Sistematic Review: Mathematics Model Epidemiology of Dengue Fever

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Sistematic Review: Mathematics Model Epidemiology of Dengue Fever

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Abstract Dengue Hemorrhagic Fever (DHF) is a disease caused by an arbovirus that enters the human body through the Aedes aegypti mosquito. Dengue Hemorrhagic Fever is characterized by symptoms, headache; reddish skin that looks like measles; and muscle and joint pain. The spread of dengue hemorrhagic fever (DHF) globally has tended to be higher in the last 50 years, thus giving rise to ideas for systematic prevention. Many factors cause this dengue fever, climate factors, weather, residential density, and other factors. The Epidemiological Model of DHF can provide a pattern of prevention against dengue outbreaks so that the problem can be modeled mathematically and through the stability of the equilibrium point, the dynamics or behavior of the model can be determined. The spread of DHF can be suppressed by providing control in the form of vaccines, eradication with insecticides and treatment. This review article aims to provide a systematic description of the causative factors, a mathematical model of DHF with an epidemiological approach. To get the right model related to the SIR epidemiological mathematical model and its modifications which can be an alternative solution to describe and analyze the model mathematically. The methodology used is to systematically search for journals and articles from August 2021 to April 2022. This is done by accessing electronic journal portals such as: Elsevier, Springer, ResearchGate, google scholar, Scient direct and so on. Other references also use national journals and information on the Ministry of Health's website. The results of a review of factors that cause dengue fever are physical environmental factors that have a significant influence on rainfall and air temperature. Mathematical models with Optimal Control can be used as an alternative to mathematical analysis which is expected to help solutions to reduce the spread of dengue fever. The recommendation given is to investigate the disease-causing factors from the chemical aspect related to the chemical effect in water that influences the growth of mosquito larvae in water which can indirectly affect DHF disease and involves these parameters in mathematical models and optimal control.

Keywords Dengue Hemorrhagic Fever, Mathematical Model, Optimal Control

1. Introduction

One of the bases that started the discussion about the effect of disease spread that can be detected through mathematical modeling, is the reference book published by Kermack, WO and Mc Kendrick, A. G [1], known as the Kermack-Mc Kendrick SIR model flow chart, this model done by dividing the human population into 3 classes (Susceptible, Infected, Recovered), which is known as the SIR model. So that there is a lot of literature related to the spread of diseases that can be detected through mathematical modeling [2], including Dengue

Hemorrhagic Fever, which was initiated by the journal Fischer D.B. [3].

Dengue Hemorrhagic Fever is commonly found in tropical and subtropical areas, caused by the Aedes aegypti mosquito [4]. This DHF disease originally came from the Philippines in 1953 and then spread in Thailand in 1955 [5]. The first case of dengue fever was found in Indonesia in the city of Surabaya in 1968 [6], including the city of Blitar [7], then spread to other cities. The regencies of Gowa, Maros and Bone [8] in South Sulawesi are also endemic areas [9] including the Banjarbaru area of South Kalimantan Province [10],[11]. Dengue fever is caused by a viral infection, namely the dengue virus which consists of 4 serotypes which are denoted by DEN 1, DEN 2, DEN 3, and DEN 4 [12]. This dengue-transmitting mosquito is found in almost all corners of Indonesia, except in places that have an altitude of more than 1000 meters above sea level [13].

This virus is carried and spread through mosquito bites. There are three factors for transmission of dengue virus infection, including humans, viruses, and intermediary vectors [14]. This disease is characterized by high fever, bleeding and can cause death and cause outbreaks [15], some of the symptoms of dengue are fever; headache; reddish skin that looks like measles; and muscle and joint pain. In some patients, dengue fever can develop into one of two life-threatening forms [16]. DHF cases increase every year in almost all parts of Indonesia [17].

The breeding of mosquito life is much influenced by physical and non-physical factors such as density level [18], climate, rainfall, humidity and population density have an influence on the incidence of dengue fever [19]. Climate also affects parasites and vectors such as weather, temperature, and humidity. Temperature factor Temperature or air temperature also includes environmental factors that affect the life of the Aedes Aegypti mosquito which also directly affects DHF [20]. The rainfall factor [10], can create a lot of puddles where mosquitoes breed, while humidity affects the lifespan of mosquitoes where low humidity will shorten the lifespan of mosquitoes. The humidity level of 60% is the lowest limit to allow mosquito life, the transmission of this disease is strongly influenced by climatic factors [21].

