SCIREA Journal of Mathematics
http://www.scirea.org/journal/Mathematics
December 13, 2021
Volume 6, Issue 6, December 2021
https://doi.org/10.54647/mathematics11303

Optimum Control in the model of blood fever disease with vaccines and treatment

PARDI AFFANDI [1*], M.Mahfudz S [1], Oscar A.B [1], A. Rahim [2]

[1] Faculty of Mathematics and Natural Science, Lambung Mangkurat University

[2] Kopertis Wilayah XI Kalimantan

Abstract.

Dengue Hemorrhagic Fever (DHF) is a disease caused by an arbovirus that enters the human body through the Aedes aegypti or Aedes albopictus mosquito. Dengue Hemorrhagic Fever (DHF) is characterized by symptoms of dengue fever; headache; reddish skin that looks like measles; and muscle and joint pain. In some patients, dengue fever can turn into one of two life-threatening forms that lead to decreased immunity. Various ways have been done to prevent the cause of DHF, but the results have not been optimal. The problem of the spread of the dengue virus can also be modeled mathematically and through the stability of the equilibrium point, the dynamics or behavior of the model can be determined. DHF spread can be suppressed by giving control in the form of treatment. This type of treatment is given to infected individuals. This treatment can be controlled optimally by applying the Pontryagin maximum principle. Pontryagin's maximum principle is the optimal control solution in accordance with the objective of maximizing the performance index. The purpose of this study is to discuss a mathematical model for the transmission of the dengue virus in the human body. As an effort to inhibit dengue virus replication, treatment control is used in the model, starting from the formation of a model from determining assumptions, parameters so that the SIV-T model is obtained, determining stability analysis, and then involving optimal control with Pontryagin's minimum principle to carry out optimal control strategies for the fever disease model. Dengue Hemorrhagic Fever (DHF) was also simulated using the software. The results of this study are to explain how the model of the spread of the dengue virus in the human body is formed, obtained 2 equilibrium points, namely a disease-free equilibrium point, local asymptotically stable, and a local asymptotically stable endemic point. The optimal control strategy in the spread model of the dengue virus aims to maximize the number of healthy cells by administering a control in the form of treatment.

Keywords: DHF disease model, optimal control, Pontryagin's maximum principle.

INTRODUCTION

Instruments that underlie the influence of disease spread can be detected through mathematical modeling, applying control strategies, and their applications. Many references that apply control theory to disease problems include [1], [2], [3], [4], [5], [6] also by Kermack, WO and Mc Kendrick, A. G [7], Bellomo, N. and Preziosi, L. [8]. However, control theory is also widely applied to industrial and inventory problems [9], [10]. This study used many disease models were used as objects in this study, including malaria, scabies, diarrhea, dysentery, and dengue hemorrhagic fever (DHF).

DHF is an infection caused by the dengue virus. Several types of mosquitoes transmit or spread the dengue virus. Some symptoms of dengue are fever; headache; reddish skin that looks like measles; and muscle and joint pain. In some patients, dengue fever can change into two life-threatening forms [16], [17]. Much research on the spread of dengue fever has been carried out, which is applied to the host-vector model used. The controls such as prevention and insecticide could use the best role in the disease eradication from the community [28].

Based on Banjarmasin City Health Service Report [14] Kalimantan Province Health Profile data for [15], this disease is related to environmental conditions and community behavior, DHF is endemic both in urban areas and well in rural areas.

Figure 1 shows that the morbidity rate in South Kalimantan Province in 2019 is 56.6 per 100,000 with 2,401 cases with a total of 14 cases of dengue fever (CFR / death rate 0.6%).

