is one of operational strategies at IVM applied for controlling mosquitos in adult stages. Space spray using a suitable insecticide is recommended for controlling adult vector population. Integrated with the non-chemical control strategy, interrupting human-vector contact is the other control strategy that was recommended by IVM for reducing dengue virus transmission. This includes transmission control activities especially at the public places where the transmission could be occur such as schools, hospitals and workplaces. Environmental management is the IVM's control strategy seeking to change the environment in order to prevent or minimize the human-vector contact [16]. One of the three types of environmental management recommended by WHO is by changing the human habitat or behavior such as installing mosquito screening on windows, doors and other entry points, and using mosquito nets while sleeping during daytime [16]. If we assume that the environmental management as the non-chemical control strategy is successfully applied in the system then there exists u_1 percent of susceptible individuals who will be free from the infection. This is due to the prevention

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strategy applied for reducing the contact with the vector-pathogen. Moreover, if we assume that the space spray strategy also works properly for suppressing the growth rate of the vector population then the mosquito population will decrease at $u_2 S_m$ and $u_2 I_m$ individuals per time unit. By using these assumptions, we then derive the epidemic model for dengue as follows:

$$\begin{aligned}
\frac{dS_h(t)}{dt} &= \mu_h N_h - \left(B\beta_{mh}\frac{I_m(t)}{N_h}(1-u_1(t)) + \mu_h\right)S_h(t) + \theta R_h(t),\\
\frac{dI_h(t)}{dt} &= B\beta_{mh}\frac{I_m(t)}{N_h}S_h(t)(1-u_1(t)) - (\eta_h+\mu_h)I_h(t),\\
\frac{dR_h(t)}{dt} &= \eta_h I_h(t) - (\theta+\mu_h)R_h(t),\\
\frac{dA_m(t)}{dt} &= \varphi\left(1-\frac{A_m(t)}{kN_h}\right)(S_m(t)+I_m(t)) - (\eta_A+\mu_A)A_m(t),\\
\frac{dS_m(t)}{dt} &= \eta_A A_m(t) - \left(B\beta_{hm}\frac{I_h(t)}{N_h} + \mu_m + u_2(t)\right)S_m(t),\\
\frac{dI_m(t)}{dt} &= \left(B\beta_{hm}\frac{I_h(t)}{N_h}\right)S_m(t) - (\mu_m+u_2(t))I_m(t).
\end{aligned} \tag{1}$$

Here N_h is the total human population and N_m is the total population of adult mosquitoes. We assume that the total human population in the system is constant so that $N_h = S_h + I_h + R_h$. In addition, total population of adult mosquitoes is assumed constant, i.e. $N_m = S_m + I_m$ hence it is obtained that the number of larvae in the system lies in the interval $0 \le A_m \le \left(\frac{\mu_m+u_2}{\eta_A}\right)N_m$. Initial values for each variable are assumed as follows:

$$S_h(0) = S_{h0}, I_h(0) = I_{h0}, R_h(0) = R_{h0}, A_m(0) = A_{m0}, S_m(0) = S_{m0}, I_m(0) = I_{m0},$$

where $S_{h0}, I_{h0}, R_{h0}, A_{m0}, S_{m0}, I_{m0} \ge 0$. It is assumed that all parameters in the model are positive. A description of all variables and parameters in the model (1) is given in Table 1. To simplify our model and to make our analysis interpretable, it is convenient to introduce new variables, i.e.

$$x_1 = \frac{S_h}{N_h}, x_2 = \frac{I_h}{N_h}, x_3 = \frac{R_h}{N_h}, x_4 = \frac{A_m}{N_m}, x_5 = \frac{S_m}{N_m}, x_6 = \frac{I_m}{N_m}, \tag{2}$$

which represent the proportion of population in both human and mosquito populations. If the dimensionless variables (2) are substituted into model (1) then we obtain a new model with dimensionless variables i.e.

$$\dot{\boldsymbol{x}}(t) = \begin{bmatrix}
\mu_h - \left(B\beta_{mh}\frac{N_m}{N_h}x_6(1-u_1) + \mu_h\right)x_1 + \theta x_3\\
B\beta_{mh}\frac{N_m}{N_h}x_6 x_1(1-u_1) - (\eta_h+\mu_h)x_2\\
\eta_h x_2 - (\theta+\mu_h)x_3\\
\varphi\left(1-\frac{N_m}{kN_h}x_4\right)(x_5+x_6) - (\eta_A+\mu_A)x_4\\
\eta_A x_4 - (B\beta_{hm}x_2 + \mu_m + u_2)x_5\\
B\beta_{hm}x_2 x_5 - (\mu_m+u_2)x_6
\end{bmatrix}, \tag{3}$$

where $\boldsymbol{x} = (x_1, x_2, x_3, x_4, x_5, x_6)$ and dimensionless initial values

$$x_1(0) = x_a,\ x_2(0) = x_b,\ x_3(0) = x_c,\ x_4(0) = x_d,\ x_5(0) = x_e,\ x_6(0) = x_f.$$

