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Mathematical model, stability analysis and numerical simulations for the spread of malaria disease in Yogyakarta city, Indonesia

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Abstrak

Indonesia merupakan negara yang sering terjadi penyakit malaria. Oleh karena itu, diperlukan model matematika yang mampu memodelkan distribusi malaria. Tujuan dari penelitian ini adalah untuk membuat model dengan variabel yang memperhatikan *suspected*, infeksi, dorman dan pulih. Hasil model yang terbentuk kemudian disimulasikan dengan menggunakan software maple 18. Dari hasil simulasi dapat disimpulkan bahwa terjadi penurunan populasi yang terinfeksi dan peningkatan populasi yang pulih dari waktu ke waktu.

Kata Kunci: Model Matematika; SIDR; Analisis Kestabilan

Abstract

Indonesia is a country with frequent malaria cases. Therefore, a mathematical model is needed to model the distribution of malaria. The purpose of this study is to create a model with susceptible, infected, dormant and recovered compartments and to see the results of the simulation performed using maple 18 software. From the simulation results, it can be concluded that there is a decrease in the infected population and an increase in the recovered population over time.

Keywords: Mathematical Model; SIDR; Stability Analysis

Introduction

Malaria has long been one of the leading causes of death in the world, and Indonesia is no exception. With the annual average of cases reaching hundreds of thousands of cases, malaria should be an important spotlight in the world of health. Some of the regions in Indonesia with the highest malaria cases include Papua, West Papua, East Nusa Tenggara, and East Kalimantan. Malaria is caused by the Plasmodium parasite and is spread to humans through the bite of an infected female Anopheles mosquito. Symptoms of malaria usually appear 10-15 days after the parasite enters the human body. If there is no medical treatment within 24 hours, then the symptoms will quickly become a chronic disease that often leads to death. [1].

The life cycle of malaria is inseparable from the transmission process of Plasmodium spp. from the mosquito body to the human body or vice versa. When an infective mosquito sucks human blood, the sporozoites contained in the mosquito's salivary glands will enter through the human blood circulation to the liver cells. The sporozoites then develop into hepatic trophozoites. Liver trophozoites develop into liver schizonts. The liver schizont then ruptures to release merozoites with numbers reaching 10,000-30,000 merozoites. This cycle is known as the exoerythrocytic cycle which lasts for approximately 2 weeks. [2]. In determining most mathematical models according to biological developments so far, it takes a cycle of transmission from humans to diseases caused by this parasite. Malaria can be transmitted by living things. The Anopheles mosquito plays an important role in the spread of the Plasmodium

parasite in this natural mode of transmission. Plasmodium parasites that occur due to the bite of the Anopheles mosquito have 2 life cycle phases that can occur continuously and will occur repeatedly [3]. Therefore, in order to model the pattern of data that has the effect of the dispersion varies, the SIDR population approach can be used. In this study, researchers focused more on places that were susceptible to malaria incident and did not pay attention to time so that the time variable can't affect the model.

This study used the basis and literacy of relevant studies. The previous relevant research has been done about prevalence of malaria in Indonesia [3], global stability analysis of a delayed susceptible, infected, dormant and recovered from epidemic model with latent and quarantine [4] and stability of a mathematics model of malaria transmission with relapse [2]. The novelty of this research is to make a model of the data pattern which has the effect of the spread of malaria, the SIDR population approach can be used.

Research Method

A. Data Collection

The first step was data of malaria cases in Yogyakarta, Indonesia based on simulation and assumption in the region of Yogyakarta.

B. Modelling Infection

In general, the mathematical model of *Plasmodium vivax* malaria illustrates the path of the spread of the disease from susceptible individual group to infected group, the individual who infected with this disease, who are able to survive will recover but they will be recured if the *hymnozoit* is being active again, entering the dormant group. The subsequent infected individuals who are able to withstand the disease will recover and enter the recovered group and have permanent immunity to malaria. In malaria there is a period of time before the individual becomes infected.

C. SIDR Model

SIDR modeling was done by determining the following variables: Susceptible, is a group of healthy individuals but infected with malaria; Infected, is a group of infected individuals and can recover from malaria; Dormant, is a group of individuals who can recover but can recure, Recovered, is a group of individuals who have recovered from malaria with vaccines [5].

D. Interpretation

The result of malaria disease model with SIDR compartment is then interpreted into the differential equation obtained from the process of making model analysis in order to be more easily understood. The obtained SIDR model is then used to predict the number of malarial patients.