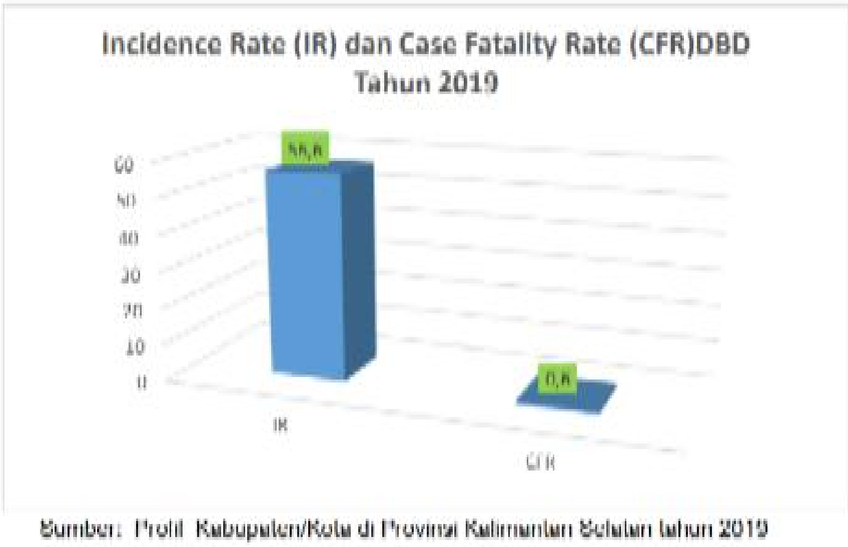

Figure 1 Incidence Rate (IR) and Case Fatality Rate (CFR) of DHF in South Kalimantan in 2019.

Dengue Hemorrhagic Fever (DHF) always increases at the beginning of the rainy season, this is due to a large amount of water where is a place for Aedes aegypti mosquitoes, Aedes albopictus, Aedes Africanus, anopheles, and others. However, Aedes aegypti is the most dangerous and mosquito found in the environment. This mosquito cause dengue hemorrhagic fever (DHF). Specially flood impact that hit, South Kalimantan region in mid-January 2021 brought out a high risk of this disease. The flood submerged thousands of houses, according to Head of BNPB Disaster Data, Information, and Communication Center Raditya Jati, it came from Tapin Regency, Banjarbaru city, Hulu Sungai Tengah Regency, Hulu Sungai Selatan Regency, Banjarmasin City, and Banjar Regency. This condition is feared to be a potential condition named extraordinary event (KLB) of Dengue Hemorrhagic Fever (DHF).

There are many ways that the government through the South Kalimantan Health Office, especially the Banjar Regency and Banjarmasin City governments, can overcome this dengue problem, but cooperation is still needed to solve this problem properly. This research involves optimal control models and theories. Prevention of disease spread through optimal control has been widely studied, such as optimal control studies on the spread model of dengue fever with insecticide control [16], and chemical cure [17].

The model used is a system of differential equations that represents the SIV-T epidemic that describes Dengue Hemorrhagic Fever. The optimal control strategy is proposed to reduce the number of infected humans by using a control in the form of treatment. The type of treatment used is appropriate [15], [19], given to infected individuals. This treatment can be optimally controlled by applying the Pontryagin maximum principle. The Pontryagin maximum principle is used to find the necessary conditions for the existence of optimal control. The numerical approximation method is used to solve the optimal control system.

The purpose of discussing a mathematical model for the transmission of the dengue virus in the human body. In an effort to inhibit dengue virus replication, treatment control is used in the model, starting from the formation of a model from determining assumptions, parameters so that the SIV-T model is obtained, determining stability analysis, and then involving optimal control with Pontryagin's minimum principle to carry out optimal control strategies for the model of fever. Dengue Hemorrhagic Fever (DHF) was also simulated using the software.

METHODOLOGY

This research begins with implying the previous DHF model in order to compile initial assumptions and determine the initial model. Model mathematical discussed is the transmission of the dengue virus in the body [9]. Secondary data are collected by questionnaires distributed to the community around Martapura river banks to obtain appropriate, reliable, and valid data. These data highly relevant to the research objectives are collected, a good data collection mechanism must first be prepared so that the data obtained will be valid, accurate, and reliable in model formation.

The data that will be used in this research is survey data distributed to the community around Martapura River banks in Banjarmasin City. The processing research data, start with determining the most influential parameters as the causative factors for dengue hemorrhagic fever (DHF). This process uses a regression method so that the dominant factor is obtained from several factors.

