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Modelling The Immune Response And Viral Dynamics In HBV Infection

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Abstract

Hepatitis B virus (HBV) infection remains a significant global public health challenge, affecting approximately 250 million people worldwide and leading to severe liver complications including cirrhosis and hepatocellular carcinoma. This study presents a deterministic compartmental mathematical model to investigate the transmission dynamics of HBV infection and its progression to liver cirrhosis. The total population is divided into six compartments: susceptible (S), exposed (E), infected (I), hospitalized (H), cirrhotic (C), and recovered (R). The model incorporates key epidemiological parameters including recruitment rate, transmission rate, progression rates between disease stages, recovery rates, and disease-induced mortality rates. We establish the well-posedness of the model by proving the positivity and boundedness of solutions. The basic reproduction number R_0 is derived using the next-generation matrix approach, serving as a threshold parameter for disease persistence or elimination. Rigorous stability analysis demonstrates that the disease-free equilibrium is locally and globally asymptotically stable when $R_0 < 1$, indicating disease eradication, while the endemic equilibrium is globally asymptotically stable when $R_0 > 1$, signifying sustained transmission. Sensitivity analysis identifies the transmission rate β and recruitment rate Λ as the most influential parameters affecting disease dynamics. Numerical simulations using MATLAB validate the theoretical findings and illustrate the temporal evolution of all population compartments under different parameter scenarios. The results emphasize the critical importance of early diagnosis, timely medical intervention, and integrated control strategies including vaccination and antiviral therapy in reducing HBV burden. This modelling framework provides valuable insights for public health policymakers and can be extended to study other chronic infectious diseases with similar transmission patterns.

Introduction

Hepatitis B virus (HBV) is a major global public health concern because it is associated with a wide range of liver diseases. HBV infection can lead to severe complications, including acute and chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma (liver cancer). Owing to its high prevalence and serious health consequences, HBV remains a significant challenge for healthcare systems worldwide. According to the World Health Organization (WHO), approximately two billion people have been infected with HBV at some point in their lives, while nearly 250 million people are living with chronic HBV infection [1], [2].

HBV is transmitted through contact with infected blood and other body fluids. The major routes of transmission include mother-to-child transmission during childbirth, unsafe medical practices such as contaminated injections, exposure to infected blood, sexual contact, and the sharing of contaminated needles or sharp instruments. Infection is particularly common in regions where HBV is endemic, with many infections occurring during infancy or early childhood. Following infection, HBV attacks liver cells and causes acute hepatitis, which may either resolve naturally or progress to chronic hepatitis B; chronic HBV infection significantly increases the risk of developing liver cirrhosis and hepatocellular carcinoma [3]–[6].

Vaccination is the most effective strategy for preventing HBV infection. In addition, the administration of hepatitis B immune globulin (HBIG), together with vaccination, greatly reduces the risk of mother-to-child transmission. Antiviral therapies are also available to suppress viral replication, delay disease progression, and reduce the risk of severe liver complications. Despite these preventive and therapeutic measures, HBV continues to pose a major public health burden, particularly in developing countries [7], [8].

Mathematical modeling has become an essential tool for understanding the transmission dynamics of HBV and for evaluating effective control strategies. Such models provide valuable insights into disease progression, predict future trends, and assess the impact of intervention measures. Several researchers have developed mathematical models to investigate the transmission dynamics of HBV. For instance, Zou et al. proposed a mathematical model to study the spread of HBV in different population groups [9]. Their model divided the population into six compartments susceptible, latent, infectious, carrier, vaccinated, and recovered individuals and demonstrated that increasing vaccination coverage and reducing transmission from carrier individuals are effective strategies for controlling HBV.

Similarly, Tahir et al. [10] investigated the transmission dynamics of HBV by considering different stages of infection and disease progression. Their model incorporates susceptible, exposed, infected, hospitalized, and recovered individuals together with a class representing liver dysfunction. At any time t, the total human population is divided into six mutually exclusive compartments, namely susceptible S(t), exposed E(t), infected I(t), hospitalized H(t), individuals with liver dysfunction C(t), and recovered R(t), so that the total population is given by

$$N(t) = S(t) + E(t) + I(t) + H(t) + C(t) + R(t) \quad (1)$$

and the dynamics of HBV infection spread are described by the following system of ordinary differential equations:

$$
\begin{cases}
\dfrac{dS}{dt} = \mu\omega(1-\nu C) + \psi V - (\mu_0 + \beta I + \varepsilon\beta C + \gamma_3) S, \\
\dfrac{dL}{dt} = (\beta I + \varepsilon\beta C) S - (\mu_0 + \sigma) L, \\
\dfrac{dI}{dt} = \sigma L - (\mu_0 + \gamma_1) I, \\
\dfrac{dC}{dt} = \mu\omega\nu C + q\gamma_1 I - (\mu_0 + \mu_1 + \gamma_2) C, \\
\dfrac{dV}{dt} = \mu(1-\omega) + \gamma_3 S - (\mu_0 + \psi) V, \\
\dfrac{dR}{dt} = (1-q)\gamma_1 I + \gamma_2 C - \mu_0 R.
\end{cases}
$$

Building on this line of work, the present study formulates a compartmental HBV model that explicitly tracks progression from infection through hospitalization to liver cirrhosis, and investigates its well-pawedness, equilibria, stability, sensitivity, and numerical behavior.

