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Increase and Decrease in Toxoplasmosis Infected Birth Rate from the Sensitivity Analysis

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ABSTRACT

This article aims to look at the dynamics of the toxoplasmosis epidemic with the effect of vaccination by increasing and decreasing the birth rate of infected with toxoplasmosis. The method used in this research is literature study and continued by using numerical simulation analysis. The research procedure used in this study is to simulate and analyze the parameters that affect the population. Some of the data used are secondary data on toxoplasmosis sufferers obtained from the Banda Aceh Health Office in 2018. From the numerical simulation results of the toxoplasmosis epidemic model with the vaccination effect, it was found that when the birth rate was infected with toxoplasmosis increased by at 5% then the number of individuals infected with toxoplasmosis, controlled individuals and the number of vaccinated individuals increases with the basic reproductive number $Ro > 1$. In this condition, there are no individuals who are susceptible to toxoplasmosis again so that vaccination for susceptible individuals can quickly overcome the spread of toxoplasmosis. Furthermore, the rate of births infected with toxoplasmosis decreases of 5% is obtained search population in the toxoplasmosis epidemic model has decreased with the basic reproduction number $Ro <1$. In this condition, the number of individuals in each population has decreased, resulting in the spread of toxoplasmosis disappeared from the population. So that this research can contribute to health science and the government in overcoming the toxoplasmosis epidemic.

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A. INTRODUCTION

Mathematical models are a set of equations or inequalities that reveal the behavior of real problems. Mathematical models are made based on assumptions and an analysis is carried out so that the model is made representative of the problems discussed. After the mathematical model is formed, analysis is carried out both analytically and numerically until a simulation is carried out to obtain a solution approach to a problem by looking at every dynamic that appears in the model being formed (Ndii, 2018).

Simulation is a technique to imitate or process an event that occurs in a system with the help of a computer device which is based on certain assumptions so that a system can be studied scientifically (Schotanus, 2013). Simulation is an appropriate tool to use in conducting experiments in order to obtain the best information from a component of the system.

Simulations are carried out to find an approach to a system component in real life by paying attention to the dynamics that occur in the environment and the object to be carried out. This is because it is very expensive and takes a long time if the experiment is done in real terms. One approach to explaining solutions to problems that occur in the real world is modeling or formulating real problems into mathematical language, one of which is an epidemic model. In this case, the epidemic model carried out on the spread of toxoplasmosis with vaccination in Banda Aceh City.

Toxoplasmosis is an infectious disease in humans and animals caused by the toxoplasma gondi parasite with the main source of its development through felidae (Cats) (cc) (Dubey, 2010). This disease is asymptomatic and can affect anyone, both adults, children and fetuses in pregnant women (Suparman et al., 2012). Toxoplasmosis in pregnant women can have a serious effect on the fetus while it is developing (Chaudhry, 2014). Although the majority of infected fetuses (about 75%) do not show obvious clinical signs at birth, many of them already have manifestations such as chorioretinitis and mental retardation later in life (Hamdan, 2015; Singh, 2016). Infection in the first trimester can lead to spontaneous abortion (Kheirandish et al., 2019)

In the current condition, treatment for toxoplasmosis is only given to individuals who are infected orally, that is, taking drugs (Paquet & Yudin, 2013). However, when the body's immune system conditions decline, toxoplasmosis can become active again (Bruna-romero et al., 2012; Robert-gangneux & Dardé, 2012). Giving the Toxovax® vaccine is a live vaccine that is licensed for mammals, one of which is sheep (Zhang et al., 2016). All toxoplasmosis vaccines provide protection in cats, but developments are still underway in making recombinant vaccines that can be used in humans (Innes et al., 2019). This is because the effectiveness in administering Toxoplasma vaccine to humans is still a health problem in disease transmission (Liu et al., 2012).

