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MATHEMATICAL MODELING AND ANALYSIS OF THE DYNAMICS OF HEPATITIS B WITH OPTIMAL CONTROL

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Abstract. Limited resources hinder the control and prevention of hepatitis B in some communities in Ghana and the Brong Ahafo region is no different. In this paper, we formulated a model that explains the spread of hepatitis B and suggested an intervention to minimise its effect. We analysed the local and global stability of the disease as well as the basic reproduction number. It was established that the disease is locally asymptotically stable whenever the basic reproduction number is less than unity and unstable otherwise. Optimal control theory was incorporated to determine the best control strategy in combating the spread of hepatitis B in the environment. The following control strategies were employed; treatment, vaccination and prevention. The results of the numerical simulation showed that the best optimal control strategy in combating the spread of the infection was vaccination of susceptible and treatment of the infected population.

Keywords: hepatitis B; vaccination; reproductive number; local and global stability; optimal control.

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1. Introduction

The hepatitis B virus infects the liver to result in a disease known as hepatitis B. Hepatitis B is among the world's leading health worries [1]. It can cause chronic infection, and if not well

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managed, can result in death from cirrhosis and hepatocellular carcinoma [2]. It is estimated that hepatitis B deaths in a year range between five hundred thousand to one million two hundred thousand people annually, and therefore among the top ten causes of death worldwide [2]. A person gets infected when the virus enters his or her bloodstream either through mother to child transmission (known as vertical transmission) or through blood, semen and other bodily fluids of infected persons [3]. Sufficient contact with an infectious person leading to infection can occur through sex, sharing needles, syringes and drug preparation equipment that are contaminated, sharing of toothbrushes, razors, medical equipment, etc., direct contact with blood or open sore [4, 5].The virus, after it has left its host for some days, can still infect susceptible individuals [6]. Infected individuals who are not able to fight off the hepatitis B virus become chronically infected after about 180 days of infection [7]. This stage of contagiousness in the transmission model of the diseases is known as the chronic class. If left untreated, the chronically infected is very likely to die from liver cancer or hepatocellular carcinoma [8].

There are safe and effective vaccines since 1982 for the prevention of hepatitis B infection through vaccination [9]. The vaccines work by activating the body to produce antibodies that ensure protection against contracting the virus. Susceptible individuals who are predisposed to the infection or are at high risk because of their particular circumstances are candidates for vaccination. Therefore, it is necessary to screen people to ascertain whether they are candidates for vaccination or not.

Research is still in progress to find a cure for chronic hepatitis B infection. Reports estimate that about one percent of the chronically infected break free from the virus each year [10]. One goal of available antiviral therapies is to help bring down the viral load and thus reduce the chance of disease progression towards liver scarring and liver cancer that are both extremely life-threatening [2].

Epidemic models generally explain the spread mechanism of diseases, determine the best optimal control mechanism and the most effective cost to be employed in combating the infections [11, 12].

A real world phenomenon is translated by a disease model for optimal cost control and employ sensitivity analysis to determine the best control measure [13, 14]

2. Model Description and Formulation

We Formulated an $SEITVR$ model for the transmission Dynamics of Hepatitis B by partitioning the human population into six compartments with respect to their disease status at any given time t. Table 1 shows the parameters and their description used in the model.

TABLE 1. Parameter description

Parameter	Description
μ_1	The rate at which people give birth.
μ_2	The rate at which people die .
σ_1	Vaccination rate of susceptible individuals.
η	Unsuccessful vaccination rate.
β_1	Horizontal transmission rate cause by the infected compartment.
β_2	The rate of transmission for the treated population.
α	The rate at which the expose population move to the infected population .
p_1	The probability that the an infected individuals clear the virus.
p_2	The probability that infected mothers give birth to infected babies.
σ_2	Rate of moving from the vaccinated class to the recovered class.
σ_3	The rate at which the recovered population move to the susceptible population due to loss of immunity.
σ_4	The rate at which the treated population move to the recovered population.
$(1-p_1)$	The probability that an infected fail to clear the virus .
λ	The rate at which infected population move to any other class

Table 2 shows the various variables used in the model formulation and description.

TABLE 2. Variable description

Variable	Description of Population at a time t
$S(t)$	Susceptible Human
$E(t)$	Expose Population
$I(t)$	Infected Population
$T(t)$	Treated Population
$V(t)$	Vaccinated Population
$R(t)$	Recovered Population

The total population $N(t)$ is given by;

$$N = S(t) + E(t) + I(t) + T(t) + V(t) + R(t). \tag{1}$$

System of differential equation of the model is given by;

$$\begin{cases} \dfrac{dS}{dt} &= \mu_1(1-p_2I) + \eta V + \sigma_3 R - [(\beta_1 I + \beta_2 T) + \mu_2 + \sigma_1]S \\ \dfrac{dE}{dt} &= (\beta_1 I + \beta_2 T)S + \mu_1 p_2 I - [\mu_2 + \alpha]E \\ \dfrac{dI}{dt} &= \alpha E - [p_1\lambda + (1-p_1)\lambda + \mu_2]I \\ \dfrac{dT}{dt} &= (1-p_1)\lambda I - [\sigma_4 + \mu_2]T \\ \dfrac{dV}{dt} &= \sigma_1 S - [\eta + \sigma_2 + \mu_2]V \\ \dfrac{dR}{dt} &= \sigma_2 V + p_1\lambda I + \sigma_4 T - [\sigma_3 + \mu_2]R \end{cases} \tag{2}$$

3. Model Analysis

This section, provides evidence of the well-posedness of the model by proving the boundedness and positivity of the model solution.

3.1. Feasible region.

The invariant region is given by,
$\Upsilon = \{(S(t)+E(t)+I(t)+T(t)+V(t)+R(t))) \in \mathbb{R}^6_+; S(t)+E(t)+I(t)+T(t)+V(t)+R(t) = N \leq \dfrac{\mu_1}{\mu_2}\}.$

Consider the model equation the total population N is given by;

$$\begin{cases} \frac{dN}{dt} & = \frac{dS}{dt} + \frac{dE}{dt} + \frac{dI}{dt} + \frac{dT}{dt} + \frac{dV}{dt} + \frac{dR}{dt} \\ & = [\mu_1 - (S+E+I+T+V+R)\mu_2] \\ & = \mu_1 - N\mu_2. \end{cases} \tag{3}$$

$$\frac{dN}{dt} = \mu_1 - N\mu_2. \tag{4}$$

solving the equation

$$\frac{dN}{\mu_1 - N\mu_2} = dt$$
$$\int \frac{dN}{\mu_1 - N\mu_2} = \int dt$$
$$\frac{-\ln|\mu_1 - N\mu_2|}{\mu_2} = t + c$$
$$-\ln|\mu_1 - N\mu_2| = \mu_2 t + c_1$$
$$\mu_1 - N\mu_2 = e^{-\mu_2 t + c_1}$$
$$\mu_1 - N\mu_2 = c_2 e^{-\mu_2 t}$$
$$N(t) = \frac{c_2 e^{-\mu_2 t} - \mu_1}{-\mu_2}$$
$$N(t) = \frac{\mu_1}{\mu_2} - c_2 e^{-\mu_2 t}$$

When $t = 0, N(t) = N(0)$

$$N(0) = \frac{\mu_1}{\mu_2} - c_2$$
$$c_2 = \frac{\mu_1}{\mu_2} - N(0)$$

Therefore,

$$N(t) = \frac{\mu_1}{\mu_2} - \left(\frac{\mu_1}{\mu_2} - N(0)\right) e^{-\mu_2 t} \tag{5}$$

now as t $\to \infty$

$$N(t) \leq \frac{\mu_1}{\mu_2}$$

hence; Υ is positively invariant [15].

3.2. Positivity of model solutions. For the model to be biologically meaningful we prove the positivity of the solution.

Let the initial values of the parameters be $\{S(t) \geq 0, E(t) \geq 0, I(t) \geq 0, T(t) \geq 0, V(t) \geq 0, R(t) \geq 0\} \in \Upsilon$ then the solution set
$\{S(t), E(t), I(t), T(t), V(t), R(t)\} \geq 0 \; \forall \; t \geq 0$

Proof. From

$$\frac{dS}{dt} = \mu_1(1-p_2 I) + \eta V + \sigma_3 R - [(\beta_1 I + \beta_2 T) + \mu_2 + \sigma_1]S \tag{6}$$

now we have

$$\frac{dS}{dt} \geq -[(\beta_1 I + \beta_2 T) + \mu_2 + \sigma_1]S(t)$$
$$\frac{dS}{S(t)} \geq -[(\beta_1 I + \beta_2 T) + \mu_2 + \sigma_1]dt$$

applying anti-derivate on both sides we have

$$\int \frac{dS}{S(t)} \geq \int -[(\beta_1 I + \beta_2 T) + \mu_2 + \sigma_1]dt$$
$$\ln|S(t)| \geq -[(\beta_1 I + \beta_2 T) + \mu_2 + \sigma_1]t + c$$
$$S(t) \geq e^{-[(\beta_1 I + \beta_2 T) + \mu_2 + \sigma_1]t + c}$$

for $t \geq 0$

$$S(t) \geq S(0)e^{-[(\beta_1 I + \beta_2 T) + \mu_2 + \sigma_1]t} \geq 0$$

Therefore

$$S(t) \geq 0$$

Next,consider the second equation in the model

$$\frac{dE}{dt} = (\beta_1 I + \beta_2 T)S + \mu_1 p_2 I - [\mu_2 + \alpha]E \tag{7}$$

now we have

$$\frac{dE}{dt} \geq -[\mu_2+\alpha]E(t)$$
$$\frac{dE}{E(t)} \geq -[\mu_2+\alpha]dt$$

taking anti derivative of both sides of the equation, we have

$$\int \frac{dE}{E(t)} \geq \int -[\mu_2+\alpha]dt$$

$$\ln|E(t)| \geq -[\mu_2+\alpha]t+c$$

$$E(t) \geq e^{-[\mu_2+\alpha]t+c}$$

for non-negative values of t

$$E(t) \geq E(0)e^{-[\mu_2+\alpha]t} \geq 0$$

Hence,

$$E(t) \geq 0$$

similarly, it can be proved that $I(t), T(t), V(t)$ and $R(t)$ are all positively invariant for all non-negative values of t [16, 17]. □

