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SACR EPIDEMIC MODEL FOR THE SPREAD OF HEPATITIS B DISEASE BY CONSIDERING VERTICAL TRANSMISSION

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ABSTRACT

Hepatitis B is an infectious disease that causes inflammation of the liver due to infection with the Hepatitis B virus. Hepatitis B is divided into two phases: the acute phase and the chronic phase. Hepatitis B virus (HBV) can be prevented through vaccination and treatment of susceptible and infected individuals. The spread of the virus can be modeled using mathematical modeling of epidemics. In this study, the model used consists of four classes, namely vulnerable individuals (S), acute individuals (A), chronic individuals (C), and recovered individuals (R). The purpose of this study is to explain the formation of the Hepatitis B disease epidemic model, analyze the stability of the model, perform simulations, and conduct parameter sensitivity analysis on the basic reproductive number. The result of this study is the construction of an epidemic model of the spread of hepatitis B disease in the form of a SACR model. This model takes into account the transmission that occurs not only through interactions between susceptible individuals and chronic individuals but also through the birth process, which occurs in chronic subpopulations because babies born can be chronically infected (vertical transmission from mother to baby). The model produces two equilibrium points, the disease-free equilibrium and the endemic equilibrium. Both points were analyzed for stability using the linearization method and were found to be asymptotically stable. Furthermore, the model simulation was carried out using the fourth-order Runge-Kutta method and sensitivity analysis of the basic reproduction number. From the results obtained, it can be concluded that the spread of hepatitis B disease can be minimized by reducing contact between susceptible and chronic individuals, increasing treatment of chronic individuals, and increasing the number of vaccinated individuals in susceptible populations.

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1. INTRODUCTION

Viral hepatitis is a systemic infection that predominantly affects the liver. Almost all cases of viral hepatitis are caused by one of the five types of viruses, namely Hepatitis A virus (HAV), Hepatitis B virus (HBV), Hepatitis C virus (HCV), Hepatitis D virus (HDV), and Hepatitis E virus (HEV). Other types of viruses transmitted post-transfusion, such as the Hepatitis G virus and TT virus, have been identified but have not been confirmed to be the same as other hepatitis. All types of hepatitis viruses that affect humans are RNA viruses, except the hepatitis B virus, which is a DNA virus [1].

Hepatitis B is an infectious disease that causes inflammation of the liver from infection with the Hepatitis B virus. It should be noted that the hepatitis B virus (HBV) is not cell-destroying (cytopathic), but rather takes over the host system and produces cancer cells. Once inside the body, HBV infects hepatocyte cells in the liver. The immune system, in response to such an infection, causes inflammation of the liver. Most hepatitis B infections are caused by viruses, bacteria, or active exposure to alcohol and drugs. Usually, HBV infection has two stages: incubation and chronic. The former refers to the initial six months of HBV infection after exposure. During this phase, most immune systems are strong enough to clear the hepatitis B virus from the infected body, and as a result, one can recover in less than a year. For other individuals with weakened immunity, the infection spreads gradually and leads to a more severe phase of hepatitis B, i.e., the chronic stage [2]. Half of all hepatitis B patients are known to be unable to transmit the viral infection after 7 weeks from the onset of symptoms. In addition, all patients who do not have chronic hepatitis B infection will become Hepatitis B Surface Antigen (HbsAg) negative within 15 weeks after the onset of symptoms. The incubation period in patients with hepatitis B generally occurs for a long time and is different from the incubation period of other viral diseases. WHO states that it takes about 30-60 days to detect the presence of the virus. Only then will symptoms appear for an average of 90 days, or a range of 60-150 days after exposure to the virus. The incubation period for hepatitis B (HBV) is 45-160 days. Please also note that the hepatitis B virus (HBV) can survive outside the body and can cause infection for approximately 7 days [3].

Hepatitis B is an infectious disease that is mostly transmitted from mother to child. The disease can be transmitted through blood, semen, breast milk, and other body fluids. Other than sexually, transmission can occur vertically in utero, which generally occurs due to antepartum hemorrhage and placental rupture, or through perinatal transmission by mothers who are seropositive with HBV viremia and transmit it to their babies during or shortly after delivery [4]. Data from Kementerian Kesehatan (Kemenkes) mentioned that there will be 50,744 pregnant women infected with hepatitis B in 2022. According to the provinces, the most hepatitis B-positive pregnant women came from East Java, with 8,269, or 16.3%, of the total hepatitis B-positive pregnant women nationally last year. West Java was next, with 6,779 pregnant women infected with hepatitis B last year. This was followed by Central Java and East Nusa Tenggara [5].

The spread of the hepatitis B virus can be built into a mathematical model in the form of ordinary differential equations [6]. Mathematical models used to determine the behavior of the spread of infectious diseases are called epidemic models [7]. The purpose of forming a mathematical model of the spread of the hepatitis B virus is to know and understand the dynamics of the spread of the virus. The dynamics of the spread of the disease can be known through the analysis of the stability of the equilibrium point of the hepatitis B virus epidemic model. In addition, the basic reproductive number can also provide information about the level of disease spread in a population and can be a parameter for the threshold for controlling a disease [8].