Many researches related to the toxoplasmosis epidemic in the field of mathematical modeling have been carried out. Researchers in other countries are very active in conducting research on the epidemic of toxoplasmosis with various perspectives and problems that occur in society. This is because toxoplasmosis is a disease that causes enormous losses to the environment, both humans and animals. One of the toxoplasmosis epidemic researchers who are active in conducting research development is Sulivan et al, and Robert and Dardec. Sulivan explains in his journal the dynamics of the spread of toxoplasma gondi in cells in the human body (A. Sullivan et al., 2012; A. M. Sullivan, 2013). Then Robert and Dardec discussed the mechanism of the toxoplasma gondi life cycle in intermediate and definitive hosts (Robert-gangneux & Dardé, 2012)In Indonesia, research related to the modeling of the toxoplasmosis epidemic is still very rare. Utami has conducted a research on mathematical model of the spread of toxoplasmosis by considering latent population. In his research, it was explained that the spread of toxoplasmosis disease was influenced by horizontal transmission, the influence of the immune system, handling or administration of drugs against disease (Utami & Sriningsih, 2018). Furthermore, the mathematical modeling of the toxoplasmosis epidemic with the effect of vaccination has been done by Yanni before. In the research, The analysis used is a sensitivity analysis of a mathematical model by obtaining two parameters that greatly affect the toxoplasmosis epidemic in the environment (Yanni, 2020). Furthermore, researchers have also conducted research related to modeling analysis and mathematical simulation of toxoplasmosis epidemic control and continued by analyzing two parameters based on the formed bifurcation diagram (Yanni & Zulfahmi, 2019, 2020). The research was conducted in different areas with different compartments.

This article discusses the simulation and interpretation analysis of changes in parameter values that affect the toxoplasmosis epidemic. The simulation is carried out to add and decrease the parameter value so that it has a relationship with the basic reproduction number based on the sensitivity analysis that has been done previously. The purpose of this study is to simulate and analyze previous studies by taking into account the dynamics that occur in the toxoplasmosis epidemic model with the effect of vaccination. Simulations were carried out on two parameters that have a strong influence on the spread of the disease, which these parameters were obtained from the sensitivity analysis of the toxoplasmosis epidemic mathematical model with the effect of vaccination. Several parameters used in the simulation were obtained from data from the Banda Aceh Health Office and other supporting articles. Another objective is to see the relationship between the analysis carried out analytically, namely the sensitivity analysis with dynamic simulation is appropriate so that an appropriate interpretation is obtained based on the dynamics that occur.

B. METHODS

This research was conducted in the city of Banda Aceh and the data used were secondary data about toxoplasmosis. This research was conducted in several stages, namely the study of literature reviews, the preparation of criteria for research variabels that were tested and revised through interviews and interviewing sources with SpOG Doctors (Obstetrics and Gynecology Specialists). Furthermore, the construction of a mathematical model is carried out and data collection is carried out. Then the data that has been obtained is converted into the form of parameterization so that it can be used in numerical simulations of mathematical models. The numerical simulation used in this research is Matlab Software. Some of the data used in the study were obtained from the Banda Aceh City Health Office in 2018 and some other data was obtained from estimating other supporting research parameters. The research procedure used in this study is to simulate and analyze the parameters that affect the population. The parameters that affect the population are obtained from the sensitivity analysis that has been carried out in previous studies.

C. RESULT AND DISCUSSION

1. A toxoplasmosis Epidemic Model Formulation with A Vaccination Effect

A mathematical model of the toxoplasmosis epidemic with vaccination effects has been previously done by Yanni. In this study, the spread of toxoplasmosis in the human population can be categorized into 4 populations, namely population S (vulnerable) states the number of individuals who are susceptible to disease, population I (infected) states the number of individuals who are infected with the disease and have the ability to transmit the disease to other individuals. , population C (controlled) states the number of individuals controlled for toxoplasmosis, and population V (vaccination) states the number of individuals vaccinated against toxoplasmosis. Before constructing a toxoplasmosis epidemic model with the effect of vaccination, assumptions are made to limit and clarify the problem to be used.