3.3. Disease free equilibrium.

At disease free equilibrium, there are no infections and recovery, hence;

$$\frac{dS}{dt} = \frac{dE}{dt} = \frac{dI}{dt} = \frac{dT}{dt} = \frac{dV}{dt} = \frac{dR}{dt} = 0 \tag{8}$$

The DFE of the model is obtained as;

$$\Big(A_1, 0, 0, 0, A_2, 0\Big) \tag{9}$$

where;

$$A_1 = \frac{\mu_1[\eta+\sigma_2+\mu_2]}{([\mu_2+\sigma_1][\eta+\sigma_2+\mu_2]) - \eta\sigma_1}$$
$$A_2 = \frac{\sigma_1\mu_1}{([\eta+\sigma_2+\mu_2][\mu_2+\sigma_1]) - \sigma_1\eta}$$

3.4. Basic reproduction number, R_0. Using the next generation matrix approach as outlined in [18, 19]; Considering;

$$\begin{cases} \dfrac{dE}{dt} &= (\beta_1 I + \beta_2 T)S + \mu_1 p_2 I - [\mu_2 + \alpha]E \\ \dfrac{dI}{dt} &= \alpha E - [\lambda + \mu_2]I \\ \dfrac{dT}{dt} &= (1 - p_1)\lambda I - [\sigma_4 + \mu_2]T \end{cases} \tag{10}$$

let;

$$F_i(x) = \begin{bmatrix} (\beta_1 I + \beta_2 T)S(t) \\ 0 \\ 0 \end{bmatrix} \quad V_i(x) = \begin{bmatrix} -\mu_1 p_2 I + [\mu_2 + \alpha]E \\ -\alpha E + [\lambda + \mu_2]I \\ -(1 - p_1)\lambda I + [\sigma_4 + \mu_2]T \end{bmatrix}$$

Taking the partial derivative of $F_i(x)$ and $V_i(x)$ at DFE;

$$F = \begin{bmatrix} 0 & S^0\beta_1 & S^0\beta_2 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \tag{11}$$

and

$$V = \begin{pmatrix} [\mu_2 + \alpha] & -\mu_1 P_2 & 0 \\ -\alpha & [\lambda + \mu_2] & 0 \\ 0 & -\lambda(1 - p_1) & [\sigma_4 + \mu_2] \end{pmatrix} \tag{12}$$

finding the inverse of V

$$V^{-1} = \begin{pmatrix} \dfrac{\lambda + \mu_2}{[\alpha + \mu_2][\lambda + \mu_2] - \alpha\mu_1 P_2} & \dfrac{\mu_1 P_2}{[\alpha + \mu_2][\lambda + \mu_2] - \alpha\mu_1 P_2} & 0 \\ \dfrac{\alpha}{[\alpha + \mu_2][\lambda + \mu_2] - \alpha\mu_1 P_2} & \dfrac{\alpha + \mu_2}{[\alpha + \mu_2][\lambda + \mu_2] - \alpha\mu_1 P_2} & 0 \\ \dfrac{(1 - P_1)\alpha\lambda}{A_3} & \dfrac{(1 - P_1)\lambda(\alpha + \mu_2)}{A_3} & \dfrac{1}{\sigma_4 + \mu_2} \end{pmatrix} \tag{13}$$

where, $A_3 = (\mu_2 + \sigma_4)\big([\alpha + \mu_2][\lambda + \mu_2] - \alpha\mu_1 P_2\big)$

$$FV^{-1}\begin{pmatrix} D_1 & D_2 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \tag{14}$$

Where,

$$D_1 = \frac{S^0\beta_1\alpha(\sigma_4+\mu_2)+S^0\beta_2\alpha(1-P_1)\lambda}{(\mu_2+\sigma_4)\big([\alpha+\mu_2][\lambda+\mu_2]-\alpha\mu_1P_2\big)}$$
$$D_2 = \frac{S^0\beta_1(\sigma_4+\mu_2)(\alpha+\mu_2)+S^0\beta_2\alpha(1-P_1)\lambda(\alpha+\mu_2)}{(\mu_2+\sigma_4)\big([\alpha+\mu_2][\lambda+\mu_2]-\alpha\mu_1P_2\big)}$$

The spectral radius (largest eigen value) of the matrix FV^{-1} is the basic reproductive number. Since FV^{-1} is a triangular matrix the eigen values are $D_1, 0$ and 0 therefore the spectral radius is D_1 hence $R_0 = D_1$

$$R_0 = \frac{S^0\beta_1\alpha(\sigma_4+\mu_2)+S^0\beta_2\alpha(1-P_1)\lambda}{(\mu_2+\sigma_4)\big([\alpha+\mu_2][\lambda+\mu_2]-\alpha\mu_1P_2\big)} \tag{15}$$

Our model is epidemiologically meaningful if;

$$[\alpha+\mu_2][\lambda+\mu_2]-\alpha\mu_1P_2 > 0 \tag{16}$$

3.5. Local stability of disease-free equilibrium.

Theorem 3.1. *The disease-free equilibrium point is locally asymptotically stable if* $R_0 \le 1$ *and unstable if* $R_0 > 1$.

Proof. The Jacobian matrix is given by;

$$J_{DFE} = \begin{bmatrix} -H_1 & 0 & -H_7 & -H_8 & \eta & \sigma_3 \\ 0 & -H_2 & H_7 & H_8 & 0 & 0 \\ 0 & \alpha & -H_3 & 0 & 0 & 0 \\ 0 & 0 & H_9 & -H_4 & 0 & 0 \\ \sigma_1 & 0 & 0 & 0 & -H_5 & 0 \\ 0 & 0 & H_{10} & \sigma_4 & \sigma_2 & -H_6 \end{bmatrix} \tag{17}$$

where

$H_1 = [\sigma_1 + \mu_2]$ $\quad H_2 = [\mu_2 + \alpha]$

$H_3 = [\lambda + \mu_2]$ $\quad H_4 = [\sigma_4 + \mu_2]$

$H_5 = [\eta + \sigma_2 + \mu_2]$ $\quad H_6 = [\sigma_3 + \mu_2]$

$H_7 = \mu_1 P_2 + \beta_1 S^0$ $\quad H_8 = \beta_2 S^0$

$H_9 = \lambda(1 - p_1)$ $\quad H_{10} = \lambda p_1$

$S = S^0$

The characteristics equation; $P(\bar{\lambda}) = |\bar{\lambda} I - J_{DEF}| = 0$ becomes

$$P(\bar{\lambda}) = \begin{vmatrix} \bar{\lambda} + H_1 & 0 & H_7 & H_8 & -\eta & -\sigma_3 \\ 0 & \bar{\lambda} + H_2 & -H_7 & -H_8 & 0 & 0 \\ 0 & -\alpha & \bar{\lambda} + H_3 & 0 & 0 & 0 \\ 0 & 0 & -H_9 & \bar{\lambda} + H_4 & 0 & 0 \\ -\sigma_1 & 0 & 0 & 0 & \bar{\lambda} + H_5 & 0 \\ 0 & 0 & -H_{10} & -\sigma_4 & -\sigma_2 & \bar{\lambda} + H_6 \end{vmatrix} = 0 \tag{18}$$

Let

$$P(\bar{\lambda}) = P(\bar{\lambda_1}) \times P(\bar{\lambda_2}) = 0 \tag{19}$$

$$
\begin{aligned}
P(\bar{\lambda_1}) &= (\bar{\lambda}+H_6)[(\bar{\lambda}+H_1)(\bar{\lambda}+H_5)-\sigma_1\eta]-\sigma_1\sigma_2\sigma_3 = 0 \\
&= \bar{\lambda}^3+(H_1+H_5+H_6)\bar{\lambda}^2 \\
&+(H_1H_5+H_1H_6+H_5H_6-\sigma_1\eta)\bar{\lambda}+H_1H_5H_6-\sigma_1\eta H_6-\sigma_1\sigma_2\sigma_3 = 0
\end{aligned}
$$

for the other factor

$$
\begin{aligned}
P(\bar{\lambda_2}) &= (\bar{\lambda}+H_4)[(\bar{\lambda}+H_2)(\bar{\lambda}+H_3)-\alpha H_7]-\alpha H_8H_9 = 0 \\
&= \bar{\lambda}^3+(H_2+H_3+H_4)\bar{\lambda}^2+(H_2H_3+H_2H_4+H_3H_4-\alpha H_7)\bar{\lambda} \\
&+H_2H_3H_4-\alpha H_4H_7-\alpha H_8H_9 = 0
\end{aligned}
$$

