BAREKENG: Journal of Mathematics and Its Applications
December 2023 Volume 17 Issue 4 Page 2305–2316
P-ISSN: 1978-7227 E-ISSN: 2615-3017
https://doi.org/10.30598/barekengvol17iss4pp2305-2316

MATHEMATICAL MODELS OF DENGUE TRANSMISSION DYNAMICS WITH VACCINATION AND WOLBACHIA PARAMETERS AND SEASONAL ASPECTS

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Article History:

Received: 8th August 2023
Revised: 15th October 2023
Accepted: 12th November 2023

Keywords:

Dengue;
Dengue Mathematical Models;
Seasonal Effects; Vaccination;
Wolbachia.

ABSTRACT

The Aedes aegypti mosquito is the main carrier of dengue virus transmission to humans. In this study, a mathematical model for the transmission of the dengue virus is constructed using vaccination and Wolbachia parameters in an attempt to control the virus's spread. Furthermore, the fundamental reproduction number is set as a parameter of the infection threshold. Based on the stability of the equilibrium point analysis, it is found that the disease-free equilibrium point is locally asymptotically stable if $R_0 < 1$. Then, a mathematical model of dengue was created by examining the seasonal aspect and adding a periodic term to the mosquito birth rate. Dengue virus transmission in mosquito populations is controlled by air temperature in addition to seasonal variables. In this study, three weather scenarios were simulated: scenario 1 for cold weather (air temperature 14 °C), scenario 2 for hot weather (air temperature 26 °C), and scenario 3 for moderate weather (air temperature between 14 and 26 °C).

How to cite this article:

A. Sa'adah and D. K. Sari, "MATHEMATICAL MODELS OF DENGUE TRANSMISSION DYNAMICS WITH VACCINATION AND WOLBACHIA PARAMETERS AND SEASONAL ASPECTS," *BAREKENG: J. Math. & App.*, vol. 17, iss. 4, pp. 2305-2316, December, 2023.

Journal homepage: *https://ojs3.unpatti.ac.id/index.php/barekeng/*
Journal e-mail: *barekeng.math@yahoo.com; barekeng.journal@mail.unpatti.ac.id*

Research Article · Open Access

1. INTRODUCTION

Dengue Hemorrhagic Fever (DHF) is an infectious disease caused by the dengue virus, which is transmitted by the mosquitoes Aedes aegypti and Aedes albopictus. Dengue fever is a major global health issue, particularly in tropical and subtropical regions. Every year, millions of people get infected with DHF, and thousands die as a result of the disease [1]. Efforts to control DHF have been carried out through various approaches, including vector control and prevention of the spread of the virus[2]. Common vector control methods involve using insecticides, fogging, eradicating mosquito breeding grounds, and vaccination[3]. Vaccines have historically been regarded as a highly effective approach in combating diseases. Consequently, persistent endeavors have been undertaken to create a potent dengue vaccine ever since the initial occurrence of the disease[3]. However, excessive use of pesticides can result in mosquito resistance to the chemicals, and other preventative measures frequently fail to effectively reduce mosquito populations[4]. The use of Wolbachia bacteria, which infect the Aedes aegypti mosquito, is one method for controlling DHF [5]. Wolbachia is a naturally occurring bacterium that can infect mosquitos and affect their capacity to transmit the dengue virus. Wolbachia can restrict the mosquito's ability to transmit the virus by suppressing virus replication in the mosquito's body, hence limiting disease transmission. Aedes aegypti carrying the symbiont Wolbachia and the introduction of natural predators of mosquito larvae are considered as biological control strategies[6], [7].

One of the important factors contributing to dengue transmission dynamics is the presence of mosquito populations, whose life cycle is influenced by climatic factors such as temperature and rainfall. In places with strong dry and rainy seasons, the mosquito population changes throughout the year, with more mosquitoes in the rainy season than in the dry season, resulting in an increase in the frequency of dengue infections during the rainy season[8], [9]. For instance, in Indonesia, the rainy season, which runs from November to March, usually has an increase in dengue fever infections. This shows that seasonal variations in mosquito populations influence the dynamics of dengue transmission[10].

Mathematical models can be used to simulate various vector control strategies and analyze their impact on disease transmission. DHF tends to show seasonal variability in its distribution[11]. Aedes mosquitoes tend to reproduce and become more active during particular seasons[8]. The rainy season, with its more humid circumstances, frequently results in an increase in mosquito population, which can raise the risk of dengue transmission. Models with a seasonal component can help identify these seasonal patterns and provide more insight into the trend of dengue transmission over time.

Several researches have created seasonal mathematical models, including the malaria transmission model[8], the chikungunya periodic model[12], the dynamic model of Zika virus transmission[13], and dengue[14], [15]. However, the dengue model constructed in[14] did not include Wolbachia as a variable controlling disease transmission. Hence, in this study, a mathematical model of the transmission of dengue was created, one that included vaccination, Wolbachia as a control variable, and seasonal aspects. The stability of the equilibrium point and the sensitivity of the basic reproduction number were then examined to determine which parameter has the most influence on the spread of the dengue virus. For seasonal variations in the dynamics of dengue virus transmission, numerical simulations were performed on dengue models with seasonal and non-seasonal aspects.

This article consists of four sections. Section one explains the background of the problem. Section two gives the research methods for this work. Section three gives the results and discussion that consist of the proposed mathematical model of dengue, its stability, sensitivity analysis, and numerical analysis. And the last, Section 4, concludes all of this work.