Aim and Objectives

The aims and objectives of this work are: (1) to investigate the well-pawedness of the proposed model; (2) to perform stability analysis of the model; (3) to perform sensitivity analysis of the proposed model; and (4) to perform numerical simulations of the proposed model.

Significance of the Study

This study aims to refine existing models of HBV infection by incorporating real-time population data, with particular emphasis on cirrhosis as a critical clinical outcome. The primary objectives are to deepen the understanding of the progression from chronic HBV infection, represented by the infected class I, to end-stage liver disease, particularly cirrhosis, denoted by the class C. The model also seeks to assess the burden of HBV-related liver failure and to support forecasting efforts for healthcare planning. The proposed framework utilizes a deterministic compartmental approach, segmenting the population into epidemiological classes, susceptible, exposed, infected, hospitalized, cirrhotic, and recovered individuals, enabling a systematic analysis of disease transmission, progression to severe outcomes, and the potential impact of interventions, including vaccination, antiviral therapy, and early screening [11]. The modeling techniques and insights gained from this work may also be applicable to other chronic liver diseases with similar progression dynamics.

PRELIMINARIES

This section presents basic definitions and mathematical techniques used throughout this paper, including modes of disease transmission, stability theory, and sensitivity analysis.

Transmission of Infectious Diseases

Direct contact transmission occurs through direct physical contact between an infected and a susceptible individual, including touching, sexual contact, biting, and similar forms of physical interaction.

Indirect contact transmission occurs when there is no direct person-to-person contact; the disease spreads through contaminated surfaces, objects, or vectors such as mosquitoes, flies, mites, fleas, ticks, rats, or dogs.

Vertical transmission refers to the transmission of pathogens from an infected pregnant mother to her fetus or newborn, as occurs in diseases such as Hepatitis B and HIV/AIDS.

Vector transmission occurs through the bite of infected arthropods such as mosquitoes, ticks, or fleas, as in malaria and dengue fever.

Horizontal transmission refers to the spread of disease between individuals through direct or indirect contact, including transmission by infected vectors or contaminated objects.

Types of Outbreaks

An epidemic is the outbreak of a disease that affects a large portion of the population of a society; it is more likely when a specific number of infectious people enter a society, and initially nobody is immune [12]. The scientific analysis of such infections is called epidemiology (e.g., COVID-19). A pandemic is a disease that spreads nearly to every part of a country, if not the entire world. An endemic is the constant presence of an infection or disease factor within a geographic region, or the usual prevalence of a given infection/disease within such a region (e.g., dengue and TB).

Differential Equations and Mathematical Modeling

An equation that involves the derivative of one or more dependent variables with respect to one or more independent variables is called a differential equation, e.g., dy/dx = x cos x. A differential equation is autonomous if the independent variable does not appear explicitly, e.g., $\frac{dy}{dx} = y^3 + 3y$

Mathematical modeling is a technique used to describe real-world problems using mathematical language, particularly systems of differential equations. A mathematical model comprises four basic steps: (1) assumption; (2) mathematical formulation, i.e., expressing assumptions as differential equations; (3) solution of the differential equations; and (4) simulation for authentication of the model.

Epidemiological models are utilized to design fitting management responses to infectious disease outbreaks, inform public policy on disease in case of future outbreaks, and plan and assess control techniques [13]. The population is arranged into classes representing distinct epidemiological states. Individuals who have no disease but are capable of catching it are labeled the susceptible class. The exposed class comprises individuals who carry the disease at an initial, asymptomatic, non-transmissible stage. The infected class comprises individuals in whom the disease is present at a developed level with symptoms and the capacity to transmit it, while the recovered class comprises individuals who have fully recovered from the disease, either through treatment or naturally through immunity. A deterministic (compartmental) model describes what occurs, on average, at the population scale.

A static system does not exhibit change over time, whereas a dynamic system evolves over time, with its behaviour typically described by differential or difference equations. A deterministic system has future states completely determined by the current state and the system's governing laws, with no randomness involved, whereas a stochastic system incorporates inherent randomness, so that identical initial conditions can produce different outcomes. Inductive reasoning derives general principles from specific observations, while deductive reasoning draws conclusions from premises assumed to be true.

Equilibrium Points and Stability

An equilibrium (critical) point of a dynamical system $\frac{dz}{dt} = f(z)$ is a solution at which the derivatives vanish, i.e., $f(\bar{z}) = 0$. The equilibrium point $\bar{z}$ is said to be stable if, for every $\varepsilon_1 > 0$, there exists $\sigma > 0$ such that $|z(0) - \bar{z}| < \sigma$ implies $|z(t) - \bar{z}| < \varepsilon_1$ for all t.

A system is locally stable if, when slightly perturbed from an equilibrium point, it tends to return to that point over time; otherwise it is unstable. Consider a system of n differential equations $dz_i/dt = k_i(z_1, z_2, \ldots, z_n)$, $i = 1, \ldots, n$, written in matrix form as $Z' = k(Z)$. Expanding k about an equilibrium $\bar{Z}$ with $k(\bar{Z}) = 0$ in a Maclaurin series and retaining first-order terms gives the linearized system

$$\frac{dZ}{dt} = JZ + P(Z) \tag{8}$$

where J is the Jacobian matrix of partial derivatives evaluated at the equilibrium and P(Z) collects the higher-order terms. When the stability of the original nonlinear system and of the linearized system $\frac{dZ}{dt} = JZ$ coincide, the analysis follows the classical result of Lyapunov (1857–1918).

