

Dynamical System of Hepatitis B in Three Groups with Vaccination

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ABSTRACT

This study aims to modify the hepatitis B transmission model in three age groups involving vaccination from the model conducted by Zhoe and Zhang. The method used is to analyze the stability of the fixed point and its basic reproduction number ($\mathcal{R}_0$). Performed stability analysis and numerical simulation to see population dynamics. Next, a sensitivity analysis of the parameters was carried out to see its effect on $\mathcal{R}_0$. From the analysis obtained two fixed points, namely disease-free and disease-endemic equilibrium. The disease-free equilibrium is locally asymptotically stable if $\mathcal{R}_0 < 1$. Meanwhile, the disease-endemic equilibrium is locally asymptotically stable if $\mathcal{R}_0 > 1$. Hepatitis vaccination affects the number of susceptible population, because the more successful the vaccination, the smaller the number of susceptible populations so that the smaller the population will be infected.

Keywords: Dynamic, Hepatitis B, Vaccine, Mathematical model.

2000 Mathematics Subject Classification: 34K20, 37N25, 37N30, 92D25.

JEL Classification : C02, C62, C63.

1 Introduction

Hepatitis B is caused by a hepatitis B virus (HBV) infection that attacks liver function and can cause acute and chronic diseases. It is an endemic disease in various countries. According to WHO 2015, HBV caused 1.34 million deaths. Globally, an estimated 257 million people are alive with chronic HBV (Organization et al., 2017)(WHO, 2019). Indonesia is listed as the second most country in the Southeast Asia Region (SEAR) as an endemic country. The prevalence of hepatitis B in Indonesia was 9,4 % in 2007 and 7,1 % in 2013 (Muljono, 2017). HBV infection in newborns who can't develop a damaged immune response is more likely to cause chronic infection than children and adults. In general, the rate of chronic infection is higher in newborns (90 %), children (30 %), and as more as in adults and adolescents (5 %) (Ganem and Prince, 2004) (Hoofnagle, Doo, Liang, Fleischer and Lok, 2007).

Many infectious diseases for which transmission can be prevented by vaccination in susceptible populations (Bakare, 2016). One of them is the spread of hepatitis b. Hepatitis b vaccination

should take in as early as possible, this is because the prevalence of the spread of the hepatitis b virus is the highest in the population of newborns.

This vaccine is given within 12 hours after the baby is born. The Ministry of Health recommends repeating the Hepatitis B vaccine in conjunction with DPT and Hib immunization at 2, 3, and 4 months of age (Afrianto, 2019). Giving the hepatitis B vaccine to adults is a continuation of the childhood immunization schedule. Before immunization, it is recommended to check HBsAg first (Afrianto, 2019).

There has been much research on the spread of HBV. Medlay *et al.* introduced and analyzed the spread of HBV by dividing the population into 5 populations, namely susceptible, exposed, infected, chronic, and immune (Medley, Lindop, Edmunds and Nokes, 2001). Furthermore, this model was developed by Pang *et al.* with the same population division by adding vaccinations to susceptible populations (Pang, Cui and Zhou, 2010). Furthermore, Zhoe and Zhang redevelop this model by dividing the population into 3 age groups, namely newborns, children (1-6 years), and adults (> 6 years), with each population divided into 5 populations as in the previous model Medlay *et al.* (Zhang and Zhou, 2014).

This study will look at Hepatitis B transmission in the three age groups involving vaccination by modified Zhoe and Zhang's model. It also involves vaccinations given to a population of susceptible newborns and adults vulnerable population. Modification of the model is done by providing further vaccinations to newborns along with DPT and Hib. That the newborn is assumed to have been vaccinated against hepatitis B first after birth.

This study aims to modify the mathematical model related to the spread of hepatitis B in three age groups by vaccination. This modification will show the equilibrium stability and basic reproduction number along with sensitivity and numerical analysis.

2 Mathematical Model

This paper built a deterministic model to involve Zhang and Zhoe models by adding the assumptions to provide a repetition of the vaccine to the newborn population. This model divided the spread of the disease into three age groups (newborns, children 1-6 years, and adult > 6 years). Where every age group was divided into five compartments, namely S was susceptible population, E was exposed population, I was population with acute infection, C was carrier population of HBV chronic, R was populations that have no immunity to HBV. This model used several assumptions. First, the susceptible individuals to get infected to HBV primary through direct contact with HBV carriers of acute or chronic that would move to the exposed population. Newborns was infected by HBV for transmission from infected mothers. The transitions between each age group are from newborn to children (μ_1) and from child to adult (μ_2) on the susceptible, exposed, of infected, chronic HBV carriers, and the is immunized population. The death of individuals of each population (d_i). Individuals in the population are exposed to acute infection ($\sigma_i E_i$). If the acute infection does not progress to chronic, then the host clears HBV, recovered, and became resistant ($(1 - q_3)\lambda_3$). Conversely, if the infection was acute, it will develop chronic HBV. The catch-up vaccination is given to the adult population so it has an immune system (p). Newborns have a risk of becoming HBV chronic-born of mothers who

both HBeAg-positive and HBeAg-negative ($\frac{b\omega v C_3}{N_3}$). Chronic HBV carried to recovered populations, hosts cleared HBV and immune (η_i). Newborns who have an immune system to HBV ($b(1-w)$). This modification model can be seen in Figure 1.

