

STABILITY ANALYSIS OF THE EFFECT OF VACCINATION AND TREATMENT ON HEPATITIS B VIRUS TRANSMISSION WITH INFECTIVE MIGRANTS

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Abstract

This study considers a deterministic model on HBV transmission with infective migrants, incorporating vaccination and treatment as control measures. The disease free equilibrium state is obtained and we compute the effective reproduction number from which we establish the endemic equilibrium state of the model. The local stability of the endemic equilibrium state was analyzed using the sign of the constant term of the characteristic equation and proved to be stable when the vaccination and treatment rates are kept below 0.6 and becomes unstable at a rate 0.6 and above. Therefore, effort should be intensified, so as to ensure high coverage with effective vaccination and treatment options, in order to curtail HBV transmission with infective migrants.

Keywords: Hepatitis B Virus, immigrant, vaccination, treatment, stability, Endemic equilibrium state.

1. INTRODUCTION

The danger of hepatitis B virus (HBV) worldwide has a major influence on the demand for health-care services mostly due to increased migration from countries with intermediate/ high HBV prevalence.

The prevalence of chronic HBV infection varies throughout regions of the world [1] and could be categorized as high (>8%) in China and Sub-Sahara Africa like Nigeria [2], moderately endemic (2-8%) in Eastern and southern Europe, and low (0.5-2%) in Northern and Western Europe [1].

Currently, HBV infects approximately 2 billion people Worldwide and over 350 million are chronic HBV surface antigen (HBsAg) carriers [3]. Without intervention, 15% to 40% will eventually develop cirrhosis, liver failure or hepatocellular carcinoma.

The modes of transmission of HBV are the same as those for the human immunodeficiency virus (HIV), but HBV is 50 to 100 times more infectious than HIV [4], and can survive outside the body for at least seven days. During this time, the virus can still infect a person who is not immunized. However, HBV can be transmitted by birth (from mother to child), sex and exchange of blood and body fluids. Though, the spread might become faster through non-standard conditions and structure of migration process.

Nigeria being an Africa most populous country is classified among countries of the world that is highly endemic for hepatitis B virus infection. About 75% of Nigeria population is reportedly likely to have been exposed to hepatitis B virus at one time or the other in their life [5]. Considering the number of Nigerians who travel on a daily basis, this is not just Nigeria's public health problem but has a global relevance. Therefore, to prevent the spread of HBV with infective migrants using vaccination and treatment seems imperative to reduce the global burden of HBV infection.

Vaccination as a control measure is the use of antigenic substance to stimulate the immune system to develop protective antibodies (>10 million IU/ML or 10 IU/L) against the virus. The administration of monovalent HB vaccine (engix-B, recombinant HB regimen) or combination vaccine (twinrix, convax, pediarix) for immunization of children and adults at risk, is administered with Hepatitis B Immune Globulin (HBIG) in order to produce immunity against HBV (USFDA, 2011). Current dosing recommendations are 0.13ml/kg HBIG immediately after delivery or within 12 hours after birth, followed by a second dose at 1-2 months and a third dose not earlier than 6 months (24 weeks) in combination with recombinant vaccine ([7], [8]). The combination results in a higher-than-90% level of protection against HBV infection [9]. Despite some successes associated with the use of vaccines and supportive therapies for acute infection, the devastating effect of HBV has increased, thus, the need for treatment of chronic carriers.

Treatment as a regulatory strategy helps to lessen viral loads to untraceable (≤ 20 IU/ML) or nearly untraceable levels (< 69 IU/ML or 400 Copies/ML) in most treated persons, subject to medication and genotype [10]. Treatment resolutions are made on the basis of Hepatitis B Virus Deoxyribonucleic Acid (HBVDNA) viral load, Hepatitis B envelope antigen (HBeAg) status, Alanine

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aminotransferase (ALT), mild to severe active necroinflammation and/or at least mild liver fibrosis severity ([11], [12], [13], [14] and [15]), the age of patient, stage of liver disease and other factors [16]. The research carried out in [17], suggest treatment to be given when ALT concentrations are more than 2 times the expected upper bound (>30 IU/L for men and 19IU/L for women) and HBVDNA have values that are continually >2,000IU/ML.