E. Validation

Furthermore, the forecast results are validated by the number of malaria cases in the same time period. Then the researchers will also conduct a survey related to the effects of SIDR compartment against people with malaria disease as well as opinion polls suggesting improvement of the method for good quality improvement in short or long term.

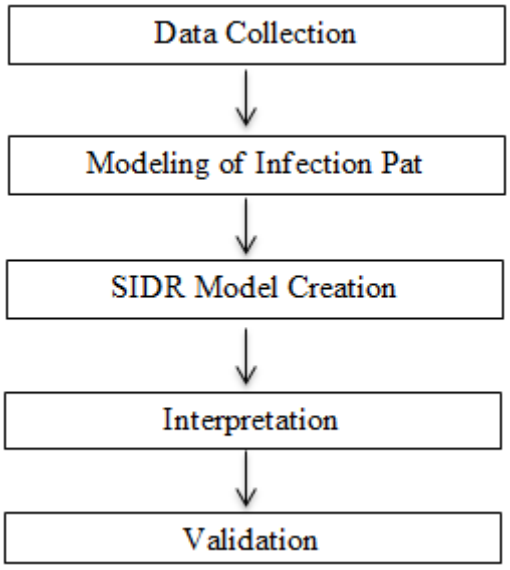

Figure 1. Flow Chart of Method

Results and Discussion

I. Mathematical Model SIDR

The model discussed in this paper was the SIDR model in which the population was divided into four distinct individual classes of *susceptible*, *symptomatic infective (is)*, *dormant* and *recovered* populations.

Malaria disease model with SIDR compartment can be formulated as follows:

Model Endemic Virus *Plasmodium vivax*

$$\frac{ds}{dt} = \delta - \alpha s(t) i_s(t) - \mu s(t) \qquad s(0) > 0$$

$$\frac{di_s}{dt} = \beta p e(t) - \theta i_s(t) - \mu i_s(t) \qquad i_s(0) > 0$$

$$\frac{dd}{dt} = \theta i(t) - \rho d(t) - \mu d(t) \qquad d(0) > 0$$

$$\frac{dr}{dt} = \rho d(t) - \mu r(t) \qquad r(0) > 0$$

$$N(t) = s(t) + +i_s(t) + d(t) + r(t)$$

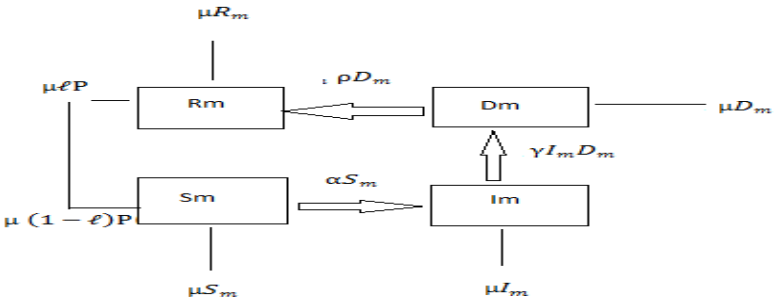

Figure 2. Flow Chart Mathematics Model *Plasmodium vivax* with *SIDR*

A. Assumption

1. Malaria virus infection occurs internally in the human body.
2. Changes in the population remain, so the rate of birth is equal to the rate of death.
3. The population of each district/city in Indonesia is equal to the number of human population in Sleman district, Yogyakarta.
4. The percentage of adding the number of human beings per compartment is the same.
5. No other microorganisms attack humans other than the Malaria virus.
6. The rate of recovery is constant.
7. Any infected quarantined will recover.
8. Viral deaths are ignored.
9. All infected humans have symptoms of Malaria disease.
10. Free viruses multiply in population Infected with rate of α (virus transmission rate).
11. The rate of recovery from infected to recovered is the same as quarantine to recovered.
12. In the model, all parameters of positive value with the immune system (p) are in the interval $0 < p < 1$.

