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Analyzing hepatitis B transmission dynamics: Insights into clinical control and passive immunity strategies through mathematical modeling and simulation

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Abstract
Hepatitis B virus (HBV) infection remains a pressing global public health concern, particularly in underserved rural regions of low and middle-income countries. Despite the availability of therapies, the prevalence of HBV infection persists, often due to neglect in these areas. This paper addresses the complex dynamics of HBV transmission by incorporating passive immunity and clinical control interventions into a deterministic mathematical model. The model, expressed as a system of non-linear differential equations with time-dependent infection rates, reveals the intricate interplay between passive immunity and infection susceptibility among infants born to HBV-infected mothers. Through comprehensive stability analysis and numerical simulations, we illuminate the dynamics of HBV infection within populations. Sensitivity analysis identifies critical parameters that significantly influence disease transmission, including the reproduction number and strength number. By exploring the effects of these key parameters and control measures, we provide insights into potential strategies for mitigating HBV spread. The study underscores the necessity of acknowledging passive immunity and its temporal nature in HBV transmission modeling. Moreover, it highlights the importance of addressing maternal antibody protection and the implications of control measures for public health policy. Ultimately, this research contributes to our understanding of HBV transmission dynamics and offers valuable guidance for effective interventions in combating Hepatitis B, particularly in resource-constrained regions.

Keywords: HBV, reproduction number, strength number, passive immunity, equilibrium point, stability, survival function, jury's test, numerical simulation

Introduction
Hepatitis B remains a significant global health concern, with millions of people affected by this viral infection. Understanding the intricate dynamics of Hepatitis B transmission is crucial for developing effective clinical control interventions and evaluating the potential impact of passive immunity strategies. This study delves into the intricate world of Hepatitis B transmission, employing mathematical modeling and simulation to uncover valuable insights. Hepatitis B virus (HBV) is a highly contagious pathogen transmitted primarily through contact with infected blood or bodily fluids. The virus can lead to acute or chronic infections, and its consequences can range from mild illness to severe liver damage, including cirrhosis and hepatocellular carcinoma. Despite the availability of vaccines and antiviral treatments, Hepatitis B continues to pose a substantial public health challenge. Mathematical modeling and simulation techniques provide a unique vantage point for comprehending the transmission dynamics of this virus. By constructing mathematical models that capture the intricacies of HBV transmission, researchers can gain insights into how the virus spreads within populations and assess the effectiveness of various control measures. This study aims to bridge the gap between theory and practice by exploring the real-world implications of Hepatitis B transmission dynamics. By integrating clinical control interventions and passive immunity strategies into the mathematical models, we seek to discern the most effective approaches for reducing Hepatitis B transmission rates and minimizing disease burden. Through rigorous mathematical analysis and numerical simulation, this research endeavors to uncover patterns, trends, and critical factors that influence the transmission of Hepatitis B. Ultimately, the goal is to provide evidence-based recommendations that can inform public health policies and

interventions, leading to more effective strategies for managing and, ultimately, mitigating the impact of Hepatitis B on global health. Hepatitis B virus (HBV) infection ranks among the most prevalent forms of viral hepatitis that target the liver, an organ of paramount importance in the human body. This infection follows a two-phase course, encompassing acute and chronic stages. Chronic HBV infection is particularly menacing as it can lead to the development of conditions such as liver cirrhosis and liver cancer, presenting a substantial global public health challenge. The primary mode of HBV transmission occurs through unprotected sexual intercourse with an individual carrying the virus, as well as through mother-to-child transmission during various stages of pregnancy, childbirth, or breastfeeding. Pregnant women and their unborn infants face the risk of contracting HBV infection if comprehensive screening is not conducted either during the course of pregnancy or prior to delivery. Additionally, it is widely presumed that HBV can be horizontally transmitted through sexual contact with an infected individual.

Screening for susceptibility plays a pivotal role in both preventing and managing Hepatitis B infection within the general population. However, it's worth noting that screening and immunization initiatives targeting HBV are not widely practiced in developing nations. Consequently, a significant number of individuals, including expectant mothers, inadvertently transmit the infection to their infants and partners. According to a report by CIHEB in 2022, Kenya faces a critical issue where nearly 90% of individuals with hepatitis remain unaware of their infection status. Furthermore, access to adequate antenatal, perinatal, and post-natal maternal care services remains severely limited in rural areas of these countries. This predicament is particularly evident in various Kenyan counties where a substantial portion of childbirth occurs in rural villages. Access to information about HBV infection is scant, particularly in rural Kenya. Nonetheless, based on existing literature, it is estimated that the overall prevalence of HBV infection in Kenya stands at approximately 7.8% among the general population. Moreover, certain demographics, particularly individuals who engage in drug injection, bear a disproportionately high burden of carriers. However, the precise contribution of each vulnerable population group to the overall prevalence of Hepatitis B remains unclear.

Another notable challenge is the cost associated with testing, which currently exceeds the cost of treatment, thus acting as a barrier to effective hepatitis control efforts. For individuals with acute HBV infection, recovery is possible with timely treatment or through natural immunity. However, when left untreated, this condition progresses to chronic Hepatitis, necessitating lifelong treatment, which places a significant strain on the country's economy. Vaccination has emerged as a highly effective strategy for controlling viral infections globally. Unfortunately, the Hepatitis B vaccine is prohibitively expensive and remains inaccessible to many individuals at risk.

HBV can cause chronic infection, resulting in cirrhosis of the liver, liver cancer, liver failure, and death. Persons with chronic infection also serve as the main reservoir for continued HBV transmission. Although chronic infection is more likely to develop in persons infected as infants or young children, rates of new infection and acute disease are highest among adults (CDC, 2016). The highest concentrations of the virus are found in blood; however, semen and saliva also have been demonstrated to be infectious (Walter W Bond, 1977) [19]. HBV remains viable and infectious in the environment for at least 7 days and can be present in high concentrations on inanimate objects, even in the absence of visible blood (Walter W Bond, *et al*., 1981) [20]. Persons with chronic HBV infection are the major source of new infections, and the primary routes of HBV transmission are sexual contact, percutaneous exposure to infectious body fluids, perinatal exposure to an infected mother, and prolonged, close personal contact with an infected person, as occurs in household contact (Eric E Mast, *et al*, 2006) [6]. No evidence exists of transmission of HBV by casual contact in the workplace, and transmission occurs rarely in childcare settings (Eric E Mast, *et al*, 2005) [7]. Few cases have been reported in which health-care workers have transmitted infection to patients, particularly since implementation of standard universal infection control precautions (RN Gunson, *et al*, 2003) [18]. Most people do not experience any symptoms when newly. However, some people have acute illness with symptoms that last several weeks, including yellowing of the skin and eyes dark urine, extreme fatigue, nausea, vomiting and abdominal pain. People with acute hepatitis can develop acute liver failure, which can lead to death if not diagnosed and treated earlier. Among the long-term complications of HBV infections, a subset of persons develops advanced liver diseases such as cirrhosis and hepatocellular carcinoma, which cause high morbidity and mortality. There is no specific treatment for acute hepatitis B, recovery can be through earlier treatment or natural immunity. Therefore, care is aimed at maintaining comfort and adequate nutritional balance, including replacement of fluids lost from vomiting and diarrhea. Most important is the avoidance of unnecessary medications. Chronic hepatitis B infection can be treated with medicines, including oral antiviral agents. Treatment can slow the progression of HBV, cirrhosis, reduce incidence of liver cancer and improve long-term survival.

In June 2022 report by the World Health Organization (WHO), it was highlighted that there are over 350 million individuals persistently carrying the Hepatitis B Virus (HBV), and approximately 0.6 million people succumb to HBV-related liver diseases or hepatocellular carcinoma each year. The African region was identified as contributing to 26% of the global burden of hepatitis B and C infections in the year 2020. To combat the transmission of HBV, several comprehensive strategies have been successfully implemented. Among these, immunizing vulnerable individuals, especially newborns, with safe and effective vaccines has proven to be the most appealing and cost-effective approach for reducing the incidence of hepatitis B. Despite the success of vaccination efforts, there are still challenges to be addressed. One significant factor in HBV transmission is passive immunity, which involves the transfer of the virus from an infected mother to her child during childbirth. Newborns acquire passive immunity from their mothers through the placenta. Unfortunately, many mothers unknowingly transmit the infection to their infants when their own immunity is compromised. Therefore, it is crucial to anticipate the long-term trends in HBV prevalence to provide valuable insights for public health decision-making. One potential strategy for predicting the prevalence of HBV infections is to employ a mathematical model that incorporates the passive immunity component within the transmission dynamics. This approach can offer a deeper understanding of the dynamics of HBV and aid in making informed public health decisions.

In 2021, the World Health Organization (WHO) conducted estimations indicating that the need for treatment among individuals with chronic hepatitis B infection ranges from 12% to 25%, with variations depending on the specific context and eligibility criteria. For effective suppression of the hepatitis B virus, WHO recommends the utilization of oral medications like tenofovir or entecavir as the most potent drugs. Individuals afflicted with chronic hepatitis B typically require lifelong treatment. In regions with limited resources, most individuals diagnosed with liver cancer sadly experience rapid deterioration and often succumb to the

disease within a few months. Conversely, in high-income areas, patients typically seek medical attention at earlier stages of the infection, allowing for access to surgical and chemotherapeutic interventions that can extend life expectancy from several months to a few years. In some high-income countries, liver transplantation is occasionally employed as a treatment option for individuals with cirrhosis or liver cancer, although success rates vary.

WHO strongly advocates for the administration of the hepatitis B vaccine to all infants as soon as possible following birth, preferably within the initial 24 hours. This should be followed by 2 or 3 additional doses of the vaccine, administered at intervals of at least 4 weeks, to complete the vaccination series. The protective immunity conferred by this vaccination lasts for a minimum of 20 years, and it is likely to be lifelong. WHO does not recommend booster vaccinations for those who have successfully completed the 3-dose vaccination schedule. In addition to infant vaccination, WHO advises the use of antiviral prophylaxis to prevent the transmission of hepatitis B from mother to child. Regrettably, there is a lack of adequate information regarding Hepatitis B vaccines, and screening, diagnosis, and testing for Hepatitis are not commonly practiced among pregnant women during their antenatal care. This is particularly concerning for the most vulnerable population groups, especially those residing in rural areas. To mitigate the transmission of Hepatitis B, WHO suggests implementing strategies focused on blood safety and promoting safer sex practices. This includes measures such as minimizing the number of sexual partners and adopting barrier protective measures like condoms.

According to a report by Sheena, B.S. *et al*. in 2022, interventions targeting Hepatitis B, including vaccination, testing, and treatment, must be strategically reinforced and expanded to achieve the goal of Hepatitis B elimination outlined in the UN Sustainable Development Goals for 2030. The global burden of hepatitis B is marked by significant disparities, and accordingly, Kenya's AIDS Strategic Plan II for 2022 also emphasizes the importance of screening, prevention, and treatment of viral hepatitis and sexually transmitted infections.