Several studies involve the formation of mathematical models using the mathematical model of SIR epidemiology and its variations. Using the SIR-SI model involving the human population and mosquitoes as vectors [22], [23], the SIR-SI-SI model adds the human population by administering the vaccine [24]. The model used is a system of differential equations that represents the epidemiology of dengue hemorrhagic fever, such as Windawati et al (2020). This study discusses the analysis of the mathematical model of the spread of dengue fever with the effect of fogging which shows the model of the spread of dengue fever, fixed points, stability analysis, basic reproduction numbers and simulation results that show the effect of fogging [25], while in other studies carried out by Side et al (2018) discussed the analysis of a mathematical model on the spread of DHF with the Lyapunov function using secondary data from the number of patients with DHF [8]. Based on Side et al's research (2018), the SIRS mathematical model, fixed point, stability analysis and the value of the basic reproduction number [26], were obtained. Furthermore, there are also those that involve computation in the model, including that carried out [27] which discusses the dynamics model of Dengue Hemorrhagic Fever and Optimal Control Applied to Biological Models [28].

Mathematical modeling is expected to help the problem of the spread of dengue fever so that it is more efficient both time and cost in dealing with the problem. In addition, an area that has been designated as an endemic area can also be used as a sample search method in conducting an epidemiological assessment of dengue disease.

This systematic review is very important to do to find out the extent of research that has been done previously related to the causal factors, both physically and chemically, methods, variables, predictor parameters that are relevant to the DHF disease model. This is done to determine the accuracy of the DHF disease model so that it is possible to use it to identify and take appropriate steps in controlling DHF disease in a timely manner.

The purpose of this systematic review is to conduct a review of the DHF disease starting from the factors that affect DHF, a review of the mathematical model of the dengue virus in the human body, a review of the mathematical model of the dengue virus through vectors in the human body, and optimal control of the problem of dengue fever. later it can be used as a basis in developing a model of DHF disease.

From the several articles obtained in full, they have discussed the physical environmental factors that cause the emergence of DHF, but only a few have discussed the chemical factors related to DHF. So that this is an opportunity in further research that can be used as a factor that also influences the formation of mathematical models.

2. Methods

The writing of a systematic review is carried out in the period from August 2021 to April 2022. Article searches are carried out by accessing electronic journal portals such as: Elsevier, Springer, ResearchGate, google scholar, Scient direct and so on. Other references also use national journals and information on the Ministry of Health's website. Figure 1 shows the flowchart of systematic review article.

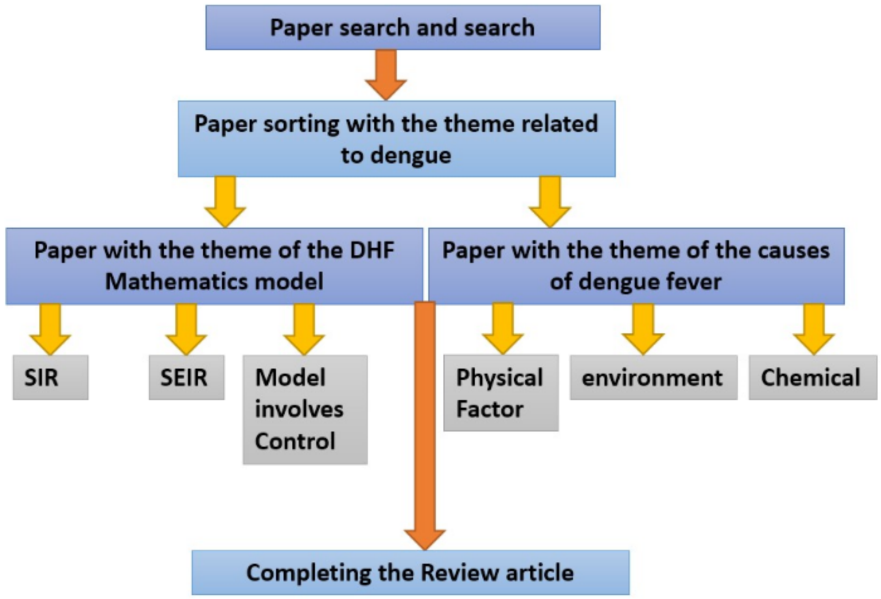

Figure 1. Flowchart of systematic review article

2.1. Article Search Techniques

The search for articles is carried out by using an article heading approach in the form of medical subject headings for themes in the health sector and using keywords in the search into categories related to DHF, namely:

i. Physical and non-physical factors related to DHF
ii. DHF Mathematical Model (SIR Differential Equation).
iii. Another Mathematical Model Analysis.
iv. Optimal control in dengue disease

2.2. Criteria

The standard criteria used are as follows:

i. Full text article producing a mathematical model of DHF. The epidemiological model obtained through several modeling approaches is in the form of a differential equation.
ii. Full text article that uses optimal control applications in DHF.