The Routh–Hurwitz criterion gives necessary and sufficient conditions for stability: the necessary condition is that all coefficients of the characteristic polynomial $b_0z^n + b_1z^{n-1} + \cdots + b_n = 0$ are non-zero and of the same sign, and the sufficient condition is that all entries in the first column of the associated Routh array share the same sign; the system is unstable otherwise.

A system is globally stable if every trajectory, regardless of initial condition, eventually converges to a single equilibrium point. A Lyapunov function V(x) is used to assess the stability of an equilibrium point through the behaviour of its derivative along trajectories. LaSalle's Invariance Principle extends this approach to cases where Lyapunov's method alone is insufficient. A function V(x) is positive definite if $V(x) > 0$ for all states x other than the equilibrium, where $V(x) = 0$; the equilibrium is asymptotically stable if $\dot{V}(x) < 0$ for all $x \neq 0$, and stable if $\dot{V}(x) \leq 0$.

Basic Reproduction Number and Sensitivity Analysis

The basic reproduction number, denoted R0, is the number of secondary infections produced by a single infected individual in an otherwise susceptible population, and can be obtained through the next-generation matrix method [14]. If $R0 < 1$, the disease-free equilibrium is stable, both locally and globally, and the disease dies out; if $R_0 > 1$, the endemic equilibrium is stable and the disease persists in the population.

Sensitivity analysis investigates the variation in model outputs brought about by changes in inputs, and identifies which initial values and parameters most influence model behaviour. A most-sensitive parameter should be estimated carefully, since even a small change in it can produce a large quantitative or qualitative change in the outcome, whereas insensitive parameters require comparatively little estimation effort. Sensitivity analysis therefore helps identify which parameters should be targeted by management strategies. At any time t, sensitivities are determined by taking partial derivatives of each state variable with respect to each parameter; the normalized forward sensitivity index of a quantity ζ that depends differentiably on a parameter θ is defined as

$$\chi_{\zeta}^{\theta} = \frac{\partial \theta}{\partial \zeta} \times \frac{\zeta}{\theta}. \tag{9}$$

Finally, numerical simulation is a technique used to approximate the behaviour of mathematical models through computational methods, using algorithms to solve equations that may be too complex for analytical solutions.

MODEL FORMULATION AND MATHEMATICAL ANALYSIS

Model Formulation

A deterministic compartmental mathematical model is proposed to describe the dynamics of HBV infection and the formation of liver cirrhosis. The total population at time t, N(t), is divided into six groups: susceptible S(t), exposed E(t), infected I(t), hospitalized H(t), cirrhotic C(t), and recovered R(t) individuals.

Susceptible individuals enter the population at rate Λ and become infected through contact with infected individuals at rate β. Exposed individuals join the infected class at rate ε. Individuals in the infected class are hospitalized at rate η, progress to the cirrhotic class at rate α, recover at rate δ, or die from disease-related complications at rate μ1. Hospitalized individuals progress to the cirrhotic class at rate ω or recover at rate τ. Individuals with cirrhosis recover at rate γ and experience disease-induced mortality at rate μ2. Each individual, regardless of class, dies naturally at rate μ. The transmission dynamics of HBV are described by the following system of ordinary differential equations:

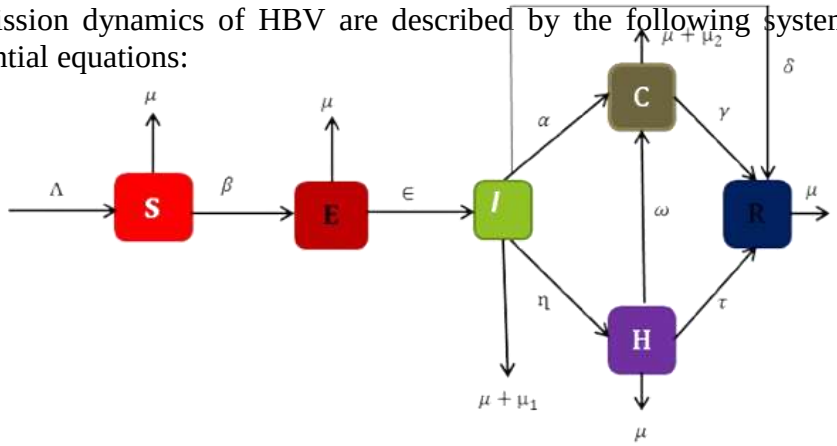

Figure3.1: The HBV Model (3.2.1) flow diagram

$$\begin{cases} \frac{dS}{dt} = \Lambda - \beta IS - \mu S \\ \frac{dE}{dt} = \beta IS - (\mu + \varepsilon)E \\ \frac{dI}{dt} = \varepsilon E - (\omega + \eta + \alpha + \mu + \mu_1)I \\ \frac{dH}{dt} = \eta I - (\mu + \tau + \omega)H \\ \frac{dC}{dt} = \alpha I + \omega H - (\gamma + \mu + \mu_2)C \\ \frac{dR}{dt} = \delta I + \tau H + \gamma C - \mu R. \end{cases} \quad (3.2.1)$$

The initial conditions are S>0,E≥0, I≥0,C≥0,R≥0.