3. Stability of the Disease-Free Equilibrium (DFE)

In this section we study the stability of the disease-free equilibrium of the generated model. Along this analysis, we assume the control functions as a constant. By setting the right-hand sides of the equations (3) to zero, we get the DFE of the model, i.e.

$$E_0(x_1^*, x_2^*, x_3^*, x_4^*, x_5^*, x_6^*) = \left(1,0,0,\frac{(\varphi\eta_A-(\eta_A+\mu_A)(\mu_m+u_2))kN_h}{\eta_A\varphi N_m}, \frac{(\varphi\eta_A-(\eta_A+\mu_A)(\mu_m+u_2))kN_h}{(\mu_m+u_2)\varphi N_m}, 0\right).$$

Table 1. Variables and parameters of model (1).

Variable	Description	Initial Value (in millions)	References
S_h	Susceptible population	$S_h(0) = 45360$	Assumed
I_h	Infected population	$I_h(0) = 240$	Assumed
R_h	Recovered population	$R_h(0) = 240$	Assumed
A_m	Larvae of mosquito	$A_m(0) = 50$	Assumed
S_m	Susceptible mosquito	$S_m(0) = 50$	Assumed
I_m	Infected mosquito	$I_m(0) = 0$	Assumed
Parameter	**Description**	**Baseline value**	
$1/\mu_h$	average lifespan of humans (days)	$71 * 365$	[13]
N_h	Total of human population	48000	Assumed
N_m	Total of mosquito population	500000	Assumed
B	average number of bites on humans by mosquitoes, per day	0.8	[13]
β_{mh}	transmission probability from infected human (per bite)	0.35	[13]
β_{hm}	transmission probability from infected mosquito (per bite)	0.375	[13]
θ	decreasing rate of human immunity per day	0.05	Assumed
$1/\eta_h$	mean of viremic period (in days)	3	[13]
η_A	maturation rate from larvae to adult (per day)	0.08	[13]
φ	number of eggs at each deposit per capita (per day);	10	Assumed
k	number of dismissed larvae per human	6	Assumed
$1/\mu_A$	natural mortality of larvae (in day)	4	[13]
$1/\mu_m$	average lifespan of adult mosquitoes (in days)	10	[13]

The DFE exists if $\varphi\eta_A > (\eta_A + \mu_A)(\mu_m + u_2)$. The stability of the DFE E_0 can be established using the basic reproduction number of model (3). It can be determined by using the next generation operator method (see for instance [17] and [18]).

By collecting the classes of non-infected individuals, infected individuals who do not transmit the disease, and infected individuals capable transmitting the disease [18], we get two functions, $\mathcal{F}_i(\boldsymbol{X})$ and

$\mathcal{V}_i(\boldsymbol{X})$, which respectively contain the rate of new infections at compartment i and the rate of transfer of individuals between the compartment i as follow,

$$\mathcal{F}_i(\boldsymbol{X}) = \begin{bmatrix} B\beta_{mh}\frac{N_m}{N_h}x_6x_1(1-u_1) \\ B\beta_{hm}x_2x_5 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix},$$

$$\mathcal{V}_i(\boldsymbol{X}) = \begin{bmatrix} (\eta_h+\mu_h)x_2 \\ (\mu_m+u_2)x_6 \\ -\mu_h + \left(B\beta_{mh}\frac{N_m}{N_h}x_6(1-u_1)+\mu_h\right)x_1 - \theta x_3 \\ -\eta_h x_2 + (\theta+\mu_h)x_3 \\ -\varphi\left(1-\frac{N_m}{kN_h}x_4\right)(x_5+x_6) + (\eta_A+\mu_A)x_4 \\ -\eta_A x_4 + (B\beta_{hm}x_2+\mu_m+u_2)x_5 \end{bmatrix},$$

where $\boldsymbol{X} = (x_2, x_6, x_1, x_3, x_4, x_5)$. By taking the Jacobian matrices of $\mathcal{F}_i(\boldsymbol{X})$ and $\mathcal{V}_i(\boldsymbol{X})$ which are evaluated at E_0, we respectively get the following block matrices,

$$\mathrm{DF}_i(E_0) = \begin{bmatrix} \mathbb{F} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} \end{bmatrix} \text{ and } \mathrm{D}\mathbb{V}_i(E_0) = \begin{bmatrix} \mathbb{V} & \mathbf{0} \\ J_1 & J_2 \end{bmatrix}$$