Many researchers have previously studied mathematical models of the hepatitis B virus. For example, Zhao, Xu, and Lu (2000) used partial differential equations to model the spread of the hepatitis B virus and concluded that vaccination coverage is the most important indicator to stop the spread of the virus [9]. Later research by Ullah, Khan, and Gómez-Aguilar [10], developed a mathematical model of hepatitis B virus infection with a population of hospitalized patients to explore the dynamics of this infection. The model is without control and all basic properties and results including local and global stability are presented. After that, the model was developed with a suitable optimal control strategy and explored the necessary optimality conditions using Pontryagin's maximum principle to minimize the spread of hepatitis B in the community. Khan, Ullah, Ali, and Zaman [11] explained the formulation of the hepatitis B epidemic model with a saturated incidence rate and concluded that in controlling the spread of the hepatitis B virus, it is necessary to isolate infected people, increase public awareness, and hospitalize treatment as control variables. Furthermore, the study was extended by Din, Li, and Liu [2]. Based on the mathematical model formed, it can be concluded that vaccination and treatment as control variables are very effective in controlling the spread of the hepatitis B virus. Whereas in the research of Hasmani, Safi, and Das [12], the vulnerable

subpopulation in the model formed consists of subpopulations aged less and equal to 5 years and subpopulations aged more than 5 years. This model discusses model parameter estimation and sensitivity analysis and presents simulations of the effect of several parameters on the number of subpopulations in the model.

In this study, the author develops a hepatitis B model with an incubation period and considers vertical transmission from a pregnant mother to her baby. After the model is formed, the equilibrium point is determined, and the results of the model stability analysis are presented. The solution of the presented model is determined through the fourth-order Runge-Kutta method. This method has four function evaluations and has a higher solution accuracy than the previous order Runge Kutta method [13]. Finally, we will examine what efforts must be made to minimize the spread of the hepatitis B virus through sensitivity analysis of the parameters involved in the basic reproduction number and contour plot of the basic reproduction number.

2. RESEARCH METHODS

The research conducted is a type of theoretical study by reviewing the literature related to mathematical modeling that can be used to solve problems by first compiling the concepts as needed regarding differential equations, to form, analyze, and simulate an epidemic model of the hepatitis B virus in the form of a system of ordinary differential equations.

In this research, the authors developed the SEIR (Susceptible, Exposed, Infected, Recovered) model based on the characteristics of the spread of hepatitis B. Hepatitis B virus infection has two phases, the first phase in the first six months of hepatitis B virus infection after exposure. In this phase, most people's immune systems are strong enough to recover in less than a year. Meanwhile, for other individuals with weakened immunity, the infection will spread gradually and lead to the more severe hepatitis B phase, the chronic stage. So this research was developed into a SACR model that is divided into four subpopulations: susceptible, denoted as ($\boldsymbol{S}$), which states the number of individuals who are healthy but susceptible to being infected with the hepatitis B virus; acute, denoted as ($\boldsymbol{A}$), which denotes the number of individuals infected with the hepatitis B virus during the incubation period (acute phase), chronic is denoted as ($\boldsymbol{C}$), which states the number of individuals infected with the hepatitis B virus in the chronic phase who can transmit the disease, and recovered is denoted as ($\boldsymbol{R}$), which states the number of individuals recovered from the hepatitis B virus.

The steps taken in this research are as follows:

1. Develop assumptions and explain the formation of the hepatitis B virus model based on the characteristics of the virus using the epidemic model.
2. Determine the hepatitis B virus equilibrium point and basic reproduction number using the Next Generation Matrix method [14]
3. Determine local stability analysis at the equilibrium point in the Hepatitis B virus epidemic model with the following stages:
   a. Perform linearization using the Jacobian matrix [15].
   b. Determine the eigenvalues using the following formula: $|\boldsymbol{M} - \boldsymbol{\lambda I}| = \boldsymbol{0}$ [15]-[16].
   c. Analyzing stability using the Routh-Hurwiz Criteria approach [17].
4. Simulate the epidemic model of the hepatitis B virus using the fourth-order Runge-Kutta method [18].
5. Present the results of the sensitivity analysis using the sensitivity index of the parameters involved [19]-[20], and [21].

3. RESULTS AND DISCUSSION

3.1 Mathematical Model

The assumptions in the mathematical model of the hepatitis B virus include, among others, that the natural death rate for each subpopulation is constant and has the same value, the vaccine is given to the susceptible subpopulation so that the individual becomes immune to the hepatitis B virus, and births that occur in each subpopulation are assumed to be susceptible subpopulations, except births occur in the chronic subpopulation because babies who are still in the womb or who have been born can become chronically

infected. This process involves the vertical transmission of the virus from a pregnant mother to her baby. The acutely affected subpopulation can recover naturally without any special treatment. If the chronic subpopulation interacts with the susceptible subpopulation, the susceptible subpopulation will become the acute subpopulation, and individuals in the acute subpopulation will become chronic individuals due to the development of the hepatitis B virus in the body. Every individual who recovers from hepatitis B virus infection in the chronic phase has permanent immunity and will not be infected again, and deaths due to hepatitis B virus can occur in the chronic subpopulation. Below is a flow diagram of the spread of the hepatitis B virus.