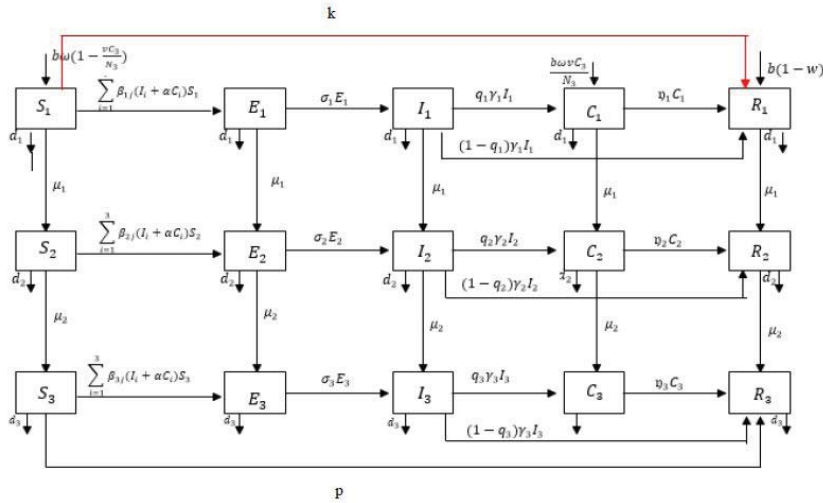


Figure 1: Compartment diagram of modified hepatitis B disease

Based on the compartment diagram of Hepatitis B, the modification results obtained the following differential equation:

$$\begin{aligned}
 S_1' &= b\omega \frac{1-vC_3}{N_3} - [\beta_{11}(I_1 + \alpha C_1) + \beta_{12}(I_2 + \alpha C_2) + \beta_{13}(I_3 + \alpha C_3)]S_1 - (k + \mu_1 + d_1)S_1 \\
 E_1' &= [\beta_{11}(I_1 + \alpha C_1) + \beta_{12}(I_2 + \alpha C_2) + \beta_{13}(I_3 + \alpha C_3)]S_1 - (\sigma_1 + \mu_1 + d_1)E_1 \\
 I_1' &= \sigma_1 E_1 - (\gamma_1 + \mu_1 + d_1)I_1 \\
 C_1' &= q_1 \gamma_1 I_1 + \frac{b\omega v C_3}{N_3} - (\eta_1 + \mu_1 + d_1)C_1 \\
 R_1' &= (1 - q_1)\gamma_1 I_1 + \eta_1 C_1 + b(1 - w) - (\mu_1 + d_1)R_1 + kS_1 \\
 S_2' &= \mu_1 S_1 - [\beta_{21}(I_1 + \alpha C_1) + \beta_{22}(I_2 + \alpha C_2) + \beta_{23}(I_3 + \alpha C_3)]S_1 - (\mu_2 + d_2)S_2 \\
 E_2' &= \mu_1 E_1 - [\beta_{21}(I_1 + \alpha C_1) + \beta_{22}(I_2 + \alpha C_2) + \beta_{23}(I_3 + \alpha C_3)]S_1 - (\sigma_2 + \mu_2 + d_2)S_2 \\
 I_2' &= \mu_1 I_1 + \sigma_2 E_2 - (\gamma_2 + \mu_2 + d_2)I_2 \\
 C_2' &= \mu_1 C_1 + q_2 \gamma_2 I_2 - (\eta_2 + \mu_2 + d_2)C_2 \\
 R_2' &= \mu_1 R_1 + \eta_2 C_2 + (1 - q_2)\gamma_2 I_2 - (\mu_2 + d_2)R_2 \\
 S_3' &= \mu_2 S_2 - [\beta_{31}(I_1 + \alpha C_1) + \beta_{32}(I_2 + \alpha C_2) + \beta_{33}(I_3 + \alpha C_3)]S_1 - (p + d_3)S_3 \\
 E_3' &= \mu_2 E_2 - [\beta_{31}(I_1 + \alpha C_1) + \beta_{32}(I_2 + \alpha C_2) + \beta_{33}(I_3 + \alpha C_3)]S_1 - (\sigma_3 + d_3)S_3 \\
 I_3' &= \mu_2 I_2 + \sigma_3 E_3 - (\gamma_3 + d_3)I_3 \\
 C_3' &= \mu_2 C_2 + q_3 \gamma_3 I_3 - (\eta_3 + d_3)C_3 \\
 R_3' &= \mu_2 R_2 + \eta_3 C_3 + (1 - q_3)\gamma_3 I_3 - d_3 R_3 + pS_3
 \end{aligned} \tag{2.1}$$

All parameters in the model are nonnegative.

Table 1: Hepatitis B model parameters

Paramaters	Information	unit
b	Recruitment rate	Person / time
w	Proportion of births that were not immunized successfully	Without units
v	Proportion of newborns that developing to be HBV carriers of mother giving birth	Without units
α	The rate of transmission of the relative operator of acute infection	1/(Person / time)
p	Rate of adults receiving catch-up vaccination	1/(Person / time)
μ_1	Transition rate from newborn to child	1/(Person / time)
μ_2	Transition rate from child to adult	1/(Person / time)
$\beta_i j$	Coefficient Transmission	Without units
σ_i	The rate at which the exposed group progresses to the acute infection group	1/(Person / time)
γ_i	The rate at which the acute infection cohort develops into the chronic HBV carrier group	1/(Person / time)
q_i	Proportion of the acute infection cohort developing chronic HBV carriers	1/(Person / time)
η_i	Chronic HBV carriers entered the HBV-immune group	1/(Person / time)
d_i	Death rate	1/(Person / time)
k	Rate of newborns receiving repetition of the vaccine	1/(Person / time)

From Zhoe and Zhang research using five equation for each age group, namely

$$\begin{aligned}
 N_1' &= b - (\mu_1 + d_1)N_1, \\
 N_2' &= \mu_1 N_1 - (\mu_2 + d_2)N_2, \\
 N_3' &= \mu_2 N_2 - d_3 N_2,
 \end{aligned}$$

3 Basic Reproduction Numbers and Stability

The basic reproduction number ($\mathfrak{R}_0$) is the number of cases estimated in a susceptible population by infected individuals. The basic reproduction can be determined using the next generation matrix. The value of the basic reproduction number according is (Van den Driessche and Watmough, 2002).

$$\mathfrak{R}_0 = \rho FV^{-1}, \quad (3.1)$$

For his modification case, a multi-group model is used so that the parameter value $\beta_{12} = \beta_{13} = \beta_{21} = \beta_{23} = \beta_{31} = \beta_{32} = 0$ dan $v = 0$. Because this model is multi-group, the sum of the basic reproduction numbers is the sum of the reproduction numbers of each group (Diekmann, Heesterbeek and Metz, 1990).