Now, we analyze $P(\bar{\lambda_1}) = 0$ and $P(\bar{\lambda_2}) = 0$ separately for the nature of their roots by using the Routh-Hurwitz criteria. Let's begin with $P(\bar{\lambda_1}) = 0$
$P(\bar{\lambda_1})$ is in the form

$$
P(\bar{\lambda_1}) = \bar{\lambda}^3+m_1\bar{\lambda}^2+m_2\bar{\lambda}+m_3 = 0 \tag{20}
$$

and

$$
\begin{aligned}
m_1 &= H_1+H_5+H_6 \\
&= \sigma_1+\mu_2+\eta+\sigma_2+\mu_2+\sigma_3+\mu_2 \\
&= \sigma_1+\sigma_2+\sigma_3+\eta+3\mu_2 \\
m_2 &= H_1H_5+H_1H_6+H_5H_6-\sigma_1\eta \\
&= (\sigma_1+\mu_2)(\eta+\sigma_2+\mu_2)+(\sigma_1+\mu_2) \\
&(\sigma_3+\mu_2)+(\eta+\sigma_2+\mu_2)(\sigma_3+\mu_2)-\sigma_1\eta \\
&= \mu_2\eta+(\sigma_1+\mu_2)(\sigma_2+\mu_2)+(\sigma_1+\mu_2)(\sigma_3+\mu_2) \\
&+(\eta+\sigma_2+\mu_2)(\sigma_3+\mu_2)
\end{aligned}
$$

$$
\begin{aligned}
m_3 &= H_1H_5H_6 - \sigma_1\eta H_6 - \sigma_1\sigma_2\sigma_3 \\
&= (\sigma_1+\mu_2)(\eta+\sigma_2+\mu_2)(\sigma_3+\mu_2) \\
&- \sigma_1\eta(\sigma_3+\mu_2) - \sigma_1\sigma_2\sigma_3 \\
&= \sigma_1\sigma_2\mu_2 + \mu_2(\sigma_1+\eta+\sigma_2+\mu_2)(\sigma_3+\mu_2)
\end{aligned}
$$

According to Routh-Hurwitz criteria, roots of $P(\bar{\lambda_1})$ will have negative real parts if the conditions below are satisfied

(i) $m_1 > 0$

(ii) $m_2 > 0$

(iii) $m_3 > 0$

(v) $m_1m_2 > m_3$

$$
\begin{aligned}
m_1 &= \sigma_1+\sigma_2+\sigma_3+\eta+3\mu_2 > 0 \\
m_3 &= \sigma_1\sigma_2\mu_2 + \mu_2(\sigma_1+\eta+\sigma_2+\mu_2)(\sigma_3+\mu_2) > 0
\end{aligned}
$$

Now

$$
\begin{aligned}
m_1m_2 &= (\sigma_1+\sigma_2+\sigma_3+\eta+3\mu_2)\big[\mu_2\eta + (\sigma_1+\mu_2)(\sigma_2+\mu_2) + (\sigma_1+\mu_2)(\sigma_3+\mu_2) \\
&\quad + (\eta+\sigma_2+\mu_2)(\sigma_3+\mu_2)\big] \\
m_3 &= \sigma_1\sigma_2\mu_2 + \mu_2(\sigma_1+\eta+\sigma_2+\mu_2)(\sigma_3+\mu_2)
\end{aligned}
$$

Notice that in expanded form , m_1m_2 contains all the terms in m_3 and will still be left with additional terms. Therefore $m_1m_2 > m_3$ is satisfied. By the Routh-Hurwitz criteria all the roots of $P(\bar{\lambda_1}) = 0$ are negative or have negative real parts.
Let's now analyze the second factor $P(\bar{\lambda_2})$
$P(\bar{\lambda_2})$ is in the form

$$
P(\bar{\lambda_2}) = \bar{\lambda}^3 + c_1\bar{\lambda}^2 + c_2\bar{\lambda} + c_3 = 0 \tag{21}
$$

Where

$$
\begin{aligned}
c_1 &= H_2 + H_3 + H_4 = \alpha + \lambda + \sigma_4 + 3\mu_2 \\
c_2 &= H_2H_3 + H_2H_4 + H_3H_4 - \alpha H_7 = (\alpha + \mu_2)(\lambda + \mu_2) + (\alpha + \mu_2)(\sigma_4 + \mu_2) \\
&\quad + (\lambda + \mu_2)(\sigma_4 + \mu_2) - \alpha(\mu_1 P_2 + \beta_1 S) \\
c_3 &= H_2H_3H_4 - \alpha H_4H_7 - \alpha H_8H_9 = (\alpha + \mu_2)(\lambda + \mu_2)(\sigma_4 + \mu_2) - \alpha\mu_1 P_2(\sigma_4 + \mu_2) \\
&\quad - \alpha\beta_1 S(\sigma_4 + \mu_2) - \alpha\lambda\beta_2 S(1 - p_1)
\end{aligned}
$$

According to the Routh-Hurwitz criterion for $P(\bar{\lambda_2}) = 0$ to have negative real parts, $c_1 > 0, c_3 > 0$ and $c_1c_2 > c_3$

$$
\begin{aligned}
&c_1 = \alpha + \lambda + \sigma_4 + 3\mu_2 > 0 \\
&c_2 > 0 \\
\implies &(\alpha + \mu_2)(\lambda + \mu_2) + (\alpha + \mu_2)(\sigma_4 + \mu_2) + (\lambda + \mu_2)(\sigma_4 + \mu_2) - \alpha\mu_1 P_2 > \alpha\beta_1 S
\end{aligned}
$$

but from $R_0 < 1$

$$
\begin{aligned}
(\alpha + \mu_2)(\lambda + \mu_2) - \mu_1 P_2 &> \alpha\beta_1 S \\
c_2 &> 0 \;\; holds
\end{aligned}
$$

$$
\begin{aligned}
c_3 = &(\alpha + \mu_2)(\lambda + \mu_2)(\sigma_4 + \mu_2) - \alpha\mu_1 P_2(\sigma_4 + \mu_2) - \alpha\beta_1 S(\sigma_4 + \mu_2) - \\
&\alpha\lambda\beta_2 S(1 - p_1) > 0 \\
&(\alpha + \mu_2)(\lambda + \mu_2)(\sigma_4 + \mu_2) - \alpha\mu_1 P_2(\sigma_4 + \mu_2) > \alpha\beta_1 S(\sigma_4 + \mu_2) + \alpha\lambda\beta_2 S(1 - p_1) \\
&\alpha\beta_1 S(\sigma_4 + \mu_2) + \alpha\lambda\beta_2 S(1 - p_1) < (\alpha + \mu_2)(\lambda + \mu_2)(\sigma_4 + \mu_2) - \alpha\mu_1 P_2(\sigma_4 + \mu_2)
\end{aligned}
$$

$$
\frac{\alpha\beta_1 S(\sigma_4 + \mu_2) + \alpha\lambda\beta_2 S(1 - p_1)}{(\alpha + \mu_2)(\lambda + \mu_2)(\sigma_4 + \mu_2) - \alpha\mu_1 P_2(\sigma_4 + \mu_2)} < 1 \tag{22}
$$

Since $R_0 < 1$,$m_3 > 0$ holds.

We now analyze $c_1c_2 > c_3$ below

$$(H_2+H_3+H_4)(H_2H_3+H_2H_4+H_3H_4-\alpha H_7) > H_2H_3H_4$$

$$-\alpha H_4H_7-\alpha H_8H_9$$

$$(H_2+H_3)(H_2H_3+H_2H_4+H_3H_4-\alpha H_7)+H_2H_3H_4+H_2H_4H_4$$

$$+H_3H_4H_4-\alpha H_4H_7 > H_2H_3H_4-\alpha H_4H_7-\alpha H_8H_9$$

$$(H_2+H_3)(H_2H_3+H_2H_4+H_3H_4)-\alpha H_7(H_2+H_3)+H_4H_4(H_2+H_3) > -\alpha H_8H_9$$

$$(H_2+H_3)(H_2H_3+H_2H_4+H_3H_4+H_4H_4) > \alpha H_7(H_2+H_3)-\alpha H_8H_9$$

$$(H_2+H_3)(H_2+H_4)(H_3+H_4) > \alpha H_7(H_2+H_3)-\alpha H_8H_9$$

$$\alpha H_7(H_2+H_3)-\alpha H_8H_9 < (H_2+H_3)(H_2+H_4)(H_3+H_4)$$

substituting the model parameters

$$\alpha(\mu_1P_2+\beta_1S)(\alpha+\lambda+2\mu_2)-\alpha\beta_2S\lambda(1-p_1) <$$

$$(\alpha+\lambda+2\mu_2)(\alpha+\sigma_4+2\mu_2)(\lambda+\sigma_4+2\mu_2)$$

$$(\alpha+\lambda+2\mu_2)\beta_1S-\alpha\beta_2S\lambda(1-p_1) < (\alpha+\lambda+2\mu_2)(\alpha+\sigma_4+2\mu_2)(\lambda+\sigma_4+2\mu_2)$$

$$-\alpha(\alpha+\lambda+2\mu_2)\mu_1P_2\alpha\beta_1S-\frac{\alpha\beta_2S\lambda(1-p_1)}{\alpha+\lambda+2\mu_2} < (\alpha+\sigma_4+2\mu_2)(\lambda+\sigma_4+2\mu_2)-$$

$$\alpha\mu_1P_2$$

$$\alpha\beta_1S < (\alpha+\sigma_4+2\mu_2)(\lambda+\sigma_4+2\mu_2)-\alpha\mu_1P_2+\frac{\alpha\beta_2S\lambda(1-p_1)}{\alpha+\lambda+2\mu_2} \tag{23}$$