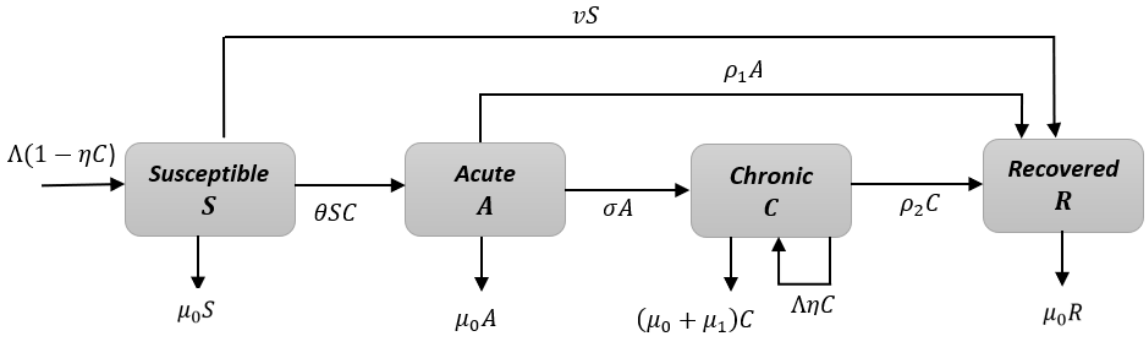

Figure 1. Flow Diagram of the Hepatitis B Virus Epidemic Model

Based on the flow diagram in **Figure 1**, it can be explained that the change in the number of susceptible subpopulations over time $\left(\frac{dS}{dt}\right)$ will increase by $\Lambda(1-\eta C)$, namely the number of babies born from the susceptible, acutely, and recovered subpopulations. Then the susceptible subpopulation decreases due to the interaction of susceptible individuals with individuals who have been infected in the chronic phase, so that susceptible individuals will move to the acute subpopulation of SB due to a natural death rate of μ_0 and a vaccination rate of v. Changes in the number of acute subpopulations over time $\left(\frac{dA}{dt}\right)$ will increase by θSC and decrease due to several factors. The first is caused by the rate of natural death, the second is caused by the rate of individuals recovering naturally (ρ_1) so that individuals will become recovered individuals, and the third is caused by the rate of development of the hepatitis B virus, which is denoted by σ, so that individuals will become chronic individuals. The number of chronic subpopulations over time $\left(\frac{dC}{dt}\right)$ increases due to the rate of development of the hepatitis B virus and the number of babies born to the chronic subpopulation. Furthermore, the chronic subpopulation is reduced due to several factors: the first is caused by the natural death rate, the second is caused by the individual death rate due to the hepatitis B virus in the chronic phase (μ_1), and the third is the individual recovery rate due to treatment in the chronic phase subpopulation (ρ_2). The number of recovered subpopulations over time $\left(\frac{dR}{dt}\right)$ increases due to several factors, namely individuals in the susceptible subpopulation who are vaccinated against the hepatitis B virus with a vaccination rate of v, the natural recovery rate in the chronic subpopulation of ρ_1, and the recovery rate due to treatment in the chronic subpopulation of ρ_2. In addition, the recovered subpopulation decreases due to natural death at a rate of μ_0.

From **Figure 1**, a mathematical model of the hepatitis B virus can be constructed as follows:

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda(1-\eta C) - \theta SC - (v+\mu_0)S \\
\frac{dA}{dt} &= \theta SC - (\mu_0+\rho_1+\sigma)A \\
\frac{dC}{dt} &= \sigma A - (\mu_0+\mu_1+\rho_2-\eta\Lambda)C \\
\frac{dR}{dt} &= \rho_1 A + \rho_2 C - \mu_0 R + vS
\end{aligned} \tag{1}$$

with initial values: $S(0) = S_0 > 0$, $A(0) = A_0 \geq 0$, $C(0) = C_0 \geq 0$, and $R(0) = R_0 > 0$.

3.2 Equilibrium Point

The equilibrium point is a point that can state that the model is in equilibrium [22], namely if the following conditions are met:

$$\frac{dS}{dt} = 0; \frac{dA}{dt} = 0; \frac{dC}{dt} = 0; \frac{dR}{dt} = 0 \tag{2}$$

Based on **Equation (2)**, **Equation (1)** can be expressed as

$$\Lambda(1 - \eta C) - \theta SC - w_1 S = 0 \tag{3}$$

$$\theta SC - w_2 A = 0 \tag{4}$$

$$\sigma A - w_3 C = 0 \tag{5}$$

$$\rho_1 A + \rho_2 C - \mu_0 R + vS = 0 \tag{6}$$

Where $w_1 = v + \mu_0, w_2 = \mu_0 + \rho_1 + \sigma, w_3 = \mu_0 + \mu_1 + \rho_2 - \eta\Lambda$, and $\mu_0 + \mu_1 + \rho_2 > \eta\Lambda$.

3.2.1 Disease-Free Equilibrium Point

The disease-free equilibrium point is a condition that shows that the value of the infected subpopulation is equal to zero. In this case, it states that in a population, there are no individuals infected with the hepatitis B virus in the incubation or chronic phase, namely $A = C = 0$. From **Equation (3)** – **Equation (6)**, the disease-free equilibrium point is obtained as follows:

$$\boldsymbol{K^1} = (S^1, A^1, C^1, R^1) = \left(\frac{\Lambda}{w_1}, 0, 0, \frac{v\Lambda}{\mu_0 w_1}\right)$$

3.2.2 Basic Reproduction Number

The basic reproduction number states the level of transmission or spread of the virus, denoted by $\mathcal{R}_0$. The stages in determining $\mathcal{R}_0$ are as follows:

a. The rate of change of the infected subpopulation over time is as follows:

$$\frac{dA}{dt} = \theta SC - w_2 A$$

$$\frac{dC}{dt} = \sigma A - w_3 C \tag{7}$$

Equation (7) can be stated as follows.

$$\frac{d\boldsymbol{x}}{dt} = \begin{pmatrix} \frac{dA}{dt} \\ \frac{dC}{dt} \end{pmatrix} = \boldsymbol{\mathcal{F}} - \boldsymbol{\mathcal{V}} \tag{8}$$