Suppose $a_i = \sigma_i + \mu_i + d_i$, $b_i = \lambda_i + \mu_i + d_i$, $g_i = \eta_i + \mu_i + d_i$, $a_3 = \sigma_3 + d_3$, $b_3 = \gamma_3 + d_3$, $g_3 = \eta_3 + d_3$. The next-generation matrix at the disease-free T^0 is given by

$$F = \begin{bmatrix} 0 & \beta_{11}S_1^0 & \beta_{11}\alpha S_1^0 & 0 & \beta_{12}S_1^0 & \beta_{12}\alpha S_1^0 & 0 & \beta_{13}S_1^0 & \beta_{13}\alpha S_1^0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \beta_{21}S_2^0 & \beta_{21}\alpha S_2^0 & 0 & \beta_{22}S_2^0 & \beta_{22}\alpha S_2^0 & 0 & \beta_{23}S_2^0 & \beta_{23}\alpha S_2^0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \beta_{31}S_3^0 & \beta_{31}\alpha S_3^0 & 0 & \beta_{32}S_3^0 & \beta_{32}\alpha S_3^0 & 0 & \beta_{33}S_3^0 & \beta_{33}\alpha S_3^0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix},$$

and

$$V = \begin{bmatrix} a_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ -\sigma_1 & b_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & -q_1\gamma_1 & g_1 & 0 & 0 & 0 & 0 & 0 & \frac{bwv}{N_3} \\ -\mu_1 & 0 & 0 & a_1 & 0 & 0 & 0 & 0 & 0 \\ 0 & -\mu_1 & 0 & -\sigma_2 & b_2 & 0 & 0 & 0 & 0 \\ 0 & 0 & -\mu_1 & 0 & -q_2\gamma_2 & g_2 & 0 & 0 & 0 \\ 0 & 0 & 0 & -\mu_2 & 0 & 0 & a_1 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\mu_2 & 0 & -\sigma_3 & b_3 & 0 \\ 0 & 0 & 0 & 0 & 0 & -\mu_2 & 0 & -q_3\gamma_3 & g_3 \end{bmatrix}.$$

From the F and V, the basic reproduction number (R_0) is obtained with dominant eigenvalue in the matrix $G = FV^{-1}$, namely

$$\mathfrak{R} = (0, 0, 0, 0, 0, 0, \frac{s_1\beta_{11}(g_1 + q_1\alpha\eta_1)\sigma_1}{a_1b_1g_1}, \frac{s_2\beta_{22}(g_2 + q_2\alpha\eta_2)\sigma_2}{a_2b_2g_2}, \frac{s_3\beta_{33}(g_3 + q_3\alpha\eta_3)\sigma_3}{a_3b_3g_3}).$$

The result show that there are three reproduction number, namely

$$R_1 = \frac{(s_1\beta_{11}(g_1 + q_1\alpha\eta_1)\sigma_1)}{a_1b_1g_1}, R_2 = \frac{(s_2\beta_{22}(g_2 + q_2\alpha\eta_2)\sigma_2)}{a_2b_2g_2}, R_3 = \frac{(s_3\beta_{33}(g_3 + q_3\alpha\eta_3)\sigma_3)}{a_3b_3g_3}.$$

So that

$$\mathfrak{R}_0 = R_1 + R_2 + R_3 \quad (3.2)$$

4 Equilibrium stability

Equilibrium of disease-free

A disease-free equilibrium is obtained if it $E_1 = I_1 = C_1 = E_2 = I_2 = C_2 = E_3 = I_3 = C_3 = 0$ is as follows :

$$T^0 = (S_1^0, 0, 0, 0, R_1^0, S_2^0, 0, 0, 0, R_2^0, S_3^0, 0, 0, 0, R_3^0),$$

with

$$S_1^0 = \frac{bw}{d_1+k+\mu_1}, \quad S_2^0 = \frac{bw\mu_1}{(d_1+k+\mu_1)(d_2+\mu_2)}, \quad S_3^0 = \frac{bw\mu_1(-d_3+\mu_2)}{(p(d_1+k+\mu_1)(d_2+\mu_2))},$$

$$R_1^0 = \frac{1}{d_1+\mu_1} - \frac{w}{d_1+k+\mu_1}, \quad R_2^0 = \frac{b\mu_1(d_1+k-d_1w+\mu_1-w\mu_1)}{(d_1+\mu_1)(d_1+k+\mu_1)(d_2+\mu_2)}, \quad R_3^0 = \frac{b\mu_1(\frac{w}{d_1+k+\mu_1} + \frac{d_3(d_1+\mu_1)}{d_2+\mu_2})}{d_2+\mu_2}$$

In this section, Theorem 4.1 will be used to be the criteria for the stability of a equilibrium of disease-free T^0 .

Theorem 4.1. *The disease-free equilibrium in (2.1) is local asymptotic if and only if $\mathfrak{R}_0 < 1$.*

Proof. The stability of the equilibrium $T^0 = (S_1^0, 0, 0, 0, R_1^0, S_2^0, 0, 0, 0, R_2^0, S_3^0, 0, 0, 0, R_3^0)$ can be determined by linearizing the system (2.1) around T^0 .