RESULTS AND DISCUSSION

Research data

The data collection method is carried out in two ways, namely offline and also online. The offline method is done by distributing questionnaires around the banks of the Martapura River. Before the step of forming the model, the first step is to conduct a data survey related to the variables that have the most influence on the model. The first step is to carry out a collection process, which is carried out in community settlements around the Martapura River. The polling process is carried out to obtain some of the most influential variables that will be used in the DHF disease model by first conducting validation and reliability tests. After obtaining valid data, then data reliability testing is carried out to find out whether an instrument is reliable enough to be used as a data collection tool. The concept of reliability refers to the notion that an instrument can be trusted to be used as a data collection tool. From the test, the output is obtained so that. After obtaining valid and reliable data, the next step is to distribute the questionnaires to respondents offline and online. The distribution of online questionnaires was carried out using a webinar involving representatives of schools on the Martapura Riverbank, Banjarmasin.

Modeling the Spread of the DHF Virus in the Human Body

Based on the Diekmann and Heesterbeek Model, the basis of the known epidemic model is the SIR model. This model divides the population into three sub-populations, namely the susceptible sub-population, the infectious sub-population, and the Removed sub-population. From this basic model, the model will be able to develop into models with other variations. The growth of each sub-population will be modeled by differential a equation so that the growth rate of the sub-population will form a differential system.

The model that will be discussed in this chapter is the SIV-T (Susceptibles, Infectious, Viruses, and Treatment) model on the transmission of the dengue virus in the human body by paying attention to the facts and assumptions used. This model is assumed to consist of four compartments, namely:

1. Susceptible group, denoted by S(t), is the number of classes of susceptible cell population at time t.

2. Infected group, denoted by I (t), namely the number of population classes of cells infected at time t.

3. Dengue virus population class group (viruses), which is then denoted by V (t)

4. Treatment group (herbal treatment) is denoted by T (t) class population of cells infected with the virus and then get herbal treatment.

The assumptions used in this model are as follows:

1. There are no other microorganisms that attack the human body apart from the dengue virus.

2. Dengue virus infection occurs internally, namely in the human body.

3. The herbal treatment given can inhibit the dengue virus reflection.
4. The population is closed and constant.
5. T cells work to kill the dengue virus
6. Herbal medicine can inhibit the replication of the dengue virus
7. The density of susceptible cells increases at a constant rate of a.

The variables and parameters used in the model of the dengue virus transmission process in the human body are presented in the table below:

Table 4.1 List of Variables

No	Variables	Explanation
1	*S(t)*	susceptible cell population class
2	*I(t)*	virus-infected cell population class
3	*T(t)*	The class population of cells infected with the virus then receive herbal medicinal treatment
4	*V(t)*	dengue virus population classes

Table 4.2 List of Parameters

No	Para meters	Explanation
1	a	The pure birth rate of susceptible cells
2	b	The proportion of the number of dengue viruses that transmit
3	d	The pure cell death rate of susceptible cells
4	w	Pure cell death of rate infected cells
5	n	Number of dengue virus duplications
6	m	The proportion number of infected cells that produce the virus
7	c_1	Dengue of virus pure death rate
8	c_2	Dengue of virus death rate caused by T cells
9	p	The death rate of dengue virus caused by herbal treatment
10	q	The rate of infected cells receiving herbal treatment

Mathematical Model Formation

The formation of a mathematical model uses the SIT-V Model, which transmits the dengue virus in the human body. In the construction of the model, it is divided into 4 (four) population class compartments, namely S class population of susceptible cells (susceptible), I class population of cells infected (infectious) virus, T class population of cells infected with the virus then get herbal treatment and population class V dengue viruses (viruses).

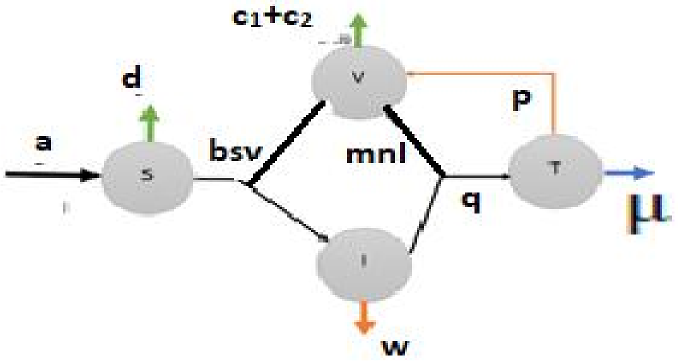

Figure 2. Diagram of the Dengue Virus Transmission Process in the Human Body

Based on the diagram above, the things that affect the spreading of. The dengue virus is presented in the mathematical model in Figure 4.1.