Where

$\boldsymbol{x} = \begin{pmatrix} A \\ C \end{pmatrix} \in \mathbb{R}^2$, $\boldsymbol{\mathcal{F}} = \begin{pmatrix} \mathcal{F}_1 \\ \mathcal{F}_2 \end{pmatrix} = \begin{pmatrix} \theta SC \\ 0 \end{pmatrix}$ and $\boldsymbol{\mathcal{V}} = \begin{pmatrix} \mathcal{V}_1 \\ \mathcal{V}_2 \end{pmatrix} = \begin{pmatrix} w_2 A \\ w_3 C - \sigma A \end{pmatrix}$

b. The Jacobian matrix from the linearization results of **Equation (8)** is respectively,

$$\boldsymbol{D\mathcal{F}} = \begin{pmatrix} \frac{\partial \mathcal{F}_1}{\partial A} & \frac{\partial \mathcal{F}_1}{\partial C} \\ \frac{\partial \mathcal{F}_2}{\partial A} & \frac{\partial \mathcal{F}_2}{\partial C} \end{pmatrix} = \begin{pmatrix} 0 & \theta S \\ 0 & 0 \end{pmatrix} \text{ and } \boldsymbol{D\mathcal{V}} = \begin{pmatrix} \frac{\partial \mathcal{V}_1}{\partial A} & \frac{\partial \mathcal{V}_1}{\partial C} \\ \frac{\partial \mathcal{V}_2}{\partial A} & \frac{\partial \mathcal{V}_2}{\partial C} \end{pmatrix} = \begin{pmatrix} w_2 & 0 \\ -\sigma & w_3 \end{pmatrix}.$$

By considering the Jacobian of $\boldsymbol{D\mathcal{F}}$ and $\boldsymbol{D\mathcal{V}}$ at equilibrium point $\boldsymbol{K^1}$, we get

$$\boldsymbol{F} = \boldsymbol{D\mathcal{F}}|_{K^1=\left(\frac{\Lambda}{w_1},0,0,\frac{v\Lambda}{\mu_0 w_1}\right)} = \begin{pmatrix} 0 & \frac{\theta\Lambda}{w_1} \\ 0 & 0 \end{pmatrix}; \quad \boldsymbol{V} = \boldsymbol{D\mathcal{V}}|_{K^1=\left(\frac{\Lambda}{w_1},0,0,\frac{v\Lambda}{\mu_0 w_1}\right)} = \begin{pmatrix} w_2 & 0 \\ -\sigma & w_3 \end{pmatrix}.$$

The next Generation Matrix can be determined as follows:

$$\boldsymbol{G} = \boldsymbol{FV^{-1}} = \begin{pmatrix} 0 & \frac{\theta\Lambda}{w_1} \\ 0 & 0 \end{pmatrix} \begin{pmatrix} \frac{1}{w_2} & 0 \\ \frac{\sigma}{w_2 w_3} & \frac{1}{w_3} \end{pmatrix} = \begin{pmatrix} \frac{\theta\Lambda\sigma}{w_1 w_2 w_3} & \frac{\theta\Lambda}{w_1 w_3} \\ 0 & 0 \end{pmatrix}$$

c. The eigenvalues of the matrix $\boldsymbol{G}$ are determined through the characteristic equation $|\boldsymbol{G} - \beta\boldsymbol{I}| = 0$, thus obtained $\beta_1 = 0$, atau $\beta_2 = \frac{\theta\Lambda\sigma}{w_1 w_2 w_3}$.

The basic reproduction number is defined as the dominant eigenvalue of the matrix $\boldsymbol{G}$ [14]. Since the absolute value of β_2 is greater than the absolute value of β_1, the basic reproduction number is obtained as follows:

$$\mathcal{R}_0 = \frac{\theta\Lambda\sigma}{w_1 w_2 w_3} = \frac{\theta\Lambda\sigma}{(v+\mu_0)(\mu_0+\rho_1+\sigma)(\mu_0+\mu_1+\rho_1-\eta\Lambda)} \tag{9}$$

3.2.3 Endemic Equilibrium Point

The endemic equilibrium point is the point determined based on the solution of Equation (3) – Equation (6), with the condition that the number of individuals from the infected subpopulation is not equal to zero. In this case, the subpopulation infected with the hepatitis B virus is the acute phase and the chronic phase, namely $A \neq 0, C \neq 0$. The result of solving Equation (3) – Equation (6) obtained the endemic equilibrium point as follows:

$$\boldsymbol{K}^* = (S^*, A^*, C^*, R^*)$$

with

$$S^* = \frac{w_2 w_3}{\theta\sigma}$$

$$A^* = \left(\frac{w_1 w_2 w_3^2}{\theta\sigma[\Lambda\eta\sigma + w_2 w_3]}(\mathcal{R}_0 - 1)\right)$$

$$C^* = \left(\frac{w_1 w_2 w_3}{\theta[\Lambda\eta\sigma + w_2 w_3]}(\mathcal{R}_0 - 1)\right)$$

$$R^* = \frac{\left(\frac{v w_2 w_3}{\theta\sigma} + \rho_1\left(\frac{w_1 w_2 w_3^2}{\theta\sigma[\Lambda\eta\sigma + w_2 w_3]}(\mathcal{R}_0 - 1)\right) + \rho_2\left(\frac{w_1 w_2 w_3}{\theta[\Lambda\eta\sigma + w_2 w_3]}(\mathcal{R}_0 - 1)\right)\right)}{\mu_0}$$

3.3 Local Stability Analysis of the Model

The local stability analysis of the Hepatitis B virus mathematical model is divided into two parts: local stability at the disease-free equilibrium point and local stability at the endemic equilibrium point. Equation (1) is linearized using the Taylor series to obtain the Jacobian matrix as follows:

$$\boldsymbol{J} = \begin{pmatrix} -\theta C - w_1 & 0 & -\eta\Lambda - \theta S & 0 \\ \theta C & -w_2 & \theta S & 0 \\ 0 & \sigma & -w_3 & 0 \\ v & \rho_1 & \rho_2 & -\mu_0 \end{pmatrix} \tag{10}$$

3.3.1 Stability of Disease-free Equilibrium Point

Based on Equation (10), the Jacobian matrix around the disease-free equilibrium point is obtained as follows:

$$\boldsymbol{J}_{K^1} = \begin{pmatrix} -w_1 & 0 & -\eta\Lambda - \theta\left(\frac{\Lambda}{w_1}\right) & 0 \\ 0 & -w_2 & \theta\left(\frac{\Lambda}{w_1}\right) & 0 \\ 0 & \sigma & -w_3 & 0 \\ v & \rho_1 & \rho_2 & -\mu_0 \end{pmatrix}.$$