In 2019, WHO estimated that 296 million individuals were living with chronic hepatitis B infection, and there were approximately 1.5 million new infections reported each year. Tragically, hepatitis B led to an estimated 820,000 deaths in 2019, primarily attributed to cirrhosis and hepatocellular carcinoma, a form of primary liver cancer. Thankfully, the availability of safe and effective vaccines presents a crucial opportunity for preventing hepatitis B infections.

Review of related Literature

In a study conducted by Emerenini and Inyama in 2018 [2], they embarked on a mathematical depiction of the intricate processes involved in the transmission of HBV while taking into account various population subgroups. Their model also factored in the influence of HBV vaccination for newborns and the treatment of individuals already infected as measures to control transmission. The foundation of their study rested upon the conventional SEIR model. This research introduced a mathematical model that elucidated the effects of vaccination and treatment on the dynamics of HBV transmission. To capture the changing proportions within different classes of the population, five differential equations were employed. Their findings revealed that the equilibrium state devoid of individuals (Referred to as the trivial equilibrium state) was inherently unstable. Subsequently, the study determined the dynamics of the Disease-Free Equilibrium (DFE) state and conducted a rigorous stability analysis, employing the Routh-Hurwitz theorem for this purpose.

In a study conducted by Wodajo *et al* in 2022 [8], put forth a model outlining the dynamics of hepatitis B virus (HBV) infection, incorporating two pivotal controls: vaccination and treatment. Initially, the research delved into the system's dynamic behavior under constant control measures. In this context of constant controls, the authors embarked on an assessment of the effective reproduction number and meticulously examined the presence and stability of equilibria. Notably, two non-negative equilibria emerged from their analysis-the disease-free equilibrium, which consistently exists and exhibits local asymptotic stability, and the endemic equilibrium, also characterized by local asymptotic stability. Furthermore, the study explored the relationship between the effective reproduction number and the exposure rate concerning each intervention, as well as their combined impact when both vaccination and treatment interventions were considered. Their investigation unveiled that a reduction in the exposure rate corresponded to a decrease in the HBV disease's reproduction number, indicating an increase in the susceptible population. This underscored the potential effectiveness of educational campaigns in reducing the population's exposure to HBV disease. Moreover, their research involved a comparative analysis of the reproduction number, revealing that both vaccination and treatment interventions played crucial roles in diminishing the HBV disease's reproduction number in contrast to scenarios without any interventions. An index based on sensitivity parameters shed light on certain factors that exerted the most significant influence in either exacerbating or mitigating the endemicity of HBV. Conversely, some parameters were found to have the most substantial impact in reducing the prevalence of HBV within the population.

In their recent study, Wang *et al*. (2022) [5] devised a mathematical model for Hepatitis B virus (HBV) transmission that follows a susceptible-infectious-recovered (SIR) framework. Notably, they incorporated the impact of waning herd immunity into their model. To explore the model's behavior, they conducted simulations using MATLAB. Their investigation, employing both steady-state solutions and computer simulations, brought to light a noteworthy finding. A shorter duration of protection induced by vaccination led to a significant rise in the proportion of susceptible individuals. Specifically, the prevalence of susceptible increased from 15% when lifelong protection was assumed to a substantial 82.16% when protection lasted for only 20 years. This observation suggests that a larger susceptible population may consequently lead to a higher incidence of acute cases and the emergence of new chronic cases. Additionally, their analysis extended to examining the effects of booster shots on the number of newly infected individuals. This analysis indicated that implementing a booster shot strategy could potentially yield positive outcomes in terms of disease control and prevention.

In a study conducted by Zu *et al* in 2018, introduced an innovative approach aimed at forecasting the extended impact of augmenting the coverage of HBV treatment within a population. Beyond the established hepatitis B vaccination strategy, the adoption of a "test and treat" strategy emerged as a highly effective measure for managing hepatitis B in China. The study recommended that substantial endeavors should be devoted to expanding the reach of the "test and treat" approach among individuals afflicted with chronic hepatitis B. Moreover, their research yielded quantifiable insights and novel information that

hold the potential to enhance both preventive and therapeutic strategies concerning hepatitis B in China and similar high-endemic regions.

In Golgeli's 2019 study, a well-established mathematical model was employed to describe how hepatitis B transmission unfolds in Turkey. The focus was exclusively on the acute phase of the disease. The study revolved around assessing the equilibrium states in both the disease-free and endemic scenarios while also delving into the stability of the equilibrium concerning the disease's dynamics. The study involved estimating critical parameters like the transmission rate and the basic reproductive number (R0) of HBV using real-world data. Through numerical simulations and sensitivity analyses, the research aimed to provide insights into the potential future trends of HBV in Turkey. Interestingly, the findings suggested that HBV in Turkey tends to maintain stability in the disease-free state. Furthermore, an analysis of real data indicated a decrease in the seroprevalence of the disease between 2005 and 2011. The study underscored that alterations in demographic parameters can transition a disease-free state into an epidemic state. Consequently, the study emphasized the importance of focusing on factors influencing demography in Turkey as a means of controlling HBV. Likewise, this approach could open the door to more comprehensive analyses of HBV transmission dynamics in Turkey. These analyses might incorporate factors like age structure, both acute and chronic phases of the disease, time-dependent parameters, vaccination processes, and more. This is because the basic reproductive rate is inherently linked to the transmission rate, making these factors critical considerations in understanding HBV dynamics in Turkey.

The research conducted by James *et al* in 2022 [12] focused on modeling Hepatitis B Virus (HBV) transmission by integrating various factors such as vaccination, on-the-spot treatment, sanatorium stays, and immigration into an existing SEIR model. The primary goals of the study were to determine the equilibrium state of the model, analyze both its local and global stability, and perform numerical simulations to understand the disease dynamics. Their approach utilized a deterministic mathematical model that divided the population into seven distinct compartments, namely: Immunized M (t), Susceptible S (t), Latent L (t), Infectious I(t), Sanatorium S(t), Vaccinated V(t), and Recovered R(t). The interactions among these compartments were characterized through a set of differential equations. From an epidemiological perspective, their findings suggested that HBV would persist unless measures to control immigration of HBV-infected individuals were implemented. The local stability analysis of the disease-free equilibrium, in the absence of HBV-infected immigrants, indicated a reproductive number below one. This stability was evident through the coefficients of the polynomial characteristics meeting the Routh-Hurwitz criterion, establishing local asymptotic stability. Also, the research explored the global stability of the disease-free equilibrium in the model. This analysis revealed that the entries in the matrix for the infected compartment remained consistently positive, indicating the overall stability of the disease-free state. To assess the effectiveness of various control strategies, such as vaccination, sanatorium stays, or a combination of both, the researchers set baseline parameter values and employed MATLAB codes for numerical computations. The results underscored that even with relatively low vaccination rates, the infected population remained notably higher than other population groups. However, when the vaccination rate was increased to 0.9, a significant decline in the infected population was observed, demonstrating the potential impact of vaccination on HBV control.

Wodajo *et al*. (2022) [8] introduced and thoroughly examined a non-linear deterministic mathematical model named SVEIRE, designed to capture the transmission dynamics and control strategies for Hepatitis B virus (HBV) disease. In their model, they incorporated a force of infection that factored in the contact rate of the susceptible population and the probability of transmission. A significant contribution of their work was demonstrating that the solution to this dynamic system remains positive and bounded. To gain insights into the model's behavior, the researchers conducted a qualitative study employing the stability theory of differential equations. They derived the basic reproductive number, a crucial epidemic indicator, from the largest eigenvalue of the next-generation matrix. This analysis encompassed both local and global asymptotic stability conditions for both disease-free and endemic equilibrium states. The results of sensitivity analysis highlighted the effectiveness of bolstering vaccination rates for newborns and providing treatment for individuals with chronic infections in halting HBV transmission. Additionally, their research underscored the considerable role played by HBV re-infection in driving up the number of infected individuals. Ultimately, the study concluded that a combination of vaccination and treatment represents the most potent strategy for controlling Hepatitis B virus infection, offering valuable insights for public health efforts in this domain.

Research Gaps

Each of the cited studies on Hepatitis B transmission dynamics and control has made significant contributions to the field. However, they also exhibit certain gaps and limitations that the current study on hepatitis B transmission dynamics with passive immunity and clinical control interventions through mathematical modelling, analysis, and simulation can address. Many of the cited studies focused on specific aspects of Hepatitis B dynamics, such as vaccination or treatment, and may not consider the full range of factors influencing transmission. The current study appears to integrate both passive immunity and clinical control interventions, offering a more comprehensive approach. Some of the previous studies employ simplified models that may not fully capture the complexities of Hepatitis B transmission. The current study's use of a mathematical model seems promising in providing a more nuanced understanding.

Some studies rely on hypothetical scenarios and may lack empirical data for validation. The current study's emphasis on numerical simulation and sensitivity analysis suggests a potential for using real-world data to inform the model. Several of the cited studies are geographically specific, which may limit the generalizability of their findings. The current study's focus on the broader topic of passive immunity and clinical control interventions suggests an opportunity to provide insights that are more universally applicable. Previous studies often neglect the role of passive immunity in Hepatitis B transmission dynamics, focusing primarily on vaccination and treatment. The current study explicitly incorporates passive immunity, addressing this gap in the existing literature. Some studies do not thoroughly consider demographic factors and population heterogeneity. The current study's mathematical modeling approach could potentially account for these aspects, leading to a more realistic representation. While previous studies discuss control strategies, they may not perform comprehensive analyses of the potential impacts of these strategies. The current study aims to provide a thorough evaluation of the effects of both passive immunity and clinical interventions, which can fill this gap. Previous research may not fully explore the policy implications of their findings for public

health interventions. The current study, through its modeling and analysis, may provide more concrete recommendations for policymakers.

In summary, while the cited studies have significantly contributed to understanding Hepatitis B transmission dynamics, they exhibit gaps related to scope, model complexity, data utilization, geographical specificity, and the consideration of passive immunity. The current study, with its focus on mathematical modeling, analysis, and simulation, has the potential to address these gaps by providing a more comprehensive and data-informed exploration of Hepatitis B transmission dynamics and control strategies. However, it's apparent that previous studies did not account for passive immunity and screening, nor did they consider demographic factors like birth and death rates. Moreover, these studies often overlooked the distinction between the acute and chronic phases of Hepatitis B. In line with the ambition of achieving the UN SDGs target of eliminating viral Hepatitis B by 2030, this research comprehensively incorporates these influential factors, along with a combination of intervention strategies. This study's primary objective is to develop and analyze a mathematical model of HBV transmission, encompassing a passive immunity component, screening, as well as vaccination and treatment control measures as recommended by Lancet in 2022. Our aim is to gain insights into how passive immunity and screening impact the basic reproduction number, identify equilibrium points, assess their stability, and conduct simulations utilizing published data. Enhancing our understanding of HBV infection prevalence and dynamics among marginalized populations will enable the government to devise more effective strategies for controlling and ultimately eradicating the infection. Moreover, the findings from this model will inform clinical care and the management of Hepatitis B infection, particularly among vulnerable population groups.

This paper is structured as follows; in Section 2, we formulate and establish the basic properties of the model. The model is analyzed in Section 3. In Section 4, we carry out some numerical simulations. Parameter estimation and numerical results are also presented in this section. The paper is concluded in Section 5.