Based on the assumptions mentioned earlier, the following should be noted to build the model: $\frac{dS}{dt}$ =rate of change of the vulnerable subpopulation per unit time; $\frac{dI}{dt}$ = rate of change in the infected subpopulation per unit time; $\frac{dC}{dt}$ = controlled rate of change in subpopulation per unit time; $\frac{dV}{dt}$ = the rate of change of the subpopulation vaccinated per unit time; δ = birth rate; θ = rate of controlled individuals becoming susceptible individuals;α = Toxoplasmosis infection rate; μ = natural death rate; d = rate of death due to toxoplasmosis; ε = individual controlled rate; σ = birth rate that has been infected with Toxoplasma; β = rate of vaccinated susceptible individuals; Ω = The rate of vaccinated individuals infected with toxoplasmosis.

The following is a diagram of the transmission of a toxoplasmosis epidemic model with the effects of vaccination

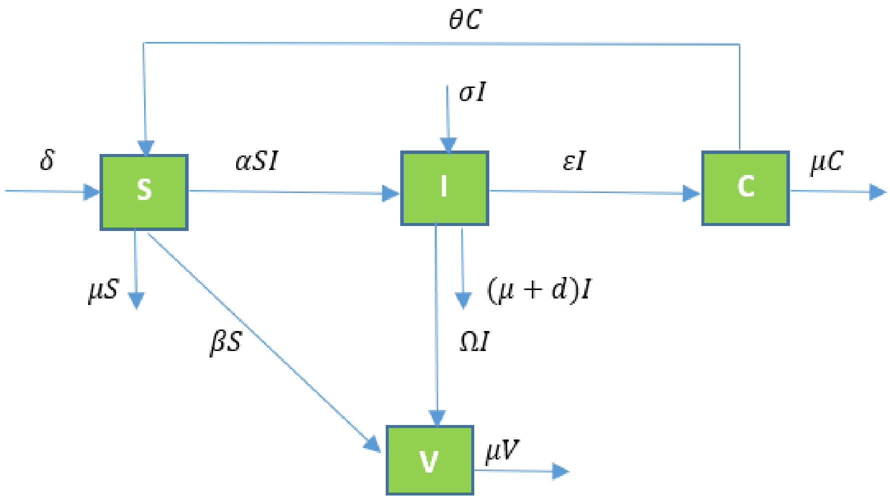

Figure 1. Compartment diagram of a toxoplasmosis epidemic model with vaccination effects

Based on the above assumptions and parameter analysis, a model for the spread of the toxoplasmosis epidemic with the effect of vaccination is obtained in the form of a differential equation as follows:

$$\frac{dS}{dt} = \delta - \alpha SI - \beta S - \mu S + \theta C \quad (1)$$

$$\frac{dI}{dt} = \alpha SI + \sigma I - \Omega I - (\mu + d)I - \varepsilon I \quad (2)$$

$$\frac{dC}{dt} = \varepsilon I - \theta C - \mu C \quad (3)$$

$$\frac{dV}{dt} = \Omega I + \beta S - \mu V \quad (4)$$

with each parameter is positive and the initial condition of each variable is positive, $S(0) \geq 0$, $I(0) \geq 0$, and $C(0) \geq 0$

2. Analysis of Disease Spread Model

Analysis of the model of the spread of toxoplasmosis with the effects of vaccination has been carried out by previous researchers. In that study, tequilibrium ducks toxoplasmosis disease free is a condition when an infected individual is zero, that is. Furthermore, for the equilibrium point the spread of toxoplasmosis with the effect of vaccination is:$E_o = \left(\frac{\delta}{\beta+\mu}, 0,0, \frac{\beta\delta}{\mu(\beta+\mu)}\right)$ dan $E_1 = (S^*, I^*, C^*, V^*)$ dengan

$$S^* = \frac{\Omega + \varepsilon + \mu + d - \sigma}{\alpha},$$

$$I^* = \frac{(\mu + \theta)[\alpha\delta - (\beta + \mu)(\Omega + \varepsilon + \mu + d - \sigma)]}{\alpha[(\mu + \theta)(\Omega + \mu + d - \sigma) + \mu\varepsilon]}$$

