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Mathematical Model of Vertical Transmission of Hepatitis B with the Effect of Treatment and Vaccination

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Abstract- Hepatitis B is a type of liver inflammation caused by infection with the Hepatitis B virus (HBV). Vertical transmissions can transmit hepatitis B. The precautions that can be taken to avoid vertical transmission of Hepatitis B are curable with treatment and vaccination. The goal of this research is to learn the mathematical model of Hepatitis B vertical transmission by observing the effects of treatment and vaccination, stability analysis, and interpreting the analysis results from the model. This research is essential. Points of equilibrium were discovered based on the model analysis. Through treatment and vaccination, vertical transmission of Hepatitis B will not become epidemic, according to the conclusions of this mathematical model's investigations. Meanwhile, as more and more effective contacts between infected individuals and vulnerable individuals occur and the average number of sexual partners per infected adult female, the vertical transmissions of Hepatitis B will grow.

1. Introduction

One of the problems faced by developing countries like Indonesia is infectious diseases. Infectious disease is caused by biological agents such as viruses, bacteria, and parasites (Semampow, 2017). One contagious disease that affects public health, mortality rates, life expectancy, and the economy of Indonesian society is Hepatitis (Kemenkes, 2018). Hepatitis is liver inflammation caused by viral infections, metabolic disorders, certain drugs, alcohol, and parasites (Sari, 2008). Hepatitis B is a liver infection caused by the VHB virus. This virus is a significant cause of acute liver failure, cirrhosis, and hepatocellular carcinoma (Friedman, 2018). It is worth noting that VHB is 100 times more infectious than HIV and 8-10 times more infectious than VHC (Jalaluddin, 2018). There are three main ways in which Hepatitis B can be transmitted, namely from mother to child, through sexual intercourse (including homosexuality), and the skin (Waluyo, 2011). Transmission of the virus from mother to child is called vertical transmission.

Vertical transmission or mother-to-child transmission (MTCT) occurs when a mother with acute or persistent Hepatitis B transmits the virus to her baby during pregnancy or delivery (Bustami, 2020). The virus can be transmitted through the umbilical cord bloodstream, during labor, or after delivery. This transmission type is more common in hyperendemic areas of Southeast Asia (Ozaras, 2018). Indonesia is a country with medium to high endemicity in Hepatitis B cases, and vertical transmission is the highest contributor to the increase in the number of chronic VHB cases. Indonesia is a country with a moderate to high endemic prevalence of Hepatitis B (Kemenkes, 2021).

The high number of Hepatitis B cases in Indonesia, especially those caused by vertical transmission, has a significant impact on human resources. Prevention efforts are crucial, primarily to protect children from the virus. The World Health Assembly (WHA) aims to achieve a world free of Hepatitis B virus infection through the 2016-2021 Global Health Sector Strategy (GHSS) program (WHO, 2019). As many as 95% of Hepatitis B virus transmission occurs vertically, and 90% of children who come into contact with the Hepatitis B virus from their mothers will develop chronic Hepatitis B (Kemenkes, 2020).

The World Health Assembly (WHA) is committed to eradicating Hepatitis B virus infection worldwide by 2030 by preventing virus transmission from mother to baby. The Indonesian government has implemented effective treatment and vaccination strategies to control and prevent vertical transmission of Hepatitis B. Vaccination is an effort to provide antigens that aim to build immunity in the body so that it can prevent attacks by pathogens (Maddeppugeng, 2018). Science and technology are powerful tools in curbing the spread of diseases. Mathematical modeling is one such tool that can be used confidently to understand and provide solutions to the spread of diseases. Mathematical modeling can be applied in various fields, such as physics, biology, medicine, engineering, social and political science, economics, business, finance, and computer network problems (Widowati & Sutimin, 2013).

Shaban and Manoza's (2016) mathematical model of vertical transmission of Hepatitis B with the effect of treatment is a confident step forward. The model divides the population into the mother and child population. The SUI model is used for both people, and the variable T (Treatment) is added to the population of mothers with acute Hepatitis B (Shaban & Manoza, 2016). The model also examines the effect of Hepatitis B treatment on vertical transmission, giving us confidence that we can fight this disease. There is also research that discusses the impact of vaccination on the spread of Hepatitis B, namely a study from Soleh (2019) on the stability of the mathematical model of Hepatitis B transmission under the influence of vaccination and treatment in the presence of migration (Soleh, 2019).

In this study, a mathematical model will be formed that combines treatment of women acutely infected with VHB with vaccination of babies born to women acutely infected with VHB. Thus, this problem can be modeled as a SUIT-SUVI mathematical model to see the effect of vaccination and treatment on vertical transmission of Hepatitis B. Therefore, research will be conducted titled "Mathematical Model of Vertical Transmission of Hepatitis B with the Effect of Treatment and Vaccination."