where

$$\mathbb{F} = \begin{bmatrix} 0 & B\beta_{mh}\frac{N_m}{N_h}(1-u_1) & 0 & 0 \\ B\beta_{hm}\frac{(\varphi\eta_A-(\eta_A+\mu_A)(\mu_m+u_2))kN_h}{(\mu_m+u_2)\varphi N_m} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix},$$

$$\mathbb{V} = \begin{bmatrix} \eta_h+\mu_h & 0 & 0 & 0 \\ 0 & \mu_m+u_2 & 0 & 0 \\ 0 & B\beta_{mh}\frac{N_m}{N_h}(1-u_1) & \mu_h & -\theta \\ -\eta_h & 0 & 0 & \theta+\mu_h \end{bmatrix},$$

$$J_1 = \begin{bmatrix} 0 & \left(\frac{\phi\eta_A-(\eta_A+\mu_A)(\mu_m+u_2)}{\eta_A}-\phi\right) & 0 & 0 \\ B\beta_{hm}\frac{(\phi\eta_A-(\eta_A+\mu_A)(\mu_m+u_2))kN_h}{(\mu_m+u_2)\phi N_m} & 0 & 0 & 0 \end{bmatrix},$$

$$J_2 = \begin{bmatrix} \frac{(\eta_A+\mu_A)(\mu_m+u_2)-\phi\eta_A}{\phi\eta_A}+(\eta_A+\mu_A) & \left(\frac{\phi\eta_A-(\eta_A+\mu_A)(\mu_m+u_2)}{\eta_A}-\phi\right) \\ -\eta_A & \mu_m+u_2 \end{bmatrix}.$$

By following [17] and [18], the basic reproduction number ($\mathcal{R}_0$) of the system (3) is the spectral radius of the next generation matrix $\mathbb{F}\mathbb{V}^{-1}$ such that we have

$$\mathcal{R}_0 = \sqrt{\frac{B^2k\beta_{mh}\beta_{hm}(\varphi\eta_A-(\eta_A+\mu_A)(\mu_m+u_2))(1-u_1)}{\varphi(\eta_h+\mu_h)(\mu_m+u_2)^2}}.$$

Furthermore, we found that the DFE E_0 is locally asymptotically stable if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$. We can observe that $\mathcal{R}_0$ is linearly depending on $(1 - u_1)$ meaning that the greater u_1 the lower $\mathcal{R}_0$, vice versa. While for u_2, we observe numerically its sensitivity to the $\mathcal{R}_0$ using parameter values given in Table 1. For simulation observation, we choose several values of u_1 and u_2 as shown in Figure 2. We could observe that for the chosen parameter values and for the varied u_1, there exists a certain value of u_2 in which $\mathcal{R}_0$ will be lower than one (see the bottom picture in Figure 2). The greater u_1, the lower u_2 to produce $\mathcal{R}_0$ <1, vice versa. Similar behavior is found for the sensitivity of u_1 to generate $\mathcal{R}_0$ <1 (see the top picture in Figure 2). In the next section, we discuss the optimal value of the both controls when we assume they are varying in time.

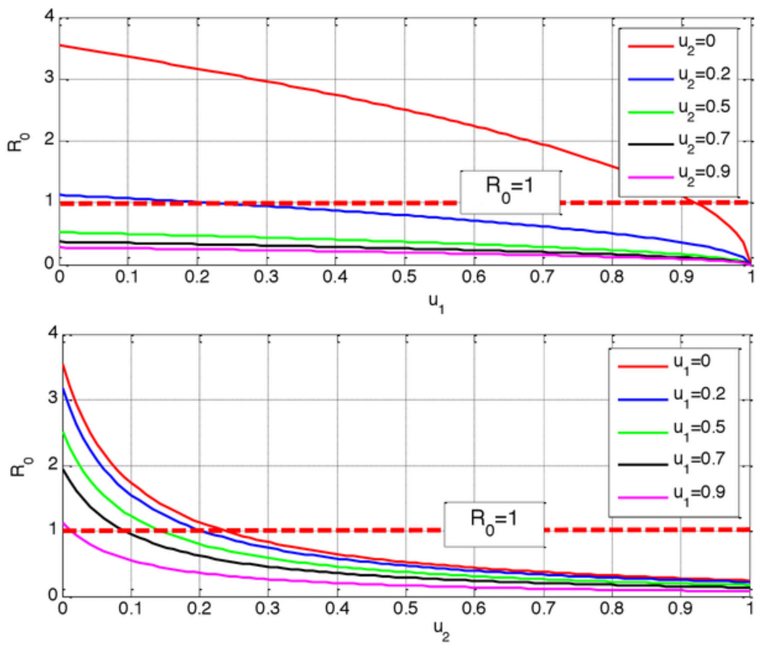

Figure 2. Sensitivity of $\mathcal{R}_0$ to the non-chemical control u_1 for fixed values of u_2 (top) and the chemical control u_2 for fixed values of u_1 (bottom).