2. RESEARCH METHODS

The method used in this research was as follow:

1. Develop a mathematical model of dengue without seasonal effect. The proposed model is based on host-vector model with human as a vector and mosquitos as a vector.
2. Calculate the equilibrium of the model by solving this equation:

$$\frac{dS_h}{dt} = \frac{dI_h}{dt} = \frac{dV_h}{dt} = \frac{dR_h}{dt} = \frac{dA_v}{dt} = \frac{dS_v}{dt} = \frac{dI_v}{dt} = \frac{dP_v}{dt} = \frac{dA_w}{dt} = \frac{dS_w}{dt} = 0 \quad (1)$$

3. Determine the basic reproduction number R_0 using the Next Generation Matrix (NGM). First, create a vector with the compartments that may induce virus transmission, $\mathbf{x} = (I_h, I_v)^T$. Then decompose $\mathbf{x}$ into $\mathcal{F} - \mathcal{V}$ to generate the Jacobi matrix of $\mathcal{F}$ and $\mathcal{V}$ which are evaluated at the non-endemic equilibrium points E_0, $\mathbb{F} = \frac{\partial \mathcal{F}}{\partial \mathbf{x}}\Big|_{E_0}$ and $\mathbb{V} = \frac{\partial \mathcal{V}}{\partial \mathbf{x}}\Big|_{E_0}$. The basic reproduction number is obtained from the largest eigenvalue modulus of the NGM,

$$R_0 = \rho(\mathbb{F}\mathbb{V}^{-1}) = \max|\lambda_i| \tag{2}$$

where λ_i is eigen values of the NGM

4. Analyze the stability of the equilibrium of the model using linearization matrix around the equilibrium point with Jacobian matrices:

$$J = \frac{\partial \boldsymbol{F}}{\partial \mathbf{x}}\Big|_{E_0} \tag{3}$$

where $\boldsymbol{F} = \left\{\frac{dS_h}{dt}, \frac{dI_h}{dt}, \frac{dV_h}{dt}, \frac{dR_h}{dt}, \frac{dA_v}{dt}, \frac{dS_v}{dt}, \frac{dI_v}{dt}, \frac{dP_v}{dt}, \frac{dA_w}{dt}, \frac{dS_w}{dt}\right\}$ and $\mathbf{x} = \{S_h, I_h, V_h, R_h, A_v, S_v, I_v, P_v, A_w, S_w\}$.

5. Determine the sensitivity index of the model parameter by using basic reproduction number. A sensitivity analysis was performed on the basic reproduction number R_0, which is the threshold for disease spread. The normalized sensitivity index of variable m to parameter k is defined by[16] :

$$\Upsilon_k^m := \frac{\partial m}{\partial k} \times \frac{k}{m}. \tag{4}$$

6. Develop a mathematical model of dengue with seasonal effect.
7. Simulate the dynamics of the model with and without seasonal effect. The solution of the proposed model is solved numerically using Runge-Kutta 4th algorithm.

3. RESULTS AND DISCUSSION

In this section, we will explain the development of mathematical model of dengue with and without seasonal effect. Then, the dynamics of the model will be analyzed, such as the equilibrium the basic reproduction number, and the stability analysis of the equilibrium. The sensitivity analysis of the basic reproduction number is carried out to determine the most influence model parameter. The numerical simulation will complete the study of the model's dynamics.

3.1 Mathematical model with non-seasonal aspect

In this sub-chapter, a mathematical model for the transmission of dengue fever will be developed, including control in the form of vaccine and Wolbachia but without taking into account the seasonal aspect. In this study, the total human population N_h was divided into four compartments, which were susceptible human S_h, dengue-infected human I_h, vaccinated human V_h, and immune human R_h. While the mosquito population is separated into two broad types, non-Wolbachia mosquitoes N_v and mosquitoes with Wolbachia N_w. The non-Wolbachia mosquito population was separated into four compartments: eggs of non-Wolbachia mosquitoes A_v, susceptible of non-Wolbachia mosquitoes S_v, mosquitoes infected with dengue I_v, and mosquitoes infected with Wolbachia P_v. Meanwhile, the Wolbachia mosquito population was separated into two compartments: mosquito eggs with Wolbachia A_w and susceptible mosquitoes with Wolbachia S_w. **Table 1** includes comprehensive explanations of each compartment.

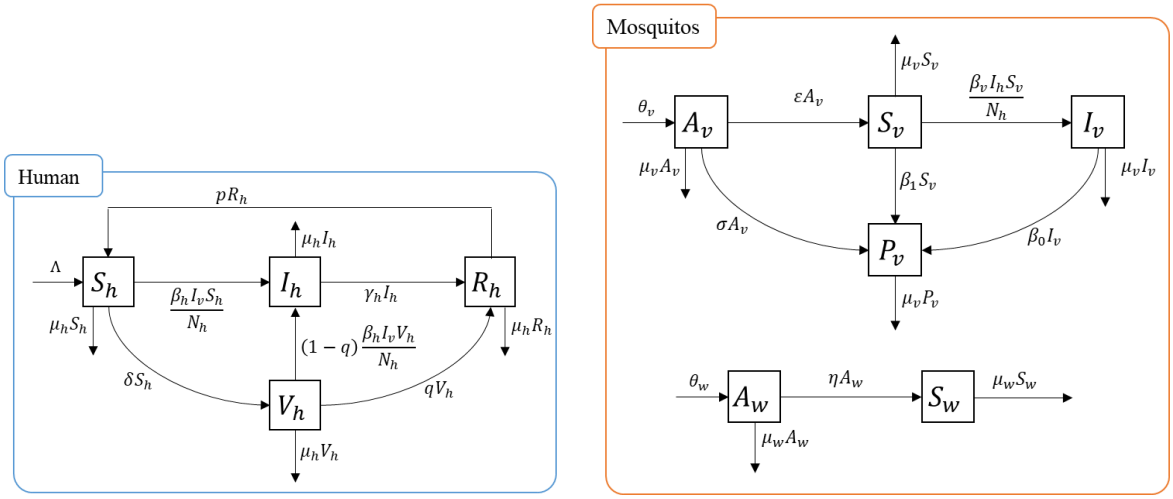
The mathematical model developed is a modification and combination of [14] and [17]. In contrast to [17] , the compartment V_h was added in this study to accommodate the number of persons who had been vaccinated. Vaccination is considered to be transitory, allowing the R_h compartment to lose its immunity and revert to the susceptible compartment S_h. Unlike [14], humans in the V_h compartment shift to the R_h compartment at a proportion equal to the vaccine's effectiveness. P_v, A_w, and S_w compartments were also included to examine the impact of Wolbachia spread on the dynamics of Aedes aegypti mosquitoes.

The model is based on assumptions about the dynamics of dengue virus transmission in real-world scenarios. The following assumptions are made in this study: i) the total human population and the total mosquito population are constant; ii) immunity from vaccination and recovery is temporary, so immune

humans will become vulnerable again when they lose their immunity; (iii) humans infected with dengue can spread the virus, causing mosquitos to become infected if they interact with infected humans; iv) mosquitos infected with dengue will remain infected for the rest of their lives; (v) there is no vertical transmission from parent to child; (vi) a Wolbachia-infected mosquito bite does not result in dengue infection.