2. Methods

This research is basic or theoretical. The method used in this research is descriptive by analyzing the theories from the problems contained in the literature study. The technique used in forming this model is:

a) Determine the assumptions, variables, and parameters of the mathematical model of vertical transmission of Hepatitis B with treatment and vaccination.
b) They formed a mathematical model of vertical transmission of Hepatitis B with treatment and vaccination.
c) Analyze the equilibrium point of the mathematical model of vertical transmission of Hepatitis B with treatment and vaccination.
d) Interpret the result of a mathematical model of vertical transmission of Hepatitis B with treatment and vaccination analysis.
e) Make a simulation using Maple 18 software for a mathematical model of vertical transmission of Hepatitis B with treatment and vaccination.
f) Conclude.

3. Results and Discussion

(a) Mathematical Model of Vertical Transmission of Hepatitis B with the Effect of Treatment and Vaccination

Based on the stages in building a mathematical model, the first step is to identify the problem obtained from various information related to the problem. This stage is carried out by determining factors considered essential or appropriate to the situation, including identifying variables and parameters and forming relationships between these parameters and variables.

The variables used to form a mathematical model of vertical transmission of Hepatitis B with the influence of treatment and vaccination are groups of adult women who are susceptible to Hepatitis B infection (S_a), groups of children who are susceptible to Hepatitis B infection (S_c), groups of adult women who are acutely infected with Hepatitis B ((U_a), groups of children who are acutely infected with Hepatitis B (U_c), groups of adult women who are chronically infected with Hepatitis B (I_a). Group of children chronically infected with Hepatitis B ((I_c). Group of adult women with acute Hepatitis B infection who are on treatment (T_a). Group of children who received vaccination after birth (V_c). Thus, the total population is N=. $S_a + U_a + I_a + T_a + S_c + U_c + I_c + V_c$.

The parameters used for model building are:

1. λ: the rate of Hepatitis B infection from susceptible individuals to acutely infected individuals in the adult female group.
2. β: the average interaction of susceptible individuals with infected individuals in the adult female cohort.
3. Λ: the number of adult females susceptible to Hepatitis
4. π: the rate of change from female children in the susceptible child group to susceptible adult women.
5. b: birth rate of children susceptible to Hepatitis B infection.
6. p: proportion of children born to mothers with acute Hepatitis B who fall into the susceptible group.
7. $(1-p)$: the proportion of children born to mothers with acute Hepatitis B who belong to the group of children with acute Hepatitis B infection.
8. γ_a: chronic infection rate among adult women.
9. γ_c: chronic infection rate of children.
10. ε: treatment rate in adult females.
11. η: cure rate after treatment in adult women with acute infection.
12. α: chronic infection rate after treatment of acutely infected adult women.
13. ρ: proportion of children born to adult women with acute Hepatitis B after treatment into the susceptible group.
14. $(1-\rho)$: the proportion of children born to adult women with acute Hepatitis B after treatment into the group of acutely infected children.
15. μ: natural mortality rate of adult women
16. μ_c: natural mortality rate of children
17. δ_a: death rate due to complications in adult women
18. δ_c: complication mortality rate among children
19. ω: rate of children who become susceptible again after vaccination
20. ξ: child vaccination rate y

The assumptions used are as follows:

1. The total population N is considered constant within the modeling period.
2. Treatment is given to adult women who are acutely infected with Hepatitis B.
3. Treatment given to adult women with acute infection is not entirely successful, so some treated women may progress to the chronic stage.
4. Adult women who recover from acute Hepatitis B infection after treatment will again become susceptible to the disease.
5. Every child born is assumed to be susceptible to Hepatitis B.
6. Children born to women with acute Hepatitis B will either fall into the group of susceptible individuals or the group of Hepatitis B-infected individuals.
7. Death can be caused by natural death and death due to complications of Hepatitis B.
8. Vaccinations given to children are not entirely successful, so some vaccinated children can be susceptible to Hepatitis B again.

Based on the variables, parameters, and assumptions used, the mathematical model of vertical transmission of Hepatitis B with the effect of treatment and vaccination can be depicted in Figure 1:

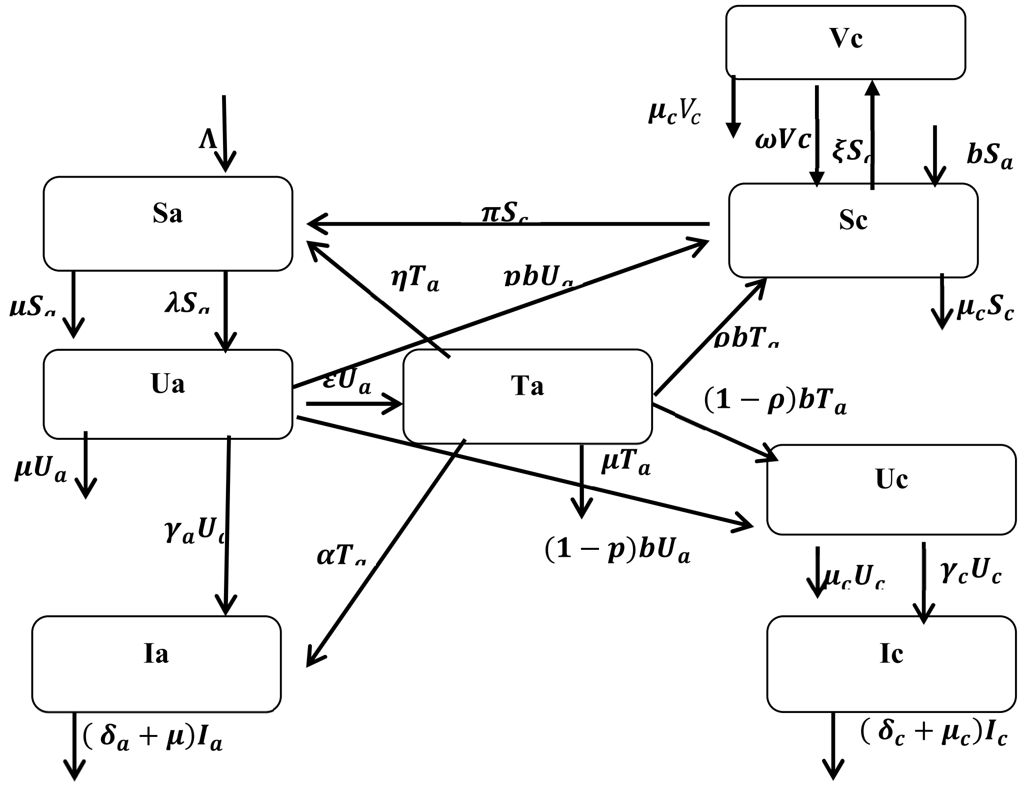


Figure 1. Mathematical Model of Vertical Transmission of Hepatitis B with the Effect of Treatment and Vaccination

Based on Figure 1, a mathematical model in the form of a system of differential equations can be formed:

$$\frac{dS_a}{dt} = \Lambda + \pi S_c + \eta T_a - (\lambda + \mu) S_a$$

$$\frac{dU_a}{dt} = \lambda S_a - (\mu + \varepsilon + \gamma_a + b) U_a$$

$$\frac{dI_a}{dt} = \gamma_a U_a + \alpha T_a - (\delta_a + \mu) I_a$$

$$\frac{dT_a}{dt} = \varepsilon U_a - (\alpha + \mu + \eta + b) T_a$$

$$\frac{dS_c}{dt} = bS_a + pbU_a + \rho bT_a + \omega V_c - (\xi + \pi + \mu_c) S_c$$

$$\frac{dU_c}{dt} = (1-p) bU_a + (1-\rho) bT_a - (\mu_c + \gamma_c) U_c$$

$$\frac{dI_c}{dt} = \gamma_c U_c - (\delta_c + \mu_c) I_c$$

$$\frac{dV_c}{dt} = \xi S_c - (\omega + \mu_c) V_c$$

It will be generalized in the following way to make the analysis easier.

$A_1 = \lambda + \mu$ $\quad A_6 = 1 - p$

$A_2 = \mu + \varepsilon + \gamma_a + b$ $\quad A_7 = 1 - \rho$

$A_3 = \delta_a + \mu$ $\quad A_8 = \mu_c + \gamma_c$

$A_4 = \alpha + \mu + \eta + b$ $\quad A_9 = \delta_c + \mu_c$

$A_5 = \xi + \pi + \mu_c$ $\quad A_{10} = \omega + \mu_c$

So that the following equation is obtained:

$$\frac{dS_a}{dt}=\Lambda+\pi S_c+\eta T_a-A_1S_a \quad (1)$$
$$\frac{dU_a}{dt}=\lambda S_a-A_2U_a \quad (2)$$
$$\frac{dI_a}{dt}=\gamma_a U_a+\alpha T_a-A_3I_a \quad (3)$$
$$\frac{dT_a}{dt}=\varepsilon U_a-A_4T_a \quad (4)$$
$$\frac{dS_c}{dt}=bS_a+pbU_a+\rho bT_a+\omega V_c-A_5S_c \quad (5)$$
$$\frac{dU_c}{dt}=A_6bU_a+A_7bT_a-A_8U_c \quad (6)$$
$$\frac{dI_c}{dt}=\gamma_c U_c-A_9I_c \quad (7)$$
$$\frac{dV_c}{dt}=\xi S_c-A_{10}V_c \quad (8)$$

(b) Mathematical Model Analysis of Vertical Transmission of Hepatitis B with the Effect of Treatment and Vaccination