4. Optimal Control Problem

In this section we will examine an optimal control problem of the model given in equation (1) by assuming that the controls u_1 and u_2 are time-dependent functions. As described in the previous section, there are two control variables applied in the model, namely chemical and non-chemical control strategies that are integrated for reducing the transmission of dengue. It is assumed that part of susceptible human population can be released from DHF virus infection such that the $u_1(t)$ function defined at interval $0 \leq u_1 \leq 1$. It represents the percentage of individuals who will be free from the infection caused by environment management where human-vector contact can be interrupted. Moreover, the function $u_2(t)$ is a control function that represents the proportion of susceptible mosquitoes and infected mosquitoes dying due to chemical control strategy per unit of time. It is also assumed that the value is defined at interval $0 \leq u_2 \leq 1$. So if $u_i(t) = 0, i = 1,2$, then the chemical and non-chemical control strategies does not have any effects on reducing the number of infected humans and mosquitos. On the contrary, when $u_i(t) = 1, i = 1,2$, it indicates that the chemical and non-chemical control strategies were totally making the system free from infections.

To obtain the optimal pair of values from both control functions, optimal control theory is applied to obtain the optimal chemical and non-chemical control effects that can reduce the transmission of dengue. In line with objective of the control functions, we then defined the objective function that should be minimized i.e.

$$\min_{(u_1,u_2)} J(u_1,u_2) = \min_{(u_1,u_2)} \int_{t_0}^{t_f} \left[a_1 {I_h}^2(t) + a_2 {I_m}^2(t) + a_3 {u_1}^2(t) + a_4 {u_2}^2(t)\right] dt, \quad (4)$$

where a_i $(i = 1,2,3,4)$ are the weighting constants for infected human, infected mosquitoes, non-chemical and chemical control efforts respectively. In the dimensionless model, the objective function (4) could be written as follows:

$$\min_{(u_1,u_2)} J(u_1,u_2) = \min_{(u_1,u_2)} \int_{t_0}^{t_f} \left[a_1 N_h^2 x_2^2(t) + a_2 N_m^2 x_6^2(t) + a_3 {u_1}^2(t) + a_4 {u_2}^2(t)\right] dt. \quad (5)$$

The objective function in (5) represents the searching for a control function pair u_1 and u_2 which minimizes the spread of dengue hemorrhagic fever disease. The set of expected control functions is defined as

$$U = \{(u_1,u_2) \in R^2 | 0 \le u_1(t) \le 1, 0 \le u_2(t) \le 1, t_0 \le t \le t_f\}.$$

Here we should determine $\boldsymbol{u}^* = ({u_1}^*, {u_2}^*) \in U$ such that $J(\boldsymbol{u}^*) \le J(\boldsymbol{u})$ for every $\boldsymbol{u} \in U$.

The optimal control search $\boldsymbol{u}^*$ could be performed using the Pontryagin maximum principle [19-20]. The principle provides the necessary conditions for optimal control problem (5) corresponding to the system given in equation (3). The Hamiltonian function of the system is given as follows:

$$\begin{aligned} H = {} & a_1 {N_h}^2 {x_2}^2 + a_2 {N_m}^2 {x_6}^2 + a_3 {u_1}^2 + a_4 u_2^2 \\ & + \lambda_1 \left(\mu_h - \left(B\beta_{mh} \frac{N_m}{N_h} x_6(1-u_1) + \mu_h\right) x_1 + \theta x_3\right) \\ & + \lambda_2 \left(B\beta_{mh} \frac{N_m}{N_h} x_6 x_1 (1-u_1) - (\eta_h + \mu_h) x_2\right) \\ & + \lambda_3(\eta_h x_2 - (\theta + \mu_h) x_3) + \lambda_4 \left(\varphi\left(1 - \frac{N_m}{kN_h} x_4\right)(x_5 + x_6) - (\eta_A + \mu_A) x_4\right) \\ & + \lambda_5(\eta_A x_4 - (B\beta_{hm} x_2 + \mu_m + u_2) x_5) + \lambda_6(B\beta_{hm} x_2 x_5 - (\mu_m + u_2) x_6), \end{aligned} \quad (6)$$

where $\lambda_1, \lambda_2, \ldots, \lambda_6$ are adjoin variables. Dynamics of the adjoin variables are given by the following differential equations

$$\dot{\boldsymbol{\lambda}} = -\frac{\partial H}{\partial \boldsymbol{x}} = \left(-\frac{\partial H}{\partial x_1}, -\frac{\partial H}{\partial x_2}, -\frac{\partial H}{\partial x_3}, -\frac{\partial H}{\partial x_4}, -\frac{\partial H}{\partial x_5}, -\frac{\partial H}{\partial x_6}\right).$$