The characteristic equation of matrix $\boldsymbol{J}_{K^1}$ is

$$|\boldsymbol{J}_{K^1} - \lambda \boldsymbol{I}| = 0$$

$$(-\mu_0 - \lambda)(-w_1 - \lambda)\left((-w_2 - \lambda)(-w_3 - \lambda) - \theta\left(\frac{\Lambda}{w_1}\right)(\sigma)\right) = 0.$$

From the characteristic equation, the eigenvalues $\lambda_1 = -\mu_0 < 0$, $\lambda_2 = -w_1 < 0$ are obtained. As for the eigenvalues, they are determined through the following equation:

$$(-w_2 - \lambda)(-w_3 - \lambda) - \theta\left(\frac{\Lambda}{w_1}\right)(\sigma) = 0 \tag{11}$$

or

$$a_0\lambda^2 + a_1\lambda + a_2 = 0 \tag{12}$$

where,
$a_0 = 1$, $a_1 = (w_2 + w_3)$ and $a_2 = w_2 w_3(1 - \mathcal{R}_0)$.

Table 1. Routh-Hurwitz Polynomial of Order 2

$a_0\lambda^2 + a_1\lambda + a_2 = 0$		
λ^2	a_0	a_2
λ^1	a_1	0
λ^0	$b_1 = \frac{a_1 a_2 - a_0 a_3}{a_1}$	$b_2 = \frac{a_1 a_4 - a_0 a_5}{a_1}$

In **Equation (12)**, the value of $a_i = 0$ for $i = 3, 4, 5, \ldots, n$, consequently the value of $b_2 = 0$. Based on the Routh-Hurwitz criterion, if all terms in the first column of **Table 1** are positive, then the eigenvalues of **Equation (12)** are negative or have negative real parts. So it must be shown that,

$$a_0 > 0, a_1 > 0, \text{and } a_1 a_2 - a_0 a_3 > 0 \tag{13}$$

Equation (13) is satisfied if the following conditions are obtained.

(1) it is clear that a is positive $(a_0 > 0)$
(2) $a_1 = w_2 + w_3 > 0$, where $w_2 = d_0 + \gamma_1 + \sigma$ and $w_3 = d_0 + d_1 + \gamma_2 - \eta\Lambda$ if $d_0 + d_1 + \gamma_2 > \eta\Lambda$.
(3) $a_1 a_2 - a_0 a_3 = (w_2 + w_3)(w_2 w_3(1 - \mathcal{R}_0) > 0$, if $\mathcal{R}_0 < 1$

Based on the Routh-Hurwitz criterion, it can be seen that the real parts of λ_3 and λ_4 in **Equation (12)** are negative. Since the real parts of $\lambda_1, \lambda_2, \lambda_3,$ and λ_4 are negative, the disease-free equilibrium point $(\boldsymbol{K^1})$ is locally asymptotically stable under the condition that $\mathcal{R}_0 < 1$.

3.3.2 Stability of Endemic Equilibrium Point

Based on **Equation (10)**, the Jacobian matrix around the endemic equilibrium point is obtained as follows:

$$\boldsymbol{J}_{K^*} = \begin{pmatrix} -\theta C^* - w_1 & 0 & -\eta\Lambda - \theta\left(\frac{w_2 w_3}{\theta\sigma}\right) & 0 \\ \theta C^* & -w_2 & \frac{w_2 w_3}{\sigma} & 0 \\ 0 & \sigma & -w_3 & 0 \\ v & \rho_1 & \rho_2 & -\mu_0 \end{pmatrix}$$

The characteristic equation of matrix $\boldsymbol{J}_{K^*}$ is $|\boldsymbol{J}_{K^*} - \lambda \boldsymbol{I}| = 0$, thus

$$(-\mu_0 - \lambda)\Big(\big((-\theta C^* - w_1) - \lambda\big)\big((-w_2 - \lambda)(-w_3 - \lambda) - w_2 w_3\big) + (\theta C^*)(-\eta\Lambda\sigma - w_2 w_3)\Big) = 0.$$

From the characteristic equation, the eigenvalue $\lambda_1 = -\mu_0 < 0$ is obtained. As for the eigenvalues, they are determined by the following equation:

$$a_0\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0 \tag{14}$$

where

$a_0 = 1,$

$a_1 = (\theta C^* + w_1 + w_2 + w_3) = \left(\frac{w_1 w_2 w_3}{\Lambda\eta\sigma + w_2 w_3}(\mathcal{R}_0 - 1)\right) + w_1 + w_2 + w_3,$

$a_2 = (\theta C^* + w_1)(w_2 + w_3) = \left(\frac{w_1 w_2 w_3}{\Lambda\eta\sigma + w_2 w_3}(\mathcal{R}_0 - 1) + w_1\right)(w_2 + w_3),$

$a_3 = (\theta C^*)\,(\sigma\eta\Lambda + w_2 w_3).$

The real part of the eigenvalues of λ_2, λ_3 and λ_4 in **Equation (14)** can be investigated using the following Routh-Hurwitz criteria.

Table 2. Routh-Hurwitz Polynomial of Order 3

$a_0\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0$		
λ^3	a_0	a_2
λ^2	a_1	a_3
λ^1	$b_1 = \frac{a_1 a_2 - a_0 a_3}{a_1}$	$b_2 = \frac{a_1 a_4 - a_0 a_5}{a_1}$
λ^0	$c_1 = \frac{b_1 a_3 - a_1 b_2}{b_1}$	$c_2 = \frac{b_1 a_5 - a_1 b_3}{b_1}$

In **Equation (14)**, the value of $a_i = 0$ for $i = 4, 5, 6, \ldots, n$, consequently the value of b_2, b_3, and c_2 equal to zero. Based on the Routh-Hurwitz criterion, if all terms in the first column of **Table 2** are positive, then the eigenvalues of **Equation (14)** are negative or have negative real parts. So it must be shown that,

$$a_0 > 0, a_1 > 0, a_1 a_2 - a_0 a_3 > 0, \text{and } \frac{b_1 a_3 - a_1 b_2}{b_1} = a_3 > 0 \tag{15}$$

Equation (15) is satisfied if the following conditions are obtained.