1. Fixed Point of Endemic Vertical Transmission of Hepatitis B with the Effect of Treatment and Vaccination.

The fixed point of endemic vertical transmission of Hepatitis B can be interpreted that there are several individuals affected by vertical transmission of Hepatitis B in the population, mathematically expressed by $S_a>0, U_a>0, I_a>0, T_a>0, S_c>0, U_c>0, I_c>0$,, dan $V_c>0$. Suppose $S_a=S_a{}^*$, $U_a=U_a{}^*$, $I_a=I_a{}^*$, $T_a=T_a{}^*$, $S_c=S_c{}^*$, $U_c=U_c{}^*$, $I_c=I_c{}^*$ dan $V_c=V_c{}^*$ The endemic fixed point is searched using Maple software so that the endemic fixed issue is obtained as follows:

$$S_a{}^*=\frac{(\mu+\varepsilon+\gamma_a+b)(\alpha+\mu+\eta+b)\Lambda}{-(\omega+\mu_C)(\alpha+\mu+\eta+b)b\lambda p\pi-(\omega+\mu_C)b\varepsilon\lambda\pi\rho+(\lambda+\mu)(\omega+\mu_C)A_2(\alpha+\mu+\eta+b)(\xi+\pi+\mu_c)-(\lambda+\mu)(\mu+\varepsilon+\gamma_a+b)}$$
$$\frac{\left((\omega+\mu_C)(\xi+\pi+\mu_c)-\omega\xi\right)}{(\alpha+\mu+\eta+b)\omega\xi-(\omega+\mu_C)(\mu+\varepsilon+\gamma_a+b)(\alpha+\mu+\eta+b)b\pi-(\omega+\mu_C)(\xi+\pi+\mu_c)\varepsilon\eta\lambda+\varepsilon\eta\lambda\omega\xi}$$

$$U_a{}^*=\frac{(\alpha+\mu+\eta+b)\lambda}{-(\omega+\mu_c)(\alpha+\mu+\eta+b)b\lambda p\pi-(\omega+\mu_c)b\varepsilon\lambda\pi\rho+(\lambda+\mu)(\omega+\mu_c)(\mu+\varepsilon+\gamma_a+b)(\alpha+\mu+\eta+b)(\xi+\pi+\mu_c)-(\lambda+\mu)}$$
$$\frac{\Lambda\left((\omega+\mu_c)(\xi+\pi+\mu_c)-\omega\xi\right)}{(\mu+\varepsilon+\gamma_a+b)(\alpha+\mu+\eta+b)\omega\xi-(\omega+\mu_c)(\mu+\varepsilon+\gamma_a+b)(\alpha+\mu+\eta+b)b\pi-(\omega+\mu_c)(\xi+\pi+\mu_c)\varepsilon\eta\lambda+\varepsilon\eta\lambda\omega\xi}$$

$$I_a{}^*=\frac{\left((\alpha+\mu+\eta+b)\gamma_a+\alpha\varepsilon\right)\lambda}{(\delta_a+\mu)\left(-(\omega+\mu_c)(\alpha+\mu+\eta+b)b\lambda p\pi-(\omega+\mu_c)b\varepsilon\lambda\pi\rho+(\lambda+\mu)(\omega+\mu_c)(\mu+\varepsilon+\gamma_a+b)(\alpha+\mu+\eta+b)(\xi+\pi+\mu_c)-(\lambda+\mu)(\mu+\varepsilon+\gamma_a+b\right)}$$
$$\frac{\Lambda\left((\omega+\mu_c)(\xi+\pi+\mu_c)-\omega\xi\right)}{(\alpha+\mu+\eta+b)\omega\xi-(\omega+\mu_c)(\mu+\varepsilon+\gamma_a+b)(\alpha+\mu+\eta+b)b\pi-(\omega+\mu_c)(\xi+\pi+\mu_c)\varepsilon\eta\lambda+\varepsilon\eta\lambda\omega\xi)}$$

$$T_a{}^*=\frac{\varepsilon\lambda\Lambda}{-(\omega+\mu_c)(\alpha+\mu+\eta+b)b\lambda p\pi-(\omega+\mu_c)b\varepsilon\lambda\pi\rho+(\lambda+\mu)(\omega+\mu_c)(\mu+\varepsilon+\gamma_a+b)(\alpha+\mu+\eta+b)(\xi+\pi+\mu_c)-(\lambda+\mu)(\mu+\varepsilon+\gamma_a+b)}$$
$$\frac{\left((\omega+\mu_c)(\xi+\pi+\mu_c)-\omega\xi\right)}{(\alpha+\mu+\eta+b)\omega\xi-(\omega+\mu_c)(\mu+\varepsilon+\gamma_a+b)(\alpha+\mu+\eta+b)b\pi-(\omega+\mu_c)(\xi+\pi+\mu_c)\varepsilon\eta\lambda+\varepsilon\eta\lambda\omega\xi}$$

$$S_c{}^*=\frac{(\omega+\mu_c)\Lambda b}{-(\omega+\mu_c)(\alpha+\mu+\eta+b)b\lambda p\pi-(\omega+\mu_c)b\varepsilon\lambda\pi\rho+(\lambda+\mu)(\omega+\mu_c)(\mu+\varepsilon+\gamma_a+b)(\alpha+\mu+\eta+b)(\xi+\pi+\mu_c)-(\lambda+\mu)(\mu+\varepsilon+\gamma_a+b)}$$
$$\frac{\left((\alpha+\mu+\eta+b)\lambda p+\varepsilon\lambda\rho+(\mu+\varepsilon+\gamma_a+b)(\alpha+\mu+\eta+b)\right)}{(\alpha+\mu+\eta+b)\omega\xi-(\omega+\mu_c)(\mu+\varepsilon+\gamma_a+b)(\alpha+\mu+\eta+b)b\pi-(\omega+\mu_c)(\xi+\pi+\mu_c)\varepsilon\eta\lambda+\varepsilon\eta\lambda\omega\xi}$$