Susceptible humans will increase with a recruitment rate of Λ. Susceptible humans will become infected if bitten by a mosquito carrying the dengue virus, with a virus transmission rate of $\frac{\beta_h I_v S_h}{N_h}$. Infected humans will recover with a recovery rate of γI_h after receiving treatment. Vaccination was administered at a rate of $\delta S_h$to the susceptible human compartment. This model examines the imperfect vaccine component, specifically conditions where the vaccine's efficiency has not reached 100%. As a result, humans who have been vaccinated have a risk of being infected with dengue at a rate of $(1-q)\frac{\beta_h I_v V_h}{N_h}$. The R_h compartment consists of immunity from medication and vaccination. As soon as immunity starts to decrease, compartment R_h will switch to compartment S_h. Each of the S_h, I_h, V_h, and R_h compartments will decrease at a rate of μ_h death on its own.

In the mosquito population, it is hypothesized that Aedes aegypti mosquitoes carrying Wolbachia are discharged into the environment and mate with non-Wolbachia Aedes aegypti mosquitoes. Wolbachia bacteria in Wolbachia-infected mosquitos will spread to other mosquitos, weakening the dengue virus in mosquitos. As a result, these mosquitoes will be unable to spread the dengue virus.



(a) **(b)**

Figure 1. Dengue Virus Transmission Diagram (a) in Human Population (b) in Mosquitos Population

Figure 1 shows the dengue virus transmission diagram. A complete description of the model parameters is given in **Table 2**. Based on the explanation above, a mathematical model for the distribution of dengue without seasonal aspects is obtained in the following **Equation (5)**:

$$
\begin{aligned}
\frac{dS_h}{dt} &= \Lambda - \beta_h \frac{I_v}{N_h} S_h - (\delta + \mu_h) S_h + pR_h \\
\frac{dI_h}{dt} &= \beta_h \frac{I_v}{N_h} S_h + (1-q)\beta_h \frac{I_v}{N_h} V_h - (\gamma + \mu_h) I_h \\
\frac{dV_h}{dt} &= \delta S_h - (1-q)\beta_h \frac{I_v}{N_h} V_h - (q + \mu_h) V_h \\
\frac{dR_h}{dt} &= \gamma I_h + qV_h - (p + \mu_h) R_h \\
\frac{dA_v}{dt} &= \theta_v - (\varepsilon + \sigma + \mu_v) A_v \\
\frac{dS_v}{dt} &= \varepsilon A_v - \frac{\beta_v I_h S_v}{N_h} - (\beta_1 + \mu_v) S_v \\
\frac{dI_v}{dt} &= \frac{\beta_v I_h S_v}{N_h} - (\beta_0 + \mu_v) I_v \\
\frac{dP_v}{dt} &= \sigma A_v + \beta_0 I_v + \beta_1 S_v - \mu_v P_v \\
\frac{dA_w}{dt} &= \theta_w - (\eta + \mu_w) A_w \\
\frac{dS_w}{dt} &= \eta A_w - \mu_w S_w
\end{aligned}
\tag{5}
$$

Table 1. Model Compartment Description

Notation	Description	Unit
$S_h(t)$	Humans who are susceptible to dengue infection when t	Person
$I_h(t)$	Humans infected with the dengue virus when t	Person
$V_h(t)$	Humans who have been vaccinated when t	Person
$R_h(t)$	Humans who are immune when t	Person
$A_w(t)$	Mosquito eggs with Wolbachia when t	Mosquito
$S_w(t)$	Wolbachia mosquitoes that are susceptible to dengue infection when t	Mosquito
$A_v(t)$	Non-Wolbachia mosquito eggs when t	Mosquito
$S_v(t)$	Non-Wolbachia mosquitoes that are susceptible to dengue infection when t	Mosquito
$I_v(t)$	Dengue-infected non-Wolbachia mosquitoes when t	Mosquito
$P_v(t)$	Non-Wolbachia mosquitoes infected with Wolbachia bacteria when t	Mosquito

Table 2. Model Parameter Description

Notation	Description	Value	Unit
Λ	Human recruitment rate	$\frac{N_h}{365\times70}$ [13]	Person.Day^{-1}
μ_h	Human mortality rate	$\frac{1}{365\times70}$ [13]	Day^{-1}
β_h	The probability of dengue virus transmission from mosquitos to humans	0.002 [14]	Person·Day^{-1} ·Mosquito^{-1}
δ	The average number of humans vaccinated	0.2 [12]	Day^{-1}
p	Waning immunity period	$\frac{1}{365}$ [Assume]	Day^{-1}
q	Vaccine effectiveness	80% [Assume]	Day^{-1}
γ	The cure rate for infected humans	$\frac{1}{14}$ [14]	Day^{-1}
θ_w	The recruitment rate of Wolbachia-infected mosquitoes	$\mu_w N_W$ [12]	Mosquito.Day^{-1}
μ_w	The death rate of Wolbachia-infected mosquitoes	$\frac{1}{21}$ [12]	Day^{-1}
η	Rate of transformation of Wolbachia mosquito eggs into Wolbachia mosquitoes	0.00854 [12]	Day^{-1}
θ_v	The recruitment rate of non-Wolbachia mosquitoes	$\mu_v N_v$ [12]	Mosquito. Day^{-1}
μ_v	The death rate of non-Wolbachia mosquitoes	$\frac{1}{21}$ [12]	Day^{-1}
ε	The transformation rate of non-Wolbachia eggs to non-Wolbachia mosquitoes	0.0238 [12]	Day^{-1}
σ	Wolbachia release rate to nature	0.2 [12]	Day^{-1}
β_v	The proportion of dengue virus transmission from an infected human individual to a mosquito	0.1718 [12]	Day^{-1}
β_1	The proportion of contact between non-Wolbachia susceptible mosquitoes and Wolbachia-infected mosquitoes	0.0087 [12]	Day^{-1}
β_0	The proportion of contact between dengue-infected mosquitos and Wolbachia-infected mosquitos	0.0195 [12]	Day^{-1}
N_h	Total human population	10^6 [Assume]	Person
N_v	Total population of non-Wolbachia mosquitos	8000 [Assume]	Mosquito
N_w	Total population of Wolbachia mosquitoes	3000 [Assume]	Mosquito