From $R_0 < 1$

$$\alpha\beta_1S(\sigma_4+\mu_2)+\alpha\beta_2\lambda S(1-p_1) < (\sigma_4+\mu_2)\left[(\alpha+\mu_2)(\lambda+\mu_2)-\alpha\mu_1P_2\right]$$

$$\alpha\beta_1S(\sigma_4+\mu_2) < (\sigma_4+\mu_2)\left[(\alpha+\mu_2)(\lambda+\mu_2)-\alpha\mu_1P_2\right]$$

$$\alpha\beta_1S < (\alpha+\mu_2)(\lambda+\mu_2)-\alpha\mu_1P_2 \tag{24}$$

Equation (24) is a true inequality when $R_0 < 1$, therefore equation (23) is also true because the right hand side of equation (23) is greater than right hand side of equation (24).
This proves that $c_1c_2 > c_3$. It follows that $P(\bar{\lambda}_2) = 0$ has its roots negative or negative real parts.
In conclusion, the roots of $P(\bar{\lambda}) = 0$ are all negatives or have negative real parts so the disease free-equilibrium is asymptotically stable when $R_0 < 1$ and unstable when $R_0 > 1$ □

4. Endemic Equilibrium

It is a constant solution of the model where the disease per exist in the system. In our model the endemic equilibrium is denoted by Q^e. To obtained the endemic equilibrium we set the system in (2) to zero.

Therefore, the endemic equilibrium points are given by;

$$\begin{cases} S^e &= k_1 \\ E^e &= \dfrac{(\lambda+\mu_2)(\sigma_4+\mu_2)(k_1k_2k_3-k_1k_4+k_5)}{\alpha\lambda(1-p_1)(k_6+k_1k_7-k_8)} \\ I^e &= \dfrac{(\sigma_4+\mu_2)(k_1k_2k_3-k_1k_4+k_5)}{\lambda(1-p_1)(k_6+k_1k_7-k_8)} \\ T^e &= \dfrac{k_1k_2k_3-k_1k_4+k_5}{k_6+k_1k_7-k_8} \\ V^e &= k_1k_2 \\ R^e &= \dfrac{\sigma_2k_1k_2(1-p_1)(k_6+k_1k_7-k_8)+D_6(k_1k_2k_3-k_1k_4+k_5)}{(\sigma_3+\mu_2)(1-p_1)(k_6+k_1k_7-k_8)} \end{cases}$$

where $D_6 = [p_1(\sigma_4+\mu_2)+\sigma_4(1-p_1)]$

$$k_1 = \frac{(\sigma_4+\mu_2)\left[(\mu_2+\alpha)(\lambda+\mu_2)-\alpha P_2\mu_1\right]}{\alpha\left[\beta_1(\sigma_4+\mu_2)+\beta_2\lambda(1-p_1)\right]} \qquad k_2 = \frac{\sigma_1}{\eta+\sigma_2+\mu_2}$$

$$k_3 = \lambda(1-p_1)(\sigma_2+\sigma_3+\eta) \qquad k_4 = \lambda(1-p_1)(\sigma_3+\mu_2)(\sigma_1+\mu_2)$$

$$k_5 = \mu_1\lambda(1-p_1) \qquad k_7 = \beta_1(\sigma_3+\mu_2)(\sigma_4+\mu_2)+\lambda\beta_2(\sigma_3+\mu_2)(1-p_1)$$

$$k_6 = \mu_1P_2(\sigma_3+\mu_2)(\sigma_4+\mu_2) \qquad k_8 = \lambda\sigma_3\left[p_1(\sigma_4+\mu_2)+\sigma_4(1-p_1)\right]$$

Hence $Q^e = \{S^e, E^e, I^e, T^e, V^e, R^e\}$

4.1. Global stability of the endemic equilibrium point.

Theorem 4.1. *If $R_0 > 1$, the endemic equilibrium Q^e of the model is globally asymptotically stable.*

Proof. The global asymptotic stability of the endemic equilibrium can be prooved using the Lyapunov function define as;

$$G(S^e,E^e,I^e,T^e,V^e,R^e) = G_1+G_2+G_3+G_4+G_5+G_6 \tag{25}$$

$$\begin{cases} G_1 &= S-S^e-S^e\ln\frac{S}{S^e}, \qquad G_2 = E-E^e-E\ln\frac{E}{E^e} \\ & G_3 = I-I^e-I^e\ln\frac{I}{I^e}, \qquad G_4 = T-T^e-T^e\ln\frac{T}{T^e} \\ & G_5 = V-V^e-V^e\ln\frac{V^e}{V}, \qquad G_6 = R-R^e-R^e\ln\frac{R}{R^e} \end{cases}$$

By setting the system of equation in (2) to zereo and taking the derivative of G along the solution of the equations, we obtain;

$$\frac{dG}{dt} = \frac{dG_1}{dt}+\frac{dG_2}{dt}+\frac{dG_3}{dt}+\frac{dG_4}{dt}+\frac{dG_5}{dt}+\frac{dG_6}{dt} \tag{26}$$

let

$$\frac{dG_1}{dt} = \left(\frac{S-S^e}{S}\right)\left[\mu_1(1-p_2I)+\eta V+\sigma_3R-[(\beta_1I+\beta_2T)+\mu_2+\sigma_1]S\right] \tag{27}$$

hence;

$$\begin{cases} \frac{dG_1}{dt} &= \left(\frac{S-S^e}{S}\right)\left[\mu_1(1-p_2I)+\eta V+\sigma_3R-[(\beta_1I+\beta_2T)+\mu_2+\sigma_1]S\right] \\ & -\mu_1+\mu_1p_2I^e-\eta V^e-\sigma_3R^e+[(\beta_1I^e+\beta_2T^e)+\mu_2+\sigma_1]S^e \\ & = \left(\frac{S-S^e}{S}\right)\left[\mu_1P_2I^e\left(1-\frac{I}{I^e}\right)+\beta_1I^eS^e\left(1-\frac{IS}{I^eS^e}\right)+\beta_2T^eS^e\right. \\ & \left(1-\frac{TS}{T^eS^e}\right)+\mu_2S^e\left(1-\frac{S}{S^e}\right)+\sigma_1S^e\left(1-\frac{S}{S^e}\right)+\eta V^e\left(\frac{V}{V^e}-1\right) \\ & \left.+\sigma_3R^e\left(\frac{R}{R^e}-1\right)\right] \end{cases} \tag{28}$$

hence;

$$
\left\{
\begin{aligned}
\frac{dG_1}{dt} \quad &= \mu_1 P_2 I^e\left(1-\frac{I}{I^e}-\frac{S^e}{S}+\frac{S^e I}{SI^e}\right)+\beta_1 I^e S^e\left(1-\frac{IS}{I^e S^e}-\frac{S^e}{S}+\frac{I}{I^e}\right)\\
&+\beta_2 T^e S^e\left(1-\frac{TI}{T^e I^e}-\frac{S^e}{S}+\frac{T}{T^e}\right)+\mu_2 S^e\left(2-\frac{S^e}{S}-\frac{S}{S^e}\right)\\
&+\sigma_1 S^e\left(2-\frac{S^e}{S}-\frac{S}{S^e}\right)+\eta V^e\left(\frac{V}{V^e}-1-\frac{S^e V}{SV^e}+\frac{S^e}{S}\right)\\
&+\sigma_3 R^e\left(\frac{R}{R^e}-1-\frac{S^e R}{SR^e}+\frac{S^e}{S}\right)
\end{aligned}
\right. \tag{29}
$$

Using the positive semi-definite function $\mathscr{M}(y) = y - 1 - \ln y$, for $y > 0$

$$
\left\{
\begin{aligned}
\frac{dG_1}{dt} \quad &= \mu_1 P_2 I^e\left[-\mathscr{M}\left(\frac{I}{I^e}\right)-\mathscr{M}\left(\frac{S^e}{S}\right)+\mathscr{M}\left(\frac{S^e I}{SI^e}\right)\right]\\
&+\beta_1 I^e S^e\left[-\mathscr{M}\left(\frac{IS}{I^e S^e}\right)-\mathscr{M}\left(\frac{S^e}{S}\right)+\mathscr{M}\left(\frac{I}{I^e}\right)\right]\\
&+\beta_2 T^e S^e\left[-\mathscr{M}\left(\frac{TS}{T^e S^e}\right)-\mathscr{M}\left(\frac{S^e}{S}\right)+\mathscr{M}\left(\frac{T}{T^e}\right)\right]\\
&+\mu_2 S^e\left[-\mathscr{M}\left(\frac{S^e}{S}\right)-\mathscr{M}\left(\frac{S}{S^e}\right)\right]\\
&+\sigma_1 S^e\left[-\mathscr{M}\left(\frac{S^e}{S}\right)-\mathscr{M}\left(\frac{S}{S^e}\right)\right]+\eta V^e\left[\mathscr{M}\left(\frac{V}{V^e}\right)-\mathscr{M}\left(\frac{S^e V}{SV^e}\right)+\mathscr{M}\left(\frac{S^e}{S}\right)\right]\\
&+\sigma_3 R^e\left[\mathscr{M}\left(\frac{R}{R^e}\right)-\mathscr{M}\left(\frac{S^e R}{SR^e}\right)+\mathscr{M}\left(\frac{S^e}{S}\right)\right]
\end{aligned}
\right. \tag{30}
$$