Hence, we found the following costate equations:

$$\dot{\lambda}_1 = -\lambda_1\left(-B\beta_{mh} \frac{N_m}{N_h} x_6(1-u_1) - \mu_h\right) - \lambda_2 B\beta_{mh} \frac{N_m}{N_h} x_6(1-u_1),$$
$$\dot{\lambda}_2 = -2a_1 {N_h}^2 x_2 - \lambda_2(-\eta_h - \mu_h) - \lambda_3 \eta_h + (\lambda_5 - \lambda_6) B\beta_{hm} x_5,$$
$$\dot{\lambda}_3 = -\lambda_1 \theta - \lambda_3(-\theta - \mu_h),$$
$$\dot{\lambda}_4 = -\lambda_4\left(-\varphi \frac{N_m}{kN_h}(x_5 + x_6) - \eta_A - \mu_A\right) - \lambda_5 \eta_A,$$
$$\dot{\lambda}_5 = -\lambda_4 \varphi\left(1 - \frac{N_m}{kN_h} x_4\right) - \lambda_5(-B\beta_{hm} x_2 - \mu_m - u_2) - \lambda_6 B\beta_{hm} x_2,$$
$$\dot{\lambda}_6 = -2a_2 {N_m}^2 x_6 + (\lambda_1 - \lambda_2) B\beta_{mh} \frac{N_m}{N_h} x_1(1-u_1) - \lambda_4 \varphi\left(1 - \frac{N_m}{kN_h} x_4\right) - \lambda_6(-\mu_m - u_2).$$

Transversality conditions for the costate equations are: $\lambda_1(t_f) = 0$, $\lambda_2(t_f) = 0$, $\lambda_3(t_f) = 0$, $\lambda_4(t_f) = 0$, $\lambda_5(t_f) = 0$, $\lambda_6(t_f) = 0$. The optimality conditions on the interior of the control set U at an optimal control pair $({u_1}^*, {u_2}^*)$ are

$$0 = \frac{\partial H}{\partial u_1} = 2u_1 a_3 + (\lambda_1 - \lambda_2) B\beta_{mh} \frac{N_m}{N_h} x_6 x_1,$$

$$0 = \frac{\partial H}{\partial u_2} = 2u_2 a_4 - \lambda_5 x_5 + \lambda_6 x_6.$$

Since $0 \leq u_1 \leq 1$ and $0 \leq u_2 \leq 1$, then we have

$$u_1^* = \begin{cases} u_1, & \text{if } 0 \leq u_1 \leq 1 \\ 0, & \text{if } u_1 < 0 \\ 1, & \text{if } u_1 > 1 \end{cases},$$

and

$$u_2^* = \begin{cases} u_2, & \text{if } 0 \leq u_2 \leq 1 \\ 0, & \text{if } u_2 < 0 \\ 1, & \text{if } u_2 > 1 \end{cases},$$

where

$$u_1 = \frac{N_m}{N_h}\left(\frac{(\lambda_2 - \lambda_1)B\beta_{mh}x_6 x_1}{2a_3}\right) \text{ and } u_2 = \frac{\lambda_5 x_5 + \lambda_6 x_6}{2a_4}.$$

5. Numerical Result

In this section, the optimal system control problem will be numerically solved using the Steepest Descent method (see Petrova and Solov'ev (1997) for details about the method [21]). This method requires an initial guess for the control function so that the state equation can be obtained by solving system (3) forward in time. Simulation of model (3) is performed using initial values and parameter values given in Table 1. The weights of each objective function are a_1=0.9, a_2=0.9, a_3=0.1, and a_4=0.1. The weights indicate that the emphasis of the optimal control problem is focused to reduce the number of infected humans and infected mosquitoes.

The numerical results show that the non-chemical control strategy for susceptible human population and the chemical control strategy for mosquito population give a significant effect in reducing number of DHF patients. Figure 3-(a-1) shows the comparison of proportion of susceptible human population with control and without control. It is found that after applying the control, proportion of susceptible human population increases around 35% compared to without control. Although the non-chemical control does not have an effect at the beginning time, but after specific time, increasing of susceptible human population is significant. A different dynamic is found in the infected population. In Figure 3-(a-2) it is found that number of infected humans with dengue hemorrhagic fever increases in the absence of the control or after applying the control. However, as time is increased, effect of the control strategy could be observed where the number of infected humans decreases and the remaining infected is around 6% of the total population. It means that the strategy is not directly affect the system. So the environment management control must be applied continuously to see the effects in the future (see also the control profile at the left picture in Figure 4). Furthermore, for recovered humans, number of removed human in the absence of control is greater than the number of removed (recovered from DHF) human after control is applied (see Figure 3-(a-3)). This is certainly due to the condition that without control the number of infective population is high enough. If the immune system in humans who have recovered from dengue hemorrhagic fever decreases, then the recovered human population will move back into susceptible human population.