2.3. Data Extraction

Article data was collected manually and then compiled in the form of a summary table. The variables collected in addition to general information related to the type of research, namely the period of data collection and the type of model used. The output category of the research is in the form of an analysis of the DHF disease model. The modeling variables are summarized in the narrative description of the study area in the time period taken from the reference starting from 1999 to 2022.

2.4. Article Statistics

There are 115 journal articles and 3 literature books which are divided into 5 categories, namely:

i. 51 journals related to the mathematical model of
ii. dengue disease.
iii. 21 journals related to DHF with other models.
iv. 20 journals using optimal control of dengue disease.
v. 23 articles on global health.
vi. 3 literature books

3. Observation Results

The following sub-chapters will describe the scope, design of the study to be carried out, and an overview of the discussion of the model. The results of the review obtained discussion of the factors that affect DHF, a review of the mathematical model of dengue virus in the human body, a review of the mathematical model of dengue virus through vectors and the human body and optimal control of the problem of dengue. Figure 2 shows the flowchart of search and article classification.

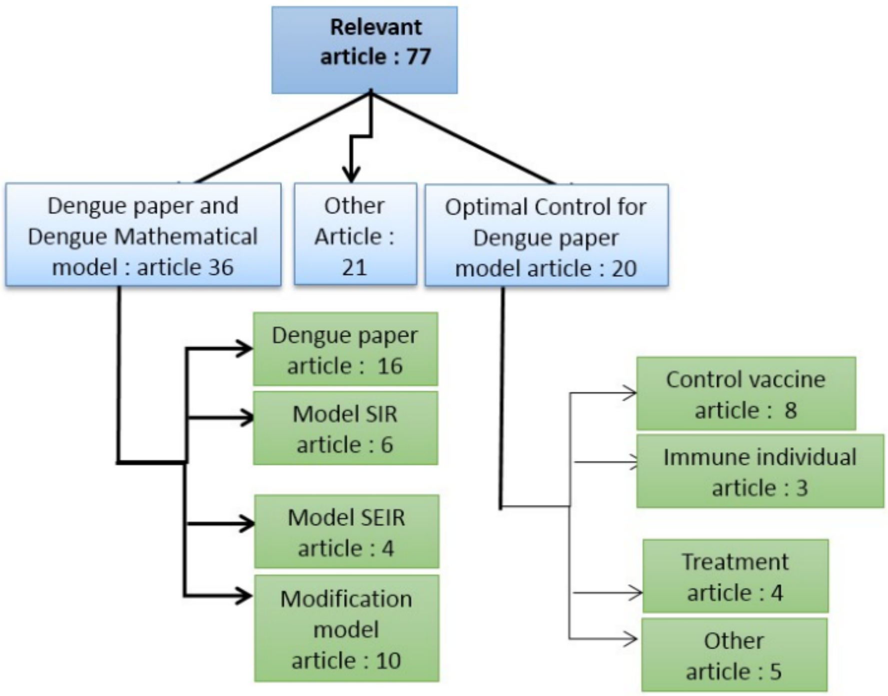

Figure 2. Flowchart of Search and Article Classification

3.1. The Scope of this Research

The scope of this research of the discussion covers many regions, several countries, and administrative levels in the search for publication articles. Most of the studies conducted on a local scale occurred in urban areas, then the information obtained that these urban areas have a high potential risk for transmission of the dengue virus.

3.2. Study Design

Most of the research conducted used secondary data on DHF cases, some used data from surveys conducted on the health surveillance system, although some studies were conducted over a shorter period of time during which dengue epidemic cases occurred.

3.3. Model Discussion

The discussion of the model in the article used uses a mathematical epidemiological model in the form of SIR, SEIR, an extension of the SIR model, and the SEIR model and some use other mathematical models.