Similarly,

$$
\left\{
\begin{aligned}
\frac{dG_2}{dt} \quad &= \left(\tfrac{E-E^e}{E}\right)\Big[(\beta_1 I+\beta_2 T)S+\mu_1 p_2 I-[\mu_2+\alpha]E-(\beta_1 I^e+\beta_2 T^e)S^e\\
&-\mu_1 p_2 I^e+[\mu_2+\alpha]E^e\Big]\\
&= \mu_1 P_2 I^e\left[\mathscr{M}\left(\frac{I}{I^e}\right)-\mathscr{M}\left(\frac{E^e I}{EI^e}\right)+\mathscr{M}\left(\frac{E^e}{E}\right)\right]\\
&+\beta_1 I^e S^e\left[\mathscr{M}\left(\frac{IS}{I^e S^e}\right)-\mathscr{M}\left(\frac{ISE^e}{I^e S^e E}\right)+\mathscr{M}\left(\frac{E^e}{E}\right)\right]\\
&+\beta_2 T^e S^e\left[\mathscr{M}\left(\frac{TS}{T^e S^e}\right)-\mathscr{M}\left(\frac{TSE^e}{T^e S^e E}\right)+\mathscr{M}\left(\frac{E^e}{E}\right)\right]\\
&+\alpha E^e\left[-\mathscr{M}\left(\frac{E^e}{E}\right)-\mathscr{M}\left(\frac{E}{E^e}\right)\right]+\mu_2 E^e\left[-\mathscr{M}\left(\frac{E^e}{E}\right)-\mathscr{M}\left(\frac{E}{E^e}\right)\right]
\end{aligned}
\right. \tag{31}
$$

$$
\left\{
\begin{aligned}
\frac{dG_3}{dt} &= \left(\tfrac{I-I^e}{I}\right)\Big[\alpha E-[p_1\lambda+(1-p_1)\lambda+\mu_2]I-\alpha E^e+[p_1\lambda+(1-p_1)\lambda+\mu_2]I^e\Big]\\
&= \alpha E^e\left[\mathscr{M}\left(\frac{E}{E^e}\right)-\mathscr{M}\left(\frac{EI^e}{IE^e}\right)+\mathscr{M}\left(\frac{I^e}{I}\right)\right]\\
&+p_1\lambda I^e\left[-\mathscr{M}\left(\frac{I^e}{I}\right)-\mathscr{M}\left(\frac{I}{I^e}\right)\right]+(1-p_1)\lambda I^e\left[-\mathscr{M}\left(\frac{I^e}{I}\right)-\mathscr{M}\left(\frac{I}{I^e}\right)\right]\\
&+\mu_2 I^e\left[-\mathscr{M}\left(\frac{I^e}{I}\right)-\mathscr{M}\left(\frac{I}{I^e}\right)\right]
\end{aligned}
\right. \tag{32}
$$

$$
\left\{
\begin{aligned}
\frac{dG_4}{dt} &= \left(\tfrac{T-T^e}{T}\right)\Big[(1-p_1)\lambda I-[\sigma_4+\mu_2]T-(1-p_1)\lambda I^e+[\sigma_4+\mu_2]T^e\Big]\\
&= (1-p_1)\lambda I^e\left[\mathscr{M}\left(\frac{I}{I^e}\right)-\mathscr{M}\left(\frac{T^eI}{TI^e}\right)+\mathscr{M}\left(\frac{T^e}{T}\right)\right]\\
&+\sigma_4 S^e\left[-\mathscr{M}\left(\frac{T^e}{T}\right)-\mathscr{M}\left(\frac{T}{T^e}\right)\right]+\mu_2 T^e\left[-\mathscr{M}\left(\frac{T^e}{T}\right)-\mathscr{M}\left(\frac{T}{T^e}\right)\right]
\end{aligned}
\right. \tag{33}
$$

$$
\left\{
\begin{aligned}
\frac{dG_5}{dt} &= \left(\tfrac{V-V^e}{V}\right)\Big[\sigma_1 S-[\eta+\sigma_2+\mu_2]V-\sigma_1 S^e+[\eta+\sigma_2+\mu_2]V^e\Big]\\
&= \sigma_1 S^e\left[\mathscr{M}\left(\frac{S}{S^e}\right)-\mathscr{M}\left(\frac{V^eS}{VS^e}\right)+\mathscr{M}\left(\frac{V^e}{V}\right)\right]\\
&+\eta V^e\left[-\mathscr{M}\left(\frac{V^e}{V}\right)-\mathscr{M}\left(\frac{V}{V^e}\right)\right]+\sigma_2 V^e\left[-\mathscr{M}\left(\frac{V^e}{V}\right)-\mathscr{M}\left(\frac{V}{V^e}\right)\right]\\
&+\mu_2 V^e\left[-\mathscr{M}\left(\frac{V^e}{V}\right)-\mathscr{M}\left(\frac{V}{V^e}\right)\right]
\end{aligned}
\right. \tag{34}
$$

$$
\left\{
\begin{aligned}
\frac{dG_6}{dt} &= \left(\tfrac{R-R^e}{R}\right)\Big[\sigma_2 V+p_1\lambda I+\sigma_4 T-[\sigma_3+\mu_2]R-\sigma_2 V^e-p_1\lambda I^e-\sigma_4 T^e\\
&+[\sigma_3+\mu_2]R^e\Big]\\
&= \sigma_2 V^e\left[\mathscr{M}\left(\frac{V}{V^e}\right)-\mathscr{M}\left(\frac{R^eV}{RV^e}\right)+\mathscr{M}\left(\frac{R^e}{R}\right)\right]\\
&+p_1\lambda I^e\left[\mathscr{M}\left(\frac{I}{I^e}\right)-\mathscr{M}\left(\frac{R^eI}{RI^e}\right)+\mathscr{M}\left(\frac{R^e}{R}\right)\right]\\
&+\sigma_4 T^e\left[\mathscr{M}\left(\frac{T}{T^e}\right)-\mathscr{M}\left(\frac{R^eT}{RT^e}\right)+\mathscr{M}\left(\frac{R^e}{R}\right)\right]\\
&+\sigma_3 R^e\left[-\mathscr{M}\left(\frac{R^e}{R}\right)-\mathscr{M}\left(\frac{R}{R^e}\right)\right]+\mu_2 R^e\left[-\mathscr{M}\left(\frac{R^e}{R}\right)-\mathscr{M}\left(\frac{R}{R^e}\right)\right]
\end{aligned}
\right. \tag{35}
$$

Adding and simplifying all terms

$$
\begin{cases}
\frac{dG}{dt} & = \mu_2 S^e\left[-\mathscr{M}\left(\frac{S^e}{S}\right)-\mathscr{M}\left(\frac{S}{S^e}\right)\right]+\mu_2 E^e\left[-\mathscr{M}\left(\frac{E^e}{E}\right)-\mathscr{M}\left(\frac{E}{E^e}\right)\right] \\
& +\mu_2 I^e\left[-\mathscr{M}\left(\frac{I^e}{I}\right)-\mathscr{M}\left(\frac{I}{I^e}\right)\right]+\mu_2 T^e\left[-\mathscr{M}\left(\frac{T^e}{T}\right)-\mathscr{M}\left(\frac{T}{T^e}\right)\right] \\
& +\mu_2 V^e\left[-\mathscr{M}\left(\frac{V^e}{V}\right)-\mathscr{M}\left(\frac{V}{V^e}\right)\right]+\mu_2 R^e\left[-\mathscr{M}\left(\frac{R^e}{R}\right)-\mathscr{M}\left(\frac{R}{R^e}\right)\right] \\
& +\mu_1 P_2 I^e\left[-\mathscr{M}\left(\frac{S^eI}{SI^e}\right)+\mathscr{M}\left(\frac{E^e}{E}\right)-\mathscr{M}\left(\frac{E^eI}{EI^e}\right)+\mathscr{M}\left(\frac{S^e}{S}\right)\right] \\
& +\sigma_1 S^e\left[-\mathscr{M}\left(\frac{S^e}{S}\right)-\mathscr{M}\left(\frac{V^eS}{VS^e}\right)+\mathscr{M}\left(\frac{V^e}{V}\right)\right]+\eta V^e\left[-\mathscr{M}\left(\frac{V^e}{V}\right)\right. \\
& \left.-\mathscr{M}\left(\frac{S^eV}{SV^e}\right)+\mathscr{M}\left(\frac{S^e}{S}\right)\right]+\sigma_3 R^e\left[-\mathscr{M}\left(\frac{R^e}{R}\right)-\mathscr{M}\left(\frac{S^eR}{SR^e}\right)+\mathscr{M}\left(\frac{S^e}{S}\right)\right] \\
& +\beta_1 I^e S^e\left[-\mathscr{M}\left(\frac{ISE^e}{I^eS^eE}\right)-\mathscr{M}\left(\frac{S^e}{S}\right)+\mathscr{M}\left(\frac{I}{I^e}\right)+\mathscr{M}\left(\frac{E^e}{E}\right)\right] \\
& +\beta_2 T^e S^e\left[-\mathscr{M}\left(\frac{TSE^e}{T^eS^eE}\right)+\mathscr{M}\left(\frac{E^e}{E}\right)-\mathscr{M}\left(\frac{S^e}{S}\right)+\mathscr{M}\left(\frac{T}{T^e}\right)\right]
\end{cases} \tag{36}
$$