Hepatitis B Model formulation

The model was constructed by compartmentalizing the epidemiological population based on an individual's state of HBV infection. The total human population, denoted as N, was divided into several categories, including susceptible (S), vaccinated (V), exposed (E), acute (A), chronic (C), treated (T), passively immune (M), and recovered (R). Specifically; Susceptible (S) represented individuals not infected but at risk of HBV infection. Exposed (E) encompassed individuals who had been infected but were not yet infectious. Acute Hepatitis B (AHB) referred to individuals in the initial, highly infectious stage of HBV infection. Chronic Hepatitis B (CHB) included individuals with chronic HBV infection, who could be infectious or non-infectious to others. Passively immune denoted infants who acquired immunity from their mothers. This approach considered that acquired immunity might wane over time, whereas immunity resulting from vaccination persisted throughout an individual's lifetime. The assumptions underlying the model were as follows:

A1: An open community with vital dynamics including the births and death rates.

A2: The population is homogeneously mixed for effective transmission of HBV infection to occur, that is, there is free interaction within the population in the compartments.

A3: Horizontal and vertical HBV transmission occurs from mother to child or through sexual contacts.

A4: All new born infants acquire passive immunity from their mothers hence they are at risk of Hepatitis B

A5: Individuals with acute and chronic HBV infection recover through treatment, that is, all recovered individuals acquire permanent immunity and subjected to treatment through serological screening/testing.

A6: Hepatitis induced death is due to fulminant hepatitis.

A7: Hep B vaccination and treatment is 100% effective. Thus, vaccinated and treated individuals do not transmit the infection.

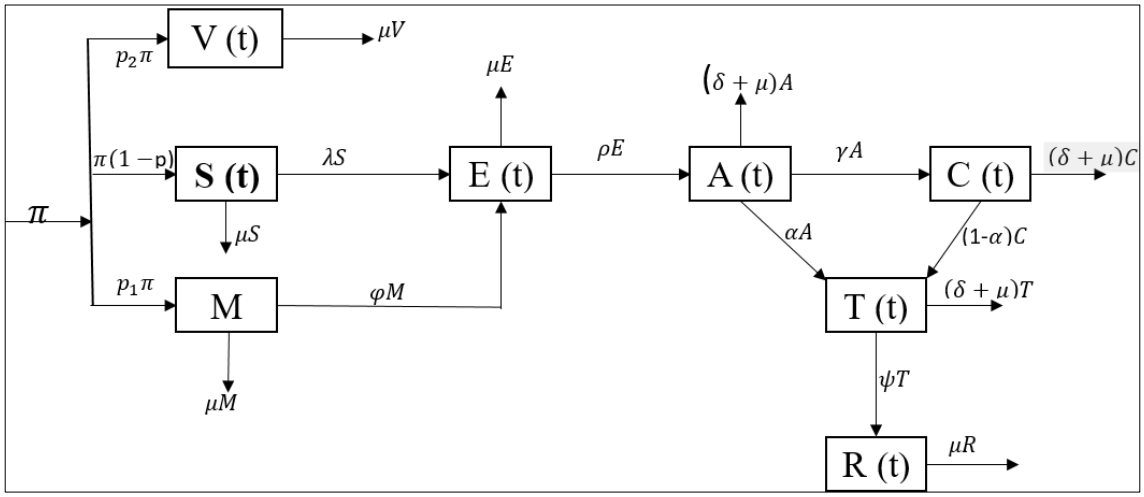

Fig 1: A flowchart of HBV model incorporating passive immunity, screening, and vaccination and treatment compartments.

Based on the stated model assumptions, the model is governed by the following non-linear ordinary differential equations deduced from each of the compartments

$$\left.\begin{aligned} \frac{dM}{dt} &= \pi p_1 - (\varphi + \mu)M \\ \frac{dV}{dt} &= \pi p_2 - \mu V \\ \frac{dS}{dt} &= \pi(1-P) - (\mu + \lambda)S \\ \frac{dE}{dt} &= (\mu + \lambda)S + \varphi M - (\mu + \rho)E \\ \frac{dA}{dt} &= \rho E - (\alpha + \gamma + \delta + \mu)A \\ \frac{dC}{dt} &= \gamma A - (1 - \alpha + \delta + \mu)C \\ \frac{dT}{dt} &= \alpha A + (1-\alpha)C - (\psi + \delta + \mu)T \\ \frac{dR}{dt} &= \psi T - \mu R \end{aligned}\right\} \quad (1)$$

Where $\lambda = \beta (E + \eta_1 A + \eta_2 C)$ with $\eta_2 > \eta_1$, $P = p_1 + p_2$

$$N(t) = M(t) + V(t) + S(t) + E(t) + A(t) + C(t) + T(t) + R(t) \quad (2)$$

Model analysis and findings

Positivity of solutions

The model deals with human population and so the solution to the differential equations (1) is non-negative for all time, $t \geq 0$. This is a crucial requirement for the model to be mathematically acceptable and biologically significant. Differential and integral calculus techniques are applied for the analysis. The following theorem is proposed to proof the positivity of model solutions.

Theorem 1: Let $M(0) \geq 0, V(0) \geq 0, S(0) \geq 0, E(0) \geq 0, A(0) \geq 0, C(0) \geq 0, T(0) \geq 0, R(0) \geq 0$ be the solution to the system of equations (1)

Proof

From model equations (1) $\frac{dM}{dt} = \pi p_1 - (\varphi + \mu)M$ since $\pi p_1 \geq 0$, by comparison theorem, we have

$$\frac{dM}{dt} \geq -(\varphi + \mu)M$$

By separation of variables, we have

$$\frac{dM}{M} \geq -(\varphi + \mu)dt$$

Integrating both sides w.r.t t, we get

$$lnM(t) \geq -(\varphi + \mu)t + h$$

$$M(t) \geq K\, exp\,(-(\varphi + \mu)t)$$

At $t = 0, K = M_0$, thus $M(t) \geq M_0 exp\,(-(\varphi + \mu)t)$

As $t \to \infty, M(t) \geq M_0 exp\,(-(\varphi + \mu)t) \geq 0$,

Hence M (t) stays positive for $t \geq 0$. By the same procedure and technique, it follows that

$$V(t) \geq V_0 \exp(-\mu t) \geq 0, S(t) \geq S_0 exp(-(\mu + \lambda)\, t) \geq 0, E(t) \geq E_0 exp(-(\mu + \rho)t) \geq 0,$$

$$A(t) \geq A_0 \exp(-(\alpha + \gamma + \delta + \mu)\, t) \geq 0, C(t) \geq C_0\, exp\,(-(1 - \alpha + \delta + \mu)t) \geq 0,$$

$$T(t) \geq T_0\, exp\,(-(\psi + \delta + \mu)\, t) \geq 0, \text{ and } R(t) \geq R_0 exp\,(-\mu\, t) \geq 0.$$ Thus S (t), V (t)

E (t), A(t), C(t),T(t) and R(t) also stays positive for all time $t \geq 0$.

Feasible region and boundedness of the solutions

This is the region of convergence to the solution of the system. The solution stays within this region throughout, that is, positively invariant. This is done by the time derivative of the total population, N. This is to say that the solution is bounded within the feasible region.

Theorem 2: The region $\Omega = \{ M(t), V(t), S(t), E(t), A(t), C(t), T(t), R(t) \in \mathbb{R}^7_+ | M(0) \geq 0, S(0) \geq 0, E(0) \geq 0, A(0) \geq 0, C(0) \geq 0, T(0) \geq 0, R(0) \geq 0, N(t) \leq N_0 \}$ is positively invariant and attracting the solutions to the system of equations (1)

Proof

We consider equation (2), $N(t) = M(t) + V(t) + S(t) + E(t) + A(t) + C(t) + T(t) + R(t)$

Taking the time derivative on both sides yields

$$\frac{dN}{dt} = \frac{dM}{dt} + \frac{dV}{dt} + \frac{dS}{dt} + \frac{dE}{dt} + \frac{dA}{dt} + \frac{dC}{dt} + \frac{dT}{dt} + \frac{dR}{dt} \tag{3}$$

Substituting for the time derivatives of M, V, S, E, A, C, T and R, we have

$$\frac{dN}{dt} = (\pi p_1 - (\varphi + \mu)M) + (\pi p_2 - \mu V) + (\pi(1 - P) - (\mu + \lambda)S) + \big((\mu + \lambda)S + \varphi M - (\mu + \rho)E\big) + (\rho E - (\alpha + \gamma + \delta + \mu)A) + (\gamma A - (1 - \alpha + \delta + \mu)C) + (\alpha A + (1 - \alpha)C - \psi T - (\delta + \mu)T) + (\psi T - \mu R) \tag{4}$$

Expanding and simplifying, we obtain

$$\frac{dN}{dt} = \pi - \delta(A + C + T) - \mu(S + A + E + C + M + R + T + V) \tag{5}$$

If there are no infectious humans $\delta = 0$, thus by comparison theorem equation (5) reduces to

$$\frac{dN}{dt} \leq \pi - \mu N \tag{6}$$

Integrating equation (6) as $t \to \infty$ yields

$$\lim_{t\to\infty} N(t) \leq \frac{\pi}{\mu} \tag{7}$$

This proves the boundedness of the solutions inside $\mathbb{R}$. This implies that all solutions of the system equations (1) starting in $\mathbb{R}$ remain in $\mathbb{R}$ for all time. Thus $\mathbb{R}$ is positively invariant and attracting and hence it is sufficient to consider the dynamics of our system in$\mathbb{R}$.

Equilibrium points and reproduction number

Hepatitis B infection free equilibrium point

This is the solution to the system of equation (1) in which HBV infection is not present in the population and the entire population is susceptible. The HBV infection-free equilibrium point (IFE) of the system (1) is gotten by setting the RHS of system (1) to zero and evaluated at infectious classes at zero. We let the IFEP as $H^0 = (M^0, V^0, S^0, E^0, A^0, C^0, T^0, R^0)$.Setting the RHS of the system (1) we have

$$\left.\begin{array}{c} \pi p_1 - (\varphi + \mu)M^0 = 0 \\ \pi p_2 - \mu V^0 = 0 \\ \pi(1 - P) - (\mu + \lambda)S^0 = 0 \\ (\mu + \lambda)S^0 + \varphi M^0 - (\mu + \rho)E^0 = 0 \\ \rho E^0 - (\alpha + \gamma + \delta + \mu)A^0 = 0 \\ \gamma A^0 - (1 - \alpha + \delta + \mu)C^0 = 0 \\ \alpha A^0 + (1 - \alpha)C^0 - (\psi + \delta + \mu)T^0 = 0 \\ \psi T^0 - \mu R^0 = 0 \end{array}\right\} \tag{8}$$

Solving (8) gives $M^0 = \frac{\pi p_1}{\varphi+\mu}, V^0 = \frac{\pi p_2}{\mu}, S^0 = \frac{\pi(1-P)}{\mu}$. Thus, $H^0 = (\frac{\pi p_1}{\varphi+\mu}, \frac{\pi p_2}{\mu}, \frac{\pi(1-P)}{\mu}, 0,0,0,0,0)$

Control Reproduction number

This parameter represents the number of secondary infections generated by a single infectious Hepatitis B host individual during its infectious lifespan when control measures are in place, and the population is entirely susceptible to the infection. In most epidemiological models, it is traditionally denoted as R_0. To calculate this reproduction number, we utilize the Next-Generation Matrix (NGM) approach, which was initially introduced by Diekmann and Heesterbeek in 1990. R_0 is essentially defined as the spectral radius of the Next-generation matrix, where the NGM is a matrix that quantifies the number of newly infected individuals across different categories in successive generations. R_0 serves as a critical metric for determining whether the infection will persist or die out within a population. Several techniques can be employed to compute the NGM, and in this study, we follow the Van den Driessche and Watmough technique. This method involves a series of fundamental steps: Identifying the infectious compartments (E, A, and C), Deriving matrices for new infections (represented as 'f') and the transfer of infections (represented as 'g'), Calculating the Jacobian matrices of 'f' and 'g,' denoted as 'F' and 'G,' respectively, evaluated at the Infectious-Free Equilibrium Point (IFEP), Obtaining the inverse of matrix 'G' as 'G^(-1).' Finally, computing the NGM as the product of FG^(-1) and determining R_0 as ρ(FG^(-1)), where ρ(A) signifies the spectral radius of matrix 'A.' The spectral radius of a matrix is defined as the maximum absolute value among its eigenvalues.