4. Discussions

Mathematical models are one of the tools in mathematics that can help describe and simplify phenomena in real life in the form of functions or equations. Mathematical models of epidemiology can be used to predict, understand, and develop strategies to control the spread of infectious diseases by helping to understand the behavior of systems under various conditions. Several epidemiological mathematical models model the spread of disease, among others in the form of: SIR, SIS, SEIR, SIAR models by involving differential equations. From these models, equations can be made that can describe the conditions of a spread of an infectious disease or an epidemic, including DHF.

The SIR epidemiological model was first introduced by Kermack and McKendrick in 1927 [1]. In this case, the model given is still a simple model that only examines the distribution in the human population. Furthermore, the Kermack-Mc Kendrick Model divides the human population into three sub-populations, namely the Susceptible sub-population or individuals who are susceptible to disease, infected or individuals who are infected and can spread the disease to susceptible individuals and recovered or individuals who are assumed to have recovered. Furthermore, this model is the initial model known as the SIR model. This SIR mathematical model has been widely used by other researchers such as Esteva and Vargas [29], M Derouich, A Boutayeb, and EH Twizell [19], Sanusi, W., Badwi, et al [9] in this model of the spread of dengue hemorrhagic fever. The human population is divided into 3 classes, namely the susceptible/susceptible (Sh) class which represents the class of individuals who have not been infected with dengue hemorrhagic fever and have the potential to be infected with the disease, the infectious/infectious (Ih) class which indicates the class of individuals infected by the dengue hemorrhagic fever virus. and has the ability to transmit the dengue virus to infectious vectors (mosquitoes), recovery class (Rh) which states the class of individuals who have recovered from viral infection. The following is the SIRS model of changes that occur in the human and mosquito classes.

From Figure 3 this can be interpreted in the form of a mathematical model of host-vector interaction which is a differential equation. Then this epidemic model continues to be developed according to the needs of researchers. In 2011 De la Sen studied with used model SEIR (Susceptible-Exposed-Infected-Recovered) [30] by adding the exposed population or individuals who were exposed to the virus but the disease had not yet emerged. Noorani explained the SEIR model by [31] constructing a mathematical model of the DHF epidemic with vaccination and vector control. The modeling is done by dividing the human population into 4 classes (Susceptible, Exposed, Infected, and Recovered), while the vector population is assumed to be Susceptible and Infected vectors. The problem-solving approach in this research is through a mathematical modeling approach. The expected result is optimal control of the dynamic model of the spread of dengue fever by vaccination of individuals who have previously been infected and vector control with mosquito nest eradication (PSN) activities.

Likewise, Khan, and Fatmawati [6] developed the SEIR model into a SEIRP-SEI model (see Figure 4) for dengue hemorrhagic fever, by adding the Hospitalized or Notified Infectious (P) subpopulation which is the number of confirmed human individuals hospitalized and identified as fever patients. dengue hemorrhagic fever at time t. Likewise this model involves human population (SEIRP) and mosquito population (SEI).

This sub-chapter will discuss an overview of the factors that affect DHF, Mathematical models of the Transmission Process of Dengue Virus in the Human Body, and Mathematical Models of the Transmission Process of Dengue Virus through vectors and the Human Body, as well as Optimal Control on the problem of DHF.

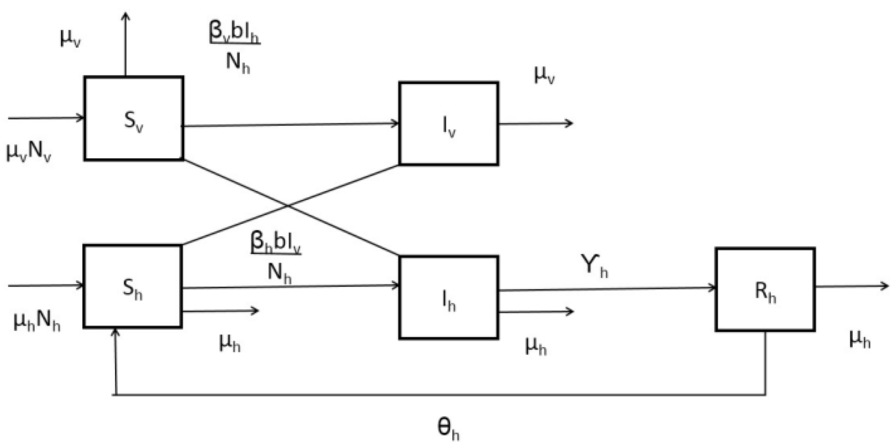

Figure 3. Human and vector SEIR model diagram [8]