$$f_1(S,I,V,T) = aS - bSI - bSV - dS$$

$$f_2(S,I,V,T) = bSI - wI - mnI - qIT$$

$$f_3(S,I,V,T) = qIT - \mu T - pTV$$

$$f_4(S,I,V,T) = mnI + pTV - (c1 + c2)V$$

Then the equilibrium point will be obtained if it is satisfied

$$aS - bSI - bSV - dS = 0$$

$$bSI - wI - mnI - qIT = 0$$

$$qIT - \mu T - pTV = 0$$

$$mnI + pTV - (c1 + c2)V = 0$$

So that it will obtain a satisfactory equilibrium point

$$Q_0 = (S_0^*, I_0^*, V_0^*, T_0^*) = \left(\frac{(mn+w)}{b}, 0,0,0\right)$$ and

$$Q_1 = (S_0^*, I_0^*, V_0^*, T_0^*) = \left(\frac{(mn+qT+w)}{b}, \frac{b(\mathrm{pT}-(c1+c2)) - bmn - d(\mathrm{pT}-(c1+c2))}{a(\mathrm{pT}-(c1+c2))}, \frac{-mnI}{(\mathrm{pT}-(c1+c2))}, \frac{\mu}{(qI+pV)}\right)$$

Basic reproduction number (R_0) is a parameter used to determine the spread of the dengue virus and $R_0$is used as a measure to express the level of dengue virus infection.

To obtain R_0, the following calculation is carried out, a population is said to be virus-free if the virus will gradually disappear over time so that endemic does not occur. Therefore R_0 can be obtained if the change in the spread of the dengue virus, to time is less, than zero, the reproduction number is othreetained

$$R_0 = \frac{bS - mn - qT}{w} < 1$$

Lemma 4.1

Free of equilibrium for DHF locally asymptotically at stable if $R_0 < 1$ and not stable if $R_0 > 1$.

Proof:

The equation model is a system of nonlinear differential equations, it can be determined by linearizing using one way with Jacobian matrix. The equation above supposes to be Jacobian matrix is obtained as follows :

$$= \begin{bmatrix} a - bI - bV + d & -bS & -bS & 0 \\ bI & bS - w - mn - qT & 0 & -qI \\ 0 & qT & -pT & qI - \mu - pV \\ 0 & mn & pT - c_1 - c_2 & pV \end{bmatrix}$$

It can determine eigenvalues of the DHF model at the virus-free equilibrium point, a substitution is used $Q_0 = (S_0^*, I_0^*, V_0^*, T_0^*) = \left(\frac{(mn+w)}{b}, 0,0,0\right)$ value will be obtained

$$J = \begin{bmatrix} a + d & -(mn + w) & -(mn + w) & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -\mu \\ 0 & mn & -(c_1 + c_2) & 0 \end{bmatrix}$$

the characteristics equation and eigen values obtained from the dengue virus spread model $\lambda_1 = -(a + d)$, $\lambda_2 = -\mu$ dan $\lambda_3 = 0$ and $R_0 < 1$

hence the virus-free equilibrium point is asymptotically stable, This explains that in a long time no dengue virus had attacked so that no cells were infected.

Than $Q_1 = (S_0^*, I_0^*, V_0^*, T_0^*) = \left(\frac{(mn+qT+w)}{b}, \frac{b(\mathrm{pT}-(c1+c2)) - bmn - d(\mathrm{pT}-(c1+c2))}{a(\mathrm{pT}-(c1+c2))}, \frac{-mnI}{(\mathrm{pT}-(c1+c2))}, \frac{\mu}{(qI+pV)}\right)$