By following these procedures, we derive the matrices for new infections and the transfer of infections from the E, A, and C compartments.

$$f = \begin{bmatrix} \lambda S \\ 0 \\ 0 \end{bmatrix} \text{ and } g = \begin{pmatrix} (\mu+\rho)E - \varphi \mathrm{M} \\ (\alpha+\gamma+\delta+\mu)A - \rho E \\ (1-\alpha+\ \delta\ +\ \mu\ )\mathrm{C} - \gamma A \end{pmatrix} \quad (9)$$

The Jacobian matrices F and G are obtained as the partial derivatives of f and g w.r.t to E, A and C evaluated at H^0

$$F = \begin{pmatrix} \beta S^0 & \beta\eta_1 S^0 & \beta\eta_2 S^0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \text{ and } G = \begin{pmatrix} \mu+\rho & 0 & 0 \\ -\rho & \alpha+\gamma+\delta+\mu & 0 \\ 0 & -\gamma & 1-\alpha+\ \delta\ +\ \mu \end{pmatrix} \quad (10)$$

The inverse of G is obtained as $G^{-1} = \begin{pmatrix} \frac{1}{\mu+\rho} & 0 & 0 \\ \frac{\rho}{(\alpha+\gamma+\delta+\mu)(\mu+\rho)} & \frac{1}{\alpha+\gamma+\delta+\mu} & 0 \\ \frac{\gamma\rho}{(1-\alpha+\delta+\mu)(\alpha+\gamma+\delta+\mu)(\mu+\rho)} & \frac{\gamma\mu+\gamma\rho}{(1-\alpha+\delta+\mu)(\alpha+\gamma+\delta+\mu)(\mu+\rho)} & \frac{1}{1-\alpha+\delta+\mu} \end{pmatrix}$ (11)

The NGM matrix is the product of $FG^{-1} = \begin{pmatrix} \frac{\pi\beta(1-\mathrm{P})}{\mu(\mu+\rho)} + \frac{\pi\beta\rho(1-\mathrm{P})\eta_1}{\mu(\alpha+\gamma+\delta+\mu)(\mu+\rho)} + \frac{\pi\beta\gamma\rho(1-\mathrm{P})\eta_2}{\mu(1-\alpha+\delta+\mu)(\alpha+\gamma+\delta+\mu)(\mu+\rho)} & \frac{\pi\beta(1-\mathrm{P})\eta_1}{\mu(\alpha+\gamma+\delta+\mu)} + \frac{\pi\beta(\gamma\mu+\gamma\rho)(1-\mathrm{P})\eta_2}{\mu(1-\alpha+\delta+\mu)(\alpha+\gamma+\delta+\mu)(\mu+\rho)} & \frac{\pi\beta(1-\mathrm{P})\eta_2}{\mu(1-\alpha+\delta+\mu)} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$ (12)

The characteristic polynomial of $|FG^{-1} - \lambda I| = 0$ is given by $\lambda^3 + b\lambda^2 + c\lambda + d = 0$, where a, b, c and d are constants. Thus, the eigenvalues of NGM are obtained as $\left\{0,0, \frac{\pi\beta(1-P)((1-\alpha+\delta+\mu)(\alpha+\gamma+\delta+\mu+\rho\eta_1)+\gamma\rho\eta_2)}{2\mu(1-\alpha+\delta+\mu)(\alpha+\gamma+\delta+\mu)(\mu+\rho)}\right\}$. R_0 is obtained as the dominant eigenvalue of the NGM $\rho(FG^{-1})$ given as

$$R_c = \frac{\pi\beta(1-P)((1-\alpha+\delta+\mu)(\alpha+\gamma+\delta+\mu+\rho\eta_1)+\gamma\rho\eta_2)}{2\mu(1-\alpha+\delta+\mu)(\alpha+\gamma+\delta+\mu)(\mu+\rho)} \quad (13)$$

The strength number, A_0

This parameter serves as an extension of R_0, yet it continues to be a parameter of future significance. Its purpose is to gauge the complexity of infection spread or pinpoint patterns of waves in a spreading process. The Next-Generation Matrix (NGM) is still employed to estimate the strength number, but in this context, we calculate the second derivative of the contagious classes, as discussed by Atangana and İğret Araz in 2021. The second derivatives of the contagious classes, determined using the mass incidence principle, are as follows:

$$\frac{\partial^2}{\partial E^2}\left(\beta S\frac{E}{N}\right), \frac{\partial^2}{\partial A^2}\left(\beta S\frac{A}{N}\right) \text{ and } \frac{\partial^2}{\partial C^2}\left(\beta S\frac{C}{N}\right) \quad (14)$$

The Jacobian of matrix of new infections and transfer of infections of the second derivative of the infectious classes

$$F_A = \begin{pmatrix} -\frac{\beta S}{N^2} & -\frac{\beta\eta_1 S}{N^2} & -\frac{\beta\eta_2 S}{N^2} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \text{ and}$$

$$G_A{}^{-1} = \begin{pmatrix} \frac{1}{\mu+\rho} & 0 & 0 \\ \frac{\rho}{(\alpha+\gamma+\delta+\mu)(\mu+\rho)} & \frac{1}{\alpha+\gamma+\delta+\mu} & 0 \\ \frac{\gamma\rho}{(1-\alpha+\delta+\mu)(\alpha+\gamma+\delta+\mu)(\mu+\rho)} & \frac{\gamma\mu+\gamma\rho}{(1-\alpha+\delta+\mu)(\alpha+\gamma+\delta+\mu)(\mu+\rho)} & \frac{1}{1-\alpha+\delta+\mu} \end{pmatrix} \quad (15)$$

The det $\left|F_A V_A{}^{-1} - \lambda I\right| = 0$, gives the strength number as $A_0 = -\frac{\mathrm{R}_C}{N^2} < 0$ (16)

Estimation of basic reproduction number by survival function

The survival function determines the number of new infections caused by an initial case using the following three components; (i) the rate at which an individual in a particular class causes new infections, $k_t b_t$ (ii) the probability, P that an individual is still in the class at time t, (iii) the probability that an initial case will enter that class. Thus, the basic reproduction number based on this approach is defined by the integral of the product of the first two terms multiplied by the third term derived from the contagious classes as follows

$R_{0,S} = \int_0^\infty k_t b_t P_t\, dt$ (Li, J., & Blakeley, D., 2011) [13] (17)

Applying this method (17) and casting to all the infectious classes we have

$$R_{0,S} = \beta S^0 \int_0^\infty e^{-(\mu+\rho)t} dt + \beta S^0 \int_0^\infty e^{-(\alpha+\gamma+\delta+\mu)t}\, dt + \beta S^0 \int_0^\infty e^{-(1-\alpha+\delta+\mu)}\, dt \quad (18)$$

Integrating (18) yields, $R_{0,S} = \beta S^0 \left(\frac{1}{\mu+\rho} + \frac{1}{\alpha+\gamma+\delta+\mu} + \frac{1}{1-\alpha+\delta+\mu}\right)$ (19)

Substituting for S^0 in (19), we get

$$R_{0,S} = \frac{\pi\beta(1-\mathrm{P})\left((\mu+\rho)(\alpha+\gamma+\delta+\mu)+(\mu+\rho)(1-\alpha+\delta+\mu)+(\alpha+\gamma+\delta+\mu)(1-\alpha+\delta+\mu)\right)}{\mu(\mu+\rho)(1-\alpha+\delta+\mu)(\alpha+\gamma+\delta+\mu)} \quad (20)$$

This method gives the correct value for the basic reproduction number as compared to the Next Generation matrix method.

Stability analysis of IFE point of HBV model

Local stability of IFE point

This is the stability of system of equations (1) around or within the neighborhood of the infection free equilibrium point. We use Jury's stability test to establish the local stability of H^0.

Theorem 3: An IFE point of the system of equations (1) is locally asymptotically stable if it all satisfies the following Jury's stability conditions for $P(z) = a_1 z^n + a_2 z^{n-1} + a_3 z^{n-2} + \cdots \ldots + a_n z^0$, and whenever ${R_C}^* < 1$.

1. $|a_0| < a_1$
2. $P(z = 1) > 0$
3. For even order, $P(z = -1) > 0$ and for odd order $P(z = -1) < 0$
4. $|b_{n-1}| > |b_0|$ For all elements in the subsequent rows of the Jury's array.

