DYNAMIC ANALYSIS OF SEITR MATHEMATICAL MODEL ON THE SPREAD OF HEPATITIS B DISEASE IN AMBON CITY

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ABSTRACT

Hepatitis B is a disease caused by infection with the HBV (Hepatitis B Virus) virus that commonly infects the liver and can develop into liver cancer. The disease can be transmitted through blood, semen, breast milk, saliva, vaginal fluids, and sperm. One effective way to prevent Hepatitis B disease is by vaccination. This study will construct a mathematical model, such as the SEITR model, to study the spread of Hepatitis B disease in Ambon City. The SEITR epidemic model is a disease spread model that divides the population into five subpopulation classes, namely the susceptible individual subpopulation class, the exposed individual subpopulation class, the infected individual subpopulation class, the treatment individual subpopulation class, and the recovered individual subpopulation class. Based on the dynamic system analysis conducted, two equilibrium points were obtained, namely the disease-free equilibrium point and the endemic equilibrium point. In addition, based on the data and simulation results, it can be concluded that the spread of Hepatitis B in Ambon City depends on the transmission rate from infected individuals to susceptible individuals.

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1. INTRODUCTION

Most hepatitis diseases caused by viral hepatitis are still endemic in Indonesia. Most viral hepatitis is caused by infection with hepatitis A, B, C, D, and E viruses [1]. Hepatitis B is a liver inflammation caused by infection with Hepatitis type B virus [2]. Hepatitis B virus infection is non-cytopathic, which does not trigger a nonspecific immune response. Hence, an adaptive/specific immune response mainly causes virus elimination. One of the immune cells that play a role in the adaptive immune response is the $CD8^+T$ cells, where these cells not only kill infected cells but also secrete cytokines that function to inhibit viral replication in a non-cytolytic manner, which in this case, results in the healing of infected cells [3]. People often do not know that they are infected with HBV infection because HBV infection can be asymptomatic for a long time due to the immune-tolerant phase (HBsAg and HBV DNA) that is positive without symptoms and signs and alanine transferase within normal limits in chronic development [4]. Currently, there are an estimated 28 million Indonesians infected with Hepatitis B [5]. Hepatitis B infection progresses to chronicity in infants at birth by 90% and in children aged 1-5 years by 30%-60% and adults by 2-6%. 21% of Hepatitis B virus infections will occur perinatally, 48% in early childhood, and 31% in adolescents or adults [6].

Hepatitis B is still one of the infectious diseases that are a health case in many parts of the world. The disease can be transmitted through blood, semen, breast milk, saliva, vaginal fluids, and sperm [7]. One of the effective ways to prevent Hepatitis B disease is vaccination [8]. Giving hepatitis B immunization to newborns should be based on whether the mother contains active hepatitis B virus at delivery. Repeat hepatitis B immunization can be considered at 10-12 years old. Suppose the child has not received hepatitis B immunization by the age of 5 years. In that case, it should be given as soon as possible [9].

The solution to the problem of the spread of Hepatitis B disease can be modeled using mathematical modeling. Mathematical modeling is a process of representing and explaining problems that occur in the real world in mathematical form [10]. Several recent studies discuss mathematical models to analyze the dynamics of disease spread, including COVID-19 spread Analysis using the SIR Model and Vaccination and parameter estimation [11], SITR model to analyze the dynamics of the spread of COVID-19 disease in India [12], the spread of Hepatitis A disease [13], the spread of Tuberculosis disease in Aceh [14], spread of Influenza disease in the body [15], and the spread of COVID-19 disease [16]. In addition, research has been conducted to analyze the spread of tuberculosis in Gorontalo Province using the MSEITR model [17], Numerical Solution of Hepatitis B Disease Model using Fourth Order Runge-Kutta Method [18], Analysis and Simulation of the SITR Model on the spread of Tuberculosis disease in Makassar City [19], Mathematical Model of Hepatitis B Transmission [20], and the SITR Model on the spread of COVID-19 [21].