Currently, the first line therapies accepted globally include injection immune stimulators (interferon Alfa-2b and pegylated interferon-2a) and oral antiviral such as entecavir (ETV) and tenofovir disoproxil fumarate (TDF) [16]. Although, combination therapy, such as TDF with ETV or emtricitabine (FTC), Encapsidation and entry inhibitors, TLR7 agonists, and therapeutic vaccines can be considered if drug-resistant mutants exist or for patients with failing first line drug ([18],[19]). Therefore, cleaving to-HBV therapies has > 95% effectiveness for sustaining utmost suppression ([20], [21], [22]). However, small tumours identified early can be treated through resection or ethanol injection. Moreover, with development in surgical technique, immunosuppression and intensive care, liver transplants have become an effective treatment option for liver failure and hepatocellular carcinoma (HCC), with 5-year survival above 75% [23].

Once you recover from Hepatitis B, you acquire antibodies that shield you from the virus for life [24].

To improve better understanding on the dynamics of HBV infection, several mathematical models have been formulated; see for example [[25], [26], [27] and [28]]. This study is motivated by the work of [28], on the transmission model of hepatitis B virus with the migration effect. Their result suggests that migrants for short visit and students should be subjected to test to reduce the number of migrants with disease. The research further recommends a more advanced model on restraining HBV transmission through migration. Therefore, guided by the work in [28] as mentioned above, the present study intends to modify their work by incorporating treatment of chronic carriers. Hence, this study intends to investigate the stability analysis of the effect of vaccination and treatment on Hepatitis B Virus transmission with infective Migrants

2 Model Formulation

2.1 The Existing Model

We consider the following assumptions of the existing model in [28] below.

- i. The population is compartmentalized into six groups namely: Susceptible individuals, S(t), Exposed individuals E(t), Acutely infected individuals, A(t), Chronic carriers, C(t), Immunised individuals, V(t), and Migrated individuals, M(t), all at time t.
- ii. The population is mixed homogeneously, that is, all people are equally likely to be infected by the infectious individuals in case of contact.
- iii. The newborns to carrier mothers infected at birth are latently infected individual.
- iv. A proportion of susceptibles is vaccinated per unit time and the vaccinated individuals do not acquire permanent immunity.
- v. By vaccination coverage we assumed the complete three dose of HBV vaccine.
- vi. There is a transmission rate from exposed to migrated class and vise-visa.
- vii. There is a transmission rate from migrated class to susceptible class and migrated class to acutely infected class.
- viii. There is a stable population with equal percapita birth and death rate δ (as disease- induced death rate is not considered in the system).

Table 1: Parameters of the Existing Model

The existing model in [28] has the following parameters:

Parameters	Description
δ	Equal per cspita birth and death rate (as disease-induced death rate is not considered in the system)
π	The proportion of failure immunization or proportion without immunization
γ_1	Rate at which exposed individuals become infectious and move to the acute infected class.
γ_2	Rate at which acutely infected individuals move to the chronic carrier class
γ_3	Rate at which carriers acquire immunity and move to the immunized class
β	The transmission coefficient
K	The infectiousness of carrier relative to acute infections.
q	Proportion of acute infected individual that become carrier.
δ_0	The loss of immunity from the immunized class to susceptible class.
P	Proportion of vaccinated susceptible per unit time.
ξ	The rate of flow from exposed to migrated class.
α	The flow from migrated to susceptible class.
μ_1	The transmission rate from migrated class to exposed class.
μ_2	The transmission rate from migrated class to acute infected class
η	Proportion of the unimmunized children born to carrier mothers
$\delta(1 - \pi)$	The newborns that are successfully immunized
$\delta\pi(1 - \eta C(t))$	Births flux into the susceptible class