3.2 Stability Analysis of Equilibrium Points

The model equilibrium point is reached when there is no change in the dynamics of the system, or when $\frac{dS_h}{dt} = \frac{dI_h}{dt} = \frac{dV_h}{dt} = \frac{dR_h}{dt} = \frac{dA_v}{dt} = \frac{dS_v}{dt} = \frac{dI_v}{dt} = \frac{dP_v}{dt} = \frac{dA_w}{dt} = \frac{dS_w}{dt} = 0$. The dengue model in the system (1) has two equilibrium points, the non-endemic equilibrium points E_0 and the endemic equilibrium point E_1. The non-endemic equilibrium point is reached when there is no disease transmission in the population ($I_h = I_v = 0$). **Equation (1)** has the following equilibrium point E_0:

$$E_0 = (S_{h0}, 0, V_{h0}, P_{v0}, A_{v0}, S_{v0}, 0, P_{v0}, A_{w0}, S_{w0}) \quad (6)$$

where $S_{h0} = \frac{\Lambda(q+\mu_h)(p+\mu_h)}{\mu_h(\mu_h^2+(p+q+\delta)\mu_h+(p+q)\delta+pq)}, V_{h0} = \frac{\Lambda\delta(p+\mu_h)}{\mu_h(\mu_h^2+(p+q+\delta)\mu_h+(p+q)\delta+pq)}, R_{h0} = \frac{\Lambda\delta q}{\mu_h(\mu_h^2+(p+q+\delta)\mu_h+(p+q)\delta+pq)}$, $A_{v0} = \frac{\theta_v}{\mu_v+\sigma+\varepsilon}$, $S_{v0} = \frac{\theta_v\varepsilon}{(\mu_v+\sigma+\varepsilon)(\mu_v+\beta_1)}, P_{v0} = \frac{(\mu_v\sigma+\beta_1\sigma+\beta_1\varepsilon)\theta_v}{(\mu_v+\sigma+\varepsilon)(\mu_v+\beta_1)\mu_v}, A_{w0} = \frac{\theta_w}{\mu_w+\eta}, S_{w0} = \frac{\eta\theta_w}{\mu_w(\mu_w+\eta)}$.

Before analyzing the stability of the equilibrium point, the basic reproduction number of the system **Equation (1)** must first be calculated. The basic reproduction number is the number of secondary infections resulting from the primary infection to which the entire population is susceptible **[18]**. The basic reproduction number R_0 is the threshold for the spread of the disease. If $R_0 < 1$ the infection will become extinct, but if $R_0 > 1$ it will result in a pandemic situation. The amount of R_0 is determined using the Next Generation Matrix (NGM) method **[18]**. First, create a vector with the compartments that may induce virus transmission, $\mathbf{x} = (I_h, I_v)^T$. Then decompose $\mathbf{x}$ into $\mathcal{F} - \mathcal{V}$ to generate the Jacobi matrix of $\mathcal{F}$ and $\mathcal{V}$ which are evaluated at the non-endemic equilibrium points E_0, $\mathbb{F} = \left.\frac{\partial\mathcal{F}}{\partial\mathbf{x}}\right|_{E_0}$ and $\mathbb{V} = \left.\frac{\partial\mathcal{V}}{\partial\mathbf{x}}\right|_{E_0}$. Obtained $\mathcal{F} = \begin{pmatrix} \frac{\beta_h I_v S_h}{N_h} + (1-q)\beta_h \frac{I_v}{N_h} V_h \\ \frac{\beta_v I_h S_v}{N_h} \end{pmatrix}$, $\mathcal{V} = \begin{pmatrix} (\gamma+\mu_h)I_h \\ (\beta_0+\mu_v)I_v \end{pmatrix}$, $\mathbb{F} = \begin{pmatrix} 0 & \frac{\beta_h S_h}{N_h} + (1-q)\frac{\beta_h V_h}{N_h} \\ \frac{\beta_v S_v}{N_h} & 0 \end{pmatrix}$, and $\mathbb{V} = \begin{pmatrix} \gamma_h+\mu_h & 0 \\ 0 & \beta_0+\mu_v \end{pmatrix}$. Furthermore, the Next Generation Matrix (NGM) can be formed using the formula $NGM = \mathbb{F}\mathbb{V}^{-1}$ as follows:

$$NGM = \begin{pmatrix} 0 & \frac{\beta_h(S_{h0}+(1-q)V_{h0})}{(\beta_0+\mu_v)N_h} \\ \frac{\beta_v S_{v0}}{N_h(\gamma_h+\mu_h)} & 0 \end{pmatrix} \quad (7)$$

where $S_{h0} = \frac{\Lambda(q+\mu_h)(p+\mu_h)}{\mu_h(\mu_h^2+(p+q+\delta)\mu_h+(p+q)\delta+pq)}, V_{h0} = \frac{\Lambda\delta(p+\mu_h)}{\mu_h(\mu_h^2+(p+q+\delta)\mu_h+(p+q)\delta+pq)}$, and $S_{v0} = \frac{\theta_v\varepsilon}{(\mu_v+\sigma+\varepsilon)(\mu_v+\beta_1)}$. The basic reproduction number is obtained from the largest eigenvalue modulus of the NGM matrix, $R_0 = \rho(\mathbb{F}\mathbb{V}^{-1}) = \max|\lambda_i|$, as follows:

$$R_0 = \frac{\sqrt{(\gamma_h+\mu_h)(\beta_0+\mu_v)\beta_h(S_{h0}+(1-q)V_{h0})\beta_v S_{v0}}}{(\gamma_h+\mu_h)(\beta_0+\mu_v)N_h}. \quad (8)$$

Theorem 1. The non-endemic equilibrium point E_0 is locally asymptotically stable if $R_0 < 1$.

