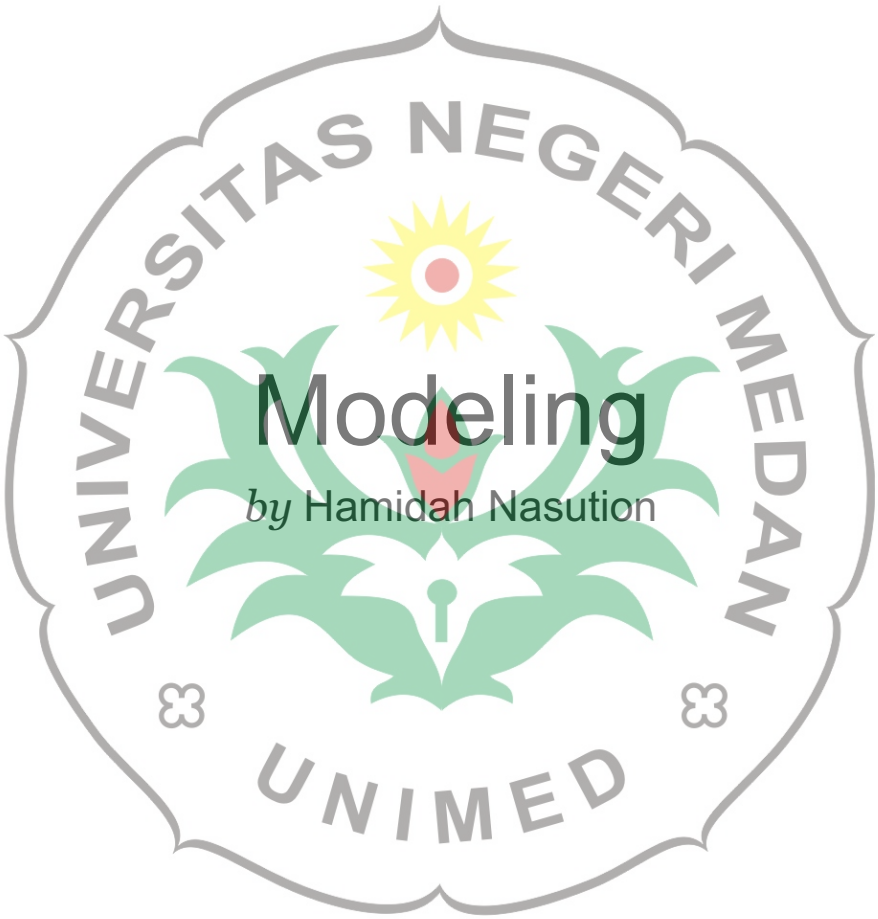

Modeling

by Hamidah Nasution

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Modeling the Existence of Basic Offspring Number on Basic Reproductive Ratio of Dengue without Vertical Transmission

Hamidah Nasution
Department of Mathematics
State University of Medan
Medan, Indonesia
Hamidah_mat67@yahoo.com

Herman Mawengkang
Department of Mathematics
University of Sumatera Utara
Medan, Indonesia
hmawengkang@yahoo.com

Syahril Pasaribu
Medical Faculty
University of Sumatera Utara
Medan, Indonesia

Abstract— Dengue fever is a *flavivirus* of the family *flaviviridae* and transmitted to human after biting the infected vectors. The main vectors of dengue are *Aedes aegypti* and *Aedes albopictus*. There are four serotypes of dengue virus, viz. DEN-1, DEN-2, DEN-3, and DEN-4. The dengue virus, one of the virus that causes classical dengue fever (DF) and dengue haemorrhagic fever (DHF) is primarily found in the tropical and subtropical regions. Indonesia with the tropical climate has become an ideal land for dengue virus transmission. The wide clinical spectrum ranges from asymptomatic infections or mild illness, to the more severe forms of infection such as dengue hemorrhagic fever and dengue shock syndrome. The transmission of virus between mosquito can occur in two mechanisms, viz., horizontally and vertically. If the infected mosquito bite a human susceptible such that the human is infected, then this kind of transmission is called horizontal. The vertically transmission can occur from infected female mosquitoes to next generation. In this paper we build what is called Basic Offspring Number (Q_0) based on the rate of change of aquatic mosquito and the total rate of change of mosquito population. Mathematical model is formulated to estimate the dynamics of the spread of disease dengue associated with basic offspring number Q_0 (how the contribution of basic offspring number on basic reproductive ratio R_0). The result shows that the existence of Q_0 is significant toward R_0.