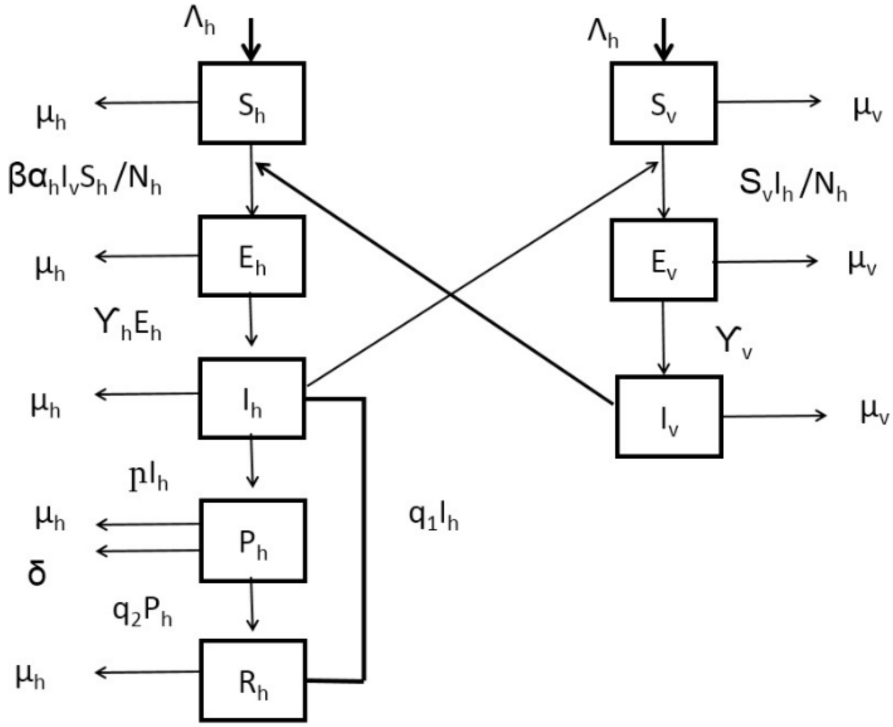

Figure 4. Human and vector SEIR model diagram [6]

4.1. Factors that affect DHF

Based on research conducted many factors that influence the disease DHF, this is supported by secondary data obtained in each research area. Rainfall, Temperature, and Humidity are physical factors that affect DHF, this was conveyed in the study [21] by taking secondary data in Semarang City in 2006 – 2015, it was found that rainfall, temperature, and humidity had an effect on the number of DHF cases in Semarang. Semarang City ($p < 0.05$). Partially (the count t = 2.621 and $p = 0.010$) only the humidity factor has a significant effect on the number of dengue cases in Semarang City, as well as research [32] in the Putat Jaya Health Center Work area in 2014-2016 Sawahan sub-district, Surabaya. temperature with cases of DHF ($p = 0.019$); ($OR = 0.319$), [33] which was observed in Bandar Lampung in 2016-2018, resulted in other factors that influence the spread of DHF, including host factors (susceptibility), environmental factors, demographic conditions, geographical location and types of mosquitoes [34] and settlement density, Pearson correlation test was performed. The results showed that there was a significant relationship between temperature and cases of DHF and no correlation between humidity and cases of DHF [35]. Physical and behavioral environmental factors are also factors in the incidence of dengue hemorrhagic fever in Mustikajaya Village, Bekasi City [36]. Statistical analysis used multivariate linear regression model [37].

However, there are also those who use climate information as an early warning signal for dengue cases, this is done in Banjarbaru, South Kalimantan [10]. Utilization and development of expert systems is also used in preventing dengue hemorrhagic fever epidemics. Expert system knowledge with information sources comes from environmental health experts, health workers, and reference searches [38].

4.2. Overview of the Mathematical Model of Dengue Virus in the Human Body

The mathematical model used to describe the Mathematical model of the Dengue Virus Transmission Process in the human body is a modified SIR model, namely the SIV (Susceptible, Infectious, Viruses) model [39]. This model has the idea of starting from [1] and [3], then specifically only analyzes the form of a mathematical model for the transmission process of dengue virus in the human body. The assumption of this model that the dengue virus is lethal, and that no other microorganism infects the human body, is defined as susceptible cells denoted by S. The infected cell compartment is I, and free virus particles are V. The diagram below illustrates the spread of the virus in body. In this model, an analysis of the disease-free and endemic equilibrium point is carried out, followed by a stability analysis followed by a numerical simulation.