In the mosquito population, the chemical control does not significantly affect the number of mosquito larvae population. However, applying of space spray is very influential on the decreasing the number of susceptible mosquitoes and infected mosquitoes (adult mosquitos). It could be seen in Figure 3-(b-2) that the number of susceptible mosquitoes after being controlled is less than before applying the control. In addition, the number of infected mosquitoes after applying space spray control is less than before applying the control (Figure 3-(b-3)). It indicates that the existence of controls in the system has an effect on the decreasing number of infected population, both in human and in mosquito populations.

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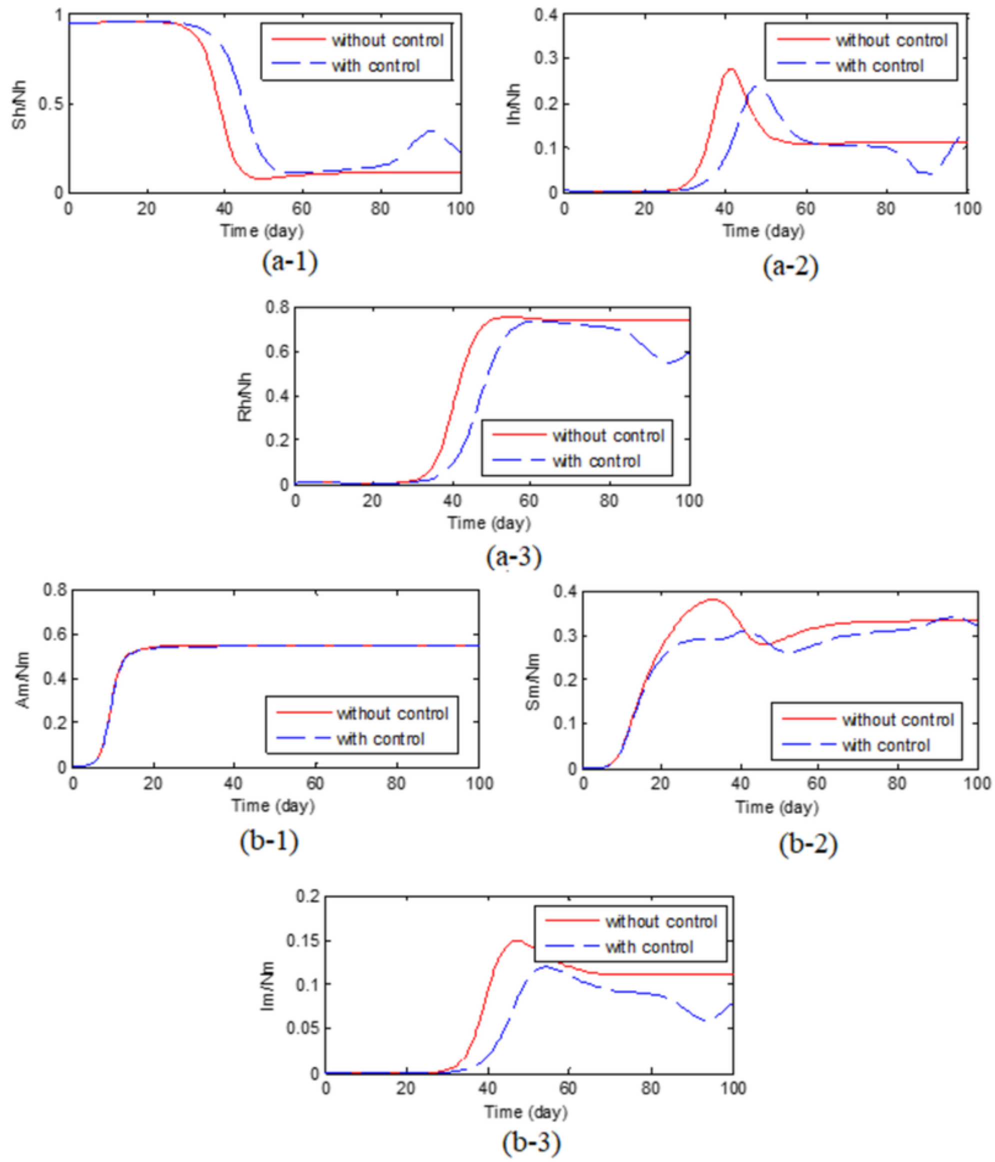

Figure 3. Simulation results for model (3) with control (dashed line) and without control (solid line) when $\beta_{mh} = 0.35$ for human population (a) and mosquito population (b).