Then the next step is to find the characteristic equation using $|\lambda I - J| = 0$ and the characteristics equation and eigenvalues obtained from the dengue virus spread model

$$\lambda^4 + A\lambda^3 + B\lambda^2 + C\lambda + D = 0$$

with

$$A = (- g - d - k - a - bc)$$

$$B = (gk + dk + dg + ei - hj + bck + bcg - bcf + ga + da - acb)$$

$$C = (- dgk - efj + eig + dhj - bcgk - bchi + bcfk + bchj - gka - dka - dga - eia + hja - acbk - acbg + acbf)$$

$$D = (dgka + efjq - eiga - dhja + acbgk + acbhi - acbfk - acbhj)$$

Furthermore, using the Routh criteria, it is known the similarities in characteristics

$$\lambda^4 + A\lambda^3 + B\lambda^2 + C\lambda + D = 0$$

Thus, the Routh table is obtained as follows:

$$\begin{array}{llll}
\lambda^4 & 1 & B & D \\
\lambda^3 & A & C & 0 \\
\lambda^2 & \frac{AB - C}{A} & \frac{D}{A} & . \\
\lambda^1 & \frac{(AB - C)C - A^2D}{AB - C} & . & . \\
\lambda^0 & \frac{(AB - C)CD - A^2D^2}{AB - C} & . & .
\end{array}$$

To be stable, then the value of $A > 0$, $AB - C > 0$, $(AB - C)C - A^2D > 0$, $(AB - C)CD - A^2D^2 > 0$.

Optimal Control of DHF Disease Model

It is known that the DHF model is locally asymptotically stable at the two equilibrium points obtained. Furthermore, because the distribution of the model is stable, the model will be controlled. Control is given in the form of treatment where the vaccin is given to individuals who are susceptible to infection.

Optimal control in the models aim to best the number of healthy cells by administering control in the form of vaccin that can inhibit infected cell in the human of body. The vaccin can be optimally controlled with maximum principle. Pontryagin's maximum principle is such a condition that the best solution will obtained in accordance with the objective of maximizing the performance index.

Equations *state* : $\dot{x} = f(x(t), u(t), t)$ with $x = \begin{bmatrix} S \\ I \\ T \\ V \end{bmatrix}$ than *state* become $\dot{x} = \begin{bmatrix} \dot{S} \\ \dot{I} \\ \dot{T} \\ \dot{V} \end{bmatrix}$ or

$$\dot{x} = \begin{bmatrix} aS - bSI - bSV - dS \\ bSI - wI - mnI - qIT \\ qIT - \mu T - pTV \\ mnI + pTV - (c1 + c2)V \end{bmatrix}$$

The performance index equation is based on the following equation:

$$J(u) = \int_{t_0}^{t_1} L(x(t), u(t), t)dt$$

where t_0 is the start time, t_f is the end time, x(t) is the state variable and u(t) is the control variable. The performance index equation is expressed as a system from the initial state to the final state, namely:

$$J(T, u) = \int_{t_0}^{t_f} (T - A(u(t))^2)\, dt$$

where T is the initial state of healthy cells, A is the weight parameter used in the control and u(t) is the vaccin control. Then, the maximum value of J(u)=1/2 for u(t)=1 which indicates that the vaccine is working optimally so that the weight parameter can be assumed to be A=1/2 γ where γ is the controlling weight in the form of treatment. Furthermore, u is squared so that it becomes a quadratic function u^2 to maximize the action of the vaccine by multiplying it so that the performance index for the model of the spread of DHF is as follows:

$$J(T, u) = \int_{t_0}^{t_f} (T - \tfrac{1}{2}\gamma(u(t))^2)\, dt$$

boundary conditions $t_0 < t < t_f$ and $0 \leq u(t) \leq 1$

where t_0 is the initial time when DHF-infected cells are given the drug and t_f is the final time when DHF-infected cells are given the vaccin. Then, based on Pontryagin's maximum principle, the step is to determine the Hamiltonian function, which is as follows:

$$H(x(t), u(t), \lambda(t), t) = L(x(t), u(t), t) + \lambda(t) f(x(t), u(t), t)$$

$$= \left(T - \tfrac{1}{2}\gamma(u(t))^2\right) + (\lambda_1 \quad \lambda_2 \quad \lambda_3 \quad \lambda_4)$$

$$\begin{pmatrix} aS - bSI - bSV((1 - u(t)) - dS \\ bSI - wI - mnI - qIT \\ qIT - \mu T - pTV((1 - u(t)) \\ mnI + pTV - (c1 + c2)V \end{pmatrix}$$