$$U_c{}^*=\frac{\left(b((\alpha+\mu+\eta+b)(1-p)+(1-\rho)\varepsilon\right)}{(\mu_c+\gamma_c)\left(-(\omega+\mu_c)(\alpha+\mu+\eta+b)b\lambda p\pi-(\omega+\mu_c)b\varepsilon\lambda\pi\rho+(\lambda+\mu)(\omega+\mu_c)(\mu+\varepsilon+\gamma_a+b)(\alpha+\mu+\eta+b)(\xi+\pi+\mu_c)\right)}$$
$$\frac{\Lambda\lambda((\omega+\mu_c)(\xi+\pi+\mu_c)-\omega\xi)}{-(\lambda+\mu)(\mu+\varepsilon+\gamma_a+b)(\alpha+\mu+\eta+b)\omega\xi-(\omega+\mu_c)(\mu+\varepsilon+\gamma_a+b)(\alpha+\mu+\eta+b)b\pi-(\omega+\mu_c)(\xi+\pi+\mu_c)\varepsilon\eta\lambda+\varepsilon\eta\lambda\omega\xi}$$

$$I_c^{*}=\frac{\left(b\gamma_c((\alpha+\mu+\eta+b)(1-p)+(1-\rho)\varepsilon\right)\Lambda}{(\delta_c+\mu_c)(\mu_c+\gamma_c)\left(-(\omega+\mu_c)(\alpha+\mu+\eta+b)b\lambda p\pi-(\omega+\mu_c)b\varepsilon\lambda\pi\rho+(\lambda+\mu)(\omega+\mu_c)(\mu+\varepsilon+\gamma_a+b)(\alpha+\mu+\eta+b)(\xi+\pi+\mu_c)\right)}$$

$$\frac{\lambda((\omega+\mu_c)(\xi+\pi+\mu_c)-\omega\xi))}{-(\lambda+\mu)(\mu+\varepsilon+\gamma_a+b)(\alpha+\mu+\eta+b)\omega\xi-(\omega+\mu_c)(\mu+\varepsilon+\gamma_a+b)(\alpha+\mu+\eta+b)b\pi-(\omega+\mu_c)(\xi+\pi+\mu_c)\varepsilon\eta\lambda+\varepsilon\eta\lambda\omega\xi}$$

$$V_c^{*}=\frac{\Lambda b\xi}{-(\omega+\mu_c)(\alpha+\mu+\eta+b)b\lambda p\pi-(\omega+\mu_c)b\varepsilon\lambda\pi\rho+(\lambda+\mu)(\omega+\mu_c)(\mu+\varepsilon+\gamma_a+b)(\alpha+\mu+\eta+b)(\xi+\pi+\mu_c)-(\lambda+\mu)(\mu+\varepsilon+\gamma_a+b)}$$

$$\frac{\left((\alpha+\mu+\eta+b)\lambda p+\varepsilon\lambda\rho+(\mu+\varepsilon+\gamma_a+b)(\alpha+\mu+\eta+b)\right)}{(\alpha+\mu+\eta+b)\omega\xi-(\omega+\mu_c)(\mu+\varepsilon+\gamma_a+b)(\alpha+\mu+\eta+b)b\pi-(\omega+\mu_c)(\xi+\pi+\mu_c)\varepsilon\eta\lambda+\varepsilon\eta\lambda\omega\xi}$$

(c) Stability Analysis of the Mathematical Model of Vertical Transmission of Hepatitis B with the Effect of Treatment and Vaccination

Fixed point stability analysis can be determined by determining the eigenvalues of the Jacobian matrix in equations (1), (2), (3), (4), (5), (6), (7) and (8). So, a Jacobian matrix is obtained, as in Figure 2.

$$\begin{bmatrix} -A1 & 0 & 0 & \eta & \phi & 0 & 0 & 0 \\ \lambda & -A2 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \gamma 1 & -A3 & \alpha & 0 & 0 & 0 & 0 \\ 0 & \varepsilon & 0 & -A4 & 0 & 0 & 0 & 0 \\ b & bp & 0 & b\rho & -A5 & 0 & 0 & \omega \\ 0 & A6b & 0 & A7b & 0 & -A8 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \gamma 2 & -A9 & 0 \\ 0 & 0 & 0 & 0 & \xi & 0 & 0 & -A10 \end{bmatrix}$$

Figure 2. Jacobian Matrix of Mathematical Model of Vertical Transmission of Hepatitis B with the Effect of Treatment and Vaccination

Since there are two fixed points, the stability of the fixed point will also be analyzed at both fixed points.