Keywords- *Dengue, vertical transmission, basic offspring number, basic reproductive ratio, mathematical modeling.*

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I. INTRODUCTION

Dengue fever (DD), Dengue hemorrhagic fever (DHF) and Dengue Shock Sindoroma (SSD) are infectious disease caused by the dengue virus. The dengue virus has four serotypes, namely DEN-TYPE I, DEN-TYPE II, DEN DEN-TYPE III and TYPE IV ([4]). The spread of dengue virus occurs when there is an interaction between the host and vector. In this case the spread of dengue virus in the human body is called the mosquito vector. Model epidemiology is a formal framework to convey ideas about the components of the host-vector interactions. The mathematical model can also be used to predict, understand and develop strategies to control the spread of infectious diseases by helping to understand the behavior of the system with a variety of conditions [1]. Through mathematical models we are able to predict the condition where dengue disease may become epidemic or not by examining the behavior of each parameter on a mathematical model constructed, and determining the equilibrium point and the basic reproduction number.

Dengue virus is transmitted from an infected human to a female *Aedes* mosquito by a bite. The mosquito, which needs regular meals of blood to feed their eggs, bites a potentially healthy human and transmit the disease. Therefore the existence of mosquitoes is very important in the spread of this virus. One way to handle the transmission of the virus is through the control of mosquito populations [12]. Because until now there is no vaccine for all four serotypes of the virus even though many efforts have been made to find the vaccine. [14].

The spread of the virus in the mosquito vectorr can occur by two mechanisms, i.e horizontally and vertically. Horizontally transmission occurs when an infected mosquito bites a human vulnerable and Vertically transmission occurs from infected female mosquitoes to next generation. In this study, we used a model SIR (susceptible, Infected and Recovered) and in particular we notice the aquatic phase at Ae. aegypti.

Further modeling of dengue dynamic is helpful to examine the aquatic and adult mosquito control [5, 6]. Ref. [13] propose an optimal control technique based on biological control to reduce the fertile female mosquitoes. Another control for mosquito using sterile insect release and habitat modification is proposed by [8] and [12]. Ref. [2] address a mathematical model that captures the essence of dengue transmission, from which they derive the main parameter related to the intensity of dengue transmission, called the Basic Reproduction Number. Recently, [3] present a mathematical model for the dengue disease transmission and finding the effective way of controlling the disease. They use multiobjective optimization to find the optimal control strategies.

In this study, we develop a mathematical model that uses existing models of SIR (susceptible, infected and recovered), especially in the mosquito vector, which will be considered the mosquito population when in aquatic. With the aquatics phase, the model of the mosquito vector is ASI (Aquatic, susceptible and Infected). Furthermore, through this model will be built a model to determine the Basic Offspring Number (Qo) by observing the aquatic compartment and the rate of change of the total population of mosquitoes. Basic Offspring Number (Qo) is a number that represents the number of mosquitoes are born to each adult mosquitoes over a period of time. Then we will construct Reproductive Ratio number (Ro) and associate it with Basic Offspring Number (Qo). Next we will analyze the relationship between Qo and Ro through simulation.

II. MODEL FORMULATION

In the model of SIR, the human population is divided into three sub-population that is susceptible human (S_h), Infected human (I_h) ,and recovered human (R_h), with total human population: $S_h + I_h + R_h = N_h$. The human population is assumed to be constant, with the birth rate (λ_h) and the mortality rate (μ_h) are the same. The mosquito population is divided into three subpopulations, namely aquatic mosquitoes (A_m), susceptible mosquitoes (S_m), and infected mosquitoes (I_m), with a total population of mosquitoes: $S_m + I_m = N_m$.

The proportion infections of human susceptible (S_h), by mosquitoes infected (I_m), per day is the ratio between chances of transmission of the dengue virus from mosquitoes to humans (θ_h) by the total number of human (N_h) multiplied by the average mosquito bites on humans per day (b) and the number of infected mosquitoes (I_m) is expressed as follows: $\frac{b\theta_h}{N_h} S_h I_m$. Human susceptible (S_h) move into humans infected (I_h). Humans are naturally infected die as much as $\mu_h I_h$.