(1) it is clear that $a_0 = 1$ is positive $(a_0 > 0)$

(2) $a_1 = \left(\frac{w_1 w_2 w_3}{\Lambda\eta\sigma + w_2 w_3}(\mathcal{R}_0 - 1)\right) + w_1 + w_2 + w_3 > 0$ if $\mathcal{R}_0 > 1$.

(3) $a_1 a_2 - a_0 a_3$

$= (\theta C^* + w_1 + w_2 + w_3)(\theta C^* + w_1)(w_2 + w_3) - (\theta C^*)\,(\sigma\eta\Lambda + w_2 w_3)$

$= (\theta C^* + w_1 + w_2 + w_3)(\theta C^* w_2 + \theta C^* w_3 + w_1 w_2 + w_1 w_3) - (\theta C^*)\,(\sigma\eta\Lambda + w_2 w_3)$

$= \theta C^*(\theta C^* w_2 + \theta C^* w_3 + 2w_1 w_2 + 2w_1 w_3 + w_2^2 + 2w_2 w_3 + w_3^2 - \sigma\eta\Lambda - w_2 w_3) +$
$w_1(w_1 w_2 + w_1 w_3 + w_2^2 + 2w_2 w_3 + w_3^2)$

$= \theta C^*(\theta C^* w_2 + \theta C^* w_3 + 2w_1 w_2 + 2w_1 w_3 + w_2^2 + w_2 w_3 + w_3^2 - \sigma\eta\Lambda) +$
$w_1(w_1 w_2 + w_1 w_3 + w_2^2 + 2w_2 w_3 + w_3^2)$

$= \theta C^*(\theta C^* w_2 + \theta C^* w_3 + 2w_1 w_2 + 2w_1 w_3 + w_2^2 + w_2 w_3 + w_3^2) - \theta C^* \sigma\eta\Lambda +$
$w_1(w_1 w_2 + w_1 w_3 + w_2^2 + 2w_2 w_3 + w_3^2)$

$= \theta C^* \tilde{p} - \theta C^* \sigma\eta\Lambda + w_1 \tilde{q} > 0$, if $\theta C^* \tilde{p} + w_1 \tilde{q} > \theta C^* \sigma\eta\Lambda$.

Where, $\tilde{p} = (\theta C^* w_2 + \theta C^* w_3 + 2w_1 w_2 + 2w_1 w_3 + w_2^2 + w_2 w_3 + w_3^2)$, and
$\tilde{q} = (w_1 w_2 + w_1 w_3 + w_2^2 + 2w_2 w_3 + w_3^2)$

(4) $a_3 = (\theta C^*)\,(\sigma\eta\Lambda + w_2 w_3) > 0$, if $\mathcal{R}_0 > 1$.

Based on the Routh-Hurwitz criterion, it can be seen that the real parts of λ_2, λ_3 and λ_4 in **Equation (14)** are negative. Since the real parts of $\lambda_1, \lambda_2, \lambda_3,$ and λ_4 are negative, the endemic equilibrium point $(\boldsymbol{K}^*)$ is locally asymptotically stable under the condition that $\mathcal{R}_0 < 1$ and $\theta C^* \tilde{p} + w_1 \tilde{q} > \theta C^* \sigma \eta \Lambda$.

3.4 Numerical Simulation

The numerical solution of the Hepatitis B virus mathematical model was determined using the fourth-order Runge-Kutta method. Numerical simulation of the model consists of two parts: numerical simulation for the disease-free equilibrium point and numerical simulation for the endemic equilibrium point. The model parameter values for numerical simulations at each equilibrium point can be seen in **Table 3**.

Table 3. Parameter Value

Parameter	Symbol	K^1	K^*	Source
Contact rate of Susceptible subpopulation individuals with Chronic subpopulation (transmission rate)	θ	0.05	0.03	**[2]**
The rate of progression of the Hepatitis B virus	σ	0.1	0.07	**[2], [10]**
Birth rate	Λ	2	2	Assumed
Rate of individuals infected before birth in the subpopulation Chronic	η	0.11	0.003	**[2]**
Recovery rate	ρ_1	0.5	0.05	**[2]**
Rate of individuals infected before birth in the subpopulation *Chronic*	ρ_2	0.6	0.4	Assumed
Natural death rate	μ_0	0.015	0.009	Assumed
Hepatitis B virus mortality rate in the chronic phase	μ_1	0.02	0.08	Assumed
Hepatitis B vaccination rate	v	0.2	0.02	**[2]**

In the simulation for the disease-free equilibrium point, the initial value $(S(0), A(0), C(0), R(0)) = (100, 20, 10, 50)$, step $h = 0$, and time interval $[0, 600]$ are given. The results of the numerical solution of the model are presented in **Table 4** and **Figure 2**.