$$C^* = \frac{\varepsilon[\alpha\delta - (\beta + \mu)(\Omega + \varepsilon + \mu + d - \sigma)]}{\alpha[(\mu + \theta)(\Omega + \mu + d - \sigma) + \mu\varepsilon]},$$

$$V^* = \frac{\begin{array}{c}[\alpha\delta - (\beta + \mu)(\Omega + \varepsilon + \mu + d - \sigma)]\Omega(\mu + \theta) + \\ \beta(\Omega + \varepsilon + \mu + d - \sigma)(\theta[(\mu + \theta)(\Omega + \mu + d - \sigma) + \mu\varepsilon])\end{array}}{\mu\alpha[(\mu + \theta)(\Omega + \mu + d - \sigma) + \mu\varepsilon]}$$

Furthermore, the basic reproduction number Ro was obtained in the mathematical model of the toxoplasmosis epidemic with the vaccination effect, namely $R_o = \frac{\alpha\delta + \sigma(\beta+\mu)}{(\beta+\mu)(\Omega+\varepsilon+\mu+d)}$.

3. Model Simulation

a. Model Simulation of Toxoplasmosis Epidemic with Vaccination effect

The dynamics of the spread of disease caused by toxoplasmosis using a model that has been constructed and simulated using the values of the following parameters.

Table 1. Mathematical model parameter values

Parameter	Score
α	0.008067
β	0.75
ξ	0.00833
Ω	0.0667
σ	0.09
μ	0.000426
d	0.0146
δ	0, 000004087
θ	0.0001

By using the above parameter values and using the Matlab software, the dynamics of each subpopulation of the toxoplasmosis epidemic model with the vaccination effect can be described as follows.

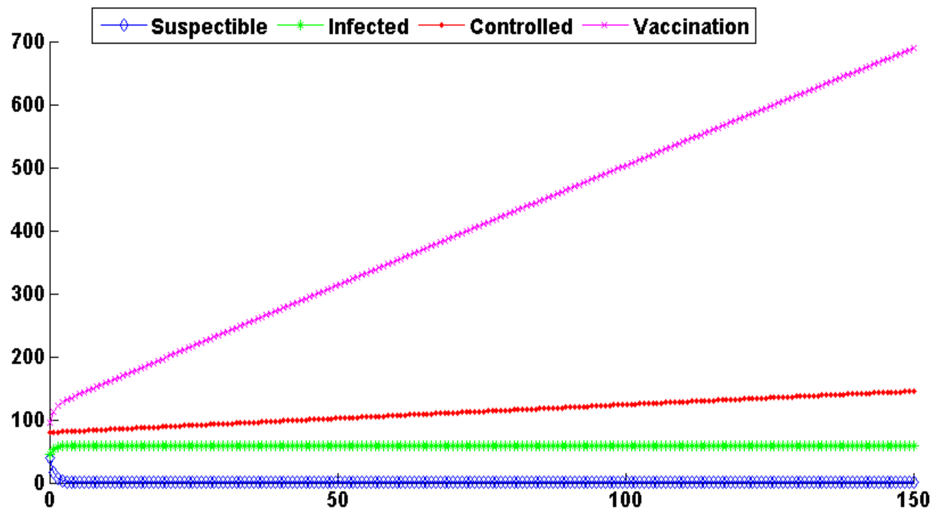

Figure 2. Disease epidemic conditions

This simulation was carried out using initial values at S = 40, I = 45, C = 80, and V = 95 with an observation time interval of 150 years. Figure 1 shows that from 40 vulnerable populations it decreases to 10 people so that with increasing time the number of subpopulations ranges decreases to very little. Furthermore, the human population infected with toxoplasmosis showed that out of 45 people infected with toxoplasmsosis slowly increased by 55 people. Then, the vaccination subpopulation experienced a very large number of increases, starting from the number of vaccination subpopulations of 95 people who were vaccinated, which increased very rapidly to 700 vaccinated people.

b. Sensitivity Analysis

Sensitivity analysis is an analysis conducted to determine the parameters that affect the mathematical model on the rate of change of the model. Sensitivity analysis is performed by calculating the sensitivity index value of these parameters (Chitnis, 2008).