The above theorem is proved as follows

We linearize the system of equations (1) by letting

$f_1\,(M,V,S,E,A,C,T,R) = \pi p_1 - (\varphi+\mu)M$

$f_2\,(M,V,S,E,A,C,T,R) = \pi p_2 - \mu V$

$f_3\,(M,V,S,E,A,C,T,R) = \pi(1-\mathrm{P}) - (\mu+\lambda)\mathrm{S}$

$f_4\,(M,V,S,E,A,C,T,R) = (\mu+\lambda)\mathrm{S} + \varphi\mathrm{M} - (\mu+\rho)\mathrm{E}$

$f_5\,(M,V,S,E,A,C,T,R) = \rho\mathrm{E} - (\alpha+\gamma+\delta+\mu)\mathrm{A}$

$f_6\,(M,V,S,E,A,C,T,R) = \gamma\mathrm{A} - (1-\alpha+\delta+\mu)\mathrm{C}$

$f_7(M,V,S,E,A,C,T,R) = \alpha\mathrm{A} + (1-\alpha)\mathrm{C} - (\psi+\delta+\mu)\mathrm{T}$

$f_8\,(M,V,S,E,A,C,T,R) = \psi T - \mu R$

The corresponding Jacobian matrix J of $f_1 - f_8$ is as follows

$$J(E^0) = \begin{pmatrix} -(\varphi+\mu) & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & -\mu & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -\mu & -\beta S^0 & -\beta\eta_1 S^0 & -\beta\eta_2 S^0 & 0 & 0 \\ \varphi & 0 & 0 & \beta S^0 - \mu - \rho & -\beta\eta_1 S^0 & -\beta\eta_2 S^0 & 0 & 0 \\ 0 & 0 & 0 & \rho & -(\alpha+\gamma+\delta+\mu) & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \gamma & -(1-\alpha+\delta+\mu) & 0 & 0 \\ 0 & 0 & 0 & 0 & \alpha & 1-\alpha & -(\psi+\delta+\mu) & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \psi & -\mu \end{pmatrix} \quad (21)$$

Reducing $J(E^0)$ by Gauss elimination method by the following row operations, we get

$R_4 \to \varphi R_1 + (\varphi+\mu)R_4$

$R_2 \to \rho R1 - (\varphi+\mu)(\beta S^0 - \mu - \rho)R_2$

$R_2 \to \gamma R_1 - \left(-\beta\rho\eta_1 S^0(\varphi+\mu) + (\varphi+\mu)(\beta S^0 - \mu - \rho)(\alpha+\gamma+\delta+\mu)\right)R_2$

$R_3 \to \alpha R_1 - \left(-\beta\rho\eta_1 S^0(\varphi+\mu) + (\varphi+\mu)(\beta S^0 - \mu - \rho)(\alpha+\gamma+\delta+\mu)\right)R_3$

$$\begin{pmatrix} -\beta\gamma\rho\eta_2 S^0(\varphi+\mu)+\left(-\beta\rho\eta_1 S^0(\varphi+\mu)+(\varphi+\mu)(\beta S^0-\mu-\rho)(\alpha+\gamma+\delta+\mu)\right)(1-\alpha+\delta+\mu) & 0 & 0 \\ -\beta\alpha\rho\eta_2 S^0(\varphi+\mu)-\left(-\beta\rho\eta_1 S^0(\varphi+\mu)+(\varphi+\mu)(\beta S^0-\mu-\rho)(\alpha+\gamma+\delta+\mu)\right)(1-\alpha) & (\psi+\delta+\mu)\left(-\beta\rho\eta_1 S^0(\varphi+\mu)+(\varphi+\mu)(\beta S^0-\mu-\rho)(\alpha+\gamma+\delta+\mu)\right) & 0 \\ 0 & \psi & -\mu \end{pmatrix} \quad (22)$$

By subsequent row reduction and inspection, the eigenvalues of the reduced $J(E^0)$ are obtained as $-(\varphi+\mu)$, $-\mu$, $(\varphi+\mu)\left(\frac{\pi\beta(1-P)}{\mu}-\mu-\rho\right)$, $-\frac{\pi\beta\rho\eta_1(1-P)}{\mu}(\varphi+\mu)+(\varphi+\mu)\left(\frac{\pi\beta(1-P)}{\mu}-\mu-\rho\right)(\alpha+\gamma+\delta+\mu)$ and the corresponding characteristic polynomial of $|J(E^0)-zG|=0$ is of order 3, where G is an identity matrix and z is a scalar expressed as

$$P(z)=a_1 z^3+a_2 z^2+a_3 z+a_0, \quad (23)$$

where a_1, a_2, a_3 and a_0 are obtained as follows;

$a_1 = -8 < 0$

$a_2 = -4\mu + 4\alpha\beta S\mu - 4\alpha^2\beta S\mu + 4\beta S\gamma\mu - 4\alpha\beta S\gamma\mu + 4\beta S\delta\mu + 4\alpha\beta S\delta\mu + 8\beta S\gamma\delta\mu + 8\beta S\delta^2\mu - 4\alpha\mu^2 + 4z^2\alpha^2\mu^2 + 4\beta S\mu^2 + 4\alpha\beta S\mu^2 - 4\gamma\mu^2 + 4\alpha\gamma\mu^2 + 8\beta S\gamma\mu^2 - 4\delta\mu^2 - 4\alpha\delta\mu^2 + 16\beta S\delta\mu^2 - 8\gamma\delta\mu^2$

$a_3 = 2(\alpha\beta S\mu^2 - \alpha^2\beta S\mu^2 + \beta S\gamma\mu^2 - \alpha\beta S\gamma\mu^2 + \beta S\delta\mu^2 + \alpha\beta S\delta\mu^2 - \alpha^2\beta S^2\delta\mu^2 + \alpha^3\beta S^2\delta\mu^2 + 2\beta S\gamma\delta\mu^2 - 2\alpha\beta S^2\gamma\delta\mu^2 + 2\alpha^2\beta S^2\gamma\delta\mu^2 - \beta S^2\gamma^2\delta\mu^2 + \alpha\beta S^2\gamma^2\delta\mu^2 + 2\beta S\delta^2\mu^2 - 2\alpha\beta S^2\delta^2\mu^2 + 2S^2\alpha\mu\varphi\psi\beta\gamma\rho\eta_1\beta\rho\eta_1 - 2S^2\delta\mu\varphi\psi\beta\gamma\rho\eta_1\beta\rho\eta_1 - 2S^2\mu^2\varphi\psi\beta\gamma\rho\eta_1\beta\rho\eta_1 - S^2\varphi^2\psi\beta\gamma\rho\eta_1\beta\rho\eta_1 + S^2\alpha\varphi^2\psi\beta\gamma\rho\eta_1\beta\rho\eta_1 - S^2\delta\varphi^2\psi\beta\gamma\rho\eta_1\beta\rho\eta_1 - S^2\mu\varphi^2\psi\beta\gamma\rho\eta_1\beta\rho\eta_1 - S^2\delta\mu^2\beta\gamma\rho\eta_2\beta\rho\eta_1 - S^2\mu^3\beta\gamma\rho\eta_2\beta\rho\eta_1 - 2S^2\delta\mu\varphi\beta\gamma\rho\eta_2\beta\rho\eta_1 - 2S^2\mu^2\varphi\beta\gamma\rho\eta_2\beta\rho\eta_1 - S^2\delta\varphi^2\beta\gamma\rho\eta_2\beta\rho\eta_1 - S^2\mu\varphi^2\beta\gamma\rho\eta_2\beta\rho\eta_1 - S^2\mu^2\psi\beta\gamma\rho\eta_2\beta\rho\eta_1 - 2S^2\mu\varphi\psi\beta\gamma\rho\eta_2\beta\rho\eta_1 - S^2\varphi^2\psi\beta\gamma\rho\eta_2\beta\rho\eta_1)$

$a_0 = S^2\alpha\mu\varphi^2\psi\beta\gamma\rho\eta_1\beta\rho\eta_1 + 2S^2\alpha\mu^2\varphi\psi\beta\gamma\rho\eta_1\beta\rho\eta_1 - 2S^2\mu^2\varphi\psi\beta\gamma\rho\eta_1\beta\rho\eta_1 - 2S^2\delta\mu^2\varphi\psi\beta\gamma\rho\eta_1\beta\rho\eta_1 - 2S^2\mu^3\varphi\psi\beta\gamma\rho\eta_1\beta\rho\eta_1 - S^2\mu\varphi^2\psi\beta\gamma\rho\eta_1\beta\rho\eta_1 - S^2\delta\mu\varphi^2\psi\beta\gamma\rho\eta_1\beta\rho\eta_1 - S^2\mu^2\varphi^2\psi\beta\gamma\rho\eta_1\beta\rho\eta_1 - S^2\delta\mu^3\beta\gamma\rho\eta_2\beta\rho\eta_1 - S^2\mu^4\beta\gamma\rho\eta_2\beta\rho\eta_1 - 2S^2\delta\mu^2\varphi\beta\gamma\rho\eta_2\beta\rho\eta_1 - 2S^2\mu^3\varphi\beta\gamma\rho\eta_2\beta\rho\eta_1 - S^2\delta\mu\varphi^2\beta\gamma\rho\eta_2\beta\rho\eta_1 - S^2\mu^2\varphi^2\beta\gamma\rho\eta_2\beta\rho\eta_1 - S^2\mu^3\psi\beta\gamma\rho\eta_2\beta\rho\eta_1 - 2S^2\mu^2\varphi\psi\beta\gamma\rho\eta_2\beta\rho\eta_1 - S^2\mu\varphi^2\psi\beta\gamma\rho\eta_2\beta\rho\eta_1$

Due to symbolic representation of the polynomial and its coefficients, numerical method is used to confirm the necessary and sufficient conditions for Jury's stability. If the Jury's condition are satisfied, then IFE point is locally asymptotically stable, an implication that the infection does not exist in the population otherwise unstable.

Global stability of IFE point

For global stability, the system will shift everywhere, if a small perturbation is introduced within the neighborhood of the equilibrium point. The Castillo-Chavez method (C.Castillo-Chavez, F. Zhilan and H. Wenzhan., 2002) [3] is applied to assess the global stability of H^0. According to this method, the conditions that must be met in order for the system to be globally asymptotically stable are;

C1: $\frac{dX}{dt} = F(X^*, 0)$, X^* is globally asymptotically stable

C2: $G(X,Z) = AZ - \hat{G}(X,Z)$, $\hat{G}(X,Z) \geq 0$ for $(X,Z) \in \Omega$, where $A = D_z G(X^*, Z)$ is a Metzler matrix.

Theorem 4: An IFE point H^0 is globally asymptotically stable if it satisfies the conditions C1 and C2 whenever ${R_C}^* < 1$

Proof

We write the reduced system as

$\frac{dX}{dt} = F(X,Z)$ and $\frac{dZ}{dt} = G(X,Z)$, where the components of X represent the number of susceptible, vaccinated, treated, Passively immune and recovered individuals who are non-infectious, that is $X = \{M, V, S, T, R\}$ and the components of Z denote the number of exposed, acute and chronic HBV infected individuals capable of transmitting the infection given as, $Z = \{E, A, C\}$

In our case,

$$(X,0) = F(M,V,S,0,0) = \begin{pmatrix} \pi p_1 - (\varphi+\mu)M \\ \pi p_2 - \mu V \\ \pi(1-P) - \mu S \\ 0 \\ 0 \end{pmatrix}, \quad (24)$$

$$D_X F(X,0) = \begin{pmatrix} -(\varphi+\mu) & 0 & 0 & 0 & 0 \\ 0 & -\mu & 0 & 0 & 0 \\ 0 & 0 & -\mu & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix} \quad (25)$$

From the above matrix it is clear that the eigenvalues are all negative, thus H^0 is globally asymptotically stable. Thus, Condition C1 satisfied.

$$G(X,Z) = \begin{pmatrix} (\mu+\lambda)S + \varphi M - (\mu+\rho)E \\ \rho E - (\alpha+\gamma+\delta+\mu)A \\ \gamma A - (1-\alpha+\delta+\mu)C \end{pmatrix} \tag{26}$$