Profile of the non-chemical control function u_1 and chemical control function u_2 can be seen in Figure 4. It is found that at the beginning of time, the environmental management effect is quite small. Over time, the control effect increased, resulting in a reduction number of infected human population. On the contrary, for the chemical control profile (u_2), it will directly affect the average value of number of died mosquitoes caused by the space spraying using a suitable insecticide. The peaks of the non-chemical control effects (environmental management strategy) occurred at the end of the observation

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time. At the time, number of infected humans decreased and number of susceptible humans significantly increased. Conversely, the peak of the chemical control effect occurs at early of the observation time. This result implies that the chemical control effect can be directly affect to the mosquito population where after $t = 40$ days, number of susceptible mosquitoes and infected mosquitoes are significantly reduced. While the non-chemical control is not directly affect the human system such that the control management should be applied continually to see the effect in the future. It indicates that campaigns related to the healthy lifestyles should be encouraged, so does for the changing human behavior especially at the public places where the transmission of the disease could be occur.

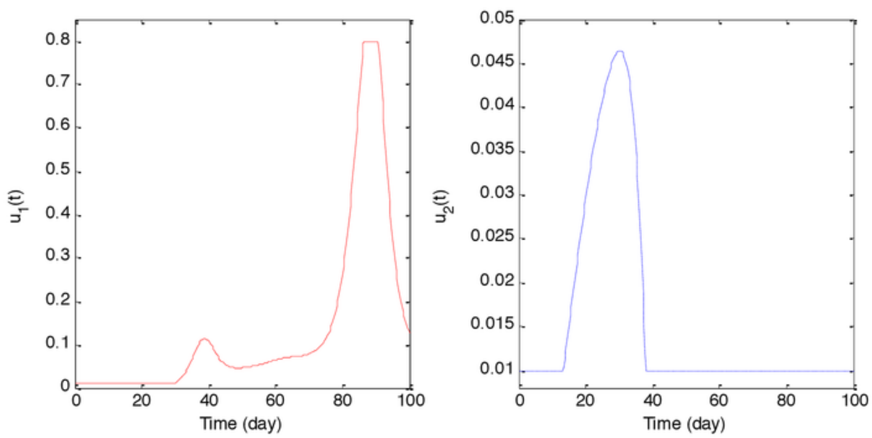

Figure 4. Graph of non-chemical (left) and chemical (right) control functions in human and mosquito populations, respectively when $\beta_{mh} = 0.35$.

In the next simulation, probability of DHF virus transmission is varying. Figure 5 presents result of the simulation when the probability value (β_{mh}) is increased twice from the previous value. In general, profile of the system solution (before and after the control) is the same as the previous simulation. It can be seen in Figure 5-(a) that the maximum number of infected individuals increases as a result of an increased probability of infection transmission. Change of the transmission probability also affects to the control variables functions u_1 and u_2 (see Figure 6), where the greater probability, the greater proportion of healthy susceptible humans should be controlled will be. Increasing of the non-chemical control proportion will reduce the number of susceptible human population that infected by DHF virus. In addition, the greater transmission probability, the greater chemical control effort should be applied will be. Increasing of the space spray effort will suppress the increasing rate of the number of infected mosquitoes (vector of the DHF virus spread) (see Figure 5-(b)). From the simulation, it is found that the more endemic the condition of a system, the greater effort should be performed to overcome the disease spread will be.