The proportion infection of mosquito susceptible (S_m), due to the biting infected humans (I_h) per day is the ratio between chances of transmission of the dengue virus from humans to mosquitoes (θ_m) by the total number of human (N_h) multiplied by the average mosquito bites on humans per day (b) and the number of humans infected (I_h) is expressed as follows: $\frac{b\theta_m}{N_h} S_m I_h$. The next step is the sensitive mosquitoes infected mosquitoes move into (I_m) and susceptible mosquitoes that die naturally as $\mu_m S_m$. Schematically, the pattern of spread of dengue disease between host (human) and vectors (mosquitoes) are illustrated in the following diagram compartment:

Oviposition

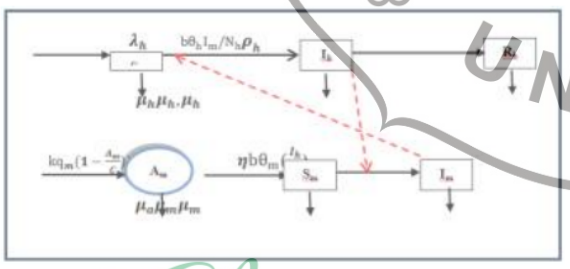


Figure 1. Flow diagram of human- vector model SIR–ASI

Fig 1. Shows the mosquito population growth rate of aquatic mosquitoes which is influenced by multiplying the proportion of births of female mosquitoes of all eggs hatched (k), the average rate of oviposition (q_m), chances between mosquitoes carrying capacity and the total number of mosquitoes. Based on the Fig. 1 system of differential equations for each compartment can be expressed as:

$$\frac{dS_h}{dt} = \mu_h N_h - \frac{b\theta_h I_m S_h}{N_h} - \mu_h S_h$$

$$\frac{dI_h}{dt} = \frac{b\theta_h I_m S_h}{N_h} - \rho_h I_h - \mu_h I_h$$

$$\frac{dR_h}{dt} = \rho_h I_h - \mu_h R_h$$

$$\frac{dA_m}{dt} = kq_m\left(1 - \frac{A_m}{C}\right)(S_m + I_m) - \eta A_m - \mu_a A_m$$

$$\frac{dS_m}{dt} = \eta A_m - \frac{b\theta_m I_h S_m}{N_h} - \mu_m S_m$$

$$\frac{dI_m}{dt} = \frac{b\theta_m I_h S_m}{N_h} - \mu_m I_m \quad (1)$$

with conditions :

$$N_h = S_h + I_h + R_h \; dan \; N_m = S_m + I_m \quad (2)$$

Where

N_h is the total number of human population
N_m is the total number of mosquitoes population
μ_h is the death rate of the human population
μ_m is the death rate of the mosquitoespopulation
λ_h is the birth rate of the human population
b is the biting rate of the mosquitoes population
θ_h is the transmission probability of dengue virus from mosquito to human population
θ_m is the transmission probability of dengue virus from human population to mosquitoes population
ρ_h is the recovery rate of human population
k is the fraction of female mosquitoes hatched from all eggs
q_m is the average oviposition rate
C is the mosquito carrying capacity
η is the average aquatic transition rate
μ_a is the average aquatic mortality rate

The total number of populations both human and mosquitoes populations were assumed constant. We obtain $\lambda_h = \mu_h$.

III. ANALYSIS OF THE MATHEMATICAL MODEL

Analysis of fixed point on the system of differential equations are often used to find a solution that does not change over time. In this sub-chapter sought a fixed point of Eq. (1) in areas that have biological significance called Ω, with:

$$\Omega = \{(S_h, I_h, R_h, A_m, S_m, I_m) \in \Re_+^6, (S_h + I_h + R_h \leq 1; S_m + I_m \leq 1\} \quad (3)$$

Fixed point on the model SIR-ASI six-dimensional is very important, because these points are the base for determining the basic offspring number (Q_0), basic reproduction ratio (R_0), point endemic and stability of each fixed point.