TABLE I: PARAMETERS AND THEIR DESCRIPTIONS

Param.	Description
Λ	Recruitment into the susceptible group
β	Transmission rate of HBV infection from infected individuals

ε	Progression rate from the exposed class to the infected class
η	Progression rate from the infected class to the hospitalized class
α	Progression rate from the infected class to the cirrhotic class
ω	Progression rate from the hospitalized class to the cirrhotic class
δ	Rate of recovery from the infected class
γ	Rate of recovery from the cirrhotic class
τ	Rate of recovery from the hospitalized class
μ	Natural death rate
$\mu 1$	HBV-induced death rate in the infected group
$\mu 2$	HBV-induced death rate in the cirrhotic group

Well-Posedness and the Feasible Region

Since the state variables represent human populations, positivity must be established for all $t \geq 0$. The following biologically feasible region is considered throughout the analysis:

$$\Omega = \{(S,E,I,H,C,R) \in \mathbb{R}_+^6 : S > 0,\ 0 \leq E,I,H,C,R \leq N,\ N(t) \leq \Lambda/\mu\} \quad (16)$$

Lemma 1.

For model (2)–(7), if the initial conditions satisfy S(t), E(t), I(t), H(t), C(t), R(t) ≥ 0, then the solutions (S(t), E(t), I(t), H(t), C(t), R(t)) remain non-negative for all $t \geq 0$.

Proof.

$By integrating the above in-equation from 0 to t, we have S(t) \geq S(0)e^{-\int_0^t [\beta I+\mu]dt} \geq 0.$ Therefore,

$S(t) \geq 0, E(t) \geq 0, I \geq 0, H(t) \geq 0, C(t) \geq 0,$ and $R(t) \geq 0$ when $t \geq 0$. □

and an analogous argument applied to each remaining equation establishes S(t), E(t), I(t), H(t), C(t), R(t) ≥ 0 for all $t \geq 0$.

Lemma 2 (Feasible region).

The feasible region of model (2)–(7) is $\Omega = \{(S,E,I,H,C,R) \in \mathbb{R}_+^6 : S > 0,\ 0 \leq E,I,H,C,R \leq N,\ N(t) \leq \Lambda/\mu\}$.

Proof.

$$N(t) = S(t) + E(t) + I(t) + H(t) + C(t) + R(t)$$

$$\frac{dN}{dt} = \Lambda - \mu(S + E + I + H + C + R) - \mu_1 I - \mu_2 C$$

Simplify the equation we get

$$\frac{dN(t)}{dt} = \Lambda - \mu N - \mu_1 I - \mu_2 C \leq \Lambda - \mu N(t),$$

using the Comparison Principle Theorem [23], we obtain that

$$N(t) \leq N(0)e^{-\mu t} + \frac{\Lambda}{\mu}(1 - e^{-\mu t}),$$

where $N(t) = S(0) + E(0) + I(0) + H(0) + C(0) + R(0)$. Hence

$$\limsup_{t \to \infty} N(t) \leq \frac{\Lambda}{\mu}.$$

Basic Reproduction Number

Here we prove the existence of the disease-free equilibrium point and calculate the basic reproduction number for Model (3.2.1). Setting the right-hand side of the model to zero yields the following disease-free equilibrium.

$$Q_0 = (S_0, E_0, I_0, H_0, C_0, R_0) = \left(\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0\right).$$

The basic reproduction number of Model (3.2.1) is derived using the next generation matrix technique [17]. Let Fi be the newly infected individuals in compartment i and Vi the transfer of individuals in each

$$\frac{dx}{dt} = F - V$$

compartment i; i.e., compartments E, I and C. Consider $x = (E, I, C)$ = and the model (3.2.1) can be written as:

where,

(21)

$$F = \begin{pmatrix} \beta IS \\ 0 \\ 0 \\ 0 \end{pmatrix}, V = \begin{bmatrix} (\mu + \varepsilon)E \\ (\delta + \eta + \alpha + \mu + \mu_1)I - \varepsilon E \\ (\mu + \tau + \omega)H - \eta I \\ (\gamma + \mu + \mu_2)C - \alpha I - \omega H \end{bmatrix}$$ **Following the calculation of the basic reproduction number based on the next generation matrix approach, we consider the infected compartments $x_i = 1, 2, 3$. In the disease-free equilibrium Q_0,**

$$F^* = \left(\frac{\partial F_i}{\partial x_i}\right)_{Q_0} = \begin{pmatrix} 0 & \beta S & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