$$
\begin{cases}
+ & \alpha E^e\left[-\mathscr{M}\left(\frac{E^e}{E}\right)-\mathscr{M}\left(\frac{EI^e}{IE^e}\right)+\mathscr{M}\left(\frac{I^e}{I}\right)\right]+p_1\lambda I^e\left[-\mathscr{M}\left(\frac{I^e}{I}\right)\right. \\
& \left.-\mathscr{M}\left(\frac{R^eI}{RI^e}\right)+\mathscr{M}\left(\frac{R^e}{R}\right)\right]+(1-p_1)\lambda I^e\left[-\mathscr{M}\left(\frac{I^e}{I}\right)-\mathscr{M}\left(\frac{T^eI}{TI^e}\right)\right. \\
& \left.+\mathscr{M}\left(\frac{T^e}{T}\right)\right]+\sigma_4 T^e\left[-\mathscr{M}\left(\frac{T^e}{T}\right)-\mathscr{M}\left(\frac{R^eT}{RT^e}\right)+\mathscr{M}\left(\frac{R^e}{R}\right)\right] \\
& +\sigma_2 V^e\left[-\mathscr{M}\left(\frac{V^e}{V}\right)-\mathscr{M}\left(\frac{R^eV}{RV^e}\right)+\mathscr{M}\left(\frac{R^e}{R}\right)\right]
\end{cases} \tag{37}
$$

Let

$$\frac{dG}{dt} = L_1 + L_2 \tag{38}$$

where

$$
\begin{cases}
L_1 & = -\mu_2 S^e\mathscr{M}\left(\frac{S}{S^e}\right)-\mu_2 E^e\mathscr{M}\left(\frac{E}{E^e}\right)-\mu_2 I^e\mathscr{M}\left(\frac{I}{I^e}\right)-\mu_2 T^e\mathscr{M}\left(\frac{T}{T^e}\right) \\
& -\mu_2 V^e\mathscr{M}\left(\frac{V}{V^e}\right)-\mu_2 R^e\mathscr{M}\left(\frac{R}{R^e}\right)-\mu_1 P_2 I^e\mathscr{M}\left(\frac{E^eI}{EI^e}\right)-\sigma_1 S^e\mathscr{M}\left(\frac{V^eS}{VS^e}\right) \\
& -\eta V^e\mathscr{M}\left(\frac{S^eV}{SV^e}\right)-\sigma_3 R^e\mathscr{M}\left(\frac{S^eR}{SR^e}\right)-\beta_1 I^eS^e\mathscr{M}\left(\frac{ISE^e}{I^eS^eE}\right)-\beta_2 T^eS^e\mathscr{M}\left(\frac{TSE^e}{T^eS^eE}\right) \\
& -\alpha E^e\mathscr{M}\left(\frac{I^eE}{IE^e}\right)-p_1\lambda I^e\mathscr{M}\left(\frac{R^eI}{RI^e}\right)-(1-p_1)\lambda I^e\mathscr{M}\left(\frac{T^eI}{TI^e}\right)-\sigma_4 T^e\mathscr{M}\left(\frac{R^eT}{RT^e}\right) \\
& -\sigma_2 V^e\mathscr{M}\left(\frac{R^eV}{RV^e}\right)
\end{cases} \tag{39}
$$

and

$$
(40)\quad \begin{cases} L_2 & = (\beta_1 I^e S^e + \beta_2 T^e S^e + \mu_1 P_2 I^e)\mathscr{M}\left(\frac{E^e}{E}\right) + (\sigma_2 V^e + \sigma_4 T^e + p_1 \lambda I^e)\mathscr{M}\left(\frac{R^e}{R}\right) \\ & +(1-p_1)\lambda I^e \mathscr{M}\left(\frac{T^e}{T}\right) + \sigma_1 S^e \mathscr{M}\left(\frac{V^e}{V}\right) + \alpha E^e \mathscr{M}\left(\frac{I^e}{I}\right) - (\mu_2 E^e + \alpha E^e) \\ & \mathscr{M}\left(\frac{E^e}{E}\right) - (\sigma_3 R^e + \mu_2 R^e)\mathscr{M}\left(\frac{R^e}{R}\right) - (\sigma_4 T^e + \mu_2 T^e)\mathscr{M}\left(\frac{T^e}{T}\right) \\ & -(\eta V^e + \sigma_2 V^e + \mu_2 V^e)\mathscr{M}\left(\frac{V^e}{V}\right) - (p_1 \lambda I^e + (1-p_1)\lambda I^e + \mu_2 I^e)\mathscr{M}\left(\frac{I^e}{I}\right) \end{cases}
$$

$$
(41)\quad \left\{ \quad +\mu_1 P_2 I^e \mathscr{M}\left(\frac{S^e I}{S I^e}\right) + \beta_1 I^e S^e \mathscr{M}\left(\frac{I}{I^e}\right) + \beta_2 T^e S^e \mathscr{M}\left(\frac{T}{T^e}\right) \right.
$$

Using endemic equilibrium relations

$$
(42)\quad L_2 = \mu_1 P_2 I^e \mathscr{M}\left(\frac{S^e I}{S I^e}\right) + \beta_1 I^e S^e \mathscr{M}\left(\frac{I}{I^e}\right) + \beta_2 T^e S^e \mathscr{M}\left(\frac{T}{T^e}\right)
$$

Observation; $|L_1|$ is greater than L_2.

Hence; $\dfrac{dG}{dt} = L_1 + L_2 \leq 0$.
Noting that $L_1 + L_2 = 0$
if $(S,E,I,T,V,R) = (S^e, E^e, I^e, T^e, V^e.R^e)$. By La Salle's invariance principle the endemic equilibrium, Q^e is globally asymptotically stable [20]. □

5. Analysis of Optimal Control Problem

Arising from the results of the our analysis, time-dependent optimal control measures are introduced into the model. An optimal control theory based on the Pontryagin's principle is employed to obtain the necessary conditions for the optimal strategies aimed at preventing and controlling the disease spread [21].

Thus, the following three optimal control variables are considered: $u_1(t)$, represents a measure for preventing hepatitis B transmission through education, $u_2(t)$ represents a measure of preventing hepatitis B transmission through vaccination and $u_3(t)$ represents a surveillance measure of availability of medical resources at health facilities to diagnose and treat people infected with the disease.

Based on these control variables, the system of differential equation is of the form;

$$
(43) \qquad \begin{cases}
\frac{dS}{dt} &= \mu_1(1-p_2I)+\eta V+\sigma_3 R-(1-u(t))[(\beta_1 I+\beta_2 T)]S-[\mu_2+u_2(t)]S \\
\frac{dE}{dt} &= (1-u_1(t))[\beta_1 I+\beta_2 T]S+\mu_1 p_2 I-[\mu_2+\alpha]E \\
\frac{dI}{dt} &= \alpha E-[\lambda+\mu_2]I \\
\frac{dT}{dt} &= (1-p_1)-[u_3(t)+\mu_2]T \\
\frac{dV}{dt} &= u_2(t)S-[\eta+\sigma_2+\mu_2]V \\
\frac{dR}{dt} &= \sigma_2 V+p_1\lambda I+u_3(t)T-[\sigma_3+\mu_2]R
\end{cases}
$$

The goal of the optimal control strategies is to minimize the number of susceptible,infected , exposed carries of human and the treated population while keeping the costs of applying the controls; $u_1(t), u_2(t), u_3(t)$ as low as possible [22, 23, 24]. The objective functional J given by ;

$$
(44) \qquad J(u_1,u_2,u_3) = \int_0^{t_f} \left[A_1 S+A_2 E+A_3 I+A_4 T+\frac{1}{2}\sum_{i=1}^{3} c_i u_i^2\right] dt
$$

where A_1, A_2, A_3, c_1, c_2 and c_3 are positive weight constants.
where; $c_1 u_1^2$ represents a measure for preventing hepatitis B transmission through education of both susceptible and disease classes so as to observe safety protocols aimed to stem the spread of infection. $c_2 u_2^2$, the control $u_2(t)$ represents a measure of preventing hepatitis B transmission through vaccination and $c_3 u_3^2$, the control $u_3(t)$ represents a surveillance measure of availability of medical resources at health facilities to diagnose and treat people infected.
The costs of controls have been chosen to be quadratic in nature because by assumption, cost is usually non-linear [25, 26].
The optimal functions; $\{u_1^*(t), u_2^*(t), u_3^*(t)\}$ are such that;

$$
(45) \qquad J(u_1^*, u_2^*, u_3^*) = min\{J(u_1,u_2,u_3) : u_1,u_2,u_3 \in \aleph\}
$$

where,

$$
\aleph = \{u_i : 0 \le u_i(t) \le 1 \quad ,Lebesgue \;\; measurable, \;\; \in [0,t_f]\}
$$

for $i = 1,\ldots,3$. is called the control set.