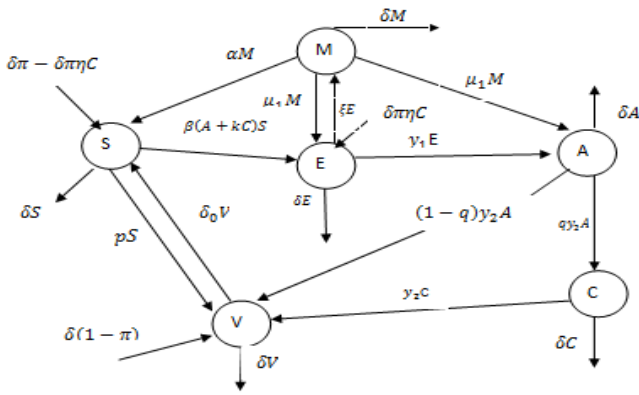


Figure 1: Flow diagram of HBV transmission dynamics for the existing model
 With the above assumptions, parameters and flow diagram in [28], the following model equations were derived.

$$\begin{aligned}
 \frac{dS}{dt} &= \delta\pi(1 - \eta C) - \delta S - \beta(A + KC)S + \delta_0 V - pS + \alpha M \\
 \frac{dE}{dt} &= \beta(A + KC)S - \delta E + \delta\pi\eta C - \gamma_1 E + \mu_1 M - \xi E \\
 \frac{dA}{dt} &= \gamma_1 E - (\delta + \gamma_2)A + \mu_2 M \\
 \frac{dC}{dt} &= q\gamma_2 A - \delta C - \gamma_3 C \\
 \frac{dV}{dt} &= \gamma_3 C + (1 - q)\gamma_2 A - \delta_0 V - \delta V + \delta(1 - \pi) + pS \\
 \frac{dM}{dt} &= \xi E - (\mu_1 + \mu_2)M - \delta M - \alpha M
 \end{aligned}
 \tag{2.1}$$

2.2 The Modified Model

In addition to the assumptions of the existing model, we make the following assumptions.

- i. The chronic carriers are treated at a rate α_0 and the treated individuals recover [29].
- Therefore, as a result of this new assumption, we change the notation of vaccinated class to remove class and redefined γ_3 as the rate at which carriers move to the removed class. Also, we redefined δ_0 as the loss of immunity from the removed class to the susceptible class.

The flow diagram for the existing model is now modified to obtain the flow diagram for the modified model as follows;

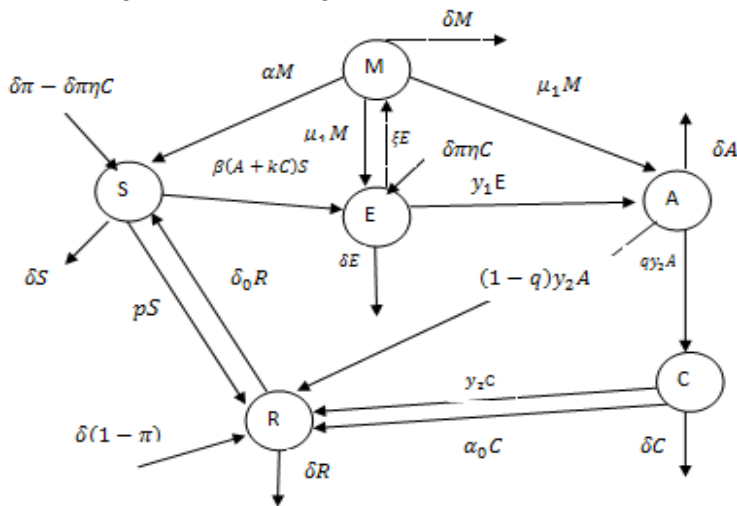


Figure 2: Flow diagram of HBV transmission dynamics for the modified model

The modified model equations are derived based on the above assumptions, parameters and flow diagram in figure 2.