And

$$V^* = \left(\frac{\partial V_i}{\partial x_i}\right)_{Q_0} = \begin{pmatrix} \mu + \varepsilon & 0 & 0 & 0 \\ -\varepsilon & \delta + \eta + \alpha + \mu + \mu_1 & 0 & 0 \\ 0 & -\eta & \mu + \tau + \omega & 0 \\ 0 & -\alpha & -\omega & \gamma + \mu + \mu_2 \end{pmatrix}$$

and,

$$(V^*)^{-1} = \begin{pmatrix} \frac{1}{a_1} & 0 & 0 & 0 \\ \frac{\varepsilon}{(a_1)(a_2)} & \frac{1}{a_2} & 0 & 0 \\ \frac{\varepsilon\eta}{(a_1)(a_2)(a_3)} & \frac{\eta}{(a_2)(a_3)} & \frac{1}{a_3} & 0 \\ \frac{\varepsilon\left(\alpha(a_3)+\omega\eta\right)}{(a_1)(a_2)(a_3)(a_4)} & \frac{\alpha(a_3)+\omega\eta}{(a_2)(a_3)(a_3)} & \frac{\omega}{(a_3)(a_4)} & \frac{1}{a_4} \end{pmatrix}$$

where

$$a_1 = \mu + \varepsilon, \qquad a_2 = \delta + \eta + \alpha + \mu + \mu_1, \qquad a_3 = \mu + \tau + \omega, \qquad a_4 = \gamma + \mu + \mu_2. \tag{3.5.1}$$

$$F^*(V^*)^{-1} = \begin{pmatrix} \frac{\beta S\varepsilon}{a_1 a_2} & \frac{\beta S}{a_2} & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

Furthermore, matrices F and V satisfy the conditions stipulated by [17] predictions

$(A1) - (A5)$**. As a result, by evaluating the spectrum of the next generation's matrix FV^{-1}, we can determine the basic reproduction number,**

$$R_0 = \frac{\beta S\varepsilon}{(\mu+\varepsilon)(\delta+\eta+\alpha+\mu+\mu_1)}$$

Enter S^0 and make the equation simpler.

$$R_0 = \frac{\beta\Lambda\varepsilon}{\mu(\,\mu+\varepsilon)(\delta+\eta+\alpha+\mu+\mu_1)} \tag{3.5.2}$$

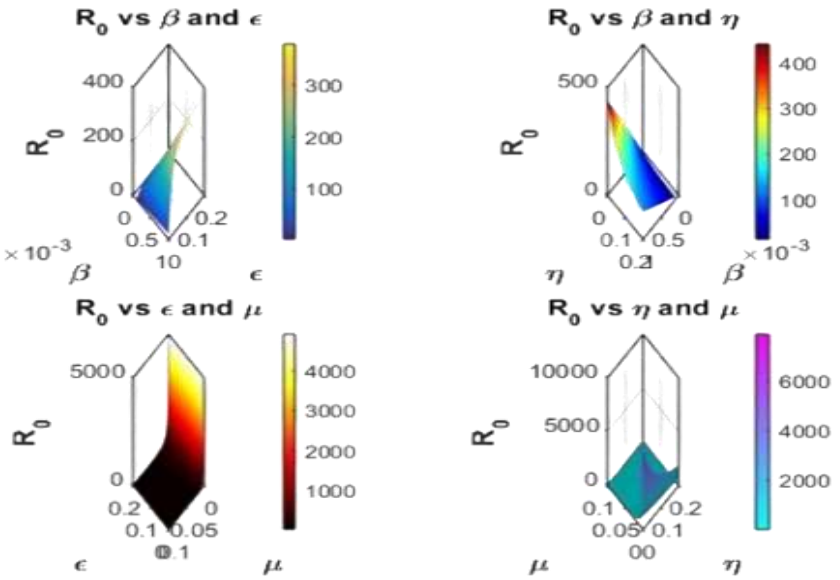

Figure 3.2: Graphical Representation of R_0

Stability of the Disease-Free Equilibrium

Theorem 1.

For model (2)–(7), the disease-free equilibrium Q_0 is locally asymptotically stable whenever $R_0 < 1$.

Proof.

The Jacobian matrix of model (2)–(7) evaluated at Q_0 has trace

$$Tr(M) = -(\delta + \eta + \alpha + \varepsilon + 2\mu + \mu 1) < 0 \quad (25)$$

and determinant

$$det(M) = (\mu+\varepsilon)(\delta+\eta+\alpha+\mu+\mu 1)(1 - R_0) \quad (26)$$

so det(M) > 0 whenever $R_0 < 1$. By the Routh–Hurwitz criterion [16], the real parts of all eigenvalues are then negative, and Q_0 is locally asymptotically stable.

Theorem 2.

For model (2)–(7), the disease-free equilibrium Q_0 is globally asymptotically stable in the feasible region Ω whenever $R_0 < 1$.

Proof.

Consider the feasible region $\Omega = \{(S,E,I,H,C,R) \in \mathbb{R}_+^6 : S+E+I+H+C+R \le \Lambda/\mu\}$. As shown above, $N(t) \le \Lambda/\mu$ as $t \to \infty$, so Ω is positively invariant and attracting, and at the disease-free equilibrium $E = I = H = C = R_0 = 0$, $S_0 = \Lambda/U_0$

Consider the Lyapunov function $V(E, I) = \varepsilon E + (\mu+\varepsilon)I$, which is positive definite in Ω. Differentiating V along solutions of the system and simplifying(27) gives

$$\frac{dV}{dt} = (\mu+\varepsilon)(\delta+\eta+\alpha+\mu+\mu_1)I\left[\frac{\varepsilon\beta S}{(\mu+\varepsilon)(\delta+\eta+\alpha+\mu+\mu_1)} - 1\right]$$

Since $S \le \frac{\Lambda}{\mu}$ in Ω, we obtain

$$\frac{dV}{dt} \le (\mu+\varepsilon)(\delta+\eta+\alpha+\mu+\mu_1)I\left[\frac{\varepsilon\beta\Lambda}{\mu(\mu+\varepsilon)(\delta+\eta+\alpha+\mu+\mu_1)} - 1\right]$$