Then, the last step is to substitute the u* (t) equation that has been obtained into the state equation to obtain the optimal solution form. Here are the results of the optimal system of equations obtained:

$$\dot{S} = \frac{\partial H}{\partial \lambda_1} = aS - bSI - bSV((1 - \left(\min\left(\max\left(0, \frac{V(\lambda_1 bS + \lambda_3 pT)}{\gamma}\right), 1\right)\right)) - dS$$

$$\dot{I} = \frac{\partial H}{\partial \lambda_2} = bSI - wI - mnI - qIT$$

$$\dot{V} = \frac{\partial H}{\partial \lambda_3} = qIT - \mu T - pTV((1 - \left(\min\left(\max\left(0, \frac{V(\lambda_1 bS + \lambda_3 pT)}{\gamma}\right), 1\right)\right))$$

$$\dot{T} = \frac{\partial H}{\partial \lambda_4} = mnI + pTV - (c1 + c2)V$$

Based on the description above, to get S, I, T, and V from the best form of u* (t), it is necessary to solve the nonlinear state and costate equations. Since nonlinear systems difficult to solve analytically, we can use solved numerically. For the model we consider a = 7, b = 0,007, d = 0.00000043, w = 0.09, n= 90.67, m = 0,02 c1= 11, c2= 18, p = 5, dan q = 10.

The optimal control on the DHF distribution model obtained can be described in graphical form. The results of the optimal system of equations that have been obtained are simulated using the MATLAB application. In the simulation of DHF spread model by defining several parameters.

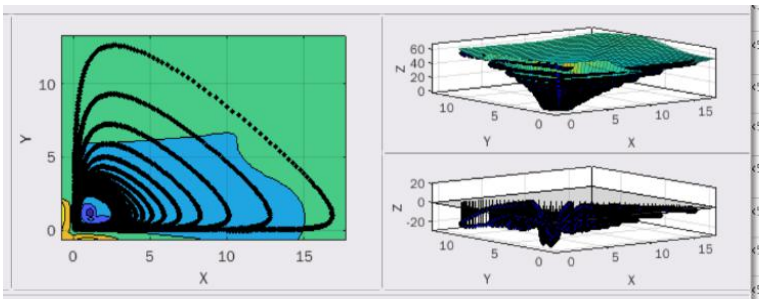

Figure 3. Simulation of the spread of DHF before given a controller

Its clear from fig 3 tend to improve from time to time. There are several simulations represented by several different images. However that everything in the picture shows that the spread of the dengue virus is increasing.

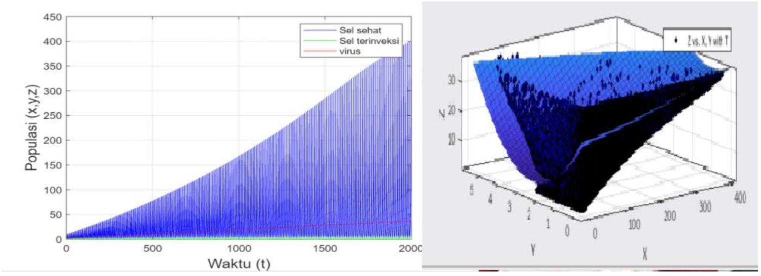

Figure 4. Simulation of the spread of DHF after being given a controller

Furthermore, in the next simulation fig 4 using the existing control variables, it is very clear that the DHF virus cells and infected cells are decreasing while healthy cells tend to increase over time.

CONCLUSION

Based on the results and discussion of this research, the following conclusions can be drawn:

1. The model of the spread of DHF in the human body can be written as follows:

$$f_1(S,I,V,T) = aS - bSI - bSV - dS$$

$$f_2(S,I,V,T) = bSI - wI - mnI - qIT$$

$$f_3(S,I,V,T) = qIT - \mu T - pTV$$

$$f_4(S,I,V,T) = mnI + pTV - (c1 + c2)V$$

2. The simulation results obtained show that the treatment given to the maximum can increase the number of cells and reduce the number of cells infected with DHF.