The fixed point of the system of differential equations (1) is obtained by determining : $\frac{dS_h}{dt} = 0, \frac{dI_h}{dt} = 0, \frac{dR_h}{dt} = 0, \frac{dA_m}{dt} = 0, \frac{dS_m}{dt} = 0 \; and \; \frac{dI_m}{dt} = 0.$ (4)

From these results it will be obtained three types of equilibrium point in Ω, ie elimination of mosquito populations (E_0), disease-free-equilibrium point(E_1) and endmicequilibrium point (E_2). This article only discusses the equilibrium pointE_0 and E_1.

A. Equilibrium $E_0(S_h, I_h, R_h, A_m, S_m, I_m) = E_l\,(N_h, 0,0,0,0,0)$

The fixed point E_0 indicates that there susceptible human population the number of susceptible human population $S_h = N_h$. This means that the total human susceptible S_h equal to the sum total of human (N_h). The E_0 point that the conditions of equilibrium occurs when the entire human population is free from dengue disease, and also shows there is no population of mosquitoes, so that at E_0 no virus and infected cells.

By analysis E_0, will be elaborated basic offspring number (Q_0), it represents the number of mosquitoes born from each adult mosquitoes during the period the productivity of adult mosquitoes. The method used to find Q_0 is the next generation matrix. In this case it is assumed that $N_m = S_m + I_m$. Furthermore, differential equations compartment of view on the mosquito population:

$$\frac{dA_m}{dt} = kq_m\left(1-\frac{A_m}{C}\right)(S_m + I_m) - \eta A_m - \mu_a A_m \; and \; dN_m = \eta A_m - \mu_m N_m . \quad (5)$$

Assuming that $\frac{dA_m}{dt} = 0$ and $N_m = 0$, then (5) becomes:

$$0 = kq_m\left(1-\frac{A_m}{C}\right)(S_m + I_m) - \eta A_m - \mu_a A_m \; dan \; 0 = \eta A_m - \mu_m N_m \quad (6)$$

Suppose that F_1 is the interaction of aquatic mosquitoes and adult mosquitoes in dA_m and F_2 is the interaction of mosquitoes aquatic and adult mosquitoes in dN_m, then V_1 and V_2 is the moving rate between compartments of dA_m and dN_m then :

$$F_1 = kq_m(1-\frac{A_m}{C})N_m; F_2 = 0 ; \quad (7)$$

$$V_1 = \eta A_m + \mu_a A_m \quad ; V_2 = -\eta A_m + \mu_m N_m \quad (8)$$

The Jaobian matrix of (7) and (8) :

$$F = \begin{bmatrix} -\frac{kq_m N_m}{C} & kq_m(1-\frac{A_m}{C}) \\ 0 & 0 \end{bmatrix} \; dan \; V = \begin{bmatrix} \eta+\mu_a & 0 \\ -\eta & \mu_m \end{bmatrix} \quad (9)$$

Let t=0, then $N_m = S_m = 0$ then:

$$E_0 = (S_h = N_h, I_m = 0, R_h = 0, A_m = 0, S_m = 0 \; and \; I_m = 0 \quad (10)$$

Subtitute Eq. (10) to Eq. (9) :

$$F = \begin{bmatrix} 0 & kq_m \\ 0 & 0 \end{bmatrix} \quad (11)$$

and

$$V^{-1} = \begin{bmatrix} \frac{1}{\eta+\mu_a} & 0 \\ \frac{\eta}{(\eta+\mu_a)\mu_m} & \frac{1}{\mu_m} \end{bmatrix} \quad (12)$$

Let $K = FV^{-1} = \begin{bmatrix} 0 & kq_m \\ 0 & 0 \end{bmatrix}\begin{bmatrix} \frac{1}{\eta+\mu_a} & 0 \\ \frac{\eta}{(\eta+\mu_a)\mu_m} & \frac{1}{\mu_m} \end{bmatrix}$ then

$$K = \begin{bmatrix} \frac{kq_m\eta}{(\eta+\mu_a)\mu_m} & \frac{kq_m}{\mu_m} \\ 0 & 0 \end{bmatrix} \quad (13)$$