By reviewing several mathematical models related to the spread of the disease above and considering that the Hepatitis B virus can survive for a long time and stay in the body of the patient [22] also because Hepatitis B disease is one of the infectious diseases that has become a health issue, in this study, we will construct a mathematical model in the form of a SEITR model to study the spread of Hepatitis B disease in Ambon City. A new model introduced in this research refers to the modified model [23] by adding a treatment subpopulation class. Based on the model, the equilibrium point of each compartment was sought in a disease-free and endemic state, as well as the basic reproduction number of the model. Furthermore, the stability of the equilibrium point was sought from the equilibrium point obtained. After that, numerical simulations were carried out using parameter values.

2. RESEARCH METHODS

The research methods used in this research are literature studies and case studies. The data used in this study are data on the number of patients infected with Hepatitis B, the number of patients who died from Hepatitis B infection, the number of patients who recovered after Hepatitis B infection, the number of Hepatitis B patients received medical treatment and data on the number of babies vaccinated. This data was obtained from the Ambon City Health Office in 2022. The research procedure used in this study is described in the following flowchart.
Based on the research flowchart, after constructing the SEITR model of the spread of Hepatitis B, the next step is to determine the disease-free and endemic equilibrium points. Then, the stability of each equilibrium point is analyzed. The next step is to find the basic reproduction number and perform simulations using Matlab software.

3. RESULTS AND DISCUSSION

3.1 Mathematical Model of Hepatitis B Virus Spread

The SEITR model of viral hepatitis spread described in this study consists of 5 sub-populations with the following assumptions:

1. The natural mortality rate is present in each subpopulation.
2. Susceptible subpopulations ($S$) increase due to the birth of humans who do not receive hepatitis B vaccination.
3. The Exposed subpopulation ($E$) increases due to contact between susceptible and infected individuals. The subpopulation of exposed individuals includes infected individuals without symptoms within the incubation period.
4. The Infected subpopulation ($I$) is the infected individuals with clinical symptoms. After the incubation period, the exposed subpopulation will become infected with clinical symptoms. It can transmit the disease to susceptible individuals.
5. The Treatment subpopulation ($T$) is individuals who are on medical treatment.
6. The Recovered subpopulation ($R$) is individuals who are cured. Infected individuals can become recovered because they have received medical treatment.
7. The Recovered subpopulation will not revert to susceptible individuals because they have a high immune system.

Based on these assumptions, hepatitis B can be schematically presented in a compartment chart, as shown in Figure 2.

\[
\begin{align*}
\frac{dS}{dt} &= (1 - \sigma)k - \beta SI - \mu_1 S \quad (1) \\
\frac{dE}{dt} &= \beta SI - (\alpha + \mu_1)E \\
\frac{dI}{dt} &= \alpha E - (\gamma + \mu_1 + \mu_2)I \\
\frac{dT}{dt} &= \gamma I - (\mu_1 + \delta)T \\
\frac{dR}{dt} &= \sigma k + \delta T - \mu_1 R \\
\end{align*}
\]

where:
- \(S\): Subpopulation class of susceptible individuals
- \(E\): Subpopulation class of exposed individuals without symptoms within the incubation period
- \(I\): Subpopulation class of infected individuals with clinical symptoms
- \(T\): Subpopulation class of individuals taking medical treatment
- \(R\): The subpopulation class of individuals who recovered from the disease
- \(k\): Natural birth rate
- \(\sigma\): Rate of vaccinated individuals
- \(\beta\): Transmission rate from infected individuals to susceptible individuals
- \(\alpha\): Rate of exposed individuals becoming infected
- \(\gamma\): Proportion of infected individuals on treatment
- \(\delta\): Rate of individuals who recover after treatment
- \(\mu_1\): Natural mortality rate
- \(\mu_2\): Death rate due to hepatitis B infection

3.2 Dynamical System Analysis of Hepatitis B Model

The equilibrium point is determined by the condition \(\frac{dS}{dt} = 0, \frac{dE}{dt} = 0, \frac{dI}{dt} = 0, \frac{dT}{dt} = 0, \frac{dR}{dt} = 0\). There are two equilibrium points, namely, the disease-free equilibrium point and the endemic equilibrium point. As for analyzing the stability of the equilibrium point, the Jacobian matrix of Equation (1) - Equation (5) can be formed as follows:
3.2.1 Disease Free Equilibrium Point