The Jacobi Matrix for the equilibrium is obtained T^0 as follows

$$J_{T^0} = \begin{pmatrix} J_{11} & 0 & -s_1\beta_{11} & J_{14} & 0 & 0 & 0 & -s_1\beta_{12} & J_{19} & 0 & 0 & 0 & -s_1\beta_{13} & J_{2114} & 0 \\ 0 & J_{22} & s_1\beta_{11} & J_{24} & 0 & 0 & 0 & s_1\beta_{12} & J_{29} & 0 & 0 & 0 & s_1\beta_{13} & J_{2214} & 0 \\ 0 & 0 & \sigma_1 & J_{33} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & q_1\gamma_1 & J_{44} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & J_{2414} & 0 \\ k & 0 & J_{53} & \eta_1 & J_{55} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \mu_1 & 0 & -s_2\beta_{21} & J_{64} & 0 & J_{66} & 0 & -s_2\beta_{22} & J_{69} & 0 & 0 & 0 & -s_2\beta_{23} & J_{2614} & 0 \\ 0 & \mu_1 & s_2\beta_{21} & J_{74} & 0 & 0 & J_{77} & s_2\beta_{22} & J_{79} & 0 & 0 & 0 & s_2\beta_{23} & J_{2714} & 0 \\ 0 & 0 & \mu_1 & 0 & 0 & 0 & \sigma_2 & J_{88} & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \mu_1 & 0 & 0 & 0 & q_2\gamma_2 & J_{99} & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \mu_1 & 0 & 0 & J_{108} & \eta_2 & J_{1010} & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -s_3\beta_{31} & J_{114} & 0 & \mu_2 & 0 & -s_3\beta_{32} & J_{119} & 0 & J_{1111} & 0 & -s_3\beta_{33} & J_{1114} & 0 \\ 0 & 0 & s_3\beta_{31} & J_{124} & 0 & 0 & \mu_2 & s_3\beta_{32} & J_{129} & 0 & 0 & J_{1212} & s_3\beta_{33} & J_{1214} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \mu_2 & 0 & 0 & 0 & \sigma_3 & J_{1313} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \mu_2 & 0 & 0 & 0 & q_3\gamma_3 & J_{1414} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \mu_2 & p & 0 & J_{1513} & \eta_3 & d_3 \end{pmatrix},$$

where

$$\begin{aligned} J_{11} &= -d_1 - k - \mu_1, & J_{22} &= -d_1 - \mu_1 - \sigma_1, & J_{33} &= -d_1 - \gamma_1 - \mu_1, & J_{53} &= (1 - q_1)\gamma_1, & J_{14} &= -s_1\alpha\beta_{11}, \\ J_{24} &= s_1\alpha\beta_{11}, & J_{44} &= -d_1 - \eta_1 - \mu_1, & J_{88} &= -d_2 - \gamma_2 - \mu_2, & J_{19} &= -s_1\alpha\beta_{12}, & J_{29} &= -s_1\alpha\beta_{12}, \\ J_{69} &= -s_2\alpha\beta_{22}, & J_{79} &= s_2\alpha\beta_{22}, & J_{99} &= -d_2 - \eta_2 - \mu_2, & J_{119} &= -s_3\alpha\beta_{32}, & J_{129} &= s_3\alpha\beta_{32}, \\ J_{1010} &= -d_2 - \mu_2, & J_{1111} &= -d_3 - p, & J_{1212} &= -d_3 - \sigma_3, & J_{64} &= -s_2\alpha\beta_{21}, & J_{74} &= s_2\alpha\beta_{21}, \\ J_{2214} &= s_1\alpha\beta_{13}, & J_{124} &= s_3\alpha\beta_{31}, & J_{55} &= -d_1 - \mu_1, & J_{66} &= -d_2 - \mu_2, & J_{77} &= -d_2 - \mu_2 - \sigma_2, \\ J_{108} &= (1 - q_2)\gamma_2, & J_{2713} &= s_2\alpha\beta_{23}, & J_{1313} &= -d_3 - \gamma_3, & J_{1513} &= (1 - q_3)\gamma_3, & J_{2114} &= -\frac{bvw}{n_3} - s_1\alpha\beta_{13}, \\ J_{2414} &= \frac{bvw}{n_3}, & J_{2614} &= -s_2\alpha\beta_{23}, & J_{2714} &= s_2\alpha\beta_{23}, & J_{1114} &= -s_3\alpha\beta_{33}, \\ J_{1214} &= s_3\alpha\beta_{33}, & J_{1414} &= -d_3 - \eta_3, & J_{114} &= -s_3\alpha\beta_{31} \end{aligned}$$

The characteristic polynomial of the matrix J_{T^0} is

$$(J_{1010} - \lambda)(J_{11} - \lambda)(J_{1111} - \lambda)(J_{1515} - \lambda)(J_{55} - \lambda)(J_{66} - \lambda)(\lambda^9 + a_1\lambda^8 + a_2\lambda^7 + a_3\lambda^5 + a_4\lambda^4 + a_5\lambda^4 + a_6\lambda^3 + a_7\lambda^2 + a_8\lambda + a_9) = 0 \quad (4.1)$$

From this equation, we obtained fifteen eigenvalues, among which six eigenvalues are negative, i.e

$$\begin{aligned} \lambda_1 &= J_{11} = -(d_1 + k + \mu_1), & \lambda_2 &= J_{55} = -(d_1 + \mu_1), & \lambda_3 &= J_{66} = -(d_2 + \mu_2), \\ \lambda_4 &= J_{1010} = -(d_2 + \mu_2), & \lambda_5 &= J_{1111} = -(d_3 + p) & \lambda_6 &= J_{1515} = -d_3 \end{aligned}$$

while the other nine eigenvalues are obtained by solving the following characteristic equations with the Routh-Hurwitz criterion.

$$(\lambda^9 + a_1\lambda^8 + a_2\lambda^7 + a_3\lambda^5 + a_4\lambda^4 + a_5\lambda^4 + a_6\lambda^3 + a_7\lambda^2 + a_8\lambda + a_9) = 0 \quad (4.2)$$

Based on the Routh-Hurwitz criterion, Equation (4.2) at a equilibrium will be stable if and only if a_k is a constant real and $k = 1, 2, \dots, 9$. Routh-Hurwitz matrix defined by using the coefficients

of the characteristic equation as follows (Edelstein-Keshet, 2005):

$$H_k = \begin{bmatrix} a_1 & 1 & 0 & \cdots & 0 \\ a_3 & a_2 & a_1 & \cdots & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \cdots & \cdots & a_k \end{bmatrix}.$$

The condition for each element in the matrix H_j with size (l, m) is

$$H_k = \begin{cases} a_{2l-m} & \text{to } 0 \leq 2l - m \leq k \\ 1 & \text{to } 2l = m \\ 0 & \text{to } 2l < m \text{ or } 2l > k + m \end{cases}$$

The equilibrium $\tilde{x}$ is stable if and only if all determinants of the matrix H_j are positive or $|H_j| > 0$ for every $j = 1, 2, \dots, k$.