Using linear algebra operations, eigenvalues of matrix K can be determined by calculating the $\det|K-\lambda I| = 0$. Where I is the identity matrix, then:

$$det\left(\begin{bmatrix} \frac{c_m\eta}{(\eta+\mu_a)\mu_m} & \frac{kq_m}{\mu_m} \\ 0 & 0 \end{bmatrix} - \begin{vmatrix} \lambda & 0 \\ 0 & \lambda \end{vmatrix}\right) = det\begin{bmatrix} \frac{kq_m\eta}{(\eta+\mu_a)\mu_m} - \lambda & \frac{kq_m}{\mu_m} \\ 0 & -\lambda \end{bmatrix} \quad (14)$$

Thus:

$$\lambda\left[\left(\lambda - \frac{c_m\eta}{(\eta+\mu_a)\mu_m}\right)\right] = 0 \quad (15)$$

We find that $\lambda_1 = 0 \; and \; \lambda_2 = \frac{kq_m\eta}{(\eta+\mu_a)\mu_m}$. The eigenvalues obtained have the maximum value and the value of these into basic offspring number (Q_0). So the basic offspring number (Q_0) from E_0 is:

$$Q_0 = \frac{kq_m\eta}{(\eta+\mu_a)\mu_m} \quad (16)$$

The value of Q_0 Eq. (16) depends on aquatic parameters and adult. If the aquatic transition rate value (η) is greater,than Q_0 value is greater too, and existence of mosquitoes in the field increases. The basic offspring number value is very important to the existence of DFE. If Q_0>1 then there must be equilibrium point E_1 (DFE).

B. Desease Free Equilibrium point (DFE)

$$E_1(S_h, I_h, R_h, A_m, S_m, I_m) = E1(N_h, 0, 0, \frac{C(\eta k q_m - \eta\mu_m - \mu_a\mu_m}{kq_m\eta}, \frac{C(\eta k q_m - \eta\mu_m - \mu_a\mu_m}{kq_m\mu_m}, 0) \quad (17)$$

The equilibrium point E_1 shows that the human susceptible population (S_h) are exist, aquatic mosquito population and mosquito populations susceptible are exist. But the point remains E_1 shows that there is not virus or infected cells.

From the analysis of equilibrium point E_1 we construct the basic reproduction ratio. The basic reproduction ratio is denoted by R_0. The R_0 is defined as the number of secondary cases or cases both produced by one patient infected and can transmit the disease. The method used to determine the basic reproduction ratio is the next generation matrix with $R_0 = \rho(FV^{-1})$ is spectral radius or the greatest eigenvalue of K= $F.V^{-1}$.

The Basic Reproduction ratio (R_0) is derived by equation compartment dengue virus infected. In this case I_h *and* I_m where:

$$\frac{dI_h}{dt} = \frac{b\theta_h I_m S_h}{N_h} - \rho_h I_h - \mu_h I_h \quad (18)$$

$$\frac{dI_m}{dt} = \frac{b\theta_m I_h S_m}{N_h} - \mu_m I_m$$

The secondary infection from (17) :

$$F_1 = \frac{b\theta_h I_m S_h}{N_h} ; F_2 = \frac{b\theta_m I_h S_m}{N_h} \quad (19)$$

and the primary infection (17):

$$V_1 = \rho_h I_h + \mu_h I_h; \; V_2 = \mu_m I_m \quad (20)$$

The Jacobian matrices of (18) and (19) are

$$F = \begin{bmatrix} 0 & \frac{b\theta_h S_h}{N_h} 0 \\ \frac{b\theta_m S_m}{N_h} & 0 \end{bmatrix} \; dan \; V = \begin{bmatrix} \rho_h + \mu_h & 0 \\ 0 & \mu_m \end{bmatrix} \quad (21)$$

Substitute Eq. (16) to Eq. (17) we get

$$E_2 = (S_h = N_h, I_h = 0, R_h = 0, A_m = C\left(1 - \frac{1}{Q_0}\right), S_m = \frac{C\eta}{\mu_m}\left(1 - \frac{1}{Q_0}\right), I_m = 0 \quad (22)$$

Substitute (22) to (21), we find :

$$F = \begin{bmatrix} 0 & b\theta_h \\ \frac{b\theta_m C\eta(1-\frac{1}{Q_0})}{\mu_m N_h} & 0 \end{bmatrix} dan\, V^{-1} = \begin{bmatrix} \frac{1}{\rho_h+\mu_h} & 0 \\ 0 & \frac{1}{\mu_m} \end{bmatrix} \quad (23)$$