If taken \( I = 0 \), we obtain a disease-free equilibrium point where no population is infected by the Hepatitis B virus. So, the disease-free equilibrium point of the Hepatitis B epidemic model is obtained:

\[
E_0(S(t), E(t), I(t), T(t), R(t)) = \left( \frac{(1 - \sigma)k}{\mu_1}, 0, 0, \frac{\sigma k}{\mu_1} \right)
\]

3.2.2 Endemic Equilibrium Point

The endemic equilibrium point is affected by the subpopulation infected with the Hepatitis B virus by \( I \neq 0 \) thus obtained:

\[
E_1(S(t), E(t), I(t), T(t), R(t)) = E_1(S(t)^*, E(t)^*, I(t)^*, T(t)^*, R(t)^*)
\]

where

\[
S(t)^* = \frac{(\alpha + \mu_1)(y + \mu_1 + \mu_2)}{\alpha \beta}
\]

\[
E(t)^* = \frac{(1 - \sigma)k\alpha \beta - \mu_1(\alpha + \mu_1)(y + \mu_1 + \mu_2)}{(\alpha + \mu_1)\alpha \beta}
\]

\[
I(t)^* = \frac{(1 - \sigma)k\alpha \beta - \mu_1(\alpha + \mu_1)(y + \mu_1 + \mu_2)}{\beta(\alpha + \mu_1)(y + \mu_1 + \mu_2)}
\]

\[
T(t)^* = \frac{y(1 - \sigma)k\alpha \beta - \gamma \mu_1(\alpha + \mu_1)(y + \mu_1 + \mu_2)}{\beta(\alpha + \mu_1)(y + \mu_1 + \mu_2)(\mu_1 + \delta)}
\]

\[
R(t)^* = \frac{\sigma k\beta(\alpha + \mu_1)(y + \mu_1 + \mu_2)(\mu_1 + \delta) - \delta \gamma (1 - \sigma)k\alpha \beta - \delta \gamma \mu_1(\alpha + \mu_1)(y + \mu_1 + \mu_2)}{\beta \mu_1(\alpha + \mu_1)(y + \mu_1 + \mu_2)(\mu_1 + \delta)}
\]

3.2.3 Basic Reproduction Numbers

Basic reproduction number \( (R_0) \) is the Number of susceptible individuals infected by infected individuals. If \( R_0 < 1 \), then the disease will disappear from the population. If \( R_0 > 1 \), then the disease will increase to an outbreak. To determine the basic reproduction number, the disease-free equilibrium point was used. In determining the basic reproduction number, the subpopulations \( E \) and \( I \) are considered by using the next generation matrix to obtain the basic reproduction number. These subpopulations are as follows:

\[
\frac{da}{dt} = \beta SI - (\alpha + \mu_1)E \quad \text{and} \quad \frac{di}{dt} = \alpha E - (y + \mu_1 + \mu_2)I.
\]

Let \( \varphi(t) \) be the matrix for new infections and \( \psi(t) \) be the matrix for subpopulation movements:

\[
\varphi(t) = \left[ \begin{array}{c}
\psi_1 \\
\psi_2
\end{array} \right] = \left[ \begin{array}{c}
\beta SI/aE \\
\alpha E
\end{array} \right] \quad \text{and} \quad \psi(t) = \left[ \begin{array}{c}
\varphi_1 \\
\varphi_2
\end{array} \right] = \left[ \begin{array}{c}
-(\alpha + \mu_1)E \\
-(y + \mu_1 + \mu_2)I
\end{array} \right]
\]

Let \( F = \frac{d}{dt} \varphi(t) \) and \( V = \frac{d}{dt} \psi(t) \) respectively denote the first derivatives with respect to \( E \) and \( I \) so that we obtain:

\[
F = \left[ \begin{array}{c}
0 & \beta S/aE \\
\alpha & 0
\end{array} \right] \quad \text{new infection rate matrix}
\]

\[
V = \left[ \begin{array}{c}
0 & (\alpha + \mu_1)E/aE \\
0 & -(y + \mu_1 + \mu_2)I
\end{array} \right] \quad \text{subpopulation movement rate matrix}
\]
After substituting the disease-free equilibrium point in new infection rate matrix, we obtain:

$$F = \begin{bmatrix} 0 & \frac{\beta(1 - \sigma)k}{\mu_1} \\ \alpha & 0 \end{bmatrix}$$