ACKNOWLEDGMENT

Thank you to the DIPA PNBP of Lambung Mangkurat University 2021 with No : SP DIPA - 023.17.2.677518/2021 and SK Rector No : 697/UN8/PG 2021 for being willing to fund this research activity.

REFERENCE

[1] Affandi, P., Faisal 2018. *Optimal control mathemathical SIR model of malaria spread in South Kalimantan*, Journal of Physics: Conference Series 1116 (2), 02200.

[2] Affandi, P., 2020. *Optimal control for dysentery epidemic model with treatment*, International Journal of Scientific and Technology Research, 2020, 9(3).

[3] Affandi, P., Salam N 2021. Optimal Control of diarrhea Disease model with Vaccination and Treatment, Journal of Physics: Conference Series, 2021, 1807(1), 012032.

[4] Affandi P., Faisal. (2017). Optimal Control Model of Malaria Spread in South Kalimantan, Halaman 54-61.

[5] Affandi, P., 2017. *Kendali Optimal pada Penentuan Interval Waktu dan Dosis Optimal pada Penyakit Malaria*. https://publikasi ilmiah.ums.ac.id /handle/11617/10150.

[6] Affandi, P., 2019. Kendali Optimal Pada Model Penyakit Scabies. Konferensi Pendidikan Nasional 1 (1), 187-196.

[7] Kermack, W. O. and McKendrick, A. G., 1927. A Contribution to the Mathematical Theory of Epidemics, Royal Society.

[8] Bellomo, N.& L. Preziosi. 1995. *Modelling Mathematical Method and Scientific Computation* . CRC press. Florida.

[9] Lotfi Tadj, A.M Sarhan, Awad El-Gohary Optimal control of an inventory system with ameliorating and deteriorating items. Applied Sciences 243-255.

[10] Affandi, P., 2015, Optimal Inventory Control Stochastic With Production Deteriorating. IOP Conference Series: Materials Science and Enginering, 300 (2018) 012019 doi:10.1088/1757-899X/300/1/012019.

[11] Esteva, L., dan Vargas, C., 1998, Analysis of a Dengue Disease Transmission Model, Mathematical Biosciences, 150, 131-151.

[12] Sheng-Qun Deng 1., Xian Yang 1., 2020. A Review on Dengue Vaccine Development, National Library of Medicine.

[13] Puntani Pongsumpun1., 2019. Optimal control of the dengue dynamical transmission with vertical transmission. Advances in Diffrence Equations. A Springer open Journal.

[14] Laporan Dinas Kesehatan Kota Banjarmasin. Kasus DBD Di Kota Banjarmasin Tahun 2013-2016. Banjarmasin: Dinas Kesehatan Kota Banjarmasin Provinsi Kalimantan Selatan; 2016.

[15] Data Profil Kesehatan Propinsi Kalimantan tahun 2019.

[16] Katrina Pareallo., W. Sanusi, 2018. Kontrol optimal pada model epidemik SIR penyakit demam berdarah *Indonesian Journal of Fundamental Sciences Vol.4, No.2, October 2018.*

[17] Rodrigues, H.S., Monteiro, M.T.T., dan Torres, D.F.M., 2010, Insecticide Control in a Dengue Epidemics Model, *Numerical Analysis and Applied Mathematics*, 1281, 979-982.

[18] Dumont, Y., dan Chiroleu, F.,, 2010, Vector Control for the Chikungunya

[19] Disease, *Mathematical Biosciences and Engineering*, 7, 313-345.
[20] Farlow, S.J.1994. *An Introduction to Differential Equation and Their Applications.* Dover Publications, United States of America.
[21] Braun, M. 1992. *Differential Equation and Their Application-Fourth Edition.* John Wiley & Sons. New York.
[22] Perko, L. 1991.*Differential Equation an Dynamical systems*. Text in Apllied Mathematic vol 7. Springer-Verlag, New York, USA.
[23] Gantmacher, F.R. 1959. *The Theory of Matrices.* Chelsea Publishing Company. New York.
[24] Burghes, D.N. 1980. *Introduction to Control Theory Including Optimal Control.* Springer-Verlag. New York.
[25] Muhammad Altaf Khan, Fatmawati, 2021, Dengue infection modeling and its optimal control analysis in East Java, Indonesia Research Article Volume 7, Issue 1.