Yanni has conducted a sensitivity analysis of the toxoplasmosis epidemic control model with the effect of vaccination. In this epidemic model, sensitivity index analysis is performed on the basic reproduction number *Ro* by using the parameter values in Table 1. The value of the sensitivity index analysis results of the parameters of the basic reproduction number *Ro* The parameters in the toxoplasmosis epidemic mathematical model with the vaccination effect are given in Table 2 below.

Table 2. Expression of parameter sensitivity to basic reproduction number

Parameter	Expression of *Ro* Sensitivity	***Ro* = 1.0010876**	
		***P* + 5%**	***P*-5%**
α	0, 0000004882	0.999348	0.9993423
σ	0.999999512	1.55453	0.44415
β	-4.87887E-07	0.9993453	0.9993454
Ω	-10.96599692	0.64258665	2,24668

Based on Table 2, it is found that the parameter in the model that most influences the Basic Reproduction Number (*Ro*) is the birth rate that has been infected with Toxoplasma and (σ) is the rate of vaccinated individuals infected with toxoplasmosis. This can be seen from the value of the result of the substitution of the parameter values on the sensitivity expression of each parameter and from this value it can also be seen that the relationship between each parameter to Ro. Parameter Ω has a negative relationship while parameter σ have a positive relationship. It is explained that when the parameter valueσ increases, the number of individuals infected with Toxoplasma increases which means that there is an epidemic of toxoplasmosis disease in the community in Banda Aceh. Furthermore, when the parameter value Ω if there is an increase, the number of vaccinated individuals infected with toxoplasmosis decreases, as a result the number of populations infected with toxoplasmosis will decrease over time so that toxoplasmosis can disappear from the population and there is no spread of toxoplasmosis in the community. Thus, giving toxoplasmosis vaccine to infected individuals greatly affects the spread of the disease so that the disease can be resolved early.

Next, a toxoplasmosis epidemic model simulation with the effect of vaccination is given by increasing and decreasing the number of parameters σ to see the relationship of toxoplasmosis epidemic dynamics.

a. Simulation when the parameter value σ + 5%.

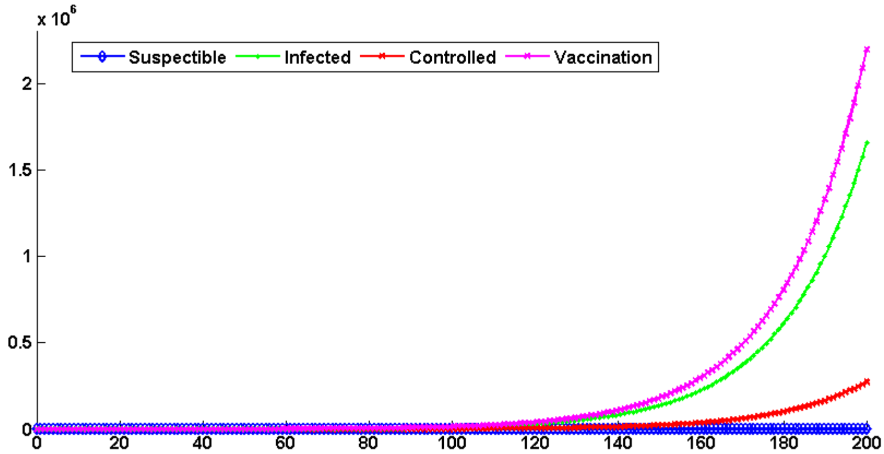

Figure 3. Population dynamics when σ + 5%.