Table 1. Parameter

Parameter	Description
$\boldsymbol{\delta}$	Constant birth rate
$\boldsymbol{\mu}$	Constant death rate
$\boldsymbol{\alpha}$	Transmission rate of *Plasmodium vivax* virus
$\boldsymbol{\beta}$	The probability of transmitting the *Plasmodium* *vivax* virus to humans
$\boldsymbol{\theta}$	The rate of increase in the population given the vaccine
$\boldsymbol{p}$	Constants $\left(\frac{1}{IP}\right)$ where IP is the virus incubation period for humans
$\boldsymbol{\rho}$	Recovery rate (constants)
$\boldsymbol{N}$	Total population

B. The Point of Illness-Free Equilibrium

By Taking $\frac{dS}{dt} = 0, \frac{dI_S}{dt} = 0$, author get the equilibrium point of the model. If take $i^0 = 0$, the disease-free equilibrium point will be obtained, where in this state all populations enter the susceptible population and no infected population can spread the disease [6]. So the free equilibrium point of the human population is $E_1 = (s^0, i_s^0, d^0) = \left(\frac{\delta}{\mu}, 0,0\right)$ [7].

C. The Point of Free Disease Equilibrium

If taken $i^0 \neq 0$, it can be shown that the point of disease (bacteria) is free where there are infective humans that can spread the disease and cause endemic. So that the epidemic equilibrium point in the human population is $E_2 = (s^*, i_s^*, d^*)$ with:

$$s^* = \frac{\beta\theta p+\beta\mu p+\theta\mu+\mu^2}{\alpha\beta p}, i_s^* = \frac{-\alpha\beta\delta p+\beta\theta\mu p+\beta\mu^2 p+\theta\mu^2+\mu^3}{(\beta\theta p+\beta\mu p+\theta\mu+\mu^2)\alpha}, d^* - \frac{\theta(-\alpha\beta\delta p+\beta\theta\mu p+\beta\mu^2 p+\theta\mu^2+\mu^3}{\alpha(\beta\theta\mu p+\beta\theta p\rho+\beta\mu^2 p+\beta\mu p\rho+\theta\mu^2+\theta\mu\rho+\mu^3+\mu^2\rho)}$$

Consequently, the equilibrium point of the mathematical model of the *Plasmodium vivax* transmission process in humans has two equilibrium points [8]:

1. The disease-free equilibrium Point

$$\boldsymbol{E_1} = (\boldsymbol{s^0}, \boldsymbol{i_s^0}, \boldsymbol{d^0}) = (\frac{\boldsymbol{\delta}}{\boldsymbol{\mu}}, \boldsymbol{0}, \boldsymbol{0})$$

2. Epidemic Equilibrium Points

$$\boldsymbol{E_2} = (\boldsymbol{s}^*, \boldsymbol{i_s^*}, \boldsymbol{d}^*).$$

D. Basic Reproduction Number ($\mathbf{R_0}$)

To determine the basic reproduction rate is to assume $I_s^* > 0$ [9]. Based on equilibrium point epidemic E_2 obtained:

$$\frac{-\alpha\beta\delta p + \beta\theta\mu p + \beta\mu^2 p + \theta\mu^2 + \mu^3}{(\beta\theta p + \beta\mu p + \theta\mu + \mu^2)\alpha} > 0$$
$$\leftrightarrow -\alpha\beta\delta p + \beta\theta\mu p + \beta\mu^2 p + \theta\mu^2 + \mu^3 > 0$$
$$\frac{(\beta\mu p + \mu^2)(\theta + \mu)}{\alpha\beta\delta p} > 1$$

Defined $R_0 = \frac{(\beta\mu p+\mu^2)(\theta+\mu)}{\alpha\beta\delta p}$

Based on the value of R_0 [10],

1. If $R_0 \leq 1$ then the quarantine model equation system has one equilibrium point ie the equilibrium-free equilibrium point $E_1 = (s^0, i_s^0, d^0)$.
2. If $\mathbf{R_0} > \mathbf{1}$ then the quarantine model equation system has two equilibrium points, ie, the equilibrium point of disease E_1 and the equilibrium point of free disease $\boldsymbol{E_2} = (\boldsymbol{s}^*, \boldsymbol{i_s^*}, \boldsymbol{d}^*)$.

II. Free Disease Equilibrium Analysis

Given a Jacobian matrix on human populations:

$$J(E_1) = \begin{bmatrix} -\mu & 0 & -\alpha\frac{\delta}{\mu} & 0 \\ 0 & -\beta p - \mu & \alpha\frac{\delta}{\mu} & 0 \\ 0 & -\beta p & -\theta - \mu & 0 \\ 0 & 0 & \theta & -\rho - \mu \end{bmatrix}$$

The eigen value is obtained from $\det(J(E_1) - \lambda I) = 0$ [11], the characteristic equation is obtained:

$$-\frac{(-\mu - \lambda)(\rho + \mu + \lambda)(\beta\mu^2 p\theta + \alpha\beta\delta p + \beta\lambda\mu p + \lambda\mu^2\theta + \mu^3\theta + \lambda^2\mu + \lambda\mu^2)}{\mu}$$