Theorem 5.1. *If the objective functional J given by is defined on a set of bounded control $\aleph$ and is subject to the non-autonomous system with initial conditions at $t = 0$, then $\exists$ an optimal control $u^* = \left(u_1^*, u_2^*, u_3^*\right)$ such that $J(u^*) = min\{J(u_i) : u_i \in \aleph\}$,for $i = 1, 2, \ldots, 3$*

6. Pontryagin's Maximum Principle

This principle gives the necessary conditions for optimality. The Hamiltonian (H) with respect to (u_1, u_2, u_3) is given by .

$$
\begin{cases}
H & = A_1S + A_2E + A_3I + A_4T + \frac{1}{2}\left(c_1u_1^2 + c_2u_2^2 + c_3u_3^2\right) \\
& +\lambda_1[u_1(1-p_2I) + \eta V + \sigma_3R - (1-u_1(t))(\beta_1I + \beta_2T)S - [\mu_2 + u_2(t)]S] \\
& +\lambda_2[(1-u_1(t))[\beta_1IS + \beta_2T]S + \mu_1p_2I - [\mu_2 + \alpha]E] \\
& +\lambda_3[\alpha E - [\lambda + \mu_2]I] \\
& +\lambda_4[(1-p_1)\lambda I - [u_3(t) + \mu_2]T] \\
& +\lambda_5[u_2(t)S - [\eta + \sigma_2 + \mu_2]V] \\
& +\lambda_6[\sigma_2V + p_1\lambda I + u_3(t)T - [\sigma_3 + \mu_2]R]
\end{cases} \tag{46}
$$

where $\lambda_i, i = 1, \ldots, 6$ are the adjoint variables. The next result presents the adjoint .

$$
\begin{aligned}
\frac{d\lambda_1}{dt} &= -\frac{\partial H}{\partial S(t)} & \frac{d\lambda_2}{dt} &= -\frac{\partial H}{\partial E(t)} \\
\frac{d\lambda_3}{dt} &= -\frac{\partial H}{\partial I(t)} & \frac{d\lambda_4}{dt} &= -\frac{\partial H}{\partial T(t)} \\
\frac{d\lambda_5}{dt} &= -\frac{\partial H}{\partial V(t)} & \frac{d\lambda_6}{dt} &= -\frac{\partial H}{\partial R(t)}
\end{aligned}
$$

with terminal conditions (48). The solutions of adjoint are;

$$
(47) \qquad \begin{cases}
\frac{d\lambda_1}{dt} & = -\frac{\partial H}{\partial S(t)} \\
 & = -A_1 + \lambda_1\left[(1-u_1(t))(\beta_1 I + \beta_2 T) + \mu_2 + u_2(t)\right] \\
 & -\lambda_2(1-u_1(t))(\beta_1 I + \beta_2 T) - \lambda_5 w_2(t) \\
\frac{d\lambda_2}{dt} & = -\frac{\partial H}{\partial E(t)} \\
 & = -A_2 + \lambda_2(\mu_2 + \alpha) - \lambda_3\alpha \\
\frac{d\lambda_3}{dt} & = -\frac{\partial H}{\partial I(t)} \\
 & = -A_3 + \lambda_1\mu_1 P_2 + \lambda_1(1-u_1(t))\beta_1 S - \lambda_2\beta_1 S(1-u_1(t)) \\
 & -\lambda_2\mu_1 P_2 + \lambda_3(\lambda + \mu_2) - \lambda_4(1-P_1)\lambda - \lambda_6 P_1\lambda \\
\frac{d\lambda_4}{dt} & = -\frac{\partial H}{\partial T(t)} \\
 & = -A_4 + \lambda_1(1-u_1(t))\beta_2 S - \lambda_2(1-u_1(t))\beta_2 S + \lambda_4(u_3(t) + \mu_2) \\
 & -\lambda_6 u_3(t) \\
\frac{d\lambda_5}{dt} & = -\frac{\partial H}{\partial V(t)} \\
 & = -\lambda_1\eta + \lambda_5(\eta + \sigma_2 + \mu_2) - \lambda_6\sigma_2 \\
\frac{d\lambda_6}{dt} & = -\frac{\partial H}{\partial R(t)} \\
 & = -\lambda_1\sigma_3 + \lambda_6(\sigma_3 + \mu_2)
\end{cases}
$$

which satisfies the transversality condition;

$$
(48) \qquad \lambda_i(t_f) = 0, \forall i = 1, 2, \ldots 6
$$

By combining the Pontryagin's Maximum Principle and the existence of optimal control.

6.1. Characterisation of optimal control. The characterisation of the optimal control given by (50) is derived by solving the partial differential equations $\frac{\partial H}{\partial w_1} = 0, \frac{\partial H}{\partial u_2} = 0$ and $\frac{\partial H}{\partial u_3} = 0$

for u_1^*, u_2^* and u_3^* respectively.

$$
\begin{cases}
\frac{\partial H}{\partial u_1(t)} & = c_1u_1 + \lambda_1 S(\beta_1 I + \beta_2 T) - \lambda_2 S(\beta_1 I + \beta_2 T) = 0 \\
\bar{u_1} & = \frac{\lambda_2 S(\beta_1 I + \beta_2 T) - \lambda_1 S(\beta_1 I + \beta_2 T)}{c_1} \\
& = \frac{(\lambda_2 - \lambda_1)(\beta_1 I + \beta_2 T)S}{c_1} \\
\frac{\partial H}{\partial u_2(t)} & = c_2u_2 - \lambda_1 S + \lambda_5 S = 0 \\
\bar{u_2} & = \frac{\lambda_1 S - \lambda_5 S}{c_2} \\
& = \frac{(\lambda_1 - \lambda_5)S}{c_2} \\
\frac{\partial H}{\partial u_3(t)} & = c_3u_3 - \lambda_4 T + \lambda_6 T = 0 \\
\bar{u_3} & = \frac{\lambda_4 T - \lambda_6 T}{c_3} \\
& = \frac{(\lambda_4 - \lambda_6)T}{c_3}
\end{cases} \tag{49}
$$

Theorem 6.1. *The optimal control vector is given by $(u_1^*(t), u_2^*(t), u_3^*(t))$ to miniimizes (J) is given by*

$$
\begin{cases}
u_1^*(t) & = max\left\{0, min\left\{1, \frac{(\lambda_2 - \lambda_1)(\beta_1 I + \beta_2 T)S}{c_1}\right\}\right\} \\
u_2^*(t) & = max\left\{0, min\left\{1, \frac{(\lambda_1 - \lambda_5)S}{c_2}\right\}\right\} \\
u_3^*(t) & = max\left\{0, min\left\{1, \frac{(\lambda_4 - \lambda_6)T}{c_3}\right\}\right\}
\end{cases} \tag{50}
$$

where $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5$ and λ_6 are obtained by solving Equation (47) and Equation (48) simultaneously. Also

$$
\begin{cases}
u_1 & = \tilde{w_1} = \frac{(\lambda_2 - \lambda_1)(\beta_1 I + \beta_2 T)S}{c_1} \\
u_2 & = \tilde{u_2} = \frac{(\lambda_1 - \lambda_5)S}{c_2} \\
u_3 & = \tilde{u_3} = \frac{(\lambda_4 - \lambda_6)T}{c_3}
\end{cases} \tag{51}
$$

By imposing bounds on the controls,

$$\begin{cases} u_1^* = \begin{cases} 0, & if\ \tilde{u_1} \leq 0 \\ \tilde{u_1}, & if\ 0 < \tilde{u_1} < 1 \\ 1, & if\ \tilde{u_1} \geq 1 \end{cases} , \quad u_2^* = \begin{cases} 0, & if\ \tilde{u_2} \leq 0 \\ \tilde{u_2}, & if\ 0 < \tilde{u_2} < 1 \\ 1, & if\ \tilde{u_2} \geq 1 \end{cases} \\ u_3^* = \begin{cases} 0, & if\ \tilde{u_3} \leq 0 \\ \tilde{u_3}, & if\ 0 < \tilde{u_3} < 1 \\ 1, & if\ \tilde{u_3} \geq 1 \end{cases} \end{cases} \tag{52}$$

The system in (52) leads to the system in (50). Every tine interval gives a unique optimality of the system.

7. Numerical Results

An iterative method of Runge-kutta's fourth order was used to solve the optimality system of the model (51). With a given initial guess, the program solves the state equation in forward time interval of [0, 100], and the results of the state equation are placed in the adjoint equation which are then solve in backward time. The state and adjoint values are used accordingly to upgrade the controls employing the characterization (50) and the process is repeated until the state, adjoint and the control values are almost exact as the next successive values when the iteration terminates. The simulation was done for different combination of the controls u_1, u_2, u_3, and the results compared for the combination that drastically minimises the exposed and the infected. Table 3 shows the various parameter values used in the numerical simulations. Some were taken from publish research and others were assumed [27, 28, 29].

TABLE 3. Numerical Values

Parameter	Value	Reference
β_1	0.0400	[30]
β_2	0.002	[31]
μ_1	0.0196	[31]
μ_2	0.0096	[31]
p_1	0.6500	Assumed
p_2	0.0025	Assumed
σ_1	0.2500	[30]
σ_2	0.0050	Assumed
σ_3	0.0020	Assumed
σ_4	0.0025	[31]
α	0.0550	Assumed
η	0.0010	Assumed
λ	0.4500	Assumed

7.1. Strategy A: Prevention and Vaccination of Susceptible. We optimise the objective functional using prevention and vaccination of susceptible as a control measure. As a result of prevention and vaccination control variables, there have been a reduction in the number of infectious population as shown in Figure 1 of the results.