Using the expression for R_0 above, this reduces to

$$dV/dt \le (\mu+\varepsilon)(\delta+\eta+\alpha+\mu+\mu 1)\, I\,(R_0 - 1) \le 0 \quad whenever\ R_0 < 1 \quad (28)$$

with dV/dt = 0 if and only if I = 0. When I = 0, dE/dt = −(μ+ε)E, so E(t) → 0, and consequently H(t) → 0, C(t) → 0, R(t) → 0, S(t) → Λ/μ. Hence the largest invariant set contained in {(S,E,I,H,C,R) ∈ Ω : dV/dt = 0} is the singleton { Q_0 }, and by LaSalle's Invariance Principle [17], Q_0 is globally asymptotically stable in Ω whenever $R_0 < 1$.

Endemic Equilibrium and Its Stability

Let Q* = (S*, E*, I*, H*, C*, R*) denote the endemic equilibrium of model (2)–(7), obtained by setting the time derivatives of the system to zero. The model possesses a unique endemic equilibrium Q* whenever the infection remains endemic, that is, whenever $R_0 > 1$.

Theorem 3.

For model (2)–(7), the endemic equilibrium Q* = (S*, E*, I*, H*, C*, R*) is locally asymptotically stable whenever R0 > 1.

Proof.

The Jacobian matrix J(Q*), evaluated at the endemic equilibrium, is block-triangular, so its characteristic polynomial factors as $\det(\lambda I - J(Q^*)) = \det(\lambda I - A)\det(\lambda I - D)$. The eigenvalues associated with block D are

$$\lambda 1 = -(\mu+\tau+\omega), \quad \lambda 2 = -(\gamma+\mu+\mu 2), \quad \lambda 3 = -\mu \tag{29}$$

which are clearly negative. The characteristic polynomial of block A is $\lambda^3 + a1\lambda^2 + a2\lambda + a3 = 0$, where

$$a1 = (\beta I^*+\mu) + (\mu+\varepsilon) + (\delta+\eta+\alpha+\mu+\mu 1) \tag{30}$$

$$a2 = (\beta I^*+\mu)(\mu+\varepsilon) + (\beta I^*+\mu)(\delta+\eta+\alpha+\mu+\mu 1) + (\mu+\varepsilon)(\delta+\eta+\alpha+\mu+\mu 1) - \beta\varepsilon S^* \tag{31}$$

$$a3 = (\beta I^*+\mu)[(\mu+\varepsilon)(\delta+\eta+\alpha+\mu+\mu 1) - \beta\varepsilon S^*] \tag{32}$$

Using the endemic equilibrium relations, the associated Routh–Hurwitz array yields the conditions

$$a1 > 0, \quad a2 > 0, \quad a3 > 0, \quad a1a2 > a3 \tag{33}$$

which are satisfied at the endemic equilibrium, so all roots of the characteristic polynomial of A have negative real parts. Since the eigenvalues of both blocks A and D have negative real parts, every eigenvalue of J(Q*) has negative real part, and the endemic equilibrium Q* is locally asymptotically stable whenever $R0 > 1$.

Global Stability of the Endemic Equilibrium

Theorem 4.

For model (2)–(7), if $R_0 > 1$, the endemic equilibrium point Q* is globally asymptotically stable in the feasible region Ω.

$$V(S,E,I,H,C,R) = \sum_{X\in\{S,E,I,H,C,R\}} \left(X - X^* - X^* \ln\frac{X}{X^*}\right).$$

Explicitly,

$$V = \left(S - S^* - S^* \ln\frac{S}{S^*}\right) + \left(E - E^* - E^* \ln\frac{E}{E^*}\right) + \left(I - I^* - I^* \ln\frac{I}{I^*}\right) + \left(H - H^* - H^* \ln\frac{H}{H^*}\right) + \left(C - C^* - C^* \ln\frac{C}{C^*}\right) + \left(R - R^* - R^* \ln\frac{R}{R^*}\right).$$

Proof.

Consider the Lyapunov function (34)

Since $x - x^* - x^* \ln(x/x^*) \geq 0$ for all $x > 0$, $V \geq 0$ with equality if and only if (S,E,I,H,C,R) = (S*,E*,I*,H*,C*,R*). Differentiating V along the solutions of model (2)–(7) and substituting the endemic-equilibrium relations

$$\Lambda = \beta S^* I^* + \mu S^*, \quad (\mu+\varepsilon)E^* = \beta S^* I^*, \quad (\delta+\eta+\alpha+\mu+\mu 1)I^* = \varepsilon E^*, \tag{35}$$

$$(\mu+\tau+\omega)H^* = \eta I^*, \quad (\gamma+\mu+\mu 2)C^* = \alpha I^* + \omega H^*, \quad \mu R^* = \delta I^* + \tau H^* + \gamma C^* \tag{36}$$

after simplification yields $dV/dt \leq 0$, with equality if and only if S=S*, E=E*, I=I*, H=H*, C=C*, R=R*. Hence the largest invariant subset of $\{(S,E,I,H,C,R) \in \Omega : dV/dt = 0\}$ is the singleton {Q*}, and by LaSalle's Invariance Principle the endemic equilibrium Q* is globally asymptotically stable in Ω whenever $R0 > 1$.