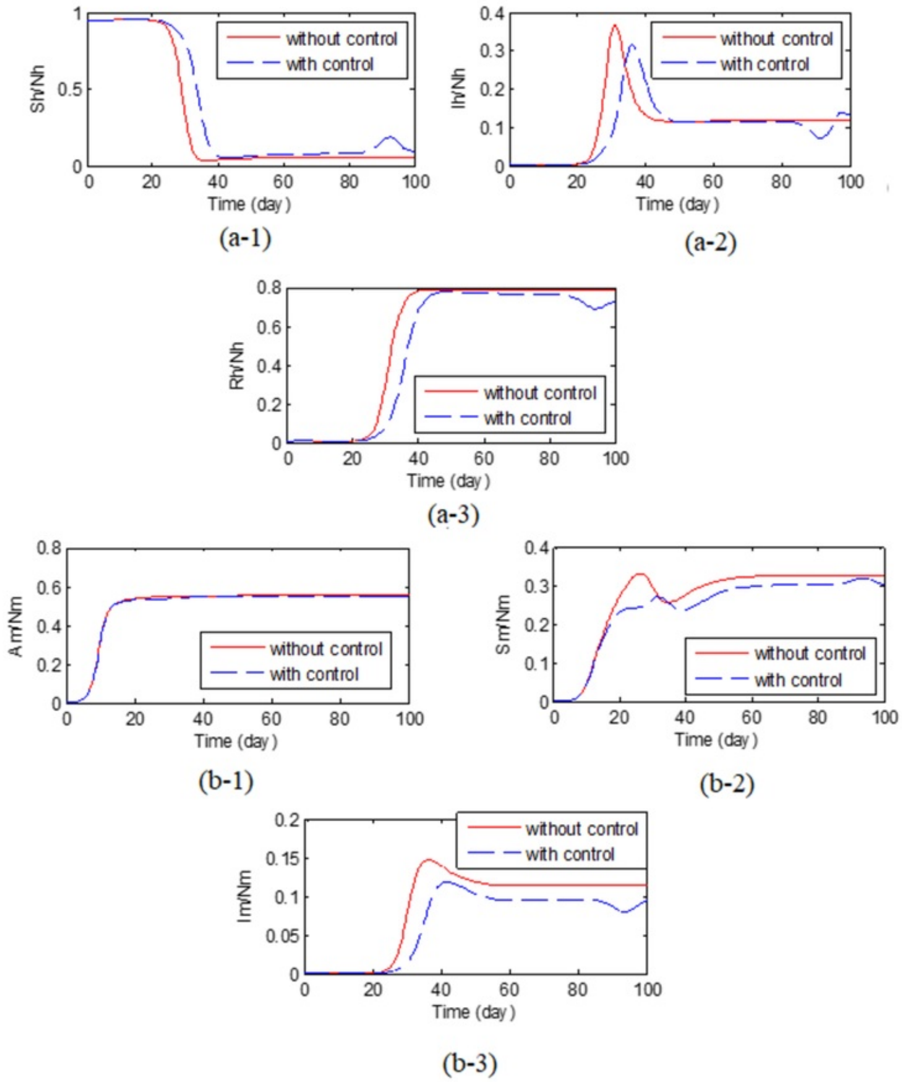

Figure 5. Simulation results for model (3) with control (dashed line) and without control (solid line) when $\beta_{mh} = 0.75$ for human population (a) and mosquito population (b).

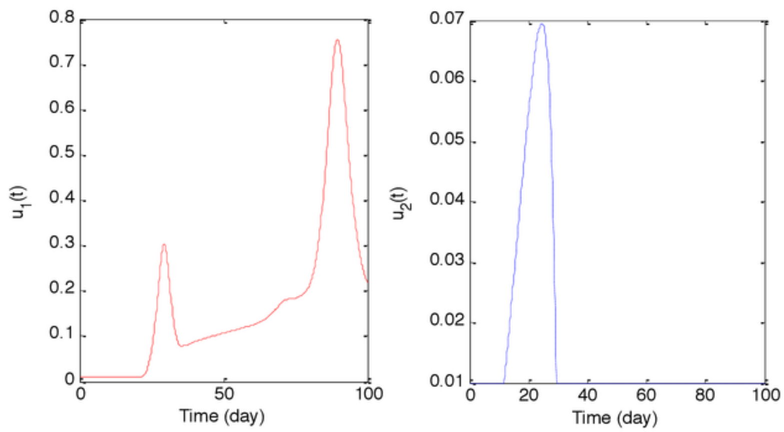

Figure 6. Graph of non-chemical (left) and chemical (right) control functions in human and mosquito populations, respectively when $\beta_{mh} = 0.75$.

6. Conclusions

In this research we have developed an epidemiology model of dengue hemorrhagic fever by including effects of the integrated vector management in term of combination of chemical and non-chemical control for reducing the transmission of the disease in the system. When the control function was considered as a constant, we found that there exists certain conditions in which controlling endemic of the system depends only on the chemical treatment. There is a critical value of chemical control effect that causes basic reproduction number value of the model is larger or smaller than one. When the chemical and non-chemical controls were considered as time dependent functions, we found analytical form of the both control functions that depend on the state and co-state of the system. The numerical simulations were performed using the Steepest Descent method to confirm the analytical results. By applying optimal control profiles, we numerically found that the peak of the non-chemical control effect occurs at the end of the observation time, while the chemical control effect reaches the maximum effect at early of the observation time. It indicated that to continuously maintain the security of the system from the endemic condition, the integrated vector control strategy should be considered as the recommended method of prevention and control *Aedes* mosquitoes. The combination of chemical and non-chemical control strategies was a relevant method in controlling of dengue infections. The greater the probability of DHF virus transmission, the greater the effort to prevent occurrence of endemic conditions in the system will be.

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