Since all parameters are positive, then a_1 is positive. The coefficient $a_2, a_3, a_4, a_5, a_6, a_7, a_8, a_9$ have positive value with condition $R_0 < 1$.

So that coefficient $a_2, a_3, a_4, a_5, a_6, a_7, a_8, a_9$ are positive. Then to prove $|H_j| > 0$, parameter values are needed when $R_0 < 1$. The parameter conditions are presented in Table 2.

So that condition $|H_j| > 0$ is met. Thus it is evident that the equilibrium disease-free T^0 is asymptotically stable. $\square$

Equilibrium for disease endemic

Disease endemic equilibrium is a condition where there are still infected individuals from a certain population. From the system of Equation (2.1), the endemic fixed point is obtained as follows:

$$T^* = (S_1^*, E_1^*, I_1^*, C_1^*, R_1^*, S_2^*, E_2^*, I_2^*, C_2^*, R_2^*, S_3^*, E_3^*, I_3^*, C_3^*, R_3^*),$$

with

$$\begin{aligned} S_1^* &= \frac{b(N_3 - C_3^* v)w}{(N_3(d_1 + p + I_1^* \beta_1 1 + C_1^* \alpha \beta_1 1 + I_2^* \beta_1 2 + C_2^* \alpha \beta_1 2 + I_3^* \beta_1 3 + C_3^* \alpha \beta_1 3 + \mu_1))}, & I_1^* &= \frac{E_1^* \sigma_1}{d_1 + \gamma_1 + \mu_1}, \\ S_2^* &= \frac{S_1^* \mu_1}{(d_2 + I_1^* \beta_2 1 + C_1^* \alpha \beta_2 1 + I_2^* \beta_2 2 + C_2^* \alpha \beta_2 2 + I_3^* \beta_2 3 + C_3^* \alpha \beta_2 3 + \mu_2)}, & I_2^* &= \frac{I_1^* \mu_1 \eta_1 + E_2^* \sigma_2}{d_2 + \gamma_2 + \mu_2}, \\ S_3^* &= \frac{S_2^* \mu_2}{(d_3 + I_1^* \beta_3 1 + C_1^* \alpha \beta_3 1 + I_2^* \beta_3 2 + C_2^* \alpha \beta_3 2 + I_3^* \beta_3 3 + C_3^* \alpha \beta_3 3)}, & I_3^* &= \frac{I_2^* \mu_2 \eta_2 + E_3^* \sigma_3}{d_3 + \gamma_3}, \\ E_1^* &= \frac{(S_1^* (I_1^* \beta_1 1 + C_1^* \alpha \beta_1 1 + I_2^* \beta_1 2 + C_2^* \alpha \beta_1 2 + I_3^* \beta_1 3 + C_3^* \alpha \beta_1 3))}{d_1 + \mu_1 + \sigma_1}, & C_1^* &= \frac{bC_3^* v w + I_1^* N_3 q_1 \gamma_1}{N_3(d_1 + \eta_1 + \mu_1)}, \\ E_2^* &= \frac{(S_2^* (I_1^* \beta_2 1 + C_1^* \alpha \beta_2 1 + I_2^* \beta_2 2 + C_2^* \alpha \beta_2 2 + I_3^* \beta_2 3 + C_3^* \alpha \beta_2 3) + E_1^* \mu_1)}{d_2 + \mu_2 + \sigma_2}, & C_2^* &= \frac{C_1^* \mu_1 \eta_1 + I_2^* q_2 \gamma_2}{d_2 + \eta_2 + \mu_2}, \\ E_3^* &= \frac{(S_3^* (I_1^* \beta_3 1 + C_1^* \alpha \beta_3 1 + I_2^* \beta_3 2 + C_2^* \alpha \beta_3 2 + I_3^* \beta_3 3 + C_3^* \alpha \beta_3 3) + E_2^* \mu_2)}{d_3 + \sigma_3}, & C_3^* &= \frac{C_2^* \mu_2 \eta_2 + I_3^* q_3 \gamma_3}{d_3 + \eta_3}, \\ R_1^* &= \frac{b + pS_1^* - bw + I_1^* q_1 \gamma_1 + C_1^* \eta_1}{d_1 + \mu_1}, & R_2^* &= \frac{R_1^* \mu_1 \eta_1 + I_2^* q_2 \gamma_2 + C_2^* \eta_2}{d_2 + \mu_2}, & R_3^* &= \frac{kS_3^* + R_2^* \mu_2 \eta_2 + I_3^* q_3 \gamma_3 - I_3^* q_3 \gamma_3}{d_3 + \mu_3}, \end{aligned}$$

In this section, theorem 4.2 will be used as the criterion for the stability of a equilibrium endemic disease T^* .