The Metzler Matrix A is obtained as

$$A = D_Z G(X,Z) = \begin{pmatrix} \beta S^0 - (\mu+\rho) & \beta\eta_1 S^0 & \beta\eta_2 S^0 \\ \rho & -(\alpha+\gamma+\delta+\mu) & 0 \\ 0 & \gamma & -(1-\alpha+\delta+\mu) \end{pmatrix} \tag{27}$$

$$AZ = \begin{pmatrix} \beta S^0 & \beta\eta_1 S^0 & \beta\eta_2 S^0 \\ \rho & -(\alpha+\gamma+\delta+\mu) & 0 \\ 0 & \gamma & -(1-\alpha+\delta+\mu) \end{pmatrix} \begin{pmatrix} E \\ A \\ C \end{pmatrix} = \begin{pmatrix} \beta S^0 E + \beta\eta_1 S^0 A + \beta\eta_2 S^0 C \\ \rho E - (\alpha+\gamma+\delta+\mu)A \\ \gamma A - (1-\alpha+\delta+\mu)C \end{pmatrix} \tag{28}$$

But

$$\hat{G}(X,Z) = AZ - G(X,Z) = \begin{pmatrix} \beta S^0 E + \beta\eta_1 S^0 A + \beta\eta_2 S^0 C \\ \rho E - (\alpha+\gamma+\delta+\mu)A \\ \gamma A - (1-\alpha+\delta+\mu)C \end{pmatrix} - \begin{pmatrix} (\mu+\lambda)S + \varphi M - (\mu+\rho)E \\ \rho E - (\alpha+\gamma+\delta+\mu)A \\ \gamma A - (1-\alpha+\delta+\mu)C \end{pmatrix} \tag{29}$$

$$\begin{pmatrix} \hat{G}_1(X,Z) \\ \hat{G}_2(X,Z) \\ \hat{G}_3(X,Z) \end{pmatrix} = \begin{pmatrix} \beta(E+\eta_1 A+\eta_2 C)(S^0 - S) - \mu S - \varphi M + (\mu+\rho)E \\ 0 \\ 0 \end{pmatrix} \tag{30}$$

Thus, if $\hat{G}(X,Z) \geq 0$ then the IFE point H0 is globally asymptotically stable otherwise unstable. Since the number of susceptible is bounded, then$S \leq S^0$. Hence $\hat{G}(X,Z) \geq 0$, implying that IFE point is globally asymptotically stable when ${R_C}^* < 1$.Condition 2 is also satisfied. Hence the prove of the theorem.

Existence of HBV Endemic equilibrium point

An endemic equilibrium point is the solution to the system of equations (1) in which HBV infection is present in the population. The solution starts in the given interval and stay in the interval for all time. We set the RHS of system of equations (1) to zero and the infectious compartments are non-zero and we denote $H^* = (M^*, V^*, S^*, E^*, A^*, C^*, T^*, R^*)$ as the endemic equilibrium point of the system of equations (1),

$$\left.\begin{aligned} \frac{dM}{dt} &= \pi p_1 - w_1 M \\ \frac{dV}{dt} &= \pi p_2 - \mu V^* \\ \frac{dS}{dt} &= \pi(1-\mathrm{P}) - (\mu+\lambda)\mathrm{S}^* \\ \frac{dE}{dt} &= (\mu+\lambda)\mathrm{S}^* + \varphi M^* - \mathrm{w}_2\mathrm{E}^* \\ \frac{dA}{dt} &= \rho\mathrm{E}^* - \mathrm{w}_3\mathrm{A}^* \\ \frac{dC}{dt} &= \gamma\mathrm{A}^* - \mathrm{w}_4\mathrm{C}^* \\ \frac{dT}{dt} &= \alpha\mathrm{A}^* + \mathrm{w}_5\mathrm{C}^* - \mathrm{w}_6\mathrm{T}^* \\ \frac{dR}{dt} &= \psi\mathrm{T}^* - \mu\mathrm{R}^* \end{aligned}\right\} \tag{31}$$

$w_1 = \varphi + \mu, \mathrm{w}_2 = (\mu+\rho), \mathrm{w}_3 = \alpha+\gamma+\delta+\mu, \mathrm{w}_4 = (1-\alpha+\delta+\mu), \mathrm{w}_5 = 1-\alpha, \mathrm{w}_6 = (\psi+\delta+\mu)$

Solving (31) for $M^*, V^*, S^*, E^*, A^*, C^*, T^*, R^*$, we obtain

$$M^* = \frac{\pi p_1}{\mathrm{w}_1},\ V^* = \frac{\pi p_2}{\mu},\ \mathrm{S}^* = \frac{\pi(1-P)}{\mu+\lambda^*},\ \mathrm{E}^* = \frac{(\mu+\lambda^*)S^* + \varphi M^*}{w_2},\ \mathrm{A}^* = \frac{\rho E^*}{w_3},\ \mathrm{C}^* = \frac{\gamma A^*}{w_4},\ T^* = \frac{\alpha A^* + w_5 C^*}{w_6},\ R^* = \frac{\psi T^*}{\mu} \tag{32}$$

Theorem 5: An E.E H^* exists whenever ${R_C}^* > 1$, otherwise it doesn't exist.

Proof

For endemic equilibrium point to exist $\frac{dE}{dt} > 0, \frac{dA}{dt} > 0$ and $\frac{dC}{dt} > 0$, that is

$$\frac{dE}{dt} = (\mu+\lambda)\mathrm{S}^0 + \varphi M^0 - \mathrm{w}_2\mathrm{E} > 0 \tag{33}$$

$$\frac{dA}{dt} = \rho E - w_3 A > 0 \quad (34)$$

$$\frac{dC}{dt} = \gamma A - w_4 C > 0 \quad (35)$$

From the inequalities 14, 15 and 16 we get

$$E = \frac{(\mu+\beta(E+\eta_1 A+\eta_2 C))S^0+\varphi M^0}{w_2} \quad (36)$$

$$A = \frac{\rho E}{w_3} \quad (37)$$

$$C = \frac{\gamma \rho E}{w_3 w_4} \quad (38)$$

Substituting (37) and (38) into (36) yields

$$E = \beta E S^0 + \beta S^0 \eta_1 \frac{\rho E}{w_3} + \beta S^0 \eta_2 \frac{\gamma \rho E}{w_3 w_4} + \mu S^0 + \varphi M^0 \quad (39)$$

By comparison theorem,

$$E < \beta E S^0 + \beta S^0 \eta_1 \frac{\rho E}{w_3} + \beta S^0 \eta_2 \frac{\gamma \rho E}{w_3 w_4} \quad (40)$$

By factoring E, (40) simplifies to $1 < \beta S^0 + \beta S^0 \eta_1 \frac{\rho}{w_3} + \beta S^0 \eta_2 \frac{\gamma \rho}{w_3 w_4} = {R_C}^*$ (41)

${R_C}^* > 1$, thus, an endemic equilibrium point H* exists.

Numerical Results and Discussion

In this section, numerical simulations were conducted using MATLAB software (R2017a) to examine the dynamics of the HBV model over time. The initial conditions for the model's variables and the parameter values used for the simulations were obtained. Table 4.1 displayed a selection of parameter values sourced from the literature, while others were computed for illustrative purposes. The numerical simulations of the model's system of ordinary differential equations were carried out using the ode45 solver. The initial values for certain state variables were determined based on an estimated Hepatitis B prevalence of 5-8%. For the model simulation, the current birth rate for Kenya in 2022 was considered to be 27.667 births per 1000 people. Additionally, the Hepatitis B birth dose vaccination coverage was set at 3.2%. The model's variables and parameters were derived from published Hepatitis B data, as presented in Table 1. As per the KDHS report of 2022, the life expectancy at birth in Kenya was reported to be 69.32 years. The birth rate was estimated at 26.78 births per 1000 population, while the death rate stood at 5.09 deaths per 1000 people. Some of the parameters were calculated based on these known rates and variables as documented in the literature.

Table 1: Parameter values and initial conditions

Parameter description	Parameter symbol	Nominal Value/Range	Source
Birth rate	π	0.027667	2021 KNBS estimates
Natural mortality rate	μ	0.00509	2021 KNBS estimates
Total population	N	54685051	Kenya Demographic profile, population estimates 2021
Effective contact rate	β	0.3- 0.9	Elena Gai Wang, 2022 [5]
HBV induced mortality rate	δ	0.041	Chao Wang and Fuqiang Cui,2022 [23]
HBV Exposure rate	ρ	0.5-0.9	Gul Zaman, Yong Han Kang, and Il Hyo Jung, 2008 [10]
Proportion of passively immune births	p	0.1-0.9	Pauline Van den Driessche and James Watmough, 2002 [17]
HBV diagnosis /screening rate	α	0-0.1	Moosarreza Shamsyeh Zahedi and Narges Shayegh Kargar, 2017 [16]
HBV recovery rate due to treatment	ψ	0.25-0.32	Pauline Van den Driessche and James Watmough, 2002 [17]
Acute HBV transition rate	γ	0.02-0.9	CDC Kenya, 2016
Passive immunity waning rate	φ	0.2-0.5	Zohreh Azarkar *et al*, 2018 [22]

Local Sensitivity analysis of R_c, R_0 and Strength number

The forward normalized sensitivity of R_0 is determined using the partial derivatives of R_0 with respect to the focal parameter as in the expression below

$$\Lambda_{\emptyset}^{R_0} = \frac{\partial R_0}{\partial \emptyset} \times \frac{\emptyset}{R_0} \quad (42)$$

The sensitivity indices based on R_c are computed from the expression (42) as tabulated below

Table 2: Sensitivity indices for Control reproduction number

Parameter	Sensitivity index for R_c
β	1
α	-0.031238
γ	-0.19082
δ	-0.000239188
φ	0
μ	-1.013047
π	1
ρ	-0.62915
P	-0.25

From the above sensitivity indices, it is evident that, the contact rate and birth rate have a strong positive correlation and directly proportional to R_c, whereas death rate has a strong negative correlation and inversely proportional to R_c. The exposure and transition rate have weak negative correlation. The implication of these indices is that decreasing the contact rate and birth rates decreases the control reproduction number and vice-versa. On the other hand, decreasing the exposure rate increases the control reproduction number.

Simulation of population dynamics and the impact of control interventions

The system of equations (1) are coded in MATLAB (R2017a) together with parameter values and initial conditions. The fourth order Runge-Kutta an inbuilt numerical scheme coded programming language is used for the numerical simulations of model system of ordinary differential equations. The results depict the dynamics of the populations with time to project future trends of the outcomes of the infection. The graphical representations are as shown in the figures below

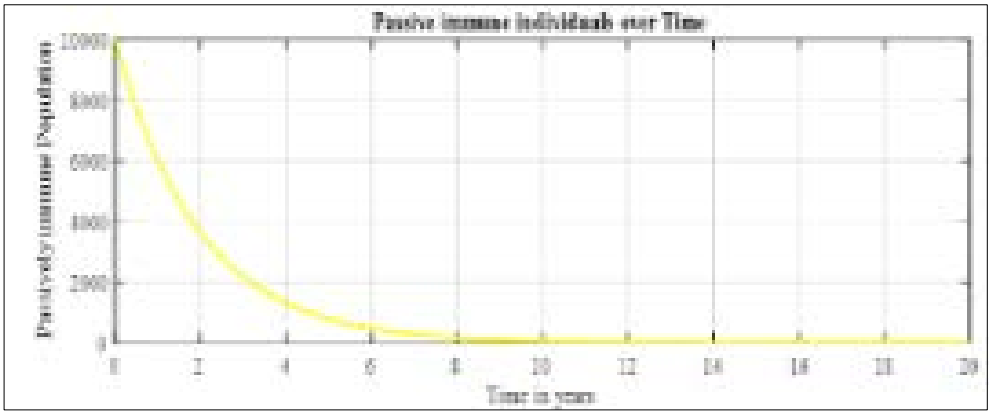

Fig 1: Simulation of M (t)

From figure 1, research findings indicated that a reduction in the rate at which passive immunity waned led to a decrease in the population with passive immunity against HBV. Consequently, immunizing infants immediately after birth emerged as a viable approach to curbing Hepatitis B transmission within the community.