Furthermore, the SIV model was added with herbal drug therapy because herbal drug therapy was needed to inhibit the replication process of the dengue virus in the human body infected with the dengue virus [40], and giving treatment, so that the SIV-T model (Figure 5) is formed [41].

4.3. An overview of the mathematical model of dengue virus through vectors and the human body

In this model of Dengue Hemorrhagic Fever, it involves the human population and the mosquito population as vectors. This model started from [1] and [3], which were further developed by further researchers. SIR-SI model [22] the human population is divided into 3 classes and the mosquito population is divided into 2 classes, as shown in Figure 6.

Furthermore, the model [24] SIRSI-SI, SIRSI as the human population and SI as the mosquito vector population.

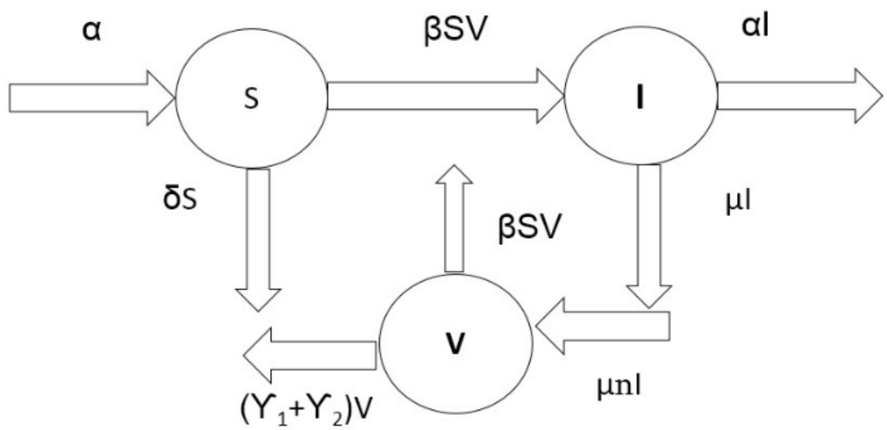

Figure 5. Transmission diagram in the SIV Model

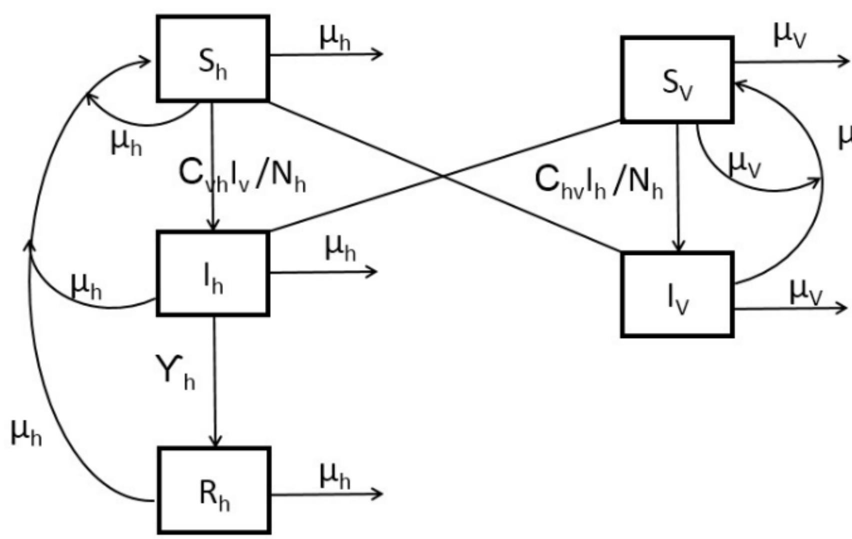

Figure 6. SIR-SI Diagram of human and mosquito transmission as vector populations