Thus, the Next Generation Matrix is obtained, namely,

$$G = FV^{-1} = \begin{bmatrix} 0 & -\frac{\beta(1 - \sigma)k}{(\gamma + \mu_1 + \mu_2)\mu_1} \\ -\alpha + \mu_1 & 0 \end{bmatrix}$$

Based on the calculation, the basic reproduction number is obtained as follows:

$$R_0 = \frac{\alpha\beta(1 - \sigma)k}{(\alpha + \mu_1)(\gamma + \mu_1 + \mu_2)\mu_1}$$

### 3.2.4 Stability Analysis of Disease-Free Equilibrium Point

Based on the disease-free equilibrium point obtained, the following Jacobian matrix is formed:

$$J(E_0) = \begin{bmatrix} -\mu_1 & 0 & -\beta \frac{(1 - \sigma)k}{\mu_1} & 0 & 0 \\ 0 & -(\alpha + \mu_1) & \beta \frac{(1 - \sigma)k}{\mu_1} & 0 & 0 \\ 0 & \alpha & -(\gamma + \mu_1 + \mu_2) & 0 & 0 \\ 0 & 0 & \gamma & -((\mu_1 + \delta)) & 0 \\ 0 & 0 & 0 & \delta & -\mu_1 \end{bmatrix}$$

From the Jacobian matrix, by using $|\lambda I - J(E_0)| = 0$ then obtained:

$$\begin{vmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{vmatrix} \begin{vmatrix} -\mu_1 & 0 & -\beta \frac{(1 - \sigma)k}{\mu_1} & 0 & 0 \\ 0 & -(\alpha + \mu_1) & \beta \frac{(1 - \sigma)k}{\mu_1} & 0 & 0 \\ 0 & \alpha & -(\gamma + \mu_1 + \mu_2) & 0 & 0 \\ 0 & 0 & \gamma & -((\mu_1 + \delta)) & 0 \\ 0 & 0 & 0 & \delta & -\mu_1 \end{vmatrix} = 0$$

By using the cofactor rule, it is obtained

$$(\lambda + \mu_1)(\lambda + (\mu_1 + \delta)) \left(\lambda^2 + \lambda(\gamma + \mu_1 + \mu_2 + \alpha + \mu_1) + (\alpha + \mu_1)(\gamma + \mu_1 + \mu_2) - \alpha\beta \frac{(1 - \sigma)k}{\mu_1}\right) = 0$$

Because the equation above is a quadratic equation where $\gamma + \mu_1 + \mu_2 + \alpha + \mu_1$ value is positive, then to ensure that the eigenvalue is negative, the form of $(\alpha + \mu_1)(\gamma + \mu_1 + \mu_2) - \alpha\beta \frac{(1 - \sigma)k}{\mu_1}$ must be positive so that:

$$\frac{\alpha\beta(1 - \sigma)k}{(\alpha + \mu_1)(\gamma + \mu_1 + \mu_2)\mu_1} < 1$$

$$R_0 < 1$$

### 3.2.5 Stability Analysis of Endemic Equilibrium Point

Based on the endemic equilibrium point obtained, the following jacobian matrix is formed:
Thus, the individual birth rate in Ambon City in 2022 is 71,014 babies.