So obtained eigen value as follows:

$$\lambda_1 = -\mu, \qquad \lambda_2 = -\rho - \mu, \qquad \lambda_3 = \frac{1}{2}\frac{\left(-\beta\mu p - \mu^2\theta - \mu^2 + \sqrt{F}\right)}{\mu},$$
$$\lambda_4 = -\frac{1}{2}\frac{\left(\beta\mu p + \mu^2\theta + \mu^2 + \sqrt{F}\right)}{\mu}$$

With $F = \beta^2\mu^2 p^2 - 2\beta\mu^3 p\theta + \mu^4\theta^2 - 4\alpha\beta\delta\mu p + 2\beta\mu^3 p - 2\mu^4\theta + \mu^4$.

The equilibrium point of a system is said to be stable if the roots of the characteristic equation of a matrix have eigen values with a real negative part [12].

Lemma 1 [13].

1. If λ < 0 then the equilibrium point E_1 of the model equations system is stable asymptotically
2. If λ > 0 then the equilibrium point E_1 of the model equation system is unstable

Evidence: From the above equation, the eigen value $\lambda_1 = -\mu$, whereas it is known that μ is positive, so the real part of the first eigen value is negative. From the above equation, the eigen value $\lambda_2 = -\rho - \mu$, whereas it is known that ρ is positif, so the real part of the second eigen value is negative.

Because the values of all compartments are positive, whereas the values of the first and second eigen are negative,

$$(-\beta\mu p - \mu^2\theta - \mu^2) = \sqrt{(-\beta\mu p - \mu^2\theta - \mu^2)^2}$$
$$> \sqrt{\beta^2\mu^2p^2 - 2\beta\mu^3p\theta + \mu^4\theta^2 - 4\alpha\beta\delta\mu p + 2\beta\mu^3p - 2\mu^4\theta + \mu^4}$$

so the eigen values of $\boldsymbol{\lambda_3}$ and $\boldsymbol{\lambda_4}$ are either negative or are complex numbers with real numbers negative.

Next author will look for the Jacobian matrix in the human population at the equilibrium point $\boldsymbol{E_2} = (\boldsymbol{s}^*, \boldsymbol{i}_s^*, \boldsymbol{d}^*)$:

$$J(E_2) = \begin{bmatrix} A & 0 & B & 0 \\ B & -\beta p - \mu & \alpha\left(\dfrac{\beta\theta p + \beta\mu p + \theta\mu + \mu^2}{\alpha\beta p}\right) & 0 \\ 0 & -\beta p & -\theta - \mu & 0 \\ 0 & 0 & \theta & -\rho - \mu \end{bmatrix}$$

With:

$$A = -\alpha\left(\frac{-\alpha\beta\delta p + \beta\theta\mu p + \beta\mu^2 p + \theta\mu^2 + \mu^3}{(\beta\theta p + \beta\mu p + \theta\mu + \mu^2)\alpha}\right) - \mu$$
$$B = -\alpha\left(\frac{\beta\theta p + \beta\mu p + \theta\mu + \mu^2}{\alpha\beta p}\right)$$
$$C = \alpha\left(\frac{-\alpha\beta\delta p + \beta\theta\mu p + \beta\mu^2 p + \theta\mu^2 + \mu^3}{(\beta\theta p + \beta\mu p + \theta\mu + \mu^2)\alpha}\right)$$

The eigen value is obtained from $\det(J(E_2) - \lambda I) = 0$, the characteristic equation is obtained [13].

According to Routh-Hurwitz criteria, it is said to be asymptotically local if the eigen value of the real part is negative. By looking for characteristic and qualifying equations:

1. $b_1, b_2, b_3 > 0$
2. $b_1 b_2 - b_3 > 0$

From according above, author use Maple 18 software to evidence that $\boldsymbol{E_2}$ is stability asymptotically with qualifying Routh-Hurwitz criteria, and author get characteristic equation with $\boldsymbol{b_1, b_2, b_3}$ and $\boldsymbol{b_0 > 0}$ and $\boldsymbol{b_1 b_2 - b_3 > 0}$ so author can conclude that $\boldsymbol{E_2}$ is asymptotic stability equilibrium [14].