Theorem 4.2. *The endemic equilibrium in Equation (2.1) is local asymptotically if and only if $R_0 > 1$*

Proof. The proof used Castillo and Song's Theorem (Castillo-Chavez and Song, 2004). Suppose $\varphi = \beta$ that the bifurcation parameter and $x_1 = S_1, x_2 = E_1, x_3 = I_1, x_4 = C_1, x_5 =$

$R_1, x_6 = S_2, x_7 = E_2, x_8 = I_2, x_9 = C_2, x_{10} = R_2, x_{11} = S_3, x_{12} = E_3, x_{13} = I_3, x_{14} = C_3, x_{15} = R_3$. Based on Equation (3) it is obtained

$$\varphi = \varphi^* = \frac{(s_1\beta_{11}(g_1 + q_1\alpha\eta_1)\sigma_1)}{a_1b_1g_1}, \frac{(s_2\beta_{22}(g_2 + q_2\alpha\eta_2)\sigma_2)}{a_2b_2g_2}, \frac{(s_3\beta_{33}(g_3 + q_3\alpha\eta_3)\sigma_3)}{a_3b_3g_3}$$

Based on Castillo and Song's Theorem (Castillo-Chavez and Song, 2004), the Jacobi matrix of the system (2.1) is evaluated at a point $T^0(J_{T^0})$ to find the eigenvalues and is obtained as equation (4.1). There are fifteen eigenvalues in the matrix J_{T^0} . Six of these eigenvalues are negative. While the other nine are determined by the Routh-Hurwitz criterion with characteristic equations such as equation (4.2).

If $\Re_0 = 0$ in equation (4.2), the coefficient a_9 must be zero, so that one eigenvalue is zero and the other eight are negative according to the Routh-Hurwitz criteria in the attachment. So there are fourteen negative eigenvalues and one zero eigenvalues. This is consistent with the Castillo-Cahves and Song Theorem. Besides, the zero eigenvalues are related to a matrix J_{T^0} that has a right eigenvector (u_i) and a left eigenvector (v_i) with $i = 1, 2, 3, \dots, 15$.

Get the right eigenvector is $u_2, u_3, u_4, u_5, u_7, u_8, u_9, u_{10}, u_{12}, u_{13}, u_{14}, u_{15} > 0$ and $u_1, u_6, u_{11} < 0$. Get the right eigenvector is $v_1 = v_5 = v_6 = v_{10} = v_{11} = v_{12} = v_{13} = v_{15} = 0$ and $v_2, v_3, v_4, v_7, v_8, v_9, v_{12}, v_{13}, v_{14} > 0$.

Suppose that Equation (2.1) is written as

$$\begin{aligned} f_1 &= bw \frac{1-vx_{14}}{N_3} - [\beta_{11}(x_3 + \alpha x_4) + \beta_{12}(x_8 + \alpha x_9) + \beta_{13}(x_{13} + \alpha x_{14})]x_1 - (k + \mu_1 + d_1)x_1 \\ f_2 &= [\beta_{11}(x_3 + \alpha x_4) + \beta_{12}(x_8 + \alpha x_9) + \beta_{13}(x_{13} + \alpha x_{14})]x_1 - (\sigma_1 + \mu_1 + d_1)x_2 \\ f_3 &= \sigma_1 x_2 - (\gamma_1 + \mu_1 + d_1)x_3 \\ f_4 &= q_1 \gamma_1 x_3 + \frac{bvw x_{14}}{N_3} - (\eta_1 + \mu_1 + d_1)x_4 \\ f_5 &= (1 - q_1)\gamma_1 x_3 + \eta_1 x_4 + b(1 - w) - (\mu_1 + d_1)x_5 + kx_1 \\ f_6 &= \mu_1 x_1 - [\beta_{21}(x_3 + \alpha x_4) + \beta_{22}(x_8 + \alpha x_9) + \beta_{23}(x_{13} + \alpha x_{14})]x_1 - (\mu_2 + d_2)x_6 \\ f_7 &= \mu_1 x_2 - [\beta_{21}(x_3 + \alpha x_4) + \beta_{22}(x_8 + \alpha x_9) + \beta_{23}(x_{13} + \alpha x_{14})]x_1 - (\sigma_2 + \mu_2 + d_2)x_6 \\ f_8 &= \mu_1 x_3 + \sigma_2 x_7 - (\gamma_2 + \mu_2 + d_2)x_8 \\ f_9 &= \mu_1 x_4 + q_2 \gamma_2 x_8 - (\eta_2 + \mu_2 + d_2)x_9 \\ f_{10} &= \mu_1 x_5 + \eta_2 x_9 + (1 - q_2)\gamma_2 x_8 - (\mu_2 + d_2)x_{10} \\ f_{11} &= \mu_2 x_6 - [\beta_{31}(x_3 + \alpha x_4) + \beta_{32}(x_8 + \alpha x_9) + \beta_{33}(x_{13} + \alpha x_{14})]x_1 - (p + d_3)x_{11} \\ f_{12} &= \mu_2 x_7 - [\beta_{31}(x_3 + \alpha x_4) + \beta_{32}(x_8 + \alpha x_9) + \beta_{33}(x_{13} + \alpha x_{14})]x_1 - (\sigma_3 + d_3)x_{11} \\ f_{13} &= \mu_2 x_8 + \sigma_3 x_{12} - (\gamma_3 + d_3)x_{13} \\ f_{14} &= \mu_2 x_9 + q_3 \gamma_3 x_{13} - (\eta_3 + d_3)x_{14} \\ f_{15} &= \mu_2 x_{10} + \eta_3 x_{14} + (1 - q_3)\gamma_3 x_{13} - d_3 x_{15} + p x_{11} \end{aligned} \quad (4.3)$$

Based on the system of Equation (4.3), a partial derivative is obtained for the following equation:

$$\begin{aligned} a &= \sum_{k,i,j=1}^n v_k u_i u_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(T^0, \varphi^*). \\ b &= \sum_{k,i,j=1}^n v_k u_i \frac{\partial^2 f_k}{\partial x_i \partial \varphi}(T^0, \varphi^*). \end{aligned}$$