Proof. The Jacobi matrix of system (1) which is evaluated at the equilibrium point E_0 as follows:

$$J_0 = \begin{pmatrix} -\frac{\beta_h I_v}{N_h} - \delta - \mu_h & 0 & 0 & p & 0 & 0 & -\frac{\beta_h S_h}{N_h} & 0 & 0 & 0 \\ \frac{\beta_h I_v}{N_h} & -\gamma-\mu_h & (1-q)\beta_h\frac{I_v}{N_h} & 0 & 0 & 0 & \frac{\beta_h S_h}{N_h} + (1-q)\beta_h\frac{V_h}{N_h} & 0 & 0 & 0 \\ \delta & 0 & -\mu_h & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \gamma & \rho & -\mu_h & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\mu_v-\sigma-\varepsilon & 0 & 0 & 0 & 0 & 0 \\ 0 & -\frac{\beta_v S_v}{N_h} & 0 & 0 & \varepsilon & -\frac{\beta_v I_h}{N_h} - \beta_1 - \mu_v & 0 & 0 & 0 & 0 \\ 0 & \frac{\beta_v S_v}{N_h} & 0 & 0 & 0 & \frac{\beta_v I_h}{N_h} & -\beta_0-\mu_v & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \sigma & \beta_1 & \beta_0 & -\mu_v & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\mu_w-\eta & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \eta & -\mu_w \end{pmatrix} \quad (9)$$

Furthermore, the eigenvalues obtained from the Jacobi matrix J_0 are $\lambda_1 = -\mu_v$, $\lambda_2 = -(\mu_v+\sigma+\varepsilon)$, $\lambda_3 = -\mu_h$, $\lambda_4 = -(\mu_h+\rho)$, $\lambda_5 = -\mu_w$, $\lambda_6 = -(\mu_w+\eta)$, $\lambda_7 = -(\delta+\mu_h)$, $\lambda_8 = -(\beta_1+\mu_v)$, and $\lambda_{9,10}$ are the roots of **Equation (6)** below:

$$\lambda^2 + a_1\lambda + a_2 = 0 \quad (10)$$

where $a_1 = \mu_h + \mu_v + \beta_0 + \gamma$ dan $a_2 = \frac{\left((\gamma+\mu_h)(\mu_h+\delta)(\mu_v+\beta_1)(\mu_v+\beta_0)(\mu_v+\sigma+\varepsilon)N_h^2 - \beta_h\beta_v\Lambda\theta_v\varepsilon\right)}{(\mu_v+\sigma+\varepsilon)(\mu_v+\beta_1)N_h^2(\mu_h+\delta)}$.

According to the assumption of parameter positivity, $a_1 > 0$. The eigenvalue $\lambda_{9,10}$ will be negative if $a_2 > 0$.

$$a_2 = \frac{\left((\gamma+\mu_h)(\mu_h+\delta)(\mu_v+\beta_1)(\mu_v+\beta_0)(\mu_v+\sigma+\varepsilon)N_h^2-\beta_h\beta_v\Lambda\theta_v\varepsilon\right)}{(\mu_v+\sigma+\varepsilon)(\mu_v+\beta_1)N_h^2(\mu_h+\delta)} > 0$$

$$\Leftrightarrow \left((\gamma+\mu_h)(\mu_h+\delta)(\mu_v+\beta_1)(\mu_v+\beta_0)(\mu_v+\sigma+\varepsilon)N_h^2-\beta_h\beta_v\Lambda\theta_v\varepsilon\right) > 0$$

$$\Leftrightarrow (\gamma+\mu_h)(\mu_h+\delta)(\mu_v+\beta_1)(\mu_v+\beta_0)(\mu_v+\sigma+\varepsilon)N_h^2 > \beta_h\beta_v\Lambda\theta_v\varepsilon$$

$$\Leftrightarrow 1 > \frac{\beta_h\beta_v\Lambda\theta_v\varepsilon}{(\gamma+\mu_h)(\mu_h+\delta)(\mu_v+\beta_1)(\mu_v+\beta_0)(\mu_v+\sigma+\varepsilon)N_h^2} = R_0^2$$

In other words, if $R_0^2 < 1 \Leftrightarrow R_0 < 1$, the eigenvalue $\lambda_{9,10}$ will be negative. Therefore, the non-endemic equilibrium point E_0 is asymptotically stable if $R_0 < 1$. ■

Based on **Theorem 1**, it is concluded that the non-endemic equilibrium point is asymptotically stable if $R_0 < 1$. This means that disease-free conditions (the spread of dengue will stop or even become extinct) will be achieved if the threshold R_0 in equation (8) can be reduced so that the value reaches $R_0 < 1$. It is possible to achieve it by decreasing parameters that have a positive impact on R_0 and increasing parameters that have a negative impact on R_0. The basic reproduction number R_0 in equation (8) has a complicated form. Therefore, in subsection 3.3, a sensitivity analysis is provided to find out which parameters have the most influence on changes in the R_0 value.

The proposed dengue mathematical model is very complicated, though, which makes it hard to figure out the endemic equilibrium point analytically. This results in difficulty in analyzing the stability of the endemic equilibrium point analytically. Therefore, the stability analysis of the endemic equilibrium point E_1 can be carried out numerically by using the phase field with the help of the parameter values in Table 2.

3.3 Sensitivity Analysis

The sensitivity index is calculated using parameter sensitivity analysis, which gives a sense of the magnitude of the influence of changes in parameter values on the dynamics of the model. The parameters with an index value of one or a negative one has the largest influence on the model change rate. A sensitivity analysis was performed on the basic reproduction number R_0, which is the threshold for disease spread. The normalized sensitivity index of variable m to parameter k is defined by**[16]**:

$$\Upsilon_k^m := \frac{\partial m}{\partial k} \times \frac{k}{m}. \tag{11}$$

Thus, to obtain the sensitivity index of the β parameter to the basic reproduction number R_0 it is calculated using the formula:

$$\Upsilon_{R_0}^{\beta} := \frac{\partial R_0}{\partial \beta} \times \frac{\beta}{R_0}. \tag{12}$$

Parameters with a positive (negative) index will be directly proportional (inversely) to the basic reproduction number R_0. In other words, an increase (reduction) in the positive index parameter will accelerate (slow down) the rate of disease transmission. In contrast, an increase (reduction) in the parameter with a negative index will halt (accelerate) the spread of the disease. By applying the formula in **Equation (7)** to the basic reproduction number R_0 in **Equation (4)**, the parameters $\{\Lambda, \beta_h, \beta_v, \theta_v\}$ each have a sensitivity index of 0.5. While the other parameters have a complex sensitivity index. Therefore, the parameter values in **Table 2** are used to obtain the sensitivity index values. In **Table 3**, all of the parameter sensitivity index values are listed. According to **Table 3**, there are parameters with positive indices such as $\{\Lambda, \beta_h, \beta_v, \theta_v, \delta, p, \varepsilon\}$ and negative indices such as $\{\mu_h, q, \mu_v, \sigma, \beta_1, \beta_0\}$. If the infection rate β_h increases (decreases) by 10%, then the value of R_0 will increase (decrease) by 5%. In the opposite case, if the effectiveness of the q vaccine increases (reduces) by 10%, the R_0 value decreases (increases) by 2.045%.