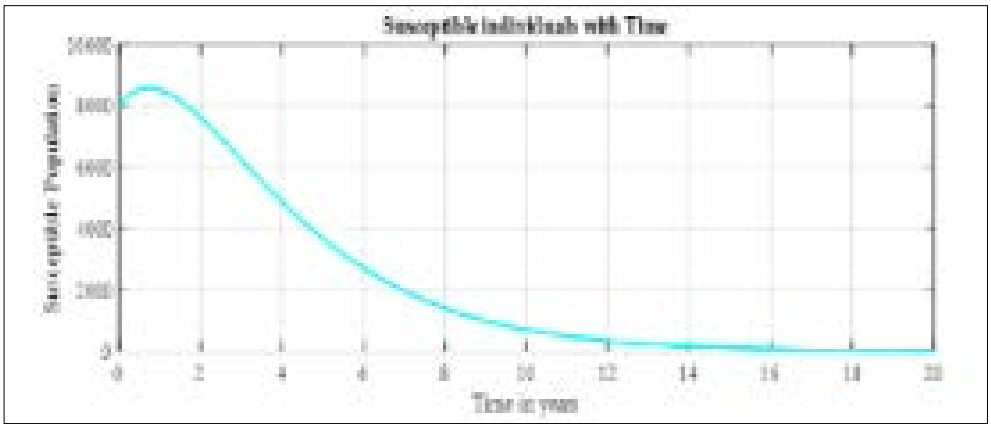

Fig 2: Simulation of S (t)

As illustrated in Figure 2, when the effective reproduction number falls below one, the susceptible population diminishes as immunity acquired at birth declines. This validates that when the average number of infected individuals transmitting the infection to susceptible individuals over time drops below one, the infected population diminishes, ultimately leading to the extinction of the infection.

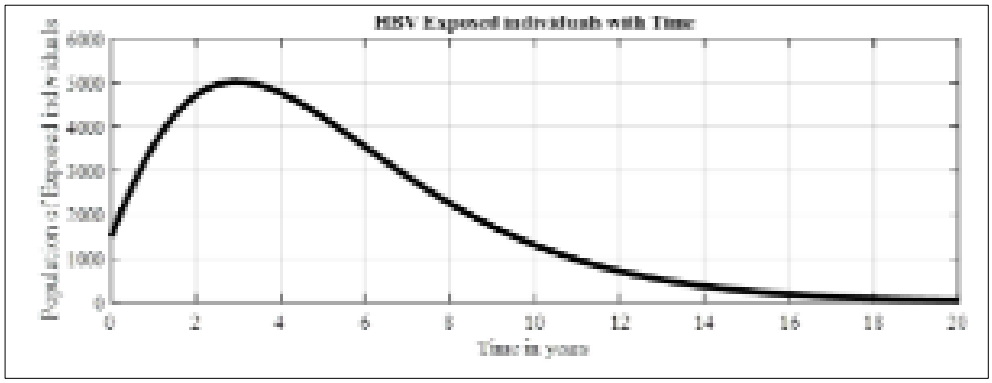

Fig 3: Simulation of E (t)

As depicted in Figure 3 above, initially, there is a rise in the number of individuals who have been exposed to the virus for a period of three years, primarily because of the high transmission rate and a relatively low level of passive immunity. Subsequently, this population of exposed individuals decreases over time due to an increase in the rate of vaccinating infants at birth and administering progressive HBV vaccine doses. As a result of ongoing efforts in diagnosing and vaccinating susceptible individuals, the population of exposed individuals diminishes steadily, ultimately leading to the eventual eradication of the infection over time.

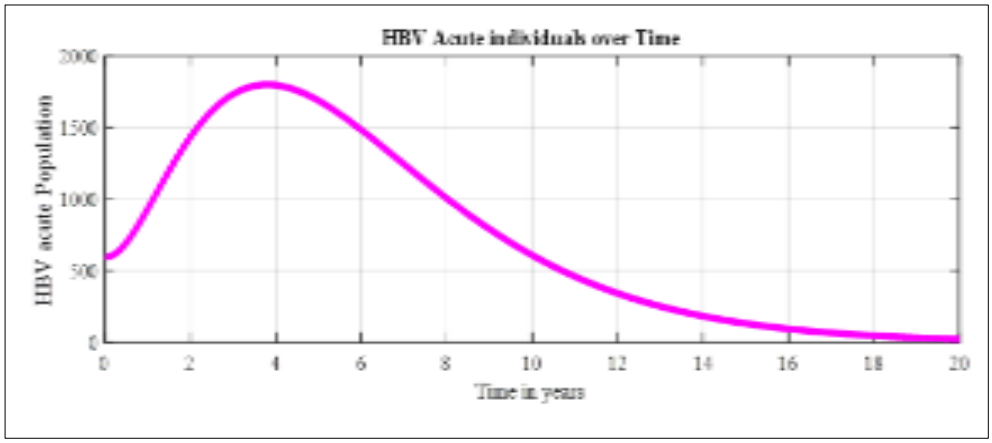

Fig 4: Simulation of A (t)

As represented in Figure 4 above, there is a notable increase in the number of individuals with acute infection, correlating with the rise in the population of individuals who have been exposed to the virus for a duration of four years. Subsequently, owing to early diagnosis and effective treatment, the number of individuals with acute infection gradually diminishes over time, preventing the progression to chronic HBV infection. This decline signifies the eventual eradication of the infection as time progresses.

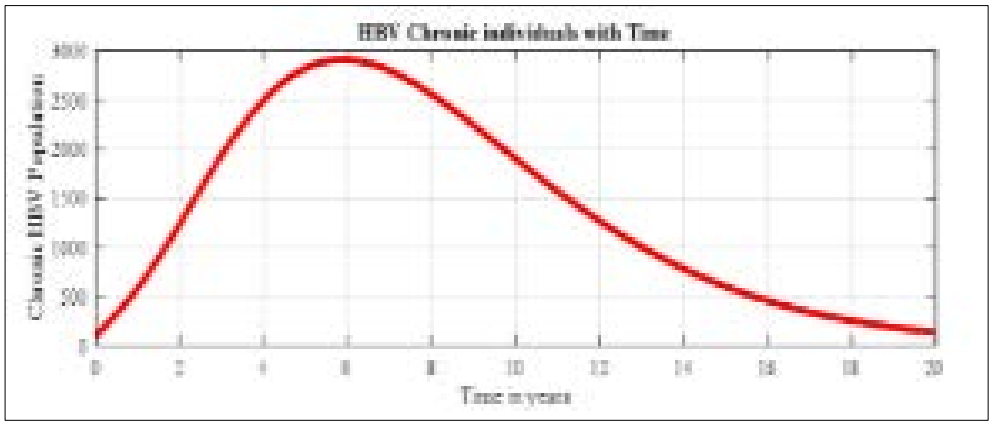

Fig 5: Simulation of C (t)

As shown in the figure 5 above, initially, the count of individuals with chronic HBV infection rises in tandem with the growth of exposed and acute populations over a span of six years. Subsequently, with the elevation of the treatment rate for individuals with acute infection, the number of those with chronic HBV infection declines. Given that there is no transition of the infection from one stage to another, the overall infected population drops over time, ultimately leading to the extinction of the infection.

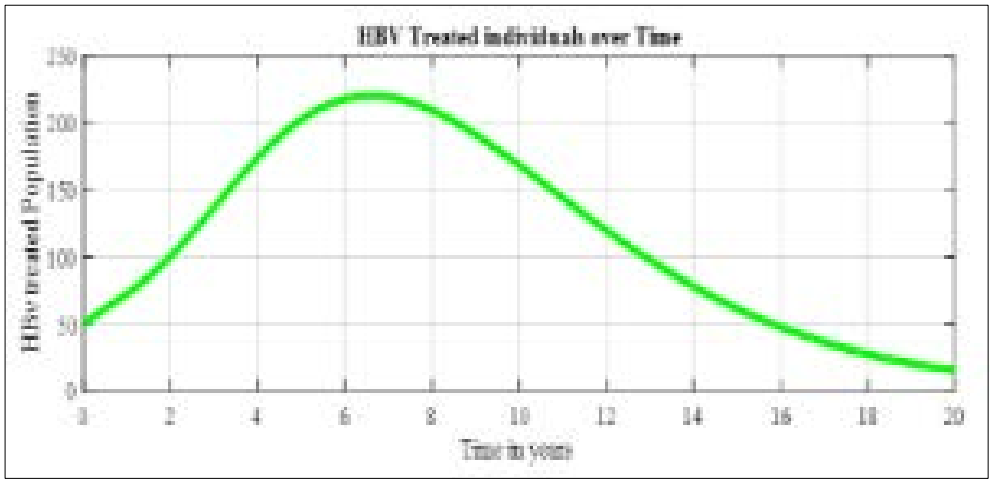

Fig 6: Simulation of T (t)

From figure 6 above, in the initial phases of the infection, there's an uptick in the count of individuals receiving treatment, driven by the heightened treatment rates for those with acute and chronic conditions. However, after a span of seven years, the population of individuals under treatment falls, corresponding to a reduction in the rate of transmission. This phenomenon signifies that treatment control measures effectively bring down the effective reproduction number to below one, ultimately leading to the gradual extinction of the infection. Consequently, the infection is successfully contained.