Numerical Simulation

The mathematical model was simulated numerically in MATLAB using a predictor–corrector method for the underlying system of nonlinear ordinary differential equations, allowing both accurate estimation and visualization of the dynamics of each compartment. The initial conditions used were S(0) = 300, E(0) = 50, I(0) = 30,

H(0) = 40, C(0) = 30, R(0) = 0, and the parameter values used were Λ = 400, β = 0.00002, α = 0.6, γ = 0.01, ε = 0.005, π = 0.02, θ = 0.01, μ = 0.02, μ1 = 0.005, μ2 = 0.003.

Initially, the susceptible population increases owing to the recruitment rate Λ; as susceptible individuals come into contact with infectious individuals, this population gradually decreases toward a steady-state level. During the early stage of the epidemic, the exposed population rises rapidly as new infections occur, then declines as individuals progress to the infected class at rate ε. The infected and hospitalized populations likewise increase initially before gradually decreasing owing to treatment and disease management, while the recovered population continuously increases. All state variables converge to positive constant values over time, confirming the existence of an endemic equilibrium: although effective treatment and control measures can significantly reduce the number of infected individuals, the disease may persist in the population under the chosen parameter values. The numerical results further indicate that the disease dynamics are highly sensitive to variations in the transmission rate β, the disease-induced mortality rate, the hospitalization rate η, the progression rate, and the recovery rate γ, which play a crucial role in determining the spread and long-term persistence of HBV infection.

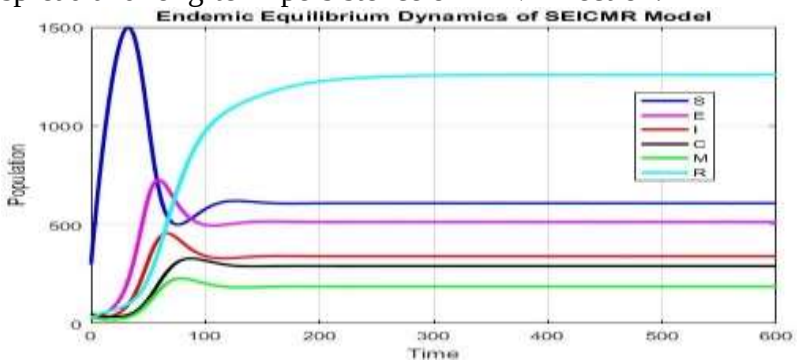

Fig. 3a. Disease-free equilibrium point (R0 < 1).

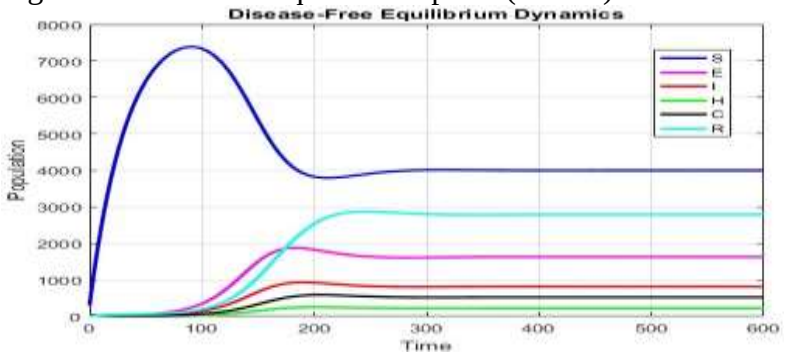

Fig. 3b. Endemic equilibrium point (R_0 > 1).

Discussion and Sensitivity Analysis

The partial rank correlation coefficients (PRCCs) of the model parameters with respect to R_0 indicate that Λ and β are positively correlated with R_0, while parameters associated with disease progression and removal from the infectious classes are negatively correlated, implying that faster recovery or removal of individuals from infectious classes limits transmission; of all parameters, β and Λ are the most influential. Fig. 3(b) presents the scenario in which the disease persists (R_0 > 1): the susceptible category decreases while the exposed, infected, cirrhotic, and recovered categories increase before stabilizing, indicating sustained circulation of the virus. Conversely, Fig. 3(a) presents the dynamics for < 1, in which the virus is controlled and eradicated underscoring the importance of reducing β and enhancing recovery-related parameters.

The normalized forward sensitivity index of R_0 with respect to a parameter r is defined as

$$\chi_r^{R_0} = \frac{\partial R_0}{\partial r} \times \frac{r}{R_0} \tag{37}$$

where

$$R_0 = \frac{\beta \Lambda \varepsilon}{\mu(\mu+\varepsilon)(\delta+\eta+\alpha+\mu+\mu_1)}$$

$$\mu \in (\beta, \Lambda, \mu, \varepsilon, \delta, \eta, \alpha, \mu_1)$$

A high transmission rate β increases R0, underscoring the importance of this parameter in the epidemic. Conversely, an increase in γ lowers R_0, while the effect of α depends on its role in the infection and cirrhosis progression mechanism. The sensitivity indices are as follows:

We calculate (4.2.1) for each parameter in (4.2.3)

$$\begin{aligned}
&1.\ X_\beta^{R_0} = \frac{\partial R_0}{\partial \beta} \times \frac{\beta}{R_0} = 1 \\
&2.\ X_\Lambda^{R_0} = \frac{\partial R_0}{\partial \Lambda} \times \frac{\Lambda}{R_0} = 1 \\
&3.\ X_\mu^{R_0} = \frac{\partial R_0}{\partial \mu} \times \frac{\mu}{R_0} = -\left(1 + \frac{\mu}{\mu+\varepsilon} + \frac{\mu}{\delta+\eta+\alpha+\mu+\mu_1}\right) \\
&4.\ X_\delta^{R_0} = \frac{\partial R_0}{\partial \delta} \times \frac{\delta}{R_0} = -\frac{\delta}{\delta+\eta+\alpha+\mu+\mu_1} \\
&5.\ X_\alpha^{R_0} = \frac{\partial R_0}{\partial \alpha} \times \frac{\alpha}{R_0} = -\frac{\alpha}{\delta+\eta+\alpha+\mu+\mu_1} \\
&6.\ X_\varepsilon^{R_0} = \frac{\partial R_0}{\partial \varepsilon} \times \frac{\varepsilon}{R_0} = -\frac{\varepsilon}{\mu+\varepsilon} \\
&7.\ X_\eta^{R_0} = \frac{\partial R_0}{\partial \eta} \times \frac{\eta}{R_0} = -\frac{\eta}{\delta+\eta+\alpha+\mu+\mu_1} \\
&8.\ X_{\mu_1}^{R_0} = \frac{\partial R_0}{\partial \mu_1} \times \frac{\mu_1}{R_0} = -\frac{\mu_1}{\delta+\eta+\alpha+\mu+\mu_1}
\end{aligned} \tag{38}$$

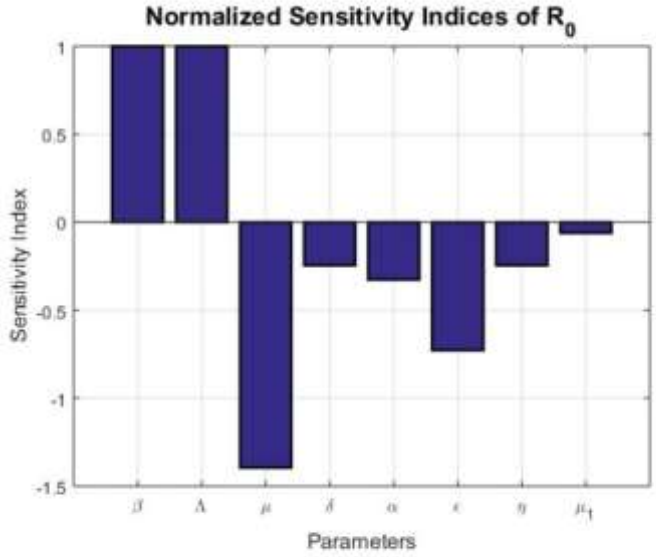

Figure 3.4: The graph show the Sensitivity of R_0 with impact of different parameters

Fig. 4. Partial rank correlation coefficients (PRCC) of model parameters with respect to R_0.

CONCLUSION AND FUTURE WORK

Conclusion

In this study, we developed a mathematical model for HBV infection that explicitly accounts for disease progression to liver cirrhosis. The model was formulated as a deterministic compartmental system and analyzed to assess its implications for the transmission dynamics and control of HBV. We derived the basic reproduction number R_0 as a threshold parameter determining whether the infection dies out or persists. Our analysis showed that the disease-free equilibrium is locally and globally asymptotically stable when R_0 < 1, indicating that the infection will eventually be eliminated, whereas the endemic equilibrium is globally asymptotically stable when R_0 > 1, implying sustained transmission in the population.

The results emphasize the importance of early diagnosis and timely medical intervention for individuals in the infected and cirrhotic compartments: prompt treatment and effective management of cirrhosis can substantially reduce the disease burden and interrupt transmission chains. The findings support the implementation of integrated control strategies including vaccination, antiviral therapy, and enhanced clinical monitoring to curb the spread of HBV. Cost considerations in the deployment of control strategies were also examined; implementing interventions in a cost-optimized manner, and improving access to screening and early-stage treatment, emerged as cost-effective approaches for reducing the long-term health and economic burden of HBV. Given the chronic progression of HBV and the difficulty of identifying infection stages without detailed clinical data, further refinement of the model is warranted as more epidemiological and patient-level data become available; the proposed framework is flexible and may be extended to incorporate factors such as coinfections, detection rates, and treatment adherence, and may also be adapted to other infectious diseases with similar chronic trajectories, including HIV, syphilis, and COVID-19.

Future Work

In future work, we intend to extend the current HBV model by incorporating additional real-world complexities, including the impact of co-infection with other diseases such as HIV, and the integration of detection and diagnosis rates as influential factors in HBV progression and control. We will also investigate the potential for HBV elimination under scenarios involving widespread vaccination and long-term antiviral treatment. To enhance the biological realism and analytical scope of the model, we propose the following extensions: (i) incorporating stochastic components to capture random variation and uncertainty in transmission and treatment outcomes; (ii) generalizing the compartmental model to a fractional-order framework, better able to represent memory and hereditary characteristics inherent in biological systems; and (iii) formulating a time-delay version of the model to account for lags in disease progression, diagnosis, and treatment initiation. These extensions are expected to yield a more comprehensive and realistic representation of HBV dynamics, supporting the development of more effective, evidence-based public health interventions.

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