III. Numeric Simulation

Thus the model equation has the root of the part whose real part is negative. So it can be concluded that E_1 is a local asymptotic stable point.With the help of Maple 18 software using parameter values $\delta = 0.72$, $\mu = 0.72$, $\beta = 1.03$, $p = 0.08$, $\rho = 0.78$, $\theta = 0.3$ and $p = 0.08$. Simulation model with quarantine is done for case $R_0 > 0$, taken $\alpha = 0.002$. Result of simulation with initial value $(80.738, 41.61, 41.756, 23.798)$.

From parameter above author get $R_0 = 4966.31 > 0$ with $E_1 = \left(\frac{\delta}{\mu}, 0,0\right) = (1,0,0)$ and $E_2 = (s^*, i_s^*, d^*) = (33.72, 359.928, 71.986)$. So author can get graphic below:

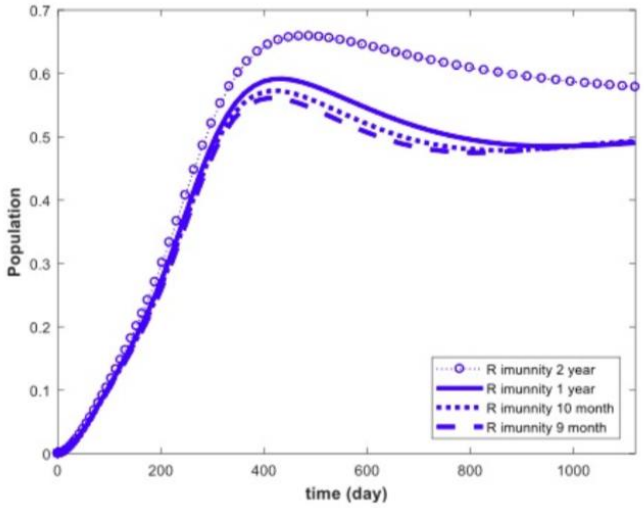

Figure 3. Recovered Graph

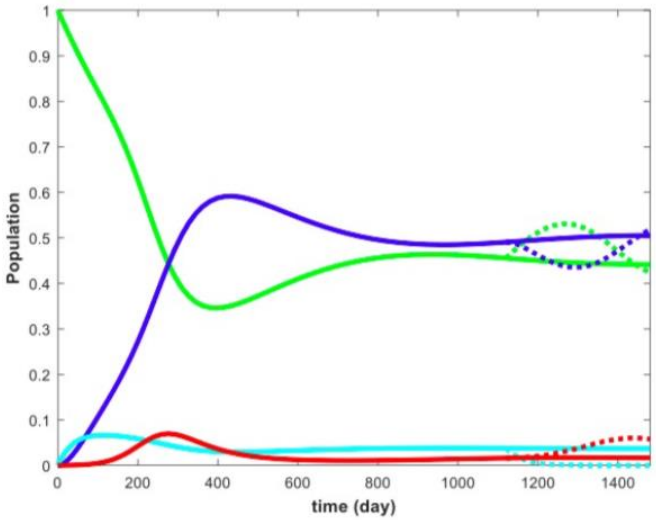

Figure 4. Numerical Simulation

In Figure 3, it showed that the growth rate of susceptible cell population decreases. This happens because the susceptible cell population is infected with the virus and enters the infectious group. At the rate of susceptible cell grow it is seen that this population will not change at a particular time t. In such circumstances, the system is in equilibrium.

In Figure 4, Exposed cell proportion is up and down. This increase is due to susceptible cells infected and eventually become infectious cell groups. But then the infectious cell goes down to the point where the movement of the infected cell is unchanged or in equilibrium. This decrease is due to the absence of the addition of susceptible cells into infected cells. These infected cells will continue to fall down to where the infectious cell growth rate is unchanged or in equilibrium.

Infected graph decreased at a certain time t. This decrease occurs because the infected cells also decreased. The population of this virus will continue to decrease to the extent that the growth rate of the virus does not change or in a state of equilibrium. Based on numerical results and recovered graph, virus population in equilibrium is **0** at a certain time ***t***, meaning Infected has switched to recovered.

Conclussion

From the results of the malaria model with SIDR compartment, it is seen that the graphs have not significant differences, but from the model charts with treatment, we know that the proportion of the population recovered with treatment is much less than the population symptomatic infected. So it can be concluded that the treatment with SIDR compartment in Malaria give positive effect on the spread of Malaria disease in humans. The conclusion that can be drawn from the above results is the mathematical model of human malaria disease with SIDR compartment is better than the before population in symptomatic infected.

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