Based on equation (4.3), we have

$$a = v_2(u_1u_3\varphi_{11}^* + u_1u_4\alpha\varphi_{11}^* + u_1u_8\varphi_{12}^* + u_1u_9\alpha\varphi_{12}^* + u_1u_{13}\varphi_{13}^* + u_1u_{14}\alpha\varphi_{13}^*) + v_7(u_6u_3\varphi_{21}^* + u_6u_4\alpha\varphi_{21}^* + u_6u_8\varphi_{22}^* + u_6u_9\alpha\varphi_{22}^* + u_6u_{13}\varphi_{23}^* + u_6u_{14}\alpha\varphi_{23}^*) + v_{12}(u_{11}u_3\varphi_{31}^* + u_{11}u_4\alpha\varphi_{31}^* + u_{11}u_8\varphi_{32}^* + u_{11}u_9\alpha\varphi_{32}^* + u_{11}u_{13}\varphi_{33}^* + u_{11}u_{14}\alpha\varphi_{33}^*).$$

Because $v_2, v_7, v_{11}, u_3, u_4, u_8, u_9, u_{13}, u_{14} > 0$, $\varphi_{11}^*, \varphi_{12}^*, \varphi_{13}^*, \varphi_{21}^*, \varphi_{22}^*, \varphi_{23}^*, \varphi_{31}^*, \varphi_{32}^*, \varphi_{33}^* > 0$, and $u_1, u_6, u_{11} < 0$, then $a < 0$ and are obtained

$$b = 3v_2u_1 + 3v_7u_6 + 3v_{12}u_{11} + u_3(v_2 + v_7 + v_{12}) + \alpha u_4(v_2 + v_7 + v_{12}) + u_8(v_2 + v_7 + v_{12}) + \alpha u_9(v_2 + v_7 + v_{12}) + u_{13}(v_2 + v_7 + v_{12}) + \alpha u_{14}(v_2 + v_7 + v_{12}).$$

Because $v_2, v_7, v_{11}, u_3, u_4, u_8, u_9, u_{13}, u_{14} > 0$ then $b > 0$.

The a and b values obtained correspond to case 4 in the Castillo-Chavez and song theorem that is The $a < 0, b > 0$, when the value of φ changes from negative to positive, then T^0 changes its stability from stable to unstable. To φ , unstable negative T^* becomes positive and locally asymptotically stable. Consequently, when φ changing from $\varphi < \varphi^*(\mathfrak{R}_0 < 1)$ to be $\varphi > \varphi^*(\mathfrak{R}_0 > 1)$, the unstable endemic equilibrium T^* changes from negative to positive and locally asymptotically stable. So it is proven if the endemic equilibrium is local asymptotic. $\square$

5 Numerical simulation

This simulation is carried out to prove the stability of each equilibrium by entering the parameter values in Table 2. The dynamics of the human population will be observed when numbers $\mathfrak{R}_0 < 1$ and $\mathfrak{R}_0 > 1$. The initial value for each sub-population is $s_1(0) = 300, e_1(0) = 150, i_1(0) = 200, c_1(0) = 200, r_1(0) = 50, s_2(0) = 200, e_2(0) = 150, i_2(0) = 200, c_2(0) = 100, r_2(0) = 332, s_3(0) = 310, e_3(0) = 100, i_3(0) = 100, c_3(0) = 50, r_3(0) = 300$.

Table 2: Parameter value in the model for T^0 and T^*

Parameters	T^0	T^*	Parameters	T^0	T^*	Parameters	T^0	T^*	source
b	40	100	σ_i	6	6	d_1	3/70	3/70	Zhoe and Zhang (2014)
w	0.45	0.45	q_1	0.885	0.885	d_2	2/70	2/70	Zhoe and Zhang (2014)
v	0.11	0.11	q_2	0.25	0.25	d_3	1/70	1/70	Zhoe and Zhang (2014)
α	0.3	0.3	q_3	0.05	0.05	β_{ij}	0.0035	0.0035	Zhoe and Zhang (2014)
p	0.05	0.05	η_i	0.025	0.025	β_{ii}	0.004	0.004	Zhoe and Zhang (2014)
k	0.3	0.3							Assumption

For the disease without equilibrium, additional values of Table 2 give $\mathfrak{R}_0 = 0.5176 < 1$. For the endemic equilibrium, additional values of Table 2 give $\mathfrak{R}_0 = 1.2940 > 1$. This can also be seen in the simulation results given in Figure 2 and 3.

This simulation shows that the system will be stable at the disease-free equilibrium when $\mathfrak{R}_0 < 1$ and will also be stable at the endemic equilibrium when $\mathfrak{R}_0 > 1$.

6 Sensitivity Analysis and Discussion

The dynamics of the spread of hepatitis B are influenced by the value of each parameter. Changes in the value of the parameter will affect the simulation value, however, the effect of each parameter is different depending on the level of sensitivity of each parameter to $\mathfrak{R}_0$. The sensitivity analysis was carried out to determine which parameters have a big influence $\mathfrak{R}_0$. The