According to data from the Central Bureau of Statistics of Ambon City, the life expectancy of people of Ambon City in 2022 is 71 years [24]. Thus, the natural mortality rate of individuals in Ambon City is

$$\mu_1 = \frac{1}{\text{life expectancy}} = \frac{1}{71} = 0.0141$$

The individual birth rate was calculated based on data on babies born in Ambon City in 2022. Based on data from the Population and Civil Registration Service of Ambon City, it is known that the number of babies born in Ambon City in 2022 is 5,341, while the population of Ambon City in 2022 is 348,225 people. Thus, the individual birth rate in Ambon City is

$$k = \frac{\text{Number of babies born}}{\text{number of population}} = \frac{5,341}{348,225} = 0.0153$$

### 3.2.6 Numerical Simulation

At this stage, a model simulation of the spread of Hepatitis B in Ambon City was carried out. The simulation was carried out by giving parameter values to the model to explain the condition of the spread of the disease, which is displayed in the form of a curve based on the data summarized in Table 1.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Definition</th>
<th>Disease Free</th>
<th>Endemic</th>
</tr>
</thead>
<tbody>
<tr>
<td>$k$</td>
<td>Natural birth rate</td>
<td>0.0153</td>
<td>0.0153</td>
</tr>
<tr>
<td>$\sigma$</td>
<td>Rate of vaccinated individuals</td>
<td>0.6497</td>
<td>0.6497</td>
</tr>
<tr>
<td>$\beta$</td>
<td>Transmission rate from infected individuals to susceptible individuals</td>
<td>0.008</td>
<td>0.072</td>
</tr>
<tr>
<td>$\alpha$</td>
<td>Rate of exposed individuals becoming infected</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>$\gamma$</td>
<td>Rate of infected individuals on treatment</td>
<td>0.1354</td>
<td>0.1354</td>
</tr>
<tr>
<td>$\delta$</td>
<td>Rate of individuals who recover after treatment</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>$\mu_1$</td>
<td>Natural mortality rate</td>
<td>0.0141</td>
<td>0.0141</td>
</tr>
<tr>
<td>$\mu_2$</td>
<td>Death rate due to Hepatitis B infection</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>$R_0$</td>
<td>Basic Reproduction Number</td>
<td>0.0203</td>
<td>1.0135</td>
</tr>
</tbody>
</table>

According to data from the Central Bureau of Statistics of Ambon City, the life expectancy of people of Ambon City in 2022 is 71 years [24]. Thus, the natural mortality rate of individuals in Ambon City is

$$\mu_1 = \frac{1}{\text{life expectancy}} = \frac{1}{71} = 0.0141$$
The rate of infected individuals on treatment, rate of vaccinated individuals, rate of individuals who recover after treatment, and death rate due to Hepatitis B infection were calculated based on the number of patients infected with Hepatitis B, the number of Hepatitis B patients received medical treatment, the number of patients who died from Hepatitis B infection, the number of patients who recovered after Hepatitis B infection, and data on the number of babies vaccinated obtained from the Ambon City Health Office in 2022 as follows:

\[ \gamma = \frac{\text{number of patients receiving medical treatments}}{\text{number of infected individuals}} = \frac{124}{916} = 0.1354 \]

\[ \sigma = \frac{\text{number of babies vaccinated}}{\text{number of babies born}} = \frac{3,470}{5,341} = 0.6497 \]

Based on data obtained from the Ambon City Health Office, it is known that no patients died due to infection with Hepatitis B in Ambon City in 2022. Thus, the death rate due to Hepatitis B infection \((\mu_2)\) is 0 and the recovery rate after treatment \((\delta)\) is 1.

\[ \alpha = \frac{1}{\text{average incubation period}} = \frac{1}{3 \text{ months}} = \frac{1}{0.25 \text{ years}} = 4 \quad [25] \]

**Table 2** shows the initial values based on data obtained from the Civil Registry Office of Ambon City in 2022, the Central Bureau of Statistics of Ambon City in 2022 and the Ambon City Health Office in 2022.

<table>
<thead>
<tr>
<th>Subpopulations on ( t = 0 )</th>
<th>Initial value</th>
</tr>
</thead>
<tbody>
<tr>
<td>( S )</td>
<td>121,663</td>
</tr>
<tr>
<td>( E )</td>
<td>0</td>
</tr>
<tr>
<td>( I )</td>
<td>792</td>
</tr>
<tr>
<td>( T )</td>
<td>124</td>
</tr>
<tr>
<td>( R )</td>
<td>225,646</td>
</tr>
</tbody>
</table>

where:

\[ S = \text{Total Population} - I - T - R \]
\[ R = \text{Total} - S - I - T \]

Numerical simulations are carried out for disease-free (Figure 3-7) and endemic (Figure 8-12) cases based on the assumed transmission rate parameter values from infected individuals to susceptible individuals \((\beta)\).