Table 3. Parameter Sensitivity Index

Parameter	Sensitivity Index	Parameter	Sensitivity Index
Λ	0.5	μ_v	-0.8652
μ_h	-0.1107	ε	0.4562
β_h	0.5	σ	-0.3684

Parameter	Sensitivity Index	Parameter	Sensitivity Index
δ	0.0016	β_v	0.5
p	0.4910	β_1	-0.0772
q	-0.2045	β_0	-0.1453
θ_v	0.5		

3.4 Mathematical Models Of Dengue Transmission Dynamics With Seasonal Aspect

In this sub-chapter, mathematical models of dengue transmission in the **Equation (1)** is modified by including the seasonal aspect. It is assumed that the birth rate of mosquitoes varies according to season using the sine function with a one-year period, as shown below:

$$\left(1 + A \sin\left(\frac{2\pi t}{365}\right)\right) \tag{13}$$

where A is the strength of seasonality, $0 \leq A \leq 1$. Thus, the mathematical model of dengue transmission dynamics with seasonal aspect can be stated as follows:

$$\begin{aligned}
\frac{dS_h}{dt} &= \Lambda - \beta_h \frac{I_v}{N_h} S_h - (\delta + \mu_h) S_h + pR_h \\
\frac{dI_h}{dt} &= \beta_h \frac{I_v}{N_h} S_h + (1-q)\beta_h \frac{I_v}{N_h} V_h - (\gamma + \mu_h) I_h \\
\frac{dV_h}{dt} &= \delta S_h - (1-q)\beta_h \frac{I_v}{N_h} V_h - (q + \mu_h) V_h \\
\frac{dR_h}{dt} &= \gamma I_h + qV_h - (p + \mu_h) R_h \\
\frac{dA_v}{dt} &= \theta_v \left(1 + A \sin\left(\frac{2\pi t}{365}\right)\right) - (\varepsilon + \sigma + \mu_v) A_v \\
\frac{dS_v}{dt} &= \varepsilon A_v - \frac{\beta_v I_h S_v}{N_h} - (\beta_1 + \mu_v) S_v \\
\frac{dI_v}{dt} &= \frac{\beta_v I_h S_v}{N_h} - (\beta_0 + \mu_v) I_v \\
\frac{dP_v}{dt} &= \sigma A_v + \beta_0 I_v + \beta_1 S_v - \mu_v P_v \\
\frac{dA_w}{dt} &= \theta_w \left(1 + A \sin\left(\frac{2\pi t}{365}\right)\right) - (\eta + \mu_w) A_w \\
\frac{dS_w}{dt} &= \eta A_w - \mu_w S_w
\end{aligned} \tag{14}$$

Compartment descriptions and parameters can be seen in **Table 1** and **Table 2**.

3.5 Numerical simulation

Air temperature has the potential to influence dengue virus transmission in mosquito populations. Therefore, three weather scenarios are included in this simulation: scenario 1 for cold weather (air temperature 14 °C), scenario 2 for hot weather (air temperature 26 °C), and scenario 3 for moderate weather (air temperature between 14 and 26 °C)**[8]** . **Table 4** shows the parameter scores in the three scenarios. Then three variations of the seasonal strength factor A are used, namely $A = 0.1$, $A = 0.3$, and $A = 0.8$ **[14]**. The simulation was carried out using the parameter values listed in **Table 2** at a simulation time of $t = 365$ days. The initial values for each compartment were $(S_{h0}, I_{h0}, V_{h0}, R_{h0}, A_{v0}, S_{v0}, I_{v0}, P_{v0}, A_{w0}, S_{w0}) = (83297, 233, 0, 90, 4500, 2500, 1500, 100, 800, 200)$. The solution of the proposed model is solved numerically using Runge-Kutta 4th algorithm.

Table 4. Parameter scores of three scenarios

Parameter	Scenario 1 (cold climate)	Scenario 2 (hot climate)	Scenario 3 (mild climate)
β_h	0.11	0.95	0.2
β_v	0.12	0.99	0.2
μ_v	0.04	0.03	1/15

Figure 2 shows the simulation results for Scenario 1 (cold climate). Based on **Figure 2**, there aren't many changes between the population dynamics I_v and I_h when there are seasonal effects and when there aren't. The simulation results for scenario 2 (hot climate) are shown in **Figure 3**. **Figure 3 (**c) shows that seasonal factors have a significant impact on the dengue infected human population I_h. The peak of infection in this scenario is the highest of the three, reaching 11 thousand people. The simulation results for scenario 3 (mild climate) are presented in **Figure 4**. According to **Figure 4**, there are very slight variations in population dynamics between I_v and I_h under seasonal and non-seasonal. Even after reaching a high peak of infection, the total human population infected with dengueI_h may decrease to zero in all three scenarios. This is due to the parameters of vaccination and the release of Wolbachia into the wild.

Meanwhile, based on the simulation results of the three scenarios in **Figure 2 – Figure (4)**, it can be seen that the population dynamics of susceptible-Wolbachia mosquitoes (S_w) are strongly influenced by seasonal effects. The greater the seasonality, the greater the fluctuation in the population of susceptible-Wolbachia mosquitoes. This means that in certain periods, the population of susceptible-Wolbachia mosquitoes will boom. And conversely, in other periods, the population of susceptible-Wolbachia mosquitoes will decrease quite drastically.

Figure 2 – Figure (4)also displays the dynamics of the vaccinated human population (V_h) based on the application of the three scenarios. In Figure 2 (scenario 1) and Figure 4 (scenario 3), the V_h population is not significantly affected by seasonal factors applied to mosquito population dynamics. However, in Figure 3 (Scenario 2), the V_h population is quite affected by seasonal factors. Based on Figure 3, the greater the seasonal effect, the greater the influence on the population size (V_h). Overall, seasonal effects influence the dynamics of the entire population in the dengue model that has been prepared.