1. Stability of the Fixed Point of the Mathematical Model of Vertical Transmission of Hepatitis B With the Effect of Treatment and Vaccination

The fixed point is stable if all eigenvalues of the Jacobian matrix at the endemic fixed point are negative. The endemic fixed point of the mathematical model of vertical transmission of Hepatitis B with the effect of treatment and vaccination is $E_1 = (S_a^*, S_c^*, U_a^*, U_c^*, I_a^*, I_c^*, T_a^*, V_c^*)$. When $\lambda = c\beta\frac{(U_a+\theta I_a+\tau T_a)}{(S_a+U_a+I_a+T_a)}$.

To facilitate the analysis, let us suppose

$S_a^* = w$ $\quad$ I_a^*=y

$U_a^* = x$ $\quad$ $T_a^* = z$

Suppose λ is an eigenvalue of the Jacobian matrix; then, it is obtained as in Figure 3.

$$\begin{bmatrix} \lambda+A1 & 0 & 0 & -\eta & -\phi & 0 & 0 & 0 \\ -\lambda & \lambda+A2 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & -\gamma 1 & \lambda+A3 & -\alpha & 0 & 0 & 0 & 0 \\ 0 & -\varepsilon & 0 & \lambda+A4 & 0 & 0 & 0 & 0 \\ -b & -bp & 0 & -b\rho & \lambda+A5 & 0 & 0 & -\omega \\ 0 & -A6b & 0 & -A7b & 0 & \lambda+A8 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -\gamma 2 & \lambda+A9 & 0 \\ 0 & 0 & 0 & 0 & -\xi & 0 & 0 & \lambda+A10 \end{bmatrix}$$

Figure 3. Eigenvalue of Jacobian Matrix of Mathematical Model of Vertical Transmission of Hepatitis B with the Effect of Treatment and Vaccination

So that the characteristic equation is obtained as follows:

$$\begin{aligned} &\big(-A10\,A4\,b\,\kappa p\phi - A10\,b\,\varepsilon\kappa\phi\rho - A10\,b\,\kappa\lambda p\phi - A4\,b\,\kappa\lambda p\phi - b\,\varepsilon\kappa\lambda\phi\rho - b\,\kappa\lambda^2 p\phi \\ &+ A1\,A10\,A2\,A4\,A5 + A1\,A10\,A2\,A4\,\lambda + A1\,A10\,A2\,A5\,\lambda + A1\,A10\,A2\,\lambda^2 \\ &+ A1\,A10\,A4\,A5\,\lambda + A1\,A10\,A4\,\lambda^2 + A1\,A10\,A5\,\lambda^2 + A1\,A10\,\lambda^3 + A1\,A2\,A4\,A5\,\lambda \\ &+ A1\,A2\,A4\,\lambda^2 - A1\,A2\,A4\,\omega\xi + A1\,A2\,A5\,\lambda^2 + A1\,A2\,\lambda^3 - A1\,A2\,\lambda\omega\xi + A1\,A4\,A5\,\lambda^2 \\ &+ A1\,A4\,\lambda^3 - A1\,A4\,\lambda\omega\xi + A1\,A5\,\lambda^3 + A1\,\lambda^4 - A1\,\lambda^2\omega\xi + A10\,A2\,A4\,A5\,\lambda \\ &- A10\,A2\,A4\,b\,\phi + A10\,A2\,A4\,\lambda^2 + A10\,A2\,A5\,\lambda^2 - A10\,A2\,b\,\lambda\phi + A10\,A2\,\lambda^3 \\ &+ A10\,A4\,A5\,\lambda^2 - A10\,A4\,b\,\lambda\phi + A10\,A4\,\lambda^3 - A10\,A5\,\varepsilon\eta\kappa + A10\,A5\,\lambda^3 - A10\,b\,\lambda^2\phi \\ &- A10\,\varepsilon\eta\kappa\lambda + A10\,\lambda^4 + A2\,A4\,A5\,\lambda^2 - A2\,A4\,b\,\lambda\phi + A2\,A4\,\lambda^3 - A2\,A4\,\lambda\omega\xi \\ &+ A2\,A5\,\lambda^3 - A2\,b\,\lambda^2\phi + A2\,\lambda^4 - A2\,\lambda^2\omega\xi + A4\,A5\,\lambda^3 - A4\,b\,\lambda^2\phi + A4\,\lambda^4 - A4\,\lambda^2\omega\xi \\ &- A5\,\varepsilon\eta\kappa\lambda + A5\,\lambda^4 - b\,\lambda^3\phi - \varepsilon\eta\kappa\lambda^2 + \varepsilon\eta\kappa\omega\xi + \lambda^5 - \lambda^3\omega\xi\big)(\lambda + A3)(\lambda \\ &+ A8)(\lambda + A9) = 0 \end{aligned}$$

Furthermore, the stability analysis of fixed points can be searched using the Routh-Hurwitz criteria. However, this has not been carried out in this study.

(d) Basic Reproduction Number

The primary reproduction number is a measure that becomes the threshold used to determine whether a population is endemic or not.