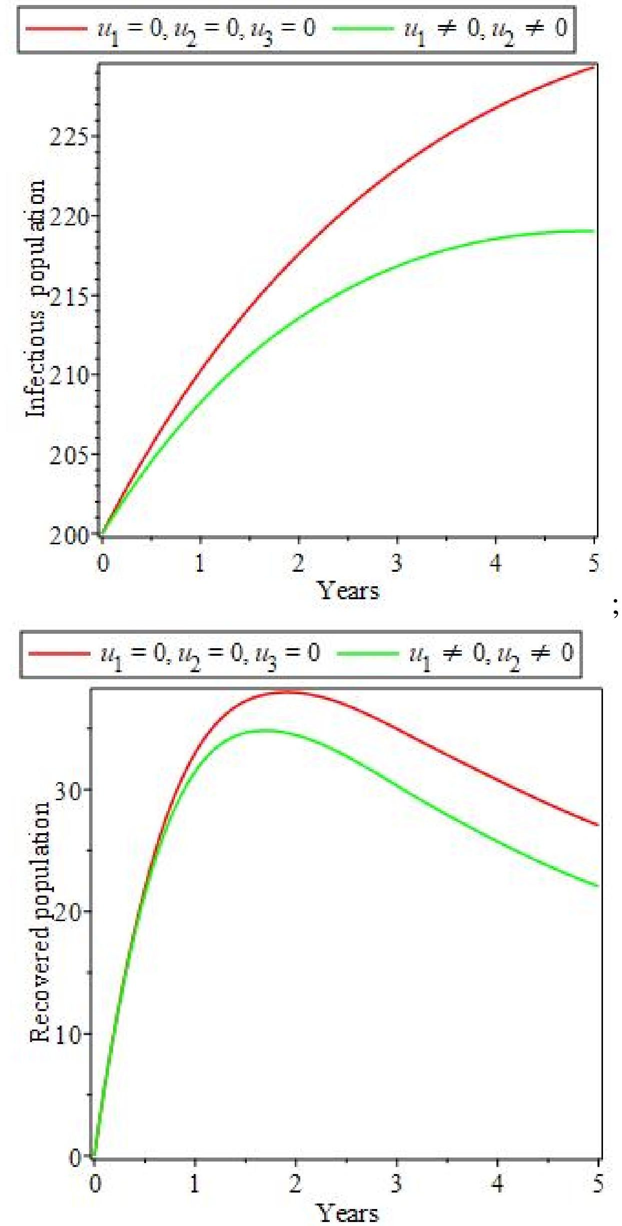

FIGURE 1. Optimal prevention and vaccination of population susceptible.

7.2. Strategy B: Prevention and Treatment of Infected population. We optimise the objective functional using prevention of susceptible and treatment of the infected population as a control measure. As a result of prevention and treatment control variables, there have been a reduction in the number of population infected. This is evidence that these control variables have an impact in controlling the spread of the infection with time as shown in Figure 2 of the plots.

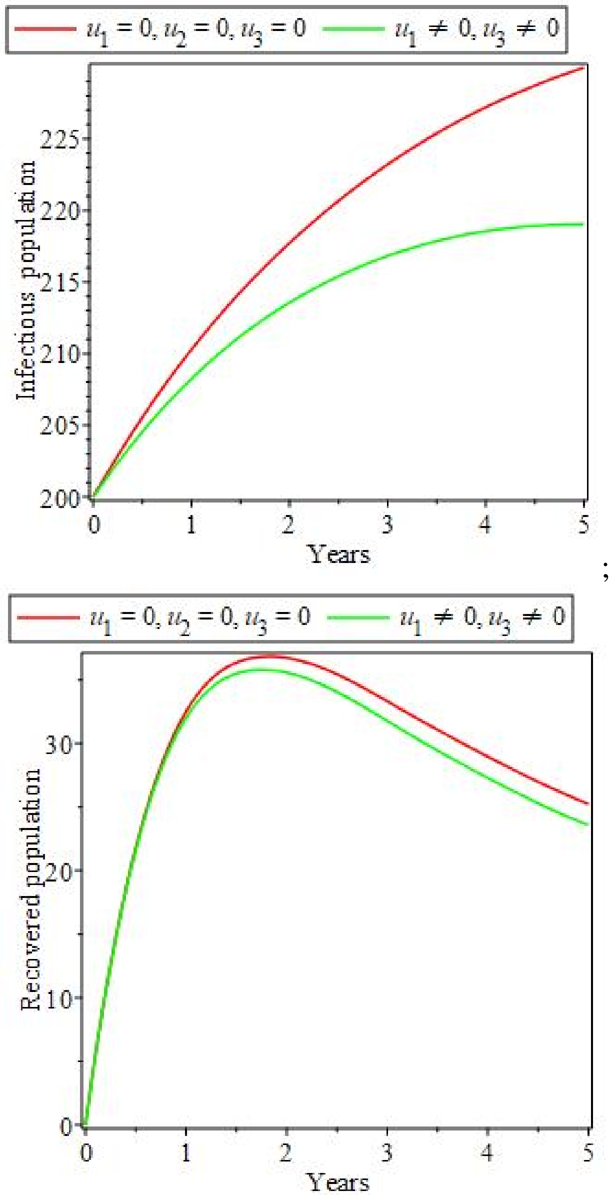

FIGURE 2. Optimal prevention and treatment of population infected.

7.3. Strategy C: Vaccination and Treatment of Infected population. We optimise the objective functional using vaccination of susceptible and treatment of infected population as a control measure. Figure 3 shows the effects of vaccination susceptible population and treatment of infected population. There have been a significant reduction in the number of population infected.

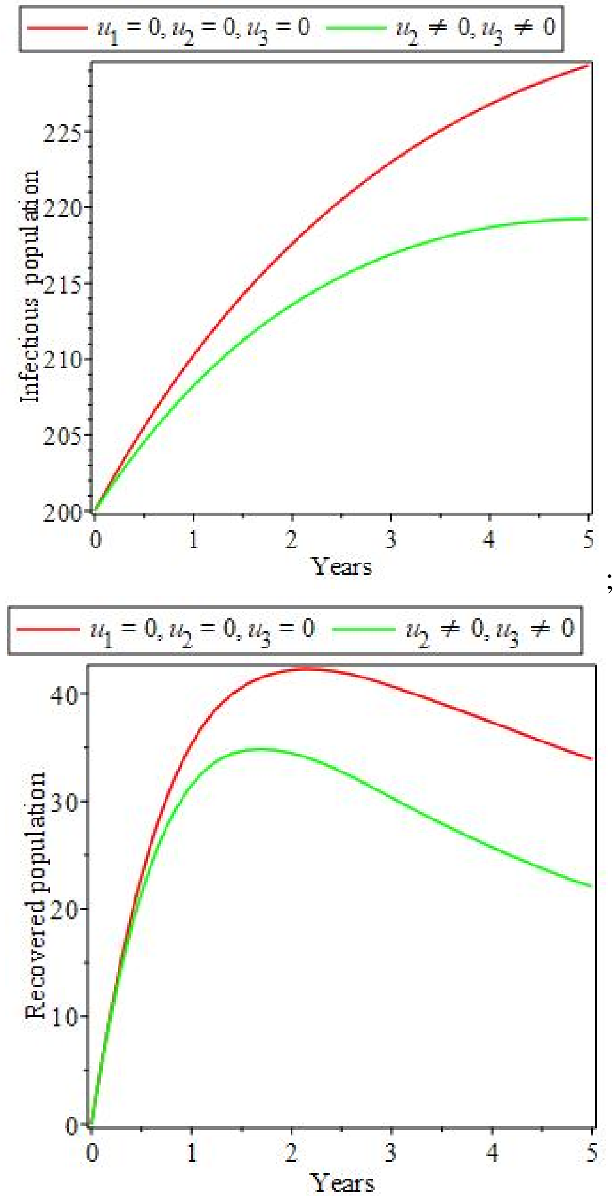

FIGURE 3. Optimal vaccination and treatment of population infected.

8. CONCLUSION

We developed a mathematical model that investigates the effect of limited medical resources on the spread of hepatitis B, and to find an optimum intervention to control and prevent the spread of hepatitis B infection.

We analysed and proved the local and global stability of the model using the Routh Hurwitz criteria and two different Lyapunov functions. The results of the stability analysis showed that depending on the control strategies adopted, the disease can persist or get eliminated from the region.

We simulated the model to investigate the impact of limited medical resources on the dynamics of the disease. Hence we increased the treatment and vaccination rates steadily. The simulation results established that limited medical resource is directly proportional to the successful fight against the spread of the disease.

We simulated the model with and without optimal control variables simultaneously. The results showed that with the incorporation of the control variables, the model significantly performed better than the model without the control variables as shown in Figure 1, Figure 2 and Figure 3 of the numerical results.

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DATA AVAILABILITY STATEMENT

Some of the parameter values are assumed and others are taken from published articles and are cited in this paper. These published articles are also cited at relevant places within the text as references.

CONFLICT OF INTERESTS

The author(s) declare that there is no conflict of interests.

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