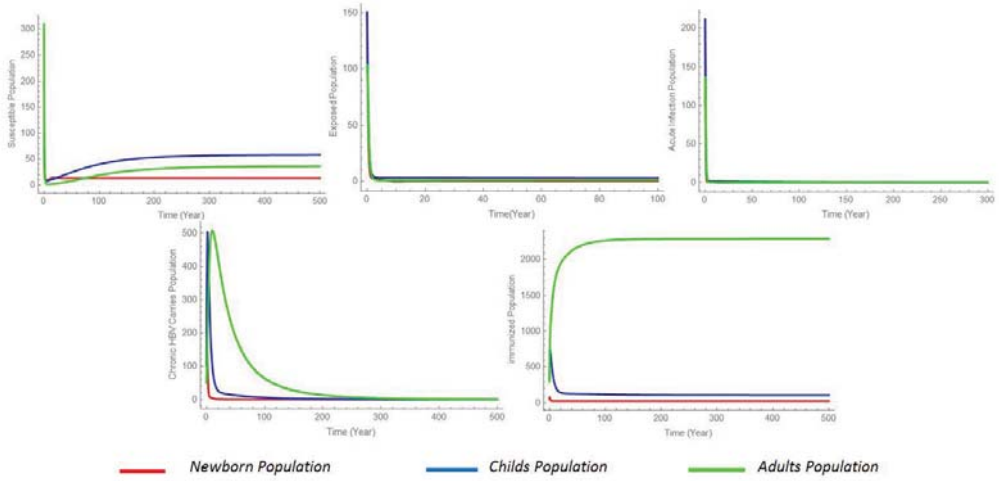


Figure 2: Dynamics of the human population for conditions $\mathfrak{R}_0 < 1$

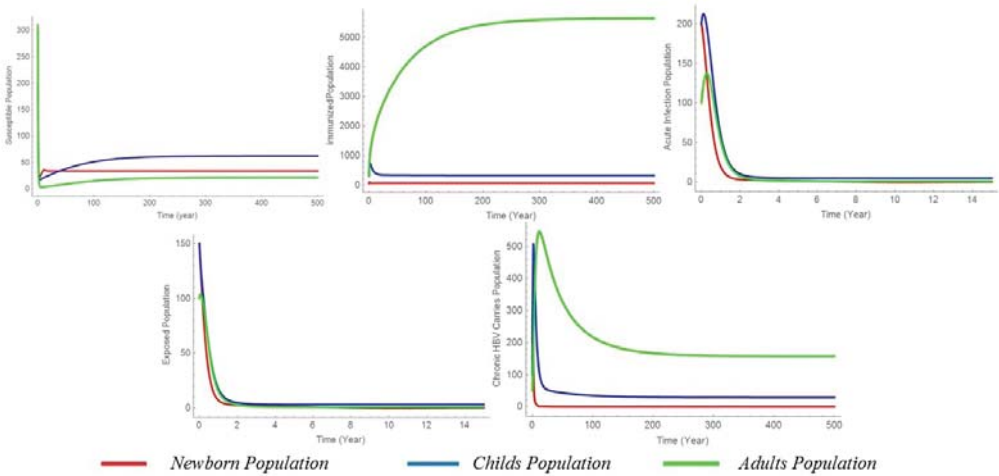


Figure 3: Dynamics of the human population for conditions $\mathfrak{R}_0 > 1$

sensitivity analysis is carried out by considering the parameter sensitivity index value obtained by using equation (3.2). The effect of rate of diseases with giving immunization newborns to $\mathcal{R}_0$ can be seen from the parameter value of immunization in newborns susceptible populations (k). The provision of immunization affects compartment S . If the k value is enlarged, the disease-free equilibrium value of S will be smaller. The effect of disease rate on HBV disease by immunizing new babies has a positive value. The greater the value of the equilibrium S on disease-free, it will increase the value $\mathcal{R}_0$.

Table 3: Effect of transmission rate on population dynamics S on parameter k

Parameter k	S_1	S_2	S_3	Basic Reproduction Numbers ($\mathcal{R}_0$)
$k_1 = 0.3$	13.4043	58.6438	36.3034	0.4009
$k_2 = 0.75$	10.0398	43.9243	27.1912	0.3003
$k_3 = 1$	8.8112	38.549	23.8636	0.2635

In Table 3 can be seen that the greater the value of the rate of immunization for newborns (k), the smaller the numerical value $\mathcal{R}_0$ or the smaller the disease-free fixed-point value, the smaller the number value $\mathcal{R}_0$. The simulation for value variations can be seen in Figure 4.

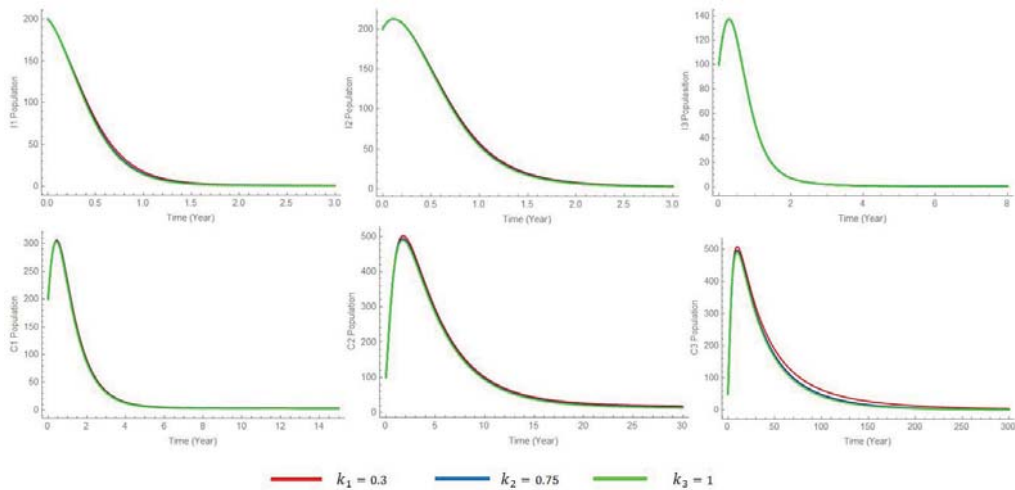


Figure 4: Dynamics of the human population with variation

7 Conclusion

This research carried out the dynamic analysis for the mathematical model of Hepatitis B which considers giving vaccinations to a population of susceptible newborns. This model obtained two equilibria, namely, disease-free equilibrium and endemic equilibrium. The disease-free equilibrium is local asymptotically stable at condition $\mathcal{R}_0 < 1$ and, the disease-endemic equilibrium is local asymptotically stable at condition $\mathcal{R}_0 > 1$. The simulation results show that the equilibrium of disease-free and of disease-endemic are the same.

Giving three doses of HB vaccination to newborns will reduce the population that is susceptible, exposed, infected, and chronic. This reduction in population does not only occur in the newborn population but also the population of children and adults. on the other hand, the immunized population of each age group will increase. this is because giving vaccinations to newborns results in a susceptible population being immune to HBV.

Therefore that the effect of hepatitis B vaccination is very important to prevent the spread of HBV. HB vaccination should be increased at both newborn and adult ages. Pregnant women are also advised to do HBsAg and anti-HBs tests. This is due to the high spread of HBV from mother to newborn.

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