Le K= $F.V^{-1}$, then :

$$K = \begin{bmatrix} 0 & \frac{b\theta_h}{\mu_m} \\ \frac{b\theta_m C\eta(1-\frac{1}{Q_0})}{\mu_m N_h(\rho_h+\mu_h)} & 0 \end{bmatrix} \quad (24)$$

Using linear algebra operations, eigenvalues of matrix K can be determined after calculating the $\det|K - \lambda I| = 0$. Where I is the identity matrix, then:

$$\tau(K) = \sqrt{\frac{C\eta(1-\frac{1}{Q_0})\theta_h\theta_m b^2}{N_h(\rho_h+\mu_h)\mu_m^2}} \; or \quad (25)$$

$$R_0 = \sqrt{\frac{C\eta(1-\frac{1}{Q_0})\theta_h\theta_m b^2}{N_h(\rho_h+\mu_h)\mu_m^2}} \quad (26)$$

The basic reproduction ratio (R_0) is :

$$R_0 = \sqrt{\frac{C\eta(1-\frac{1}{Q_0})\theta_h\theta_m b^2}{N_h(\rho_h+\mu_h)\mu_m^2}} \quad (27)$$

The R_0 value at (27) depends on the parameters of mosquitoes and humans. Multiplication coefficients and quadratic transmission from mosquito bites rate $\theta_h\theta_m b^2$, explains that the new cases of dengue fever occur only when a mosquito succeeded in transmitting the dengue virus to humans when mosquitoes bite humans had been infected and susceptible. Or susceptible mosquitoes bite humans infected with dengue virus then mosquitoes become infected and ready to transmit dengue virus to other humans [9].

IV. SIMULATION

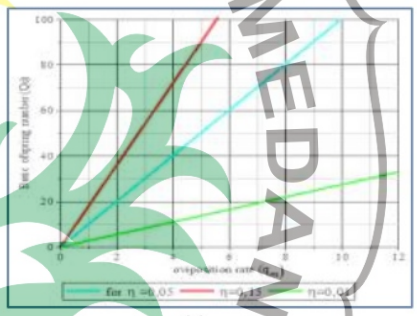
For each sub-population, here are some parameters and values to get the results of this simulation :

TABLE I. PARAMETERS VALUE

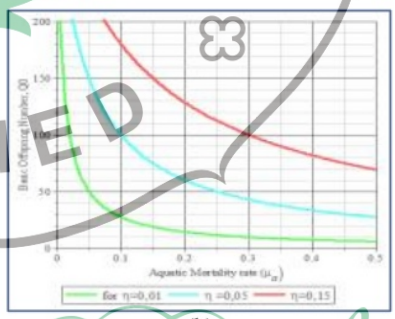
Parameter	Nilai
μ_h	0.000046
θ_h	0.75
ρ_h	0,083-0.25
μ_m	0.02-0.09
μ_a	0.01-0.47
q_m	$0 - 11.2$
η	0-0.19
θ_m	0. 75
b	0-1

Sources : ([11]; [7]; [10]; [15])

Next, we show simulation of basic offspring number (Q_0) with oviposition rate (q_m) and basic offspring number (Q_0) versus aquatic mortality rate (μ_a) in interval [0.01,0.50], and aquatic transition rate are different.



(a)

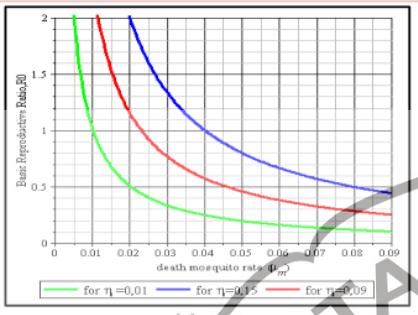


(b)

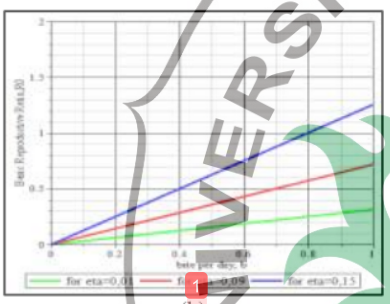
Figure 2. .(a) Baisc offspring number vs Oviposition rate; (b) Basic Offspring Number (Q_0) vs Aquatic Mortality (μ_a)

The Fig 2a, shows q_m value proportional to the value of Q_0. it means that if the q_m value increases, the value of $Q_0$is increases too. The Fig (2b) shows that if the μ_a value increases then the Q_0 value is decreased or if the Q_0 value increases then the rate of mortality of aquatic is getting smaller.