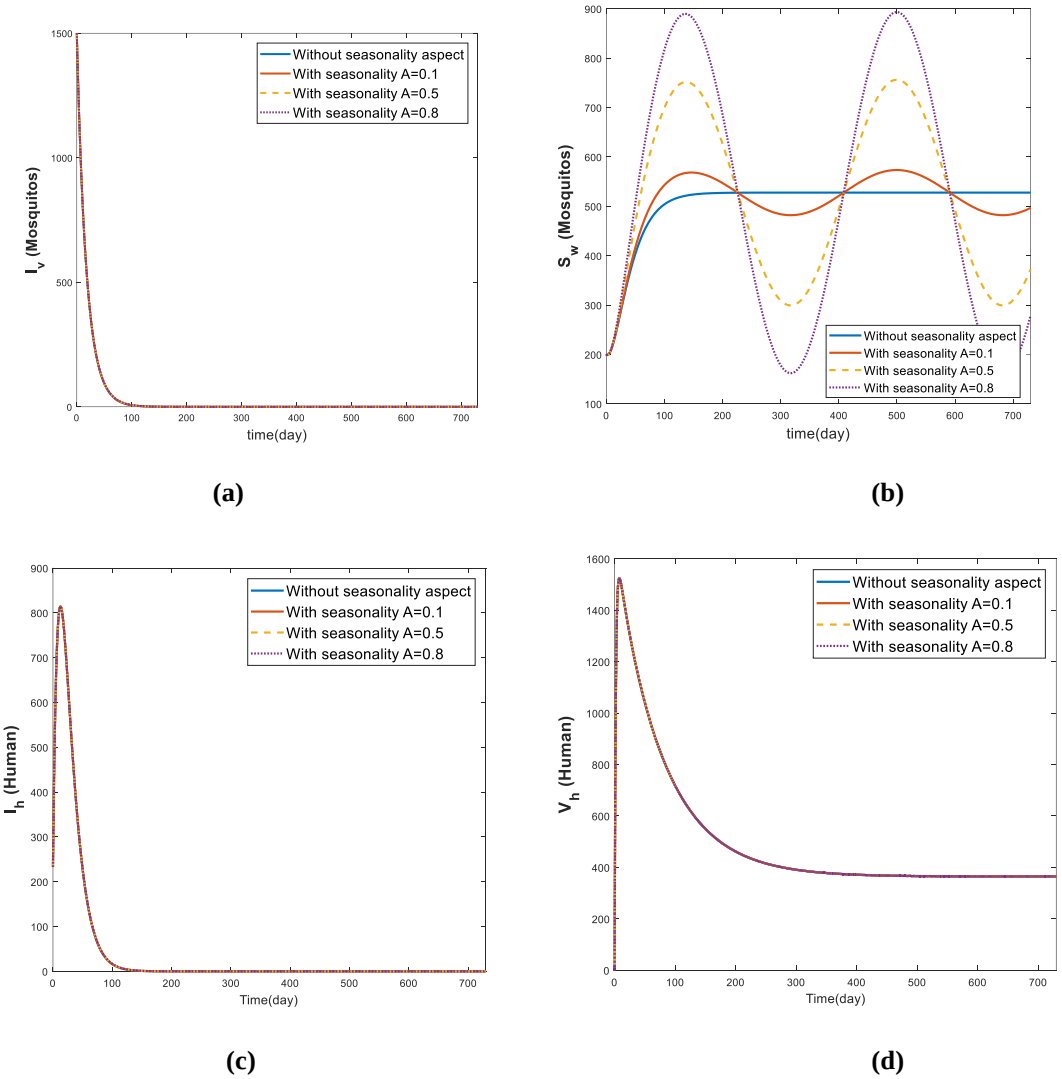


Figure 2. The Dengue Model Dynamic of (a)I_v (b)S_w (c)I_h (d)V_h with Seasonal and Non-Seasonal Aspects for Scenario 1