Table 4. Numerical Solution at the Disease-Free Equilibrium Point

t (time)	S	A	C	R
0	100.000	20.000	10.000	50.000
0.1	93.174	23.557	9.808	53.521
1	50.299	35.323	9.146	84.349
10	4.562	1.096	1.231	165.609
50	9.300	0.000	0.000	145.483
100	9.302	0.000	0.000	134.316
150	9.302	0.000	0.000	128.817
200	9.302	0.000	0.000	126.292
250	9.302	0.000	0.000	125.099
300	9.302	0.000	0.000	124.535
350	9.302	0.000	0.000	124.269
400	9.302	0.000	0.000	124.143
450	9.302	0.000	0.000	124.084
500	9.302	0.000	0.000	124.056
550	9.302	0.000	0.000	124.043
600	9.302	0.000	0.000	124.036

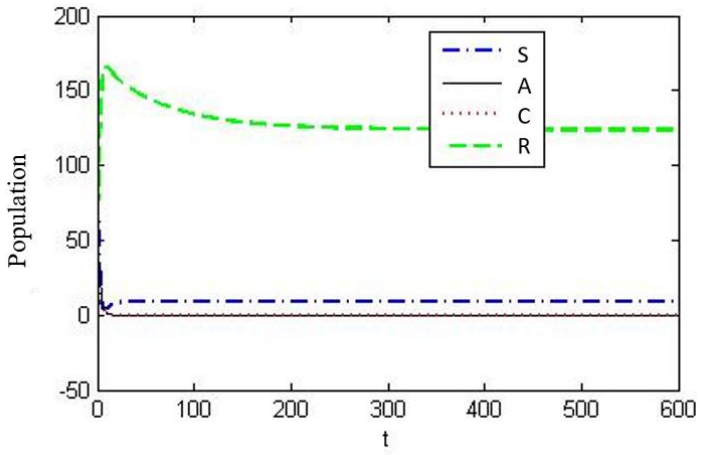

Figure 2. Simulation Graph of Disease-Free Equilibrium Point (K^1)

Based on **Table 4** and **Figure 2**, it can be seen that the model solution, from time to time, converges to point $K^1 \approx (9.30; 0; 0; 124.03)$. This supports the results obtained in Section 3.3.1 that the equilibrium point K^1 is locally asymptotically stable.

In the simulation for the endemic point, the initial value $(S(0), A(0), C(0), R(0)) = (100, 30, 30, 20)$, step $h = 0$, and time interval $[0, 900]$ are given. The results of the numerical solution of the model are presented in **Table 5** and **Figure 3** below.

Table 5. Numerical Solution at the Endemic Equilibrium Point

t (time)	S	A	C	R
0	100.000	30.000	30.000	20.000
0.1	94.310	35.335	29.212	21.013
1	46.747	75.628	21.826	34.158
10	6.401	47.824	8.565	109.843
50	27.229	6.551	0.972	146.201
100	31.112	8.953	1.282	151.098
200	29.759	8.748	1.267	163.563
300	29.672	8.772	1.271	168.118
400	29.669	8.775	1.271	169.948
500	29.670	8.775	1.271	170.692
600	29.669	8.775	1.271	170.995
700	29.669	8.775	1.271	171.118
800	29.672	8.772	1.272	171.167
900	29.670	8.774	1.272	171.188

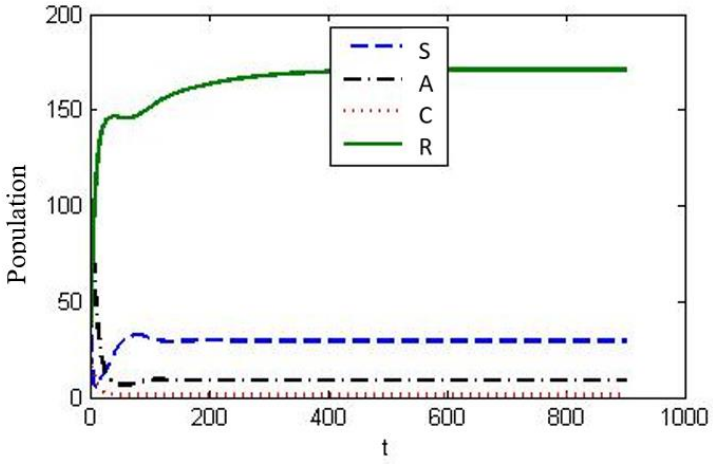

Figure 3. Simulation Graph of Endemic Equilibrium Point (K^*)

Based on **Table 5** and **Figure 3**, it can be seen that the model solution, from time to time, converges to point $\boldsymbol{K}^* \approx (29.67; 8.77; 1.27; 171.20)$. This supports the results obtained in Section 3.3.2 that the equilibrium point $\boldsymbol{K}^*$ is locally asymptotically stable.

3.5 Sensitivity Index Values

In this section, a sensitivity analysis is given to determine the parameters that affect the basic reproduction number. Sensitivity analysis is determined by calculating the sensitivity index values of the parameters involved in the basic reproduction number. The normalized sensitivity index **[19]**-**[20]** of the basic reproduction number is defined as follows:

$$\mathcal{S}_p^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial p} \times \frac{p}{\mathcal{R}_0}$$

The following is given as the value of the sensitivity index at the basic reproduction number using the parameter values in **Table 6**:

Table 6. Sensitivity Index

Parameters (p)	Sensitivity index values $\left(\mathcal{S}_p^{\mathcal{R}_0}\right)$
θ	1
σ	0.837398374
Λ	1.530120482
η	0.603607125
ρ_1	-0.813008129
ρ_2	-1.445783132
μ_0	-0.130302264
μ_1	-0.048192771
v	-0.930232557

Based on **Table 6**, the parameters $\Lambda, \theta, \sigma,$ and η cause the sensitivity index value to be positive, meaning that if these parameters change (increase/decrease), then the value also changes $\mathcal{R}_0$ (increase/decrease). While the parameters $\rho_1, \rho_2, \mu_0, \mu_1,$ and v of the sensitivity index are negative, this means that if these parameters change (increase/decrease), there will be a change in value $\mathcal{R}_0$ (decrease/increase).

The effect of changing the values of parameters θ, ρ_2 and v on the value of $\mathcal{R}_0$ is presented in **Figures 4, 5**, and **6**, respectively.