1. Primary Reproduction Number Without the Effect of Treatment and Vaccination

In this model, there are four infected classes, namely. U_c, I_c, U_a, I_a, and I_and 4 uninfected classes, namely $S_c, S_a, T_a, and\ V_c$. B Reproduction numbers are obtained by forming Matrix Next Generation (MNG) from the system of equations.
So that the primary reproduction number of the mathematical model of vertical transmission of Hepatitis B is obtained, namely:

$$R_0 = \frac{\beta c\mu(\pi+\mu_c)(\mu+\delta_a+\theta\gamma_a)}{(\mu+\delta_a)(b+\gamma_a+\mu)\mu(\pi+\mu_c)-\pi b}$$

2. Primary Reproduction Number with the Effect of Treatment and Vaccination

So that the primary reproduction number of the mathematical model of vertical transmission of Hepatitis B is obtained, namely:

$$R_e = \frac{\beta c\mu(\pi+\mu_c)((\mu+\delta_a)\varepsilon\tau+(b+\alpha+\eta+\mu)\gamma_a\theta+\alpha\varepsilon\theta+(\mu+\delta_a)(b+\alpha+\eta+\mu))}{(b+\gamma_a+\varepsilon+\mu)(\mu+\delta_a)(b+\alpha+\eta+\mu)((\mu(\pi+\mu_c)-\pi b)}$$

(e) Local Sensitivity Analysis R_e

Sensitivity analysis was conducted to see the most influential parameters in the mathematical model of vertical transmission of Hepatitis B with the effect of treatment and vaccination by inputting parameter values. Sensitivity indices were obtained as shown in Table 1:

Table 1. Index Sensitivity Local R_e

Parameter	Index Sensitivity
β	$+1$
c	+0.9999999998
μ	$+0.3681035850$
π	$+0.00001352693956$
μ_c	-0.00001352698773
δ_a	$+0.2708039958$
θ	$+0.4987245181$
γ_a	$+0.2139208687$
b	$+0.01217770640$
ε	$+0.4866623941$
η	$+0.1926697337$
τ	$+0.2018587447$
α	$+0.4556617152$

The calculation of the sensitivity index value can be seen in Appendix 2. Based on Table 1, it can be explained that every one-unit increase in the level of effective contact β results in R_e Increasing by 1 unit. Meanwhile, if there is a one-unit decrease in the practical contact level β, R_e Decreases by 1 unit, likewise for other parameters. If the sensitivity index value is positive, the parameter value increases the fundamental reproduction value with an increased index for each parameter unit, as shown in Table 1. The sensitivity index value of μ_c is -0.00001352698773, meaning that if the μ_c The parameter increases by one unit; it will cause R_e To decrease by 0.00001352698773. Likewise, with other parameters, if the sensitivity index value is negative, an increase in the parameter value results in a decrease in the essential reproduction value with an increased index of each parameter unit, as shown in Table 1. Sensitivity analysis shows that β and c are dynamically sensitive parameters.

(f) Numerical Simulation

Simulation of the stability of the fixed point of the mathematical model of vertical transmission of Hepatitis B with the effect of treatment and vaccination is carried out by forming a trajectory from the initial value that is initialized. In the resulting circuit, it can be seen that if the curve goes to the fixed point, it can be concluded that the state of the selected issue is stable, but if the angle moves away from the set point, it can be supposed that the condition of the fixed point is not stable.

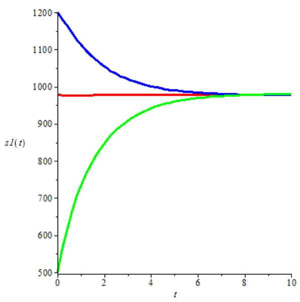
1. Simulation of Mathematical Models with Endemic Fixed Points of Vertical Transmission of Hepatitis B with the Effect of Treatment and Vaccination

In this case, the situation of individuals infected with Hepatitis B disease through vertical transmission will be simulated using the following parameters in Table 2.

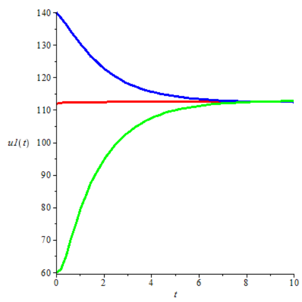
Table 2. Parameter Values for the Endemic Fixed Point

Parameter	Nilai
Λ	700
π	3.1
b	0.0121
μ	0.4
μ_c	0.054
γ_a	0.7
γ_c	0.05
ρ	0.6
p	0.7
δ_a	0.47
δ_c	0.04
η	0.53
ε	2.8
c	1.5
θ	0.88797
τ	0.34
β	0.5
α	0.47
ξ	0.94
ω	0.03-0.06
λ	0.45

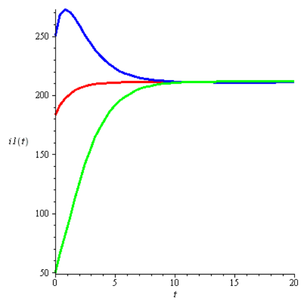
With the parameter values in Table 2, R_0=1.597223940 and R_e= 0.7927299409 are obtained. The values of R_0>1 and R_e<1 is obtained, which means that the disease does not outbreak after being given additional treatment, namely vaccination and treatment. Then, calculate the endemic fixed-point value of vertical transmission of Hepatitis B, namely. E_1= (978,112,183,222,0.6,26,0.04,64).
Based on the parameter values and initial values above, the graph of each group against time t is as follows in Figure 4:



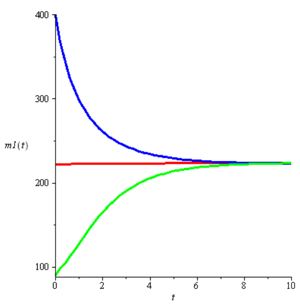
Grafik $S_a\,(t)$



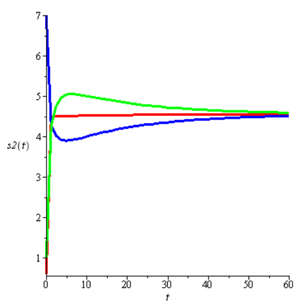
Grafik $U_a\,(t)$



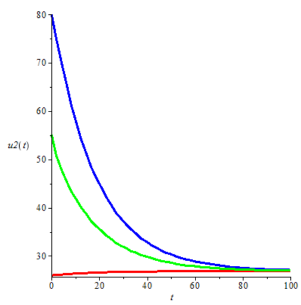
Grafik $I_a\,(t)$



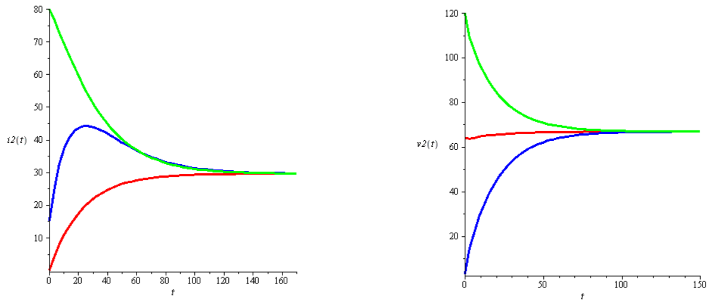
Grafik $T_a\,(t)$



Grafik $S_c\,(t)$



Grafik $U_c\,(t)$



Grafik $I_c\ (t)$ Grafik $V_c\ (t)$

Figure 4. Trajectory around the endemic fixed point (E_(1))

Based on Figure 4, the red curve represents the endemic fixed point of vertical transmission of Hepatitis B. In contrast, the blue and green curves will later determine whether or not the endemic fixed issue of vertical information of Hepatitis B is stable in each graph. It can be seen that the set point. E_1 is asymptotically stable because each graph's trajectories (blue and green curves) move closer to the endemic fixed point of vertical transmission of Hepatitis B, as shown by the red curve. The fixed point of a stable disease means that there will be vertical transmission of Hepatitis B for a long time.

2. Interpretation of the Mathematical Model of Vertical Transmission of Hepatitis B with the Effect of Treatment and Vaccination

Based on the analysis conducted on the mathematical model of vertical transmission of Hepatitis B with the effect of treatment and vaccination, several factors affect the occurrence of epidemics in the problem of vertical spread of Hepatitis B in a population. This can be seen from the local sensitivity analysis conducted on the primary reproduction number R_e

$$R_e = \frac{\beta c\mu(\pi+\mu_c)((\mu+\delta_a)\varepsilon\tau+(b+\alpha+\eta+\mu)\gamma_a\theta+\alpha\varepsilon\theta+(\mu+\delta_a)(b+\alpha+\eta+\mu))}{(b+\gamma_a+\varepsilon+\mu)(\mu+\delta_a)(b+\alpha+\eta+\mu)((\mu(\pi+\mu_c)-\pi b)}$$

Based on the sensitivity analysis conducted on the primary reproduction number R_e, it is known that the parameters that significantly affect the increase in the immediate reproduction value are contacts made with infected individuals and the average number of sexual partners in infected adult women. So, it is necessary to control these two parameters so that vertical transmission of Hepatitis B does not become an epidemic. In addition, the effectiveness of treatment and vaccination can be seen by comparing the primary reproductive number without treatment and vaccination. $R_0 = 1.597223940$, and the essential reproductive number value obtained with treatment and vaccination $R_e = 0.7927299409$.

4. Conclusion

Based on the discussion that has been done, the mathematical model of vertical transmission of Hepatitis B with the effect of treatment and vaccination is obtained in the form of a system of differential equations. There is one fixed point brought, namely the endemic fixed point. Based on the sensitivity analysis conducted on the primary reproduction number R_e, it is known that the parameters that significantly affect the increase in the immediate reproduction value are contacts made with infected individuals and the average number of sexual partners in infected adult women. So, it is necessary to control these two parameters so that vertical transmission of Hepatitis B does not become an epidemic. In addition, the effectiveness of treatment and vaccination can be seen from the comparison of the primary reproduction number with and without vaccination treatment, which shows that treatment of Hepatitis B-infected mothers and vaccination of newborns can be beneficial in controlling vertical transmission of Hepatitis B.

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