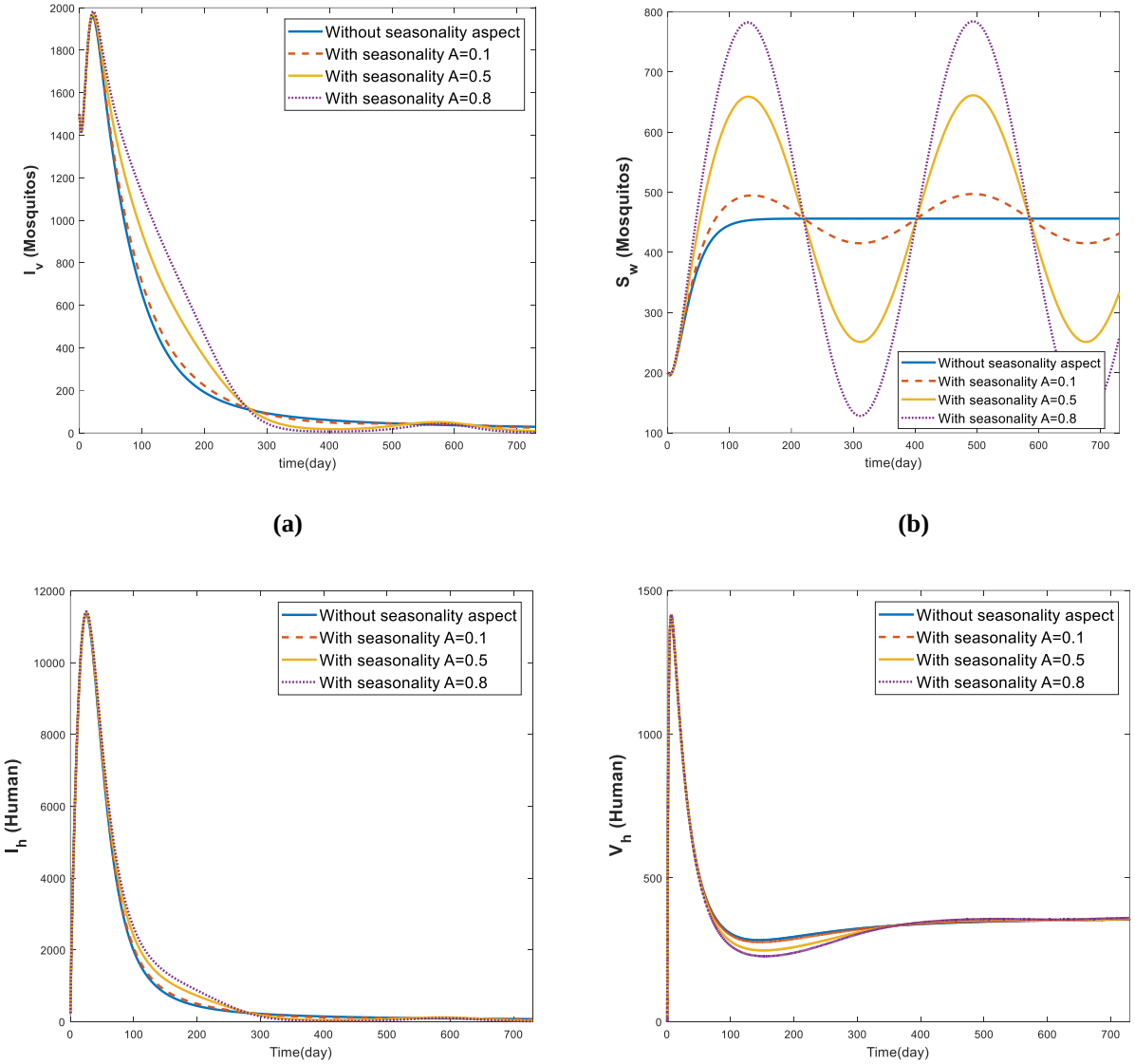


Figure 3. The Dengue Model Dynamic (a)I_v (b)S_w (c)I_h (d)V_h with Seasonal And Non-Seasonal Aspects For Scenario 2

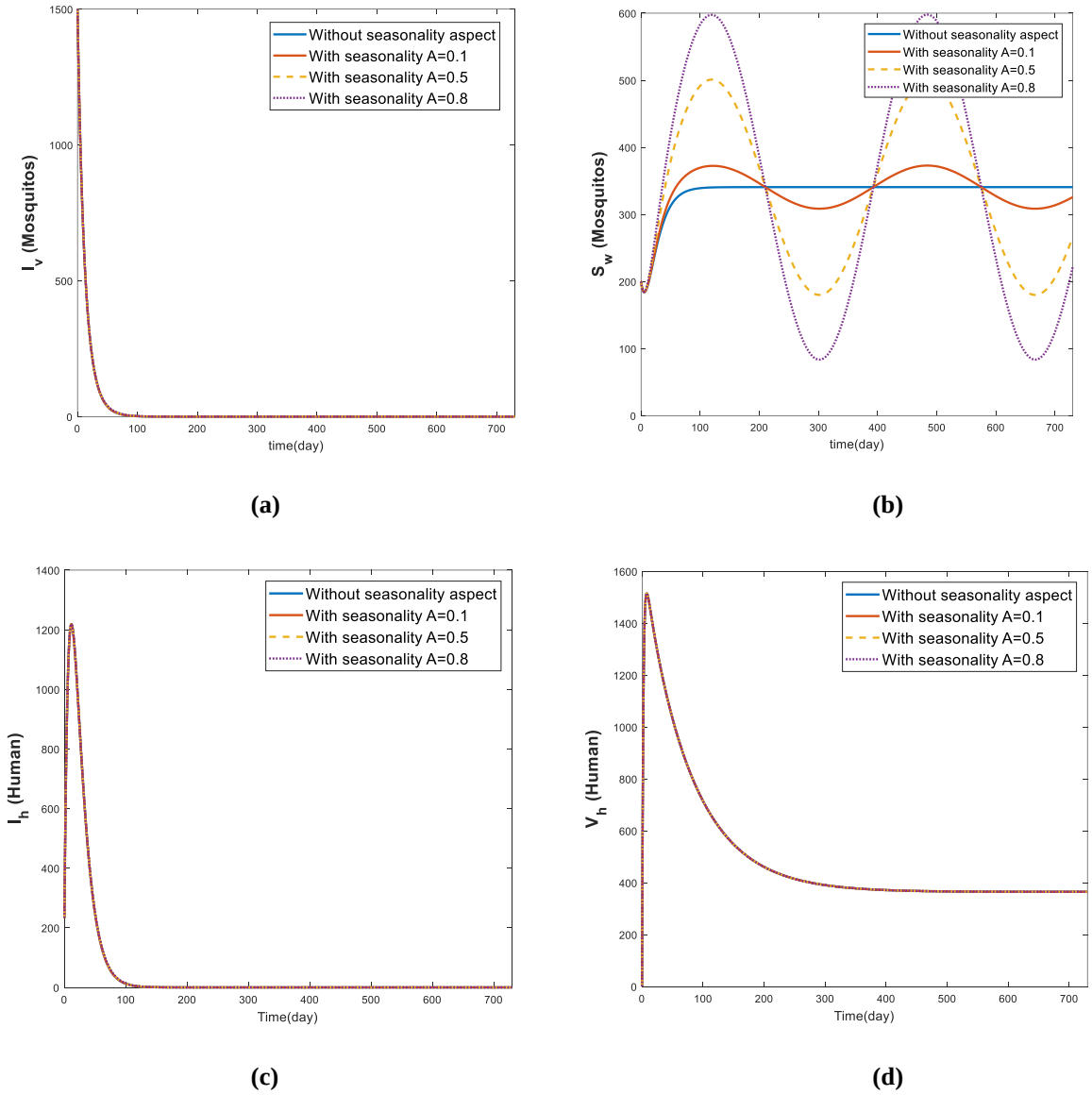


Figure 4. The Dengue Model Dynamic (a)I_v (b)S_w (c)I_h (d)V_h with Seasonal And Non-Seasonal Aspects For Scenario 3

4. CONCLUSIONS

A mathematical model for the spread of dengue has been developed by evaluating the seasonal variables that influence the dynamics of the mosquito population. The periodic term on the mosquito birth rate represents the seasonal aspect. Based on the stability of the equilibrium point analysis, it is discovered that the equilibrium point free of disease is locally asymptotically stable if $R_0 < 1$. Then, using three different scenarios based on air temperature changes, a numerical simulation was performed. Based on numerical simulations, it was discovered that seasonal variables provide mosquito dynamics with an annual recurring pattern. The largest peak of infection in humans is produced by numerical simulation in scenario 2 (air temperature 26 °C), with 11 thousand infected persons. Following the model used which involves vaccination and Wolbachia release, the peak of the infection may reduce to zero infections.

ACKNOWLEDGMENT

We appreciate LPPM Institute of Technology Telkom Purwokerto's support of research through the internal grant program. Additionally, we would want to express our gratitude to everyone who helped make the research process easier and more trouble-free.

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