For disease-free cases, the simulation process was performed with an initial time \( t_0 = 0 \) and an end time \( t_f = 40 \).

According to the initial condition \( t = 0 \), the number of individuals is 121,663. The number of susceptible subpopulations increases as the number of births of unvaccinated individuals increases. In the 40th year, the number of susceptible subpopulations is 127,790, and there are no exposed individuals in the 33rd year.
It can be concluded that at the time $t = 0$, the number of infected individuals was 792. Over time, it decreased until no more individuals were infected with Hepatitis B in the 33rd year. This is proportional to the number of individuals receiving medical treatment.

From **Figure 7**, it can be concluded that the initial condition at the time of the study was 225,646 individuals. $t = 0$ The Number of individuals is 225,646; this is in accordance with the initial conditions, and over time vulnerable individuals experience a significant increase due to the number of individuals who take treatment entering the subpopulation of cured individuals. In the 40th year, the number of cured individuals is 237,560.

Furthermore, a numerical simulation of the spread of Hepatitis B in Ambon City for endemic cases will also be presented. The simulation process was performed with $t_0 = 0$ and $t_f = 100$. 

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**Figure 5**: Infected subpopulation graph  
**Figure 6**: Treatment subpopulation graph  
**Figure 7**: Graph of the recovered subpopulation  
**Figure 8**: Susceptible subpopulation graph  
**Figure 9**: Graph of exposed subpopulations
Based on Figure 8-12, it can be seen that in the 100th year, the number of subpopulations of susceptible individuals was 134,580 people, the number of exposed individuals was eight people, the number of infected individuals was 230 people, the number of individuals receiving treatment was 30 people. The number of recovered individuals is 257,780 people.

4. CONCLUSIONS

Based on the stability analysis of the SEITR model, the spread of Hepatitis B has two equilibrium points, namely $E_0(S(t), E(t), I(t), T(t), R(t)) = \left(\frac{(1-\sigma)k}{\mu_5}, 0, 0, 0, \frac{\sigma k}{\mu_5}\right)$ as the disease-free equilibrium point and $E_1(S(t), E(t), I(t), T(t), R(t)) = E_1(S(t)^*, E(t)^*, I(t)^*, T(t)^*, R(t)^*)$ where

$$S(t)^* = \frac{a\beta}{\alpha + \mu_1(y + \mu_1 + \mu_2)}$$

$$E(t)^* = \frac{(1-\sigma)k\alpha \beta - \mu_1(\alpha + \mu_1)(y + \mu_1 + \mu_2)}{\alpha + \mu_1(a\beta)}$$

$$I(t)^* = \frac{(1-\sigma)k\alpha \beta - \mu_1(\alpha + \mu_1)(y + \mu_1 + \mu_2)}{\beta(\alpha + \mu_1)(y + \mu_1 + \mu_2)}$$

$$T(t)^* = \frac{y(1-\sigma)k\alpha \beta - y\mu_1(\alpha + \mu_1)(y + \mu_1 + \mu_2)}{\beta(\alpha + \mu_1)(y + \mu_1 + \mu_2)(\mu_1 + \delta)}$$

$$R(t)^* = \frac{\sigma k\beta(\alpha + \mu_1)(y + \mu_1 + \mu_2)(\mu_1 + \delta) - \delta y(1-\sigma)k\alpha \beta - \delta y\mu_1(\alpha + \mu_1)(y + \mu_1 + \mu_2)}{\beta \mu_1(\alpha + \mu_1)(y + \mu_1 + \mu_2)(\mu_1 + \delta)}$$

as the endemic equilibrium point with a basic reproduction number is $R_0 = \frac{a\beta(1-\sigma)k}{(\alpha + \mu_1)(y + \mu_1 + \mu_2)\mu_1}$. Based on the data and simulation results, it can be concluded that the spread of Hepatitis B in Ambon City is very dependent on the transmission rate from infected individuals to susceptible individuals.
REFERENCES