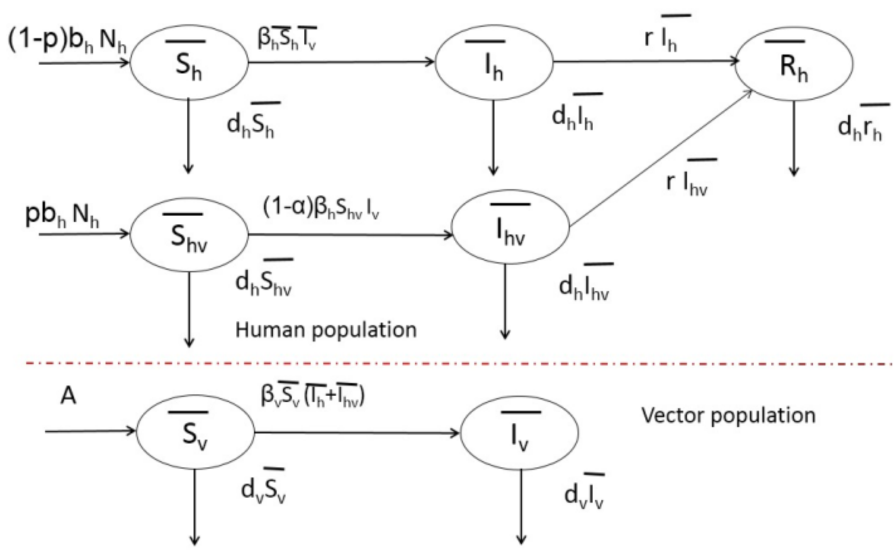

Figure 7. SIRSI-SI diagram of transmission in humans and mosquitoes as vector populations

In the SIR model in Figure 7, the population is divided into 2, namely the human host population and the vector population (mosquitoes). The human population consisted of 3 states: Suspected SH human, IH infected human, and RH cured human, while the vector population had 2 states: SV vector suspect and IV infected vector. Mosquitoes do not reach the healing stage because before they recover, they have died. The suspected mosquitoes are neither immune nor infected, while in the rate of infection, they have been infected with the dengue virus and can transmit the virus. The state of recovery in humans is someone who has recovered from a viral infection with dengue fever. Dynamic transmission in human and mosquito populations with the effect of vaccination can be seen in Figure 5.

The effect of vaccination is incorporated into the model by the presence of an effect coefficient. the setting is 1, there will be no transmission of viral infections from mosquitoes, so there will be no dengue epidemic. This is not how vaccines work. When a person is vaccinated against an attenuated virus, the weakened virus will enter humans where the body's immune system produces agents that provide immunity to the virus. Including, some people will not be able to kill the vaccine virus which causes the virus to infect that person. The effect of vaccination is to create new pathways for disease transmission

In the article [6] the formation of the SEIRP-SEI model for dengue hemorrhagic fever, begins by dividing the human population into five classes, namely: Subpopulation Susceptible (S) which states the number of healthy human individuals but susceptible to dengue hemorrhagic fever virus infection at time t. Exposed subpopulation (E) states the number of human individuals who have been exposed to the virus but have not been able to infect healthy and susceptible mosquitoes at time t. Infectious subpopulation which (I) states the number of infected human individuals who can infect at time t. Recovered subpopulation (R) represents the number of human individuals who recovered from being infected with dengue hemorrhagic fever at time t. While the Hospitalized or Notified Infectious (P) subpopulation stated the number of confirmed human individuals who were hospitalized and identified as dengue hemorrhagic fever patients at time t.

The mosquito population is divided into 3 classes, namely: Sub population Subsceptible states the number of individual mosquitoes that are healthy but susceptible to virus infection at the time. The Exposed sub population states the number of individual mosquitoes that have been exposed to the virus but have not been able to transmit it to healthy and susceptible humans at time t. And the Infectious sub population states the number of individual mosquitoes that have been infected with the virus and can transmit it at time t.

The steps taken in solving the dengue hemorrhagic fever disease model mathematically in the article discussed are carried out by determining the equilibrium point of the dengue hemorrhagic fever mathematical model, determining the basic reproduction number [31], determining local stability [42], [43], stability [9], [43] of dengue hemorrhagic fever disease model at the disease-free equilibrium point and at the endemic equilibrium point using the eigenvalues of the Jacobian matrix. Furthermore, using optimal control [44], [45] from the dengue fever model, by first determining the state variables and state equations from the Differential Equation system, determining the performance index after being given the controller.

4.4. Optimal Control on DHF problems

Many efforts to eradicate the development of Dengue Hemorrhagic Fever have been carried out, leading to restrictions on the movement and population of mosquitoes as vectors of DHF in humans. Mathematical modeling with the application of control strategies is an attractive approach tool to analyze the problem of the spread of this infectious disease of dengue fever, including by using Optimal control on the model of the spread of dengue fever by doing vaccine [46], larvicidal [47], treatment [48] also Optimal Control of Aedes Aegypti Mosquitoes [49].