Figure 3 shows that when the birth rate infected with toxoplasmosis has increased by 5% resulting in the number of individuals infected with toxoplasmosis, controlled individuals and the number of vaccinated individuals also increase with the basic reproduction number *Ro*> 1. Unlike what happens in vulnerable populations who experience a decrease very drastic. The number of individuals infected with toxoplasmosis experienced a very large increase, starting from 75 infected people 1.66×10^6 people infected with toxoplasmosis. Furthermore, the number of vaccinated individuals also experienced a very large increase, starting from 55 vaccinated people to being vaccinated. Based on these conditions, when the number of individuals infected with toxoplasmosis increases, the number of vaccinated individuals also increases. This results in no individual who returns susceptible to toxoplasmosis so that by giving vaccinations to susceptible individuals, they can quickly overcome the spread of toxoplasmosis 2.197×10^6

b. Simulation when the parameter value σ -5%.

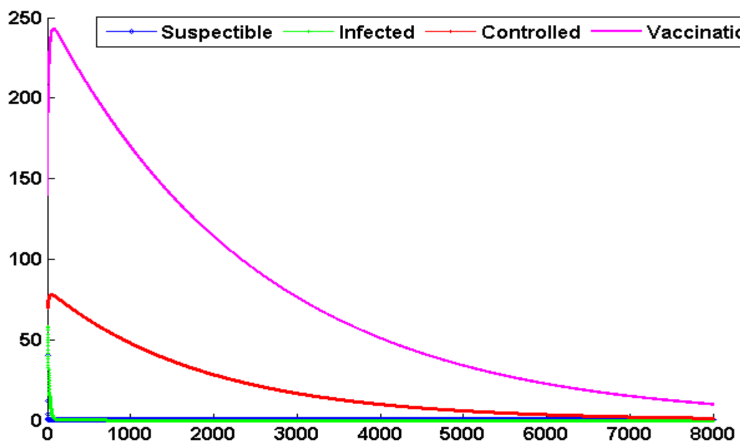

Figure 4. Population dynamics when σ -5%.

Figure 4 shows that when the birth rate infected with toxoplasmosis decreased by 5%, the number of each population in the toxoplasmosis epidemic model decreased with the basic reproduction number *Ro* <1. The number of populations infected with toxoplasmosis initially increased which then decreased, namely from 50 people who toxoplasmosis infection increased to 78 people infected with toxoplasmosis, which then decreased until there were no more individuals infected with toxoplasmosis in a population. Likewise, what happened to vulnerable and controlled populations also decreased until there were no more vulnerable and controlled populations in a population. In the vaccinated population. Based on these conditions, when the birth rate infected with toxoplasmosis decreases, the spread of toxoplasmosis can be lost from the population. Therefore, in order for the birth rate to be infected with toxoplasmosis to decrease, it is necessary to conduct socialization to the public regarding toxoplasmosis disease in pregnant women and to carry out routine toxoplasmosis examinations for pregnant women so that this disease can be resolved quickly, one of which is by adopting a healthy lifestyle and giving vaccines for pregnant women who have been infected with toxoplasmosis. Thus, in this condition, the spread of toxoplasmosis can be eliminated from the population. Thus, the results of this study are in conformity with the results of previous studies (Yanni, 2020).

D. CONCLUSION AND SUGGESTIONS

Based on the simulation results and discussion above, it can be concluded that when the parameter value σ (the birth rate infected with toxoplasmosis) increases by 5% then the number of individuals infected with toxoplasmosis, controlled individuals and the number of vaccinated individuals also increased with the basic reproduction number *Ro*> 1, while the susceptible population decreased. Any indication that this condition resulted There are no individuals who are susceptible to toxoplasmosis again so that by giving vaccinations to susceptible individuals, they can quickly overcome the spread of toxoplasmosis. Furthermore, when the parameter value σ reduced by 5% is obtained search population in the toxoplasmosis epidemic model has decreased with the basic reproduction number *Ro* <1. In this condition, each population has decreased, resulting in the spread of toxoplasmosis disappeared from the population. Thus, toxoplasmosis can be cured.

Furthermore, from the research that has been carried out, the research team recommends conducting a sensitivity analysis of the infected equilibrium point in the toxoplasmosis epidemic model with the effects of vaccination and simulations of each of the parameters that affect the infected equilibrium point.

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