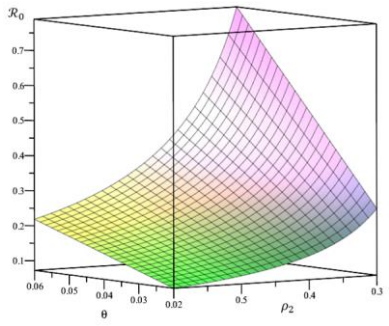

Figure 4. Graph of changes in $\mathcal{R}_0$ against changes in parameters θ and ρ_2

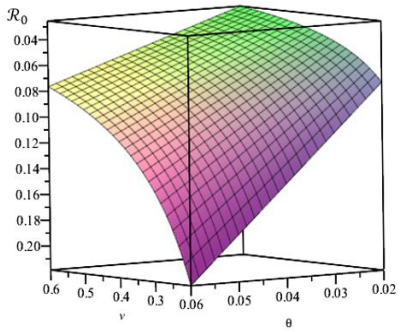

Figure 5. Graph of changes in $\mathcal{R}_0$ against changes in parameters θ and v

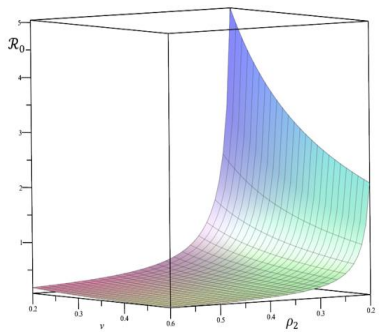

Figure 6. Graph of changes in $\mathcal{R}_0$ against changes in parameters v and ρ_2

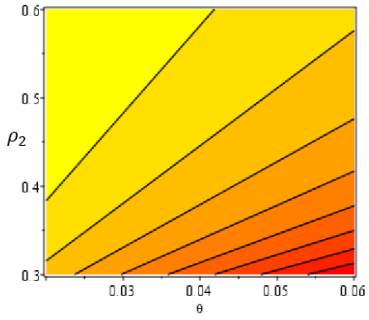

Figure 7. Contour plot of the basic reproduction number when the pair of parameters θ and ρ_2

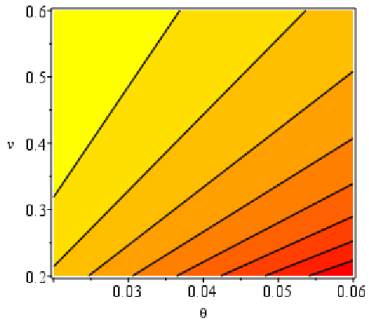

Figure 8. Contour plot of the basic reproduction number when the pair of parameters θ and v

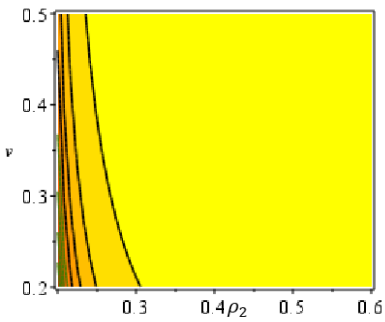

Figure 9. Contour plot of the basic reproduction number when the pair of parameters v and ρ_2

The images above present contour plots of the basic reproduction number $\mathcal{R}_0$ in relation to different pairs of parameters:

Figure 7: This contour plot illustrates how $\mathcal{R}_0$ changes based on variations in the pair of parameters θ (contact rate) and ρ_2 (rate of infection before birth in the chronic subpopulation). The darker colors represent higher values of $\mathcal{R}_0$. From this image, it is evident that an increase in both θ and ρ_2 leads to a higher $\mathcal{R}_0$, indicating a greater potential for disease spread.

Figure 8: This contour plot shows the relationship between $\mathcal{R}_0$ and the pair of parameters θ and v (vaccination rate). The darker shades represent an increase in $\mathcal{R}_0$. It is clear that while an increase in θ raises $\mathcal{R}_0$, an increase in v can lower $\mathcal{R}_0$, emphasizing the importance of vaccination in reducing the potential for disease spread, even with a high contact rate.

Figure 9: This contour plot depicts the changes in $\mathcal{R}_0$ related to variations in the pair of parameters v and ρ_2. Darker colors indicate higher $\mathcal{R}_0$ values. This figure shows that even with an increase in ρ_2, an increase in v remains effective in reducing $\mathcal{R}_0$, highlighting vaccination as a key factor in controlling the spread of the disease, even in situations of high infection risk.

Overall, these three figures emphasize the importance of controlling parameters such as contact rate, infection before birth, and especially vaccination in lowering the basic reproduction number $\mathcal{R}_0$ and managing the spread of Hepatitis B.

4. CONCLUSIONS

The Hepatitis B virus model is formed into four different subpopulations: namely susceptible, acute, chronic, and recovered. From this model, two equilibrium points (disease-free and endemic equilibrium points) and the basic reproduction number $\mathcal{R}_0 = \frac{\theta\Lambda\sigma}{w_1 w_2 w_3}$ are obtained. The disease-free equilibrium point is locally asymptotically stable under the condition that $\mathcal{R}_0 < 1$, and the endemic equilibrium point is locally asymptotically stable under the condition that $\mathcal{R}_0 > 1$ and $C^*\tilde{p} + w_1\tilde{q} > \theta C^*\sigma\eta\Lambda$. This is supported by the results of numerical simulations using the fourth-order Runge-Kutta method, and graphical visualizations are presented for two equilibrium points, each of which is locally asymptotically stable. To control the spread of hepatitis B disease, things that can be done to minimize the spread of infection are reducing the rate of individual contact in the susceptible subpopulation with the chronic subpopulation, increasing the rate of recovery due to treatment in chronic individuals, and increasing the rate of vaccination in susceptible individuals.

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