This simulation illustrates the relationship between the basic reproduction ratio (R_0) with a mortality rate of mosquitoes (μ_m) and bite mosquitoes per day (b). In this case the value of aquatic transition rate (η) is still varied.



(a)



(b)

Figure 3. (a) Basic Reproductive Ratio (R_0) vs mortality rate of mosquitoes (μ_m) and (b) Basic Reproductive Ratio (R_0) vs bite per day (b).

The existence of AedesAegyptimosquitoes population greatly influence the spread of dengue disease. Basic offspring number (Q_0) is a number that indicates the amount of aquatic mosquito born of adult female mosquitoes during the period the productivity of adult mosquitoes, its threshold indicates the existence of mosquitoes in the field. If (Q_0)> 1, then there is the possibility of dengue virus becoming endemic, but if (Q_0)<1, there would be no mosquito or in other word endemic condition may not occur. Hence, given a simulation between the basic reproduction ratio(R_0)and the basic offspring number (Q_0) with the threshold for the second point is one.

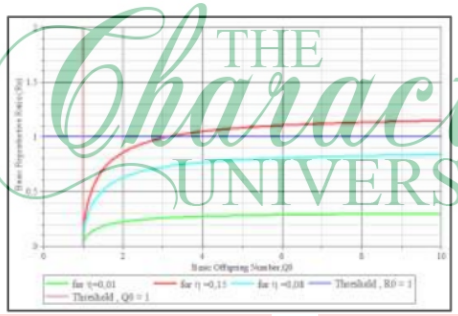


Figure 4. Basic Reproduction Ratio (R_0) with Basic Offspring Number (Q_0)

V. CONCLUSIONS

The value of Q_0 is affected by the parameters at the time of aquatic and adult mosquitoes. The greater the rate of pre-adult mosquito transition into adult mosquitoes (η), the greater the value Q_0. The greater the value of Q_0 existence of mosquitoes in the field increases. The values of basic offspring number is very big contributed on fixed point disease-free-equilibrium (DFE). Because of the existence of the disease-free-equilibrium is determined by a of basic offspring number Q_0. If $Q_0 > 1$ then the point remains disease free equilibrium must exist.

To determine of the R_0, we use of compartments taken only on subpopulations infected on the host and vector are I_h *dan* I_m, with next generation matrix method, matrix K obtained indicate dengue virus transmitted indirectly. This means that dengue virus can not be transmitted from human to human or from mosquito to other mosquito. Then from the matrix K expressed a mosquito can infect humans by $b\theta_h$ over a period of time $\frac{1}{\mu_m}$, then a person is infected can transmit the infection as much $\frac{b\theta_m C\eta(1-\frac{1}{Q_0})}{N_h}$ mosquitoes during the time period of $\frac{1}{\mu_h(\nu_h+\mu_h)}$.

The R_0 value, was also influenced by a number Q_0, where the relationship between Q_0 and R_0 provides several possibilities, among others:

1. If the basic offspring number (Q_0)<1, then R_0<1, meaning that if on the field does not exist the mosquito then dengue disease can not be transmitted because there is no vector.
2. If the basic offspring number (Q_0)>1 and R_0<1, meaning that there are mosquitoes on the field but did not transmit the dengue virus. It also shows that the presence of mosquitoes is not always transmit the disease, as shown in the fixed point disease free equilibrium.
3. If the basic offspring number (Q_0)>1, and the basic reproduction number (R_0)>1, meaning that the mosquito population is on the field, the existence of R_0 is also nothing to suggest that during the course of infection has produced more than one secondary cases. This condition also shows the endemic state. So endemic conditions arise when the value of $R_0^2 > 1$

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