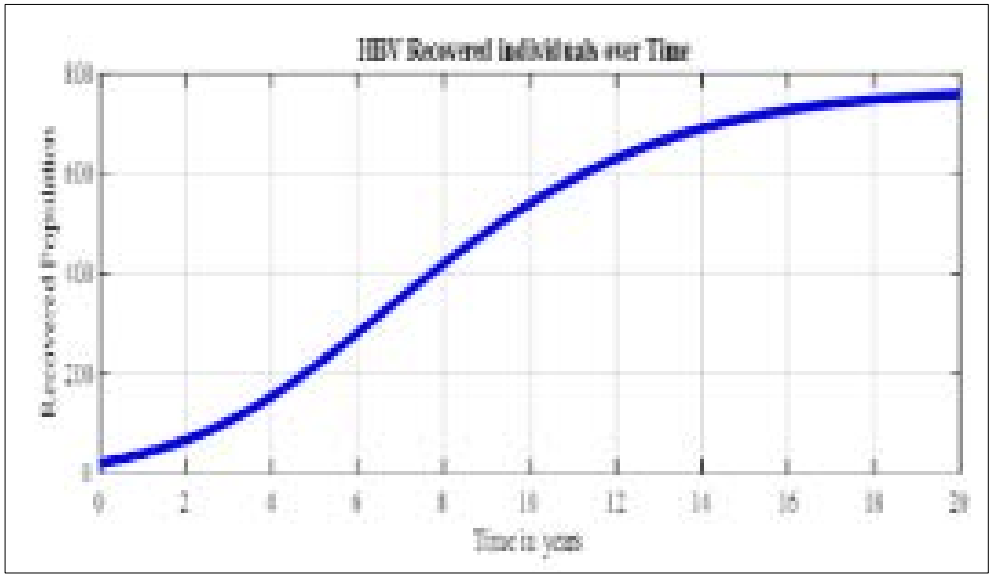

Fig 7: Simulation of R (t)

In the beginning, the count of individuals who have recovered shows a rise, and this rise is a result of an increase in the treatment rate, leading to a higher number of treated individuals. This increase can be attributed to the application of a consistent treatment regimen and the administration of effective treatment doses. It reinforces the idea that when the average number of infected individuals transmitting the infection to susceptible individuals over time drops below one, the number of infected individuals decreases, ultimately resulting in the extinction of the infection.

Variation of contact rate, screening rate and immunity waning rate on contagious populations

Figures 8 to 11 illustrates how the contact rate affects the infectious populations over a span of two decades. Within the same range of beta values, a noteworthy observation is the swift rise in the exposed population during the infection's early stages, followed by a gradual decline as it gradually diminishes within the population. This observation serves as an indicator of the presence of an infection-free equilibrium point.

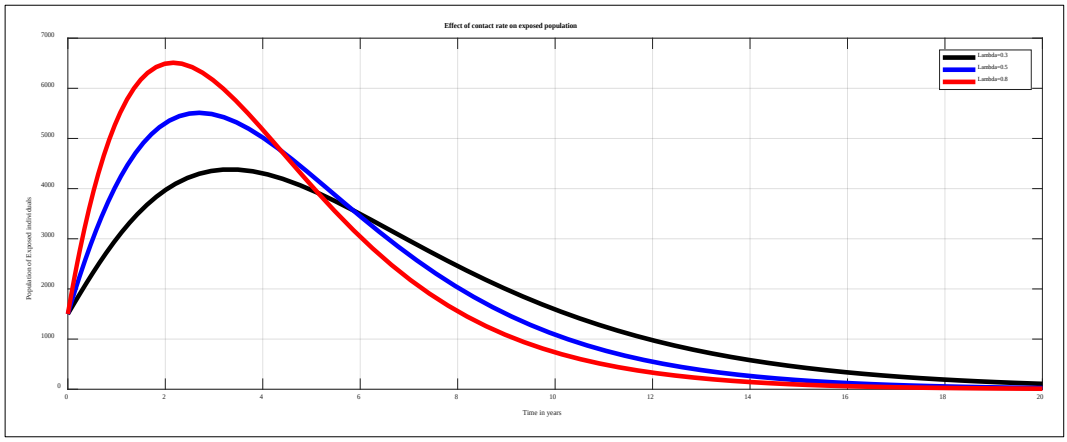

Fig 8: Effect of contact rate on exposed population

In figure 9 below the population with Acute Hepatitis B increases for different values of contact rate for about 3years and afterwards decreases slowly as the infection dies out of the population with time.

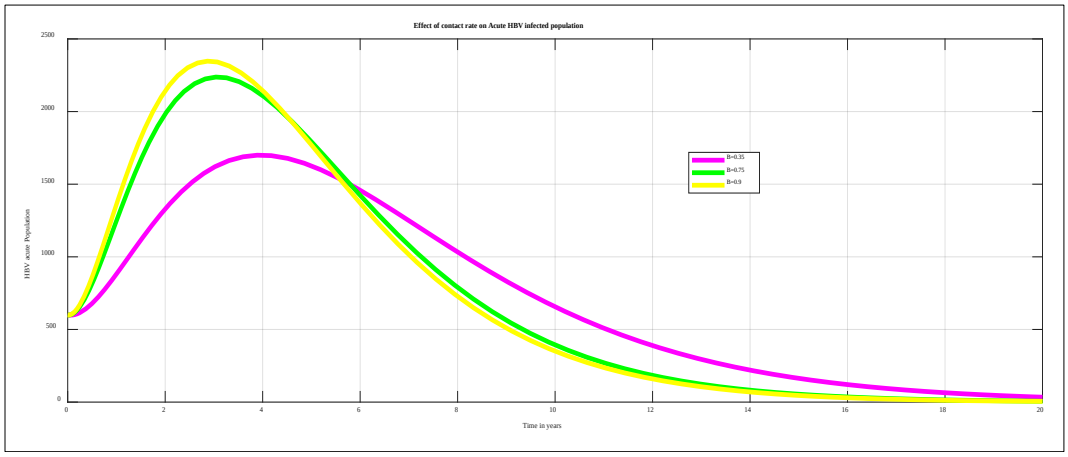

Fig 9: Effect of contact rate of acute HBV infected population

The population with chronic HBV increases steadily for a period of 5 years as shown in figure 10 below and then drops slowly as the infection goes extinct.

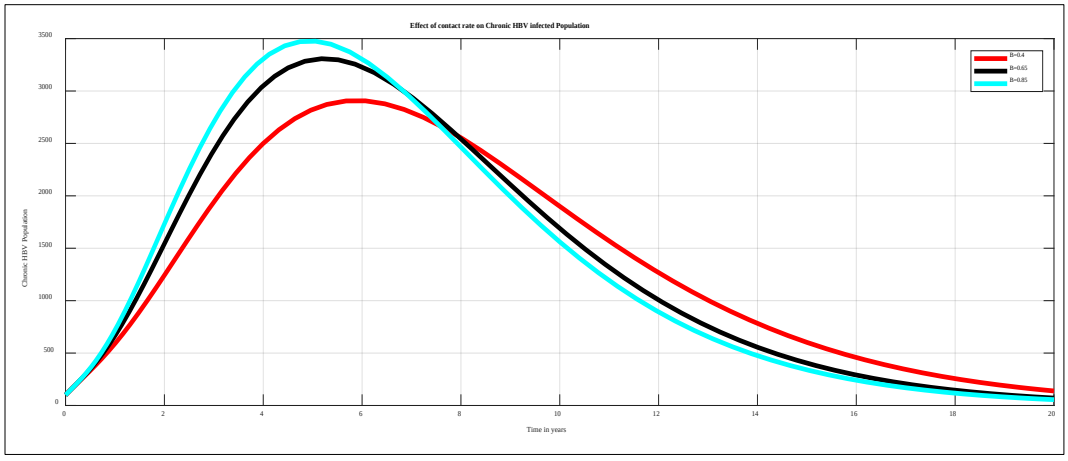

Fig 10: Effect of contact on chronic HBV infected population

In figure 11, HBV treated population increases exponentially for about 6 years with increase in the contact rate. There after the population decreases exponentially as the infection dies out with time.

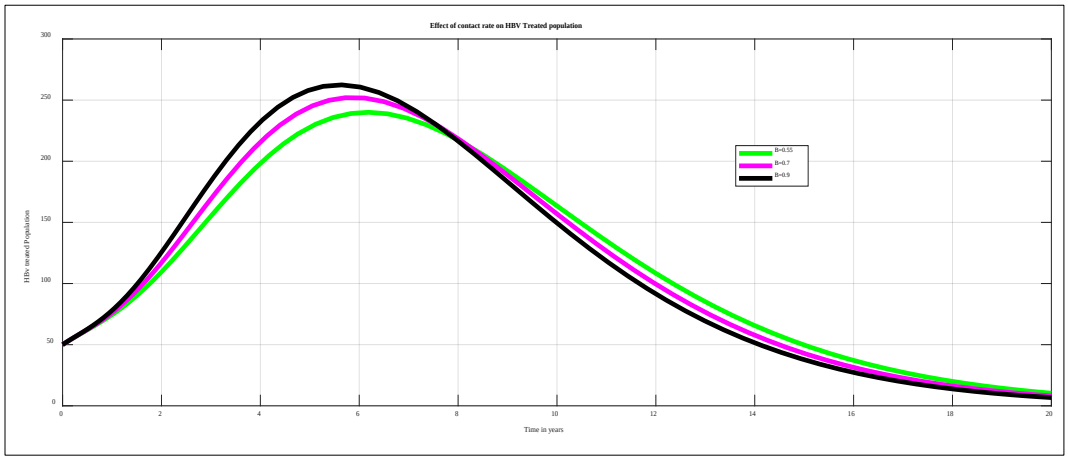

Fig 11: Effect of contact rate on HBV treated population

Many individuals are not aware of the hepatitis infection due to lack of health education focusing on creation of awareness, thus the increase. Reinforcing awareness and sensitization intervention, and people encouraged to know their hepatitis status through screening the infection fades away, hence the decrease.

Conclusion and Recommendations

In this study, a deterministic model was developed to describe the transmission dynamics of Hepatitis B, taking into account interventions such as infant vaccination at birth, screening, and treatment of acute and chronic cases. The model underwent both analytical and numerical analysis, with a focus on investigating how passive immunity, screening, vaccination, and treatment impact the transmission dynamics of Hepatitis B. The control reproductive number, denoted as R_c, was determined using the Next Generation Matrix (NGM) method, calculated as the dominant eigenvalue of the NGM. The analysis revealed that the Hepatitis B infection-free equilibrium is achieved and is both locally and globally asymptotically stable when the corresponding reproduction number falls below one. This suggests that Hepatitis B elimination is feasible with a thorough understanding and effective implementation of these interventions and risk factor management. Additionally, the study used the Jacobian approach to determine the Hepatitis B endemic equilibrium point, indicating that without control interventions, Hepatitis B would persist within the community. Numerical results were obtained through MATLAB and presented graphically. The model's findings emphasized the significance of passive immunity, which is influenced by birth rates, as a crucial transmission factor. Moreover, the contact rate was identified as a critical determinant of transmission. The impact of control interventions on the contagious population indicated a substantial reduction in transmission when cases were detected early. Consequently, the study recommends the implementation of effective detection and early treatment programs for all exposed individuals following early diagnosis, before the HBV viral load increases. This approach aims to curtail the progression of the infection to acute or chronic stages. Furthermore, the study suggests enforcing early screening of pregnant mothers for HBV during pregnancy. It also advocates for universal vaccination of infants at birth and the completion of the HBV vaccination schedule. These recommendations are seen as valuable measures to contain HBV infection, particularly among the younger population.

In conclusion, this model provides valuable insights for healthcare workers, policymakers, the Ministry of Health, and practitioners regarding the etiology and risk factors associated with Hepatitis B, as well as effective mitigation measures. The study underscores the importance of mass screening and public awareness campaigns as fundamental efforts in the prevention and control of Hepatitis B.

Further reading: Mathematical models incorporating vaccination of susceptible population as well as time delay, non-clinical interventions should be explored.

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