Overall treatment for Dengue Hemorrhagic Fever still relies on vaccines for prevention of viral infections, while drugs for Dengue Hemorrhagic Fever do not yet exist and are still in the research process, so that control is primarily aimed at breaking the chain of transmission, namely vector control. Control methods that can be carried out are preventive measures from humans such as the use of insecticide treated nets, the use of repellents such as mosquito lotions, and spraying with insecticides or fogging. To solve the optimal control problem, the necessary conditions are first determined so that optimal control is met [50] and also some applications in [51].

In the paper [52] applied optimal control on the mathematical model of the spread of dengue hemorrhagic fever, the transmission model of dengue disease with symptomatic and asymptomatic infection classes, the sensitivity of the dynamic's threshold analysis was obtained to identify the dominant factors that seriously affect dengue infection. Then in paper [53] using Optimal Control on the Dengue Hemorrhagic Fever (DHF) Disease Model by providing herbal medicine treatment with the research location on the Martapura Riverbank. Optimal control is also used when only individuals with a recorded history of past dengue infection for which the individual has been given are vaccinated, this is the case in some parts of Thailand [54], while in Johor Malaysia in 2012, control with a combination of optimal personal protection, larvicidal and adult control involving eight mutually exclusive compartments with the introduction of personal protection, the model was also adapted to data related to DHF outbreaks using the least squares method [47]. Likewise, the discussion of optimal control in the model of the spread of dengue fever using the Pontryagin minimum principle can be prevented by administering a vaccine called Chimeric Yellow Fever 17D-Tetravalent Dengue Vaccine (CYD-TDV) [55].

This necessary condition is derived using the Lagrange approach as follows:

1. Given a maximization problem of J(u) with a certain state, let's say the initial state is x(t0) = x0 and the final state, let's say x(t1) = x1.
2. Defined scalar function £ with £= (x(t), u(t), λ(t)).
3. Defined scalar function H (x, u, λ, t) with written into the Hamiltonian function.
4. It is assumed that at the optimal time, the control variables and state variables are respectively u*(t) and x*(t). Give a function.
5. Based on the above equation can be written as follows u*(t) optimally, then the deviation is very small so that it does not affect the value of the Lagrange function.

This result is further used to calculate the maximum necessary principle.

Optimal control can be used to determine alternative solutions after obtaining an epidemiological model in the form of a differential equation. Optimal control of vaccination in the model [56] and [43], but paper [43] with individuals who have previously been infected with the dengue virus, this model population (N) is divided into five classes, namely: Susceptible class (Sh) which indicates the number of humans potentially infected with the virus in healthy condition but can be infected with DHF, class Infected (Ih) states the number of humans infected with the virus including those who have become active DHF and can transmit DHF disease, Recovered (R_h) class states the number of humans who have recovered or recovered through vaccination which makes immunity permanent, Susceptible Vector (S_v) class represents the number of mosquitoes which have the potential to carry the virus, and the Infected (I_v) class indicates the number of infected mosquitoes. The size of the human population as a host is expressed as $N_h = S_h+I_h+R_h$ and the size of the mosquito population as a vector is expressed as Nv = Sv+Iv. Likewise in the SIR model [21] vaccine images are given to strengthen immunity from viral attacks.

5. Conclusions

Many factors affect DHF. Rainfall, temperature, humidity, host factors (susceptibility), environmental factors, demographic conditions, geographical location, types of mosquitoes, residential density, physical and behavioral environmental factors are also factors in the incidence of dengue hemorrhagic fever. Utilization of secondary data on the incidence of DHF is needed in data analysis for the formation of the model, which can then be presented into a model to facilitate decisions in the public health sector.

The mathematical model of dengue hemorrhagic fever, the analysis of the model is carried out by determining the equilibrium point of the mathematical model of dengue fever, determining the basic reproduction number, determining local stability, global stability of the dengue hemorrhagic fever model at the disease-free equilibrium point and at the endemic equilibrium point using values eigenvalues of the Jacobian matrix. Furthermore, using the optimal control of the dengue fever disease model, by first determining the state variables and state equations from the Differential Equation system, determining the performance index after being given the controller.

To improve improvisation in describing the dynamics of DHF disease, the formation of a future-oriented model is needed by considering the dengue virus vector variable and the human movement variable in the model so that it can also be used to predict the incidence of DHF in the future.

Optimal control can be an alternative to determine the optimal decision of reducing DHF disease with vaccines and treatments.

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