$$\begin{aligned} \frac{dS}{dt} &= \delta\pi(1 - \eta C) - \delta S - \beta(A + kC)S - pS + \delta_0 R + \alpha M \\ \frac{dE}{dt} &= \beta(A + kC)S - (\delta + \varepsilon + \gamma_1)E + \delta\pi\eta C + \mu_1 M \\ \frac{dA}{dt} &= \gamma_1 E - (\delta + \gamma_2)A + \mu_2 M \\ \frac{dC}{dt} &= q\gamma_2 A - (\delta + \alpha_0 + \gamma_3)C \\ \frac{dR}{dt} &= (\alpha_0 + \gamma_3)C + (1 - q)\gamma_2 A - (\delta_0 + \delta)R + pS + \delta(1 - \pi) \\ \frac{dM}{dt} &= \xi E - (\mu_1 + \mu_2 + \delta + \alpha)M \end{aligned} \tag{2.2}$$

$$S(0) > 0, E(0), A(0) \geq 0, C(0) \geq 0, R(0) \geq 0, M(0) \geq 0$$

The total population $N(t)$, therefore becomes

$$\frac{dN}{dt} = \delta(1 - N) \tag{2.3}$$

$$\text{If } e^{\int p dt} = e^{\int \delta dt} = e^{\delta t}$$

Multiply both sides of (2.3) by $e^{\delta t}$ and integrate, we have

$$e^{\delta t} N = \delta \int e^{\delta t} dt$$

$$N(t) = 1 + C e^{-\delta t}$$

At time $t = 0$, we have

$$N_0 - 1 = C$$

$$N(t) = 1 + (N_0 - 1)e^{-\delta t}$$

$N(t) \rightarrow 1$ as $t \rightarrow \infty$, it means that

$$S + E + A + C + R + M = 1$$

Or

$$R = 1 - S - E - A - C - M \tag{2.4}$$

Hence, substituting (2.4) in equation (2.2), the governing equation becomes

$$\begin{aligned} \frac{dS}{dt} &= \delta\pi(1 - \eta C) - \delta S - \beta(A + kC)S + \delta_0(1 - S - E - A - C - M) - pS + \alpha M \\ \frac{dE}{dt} &= \beta(A + kC)S - \delta E + \delta\pi\eta C - \gamma_1 E - \xi E + \mu_1 M \\ \frac{dA}{dt} &= \gamma_1 E - (\delta + \gamma_2)A + \mu_2 M \\ \frac{dC}{dt} &= q\gamma_2 A - (\delta + \alpha_0 + \gamma_3)C \\ \frac{dM}{dt} &= \xi E - (\mu_1 + \mu_2 + \delta + \alpha)M \end{aligned} \tag{2.5}$$

3.0 Model Analysis

The governing model equation (2.5) is shown to be biologically meaningful, epidemiologically well posed and has solutions which are contained in the region

$$\Omega = \left\{ \left((S, E, A, C, M) \in R_+^5 : N(t) \leq \frac{\delta\pi + \delta_0}{\delta_0 + \delta + p} \right), \left(S + E + A + C + M \leq \frac{\delta\pi + \delta_0}{\delta_0 + \delta + p} \right) \right\}.$$

Hence Ω is attracting and all the feasible solution of the model with initial condition in R_+^5 enters or stays in the region Ω .

3.1 The disease- Free Equilibrium State

The disease-free equilibrium state when solved gives:

$$X_0 = (S^0, 0, 0, 0, 0) = \left(\frac{\delta\pi + \delta_0}{\delta + \delta_0 + p}, 0, 0, 0, 0 \right) \tag{2.6}$$

3.2 The Effective Reproduction Number, R_e

The effective reproduction number is defined as the average number of new infection generated by a typical infectious individual in the presence of a control measure [30]. Effective reproduction number is the useful threshold for predicting outbreaks and evaluating control strategies that would reduce the spread of the disease in the population. If $R_e < 1$, the disease can be eliminated, however, when $R_e > 1$ it will persist or become endemic in the population.

The effective reproduction number for the model (2.5) is calculated using the next generation operator approach as described in [31]. Applying this approach, we rearrange our model in equation (2.5) in order of infected compartments followed by uninfected compartments. This gives

$$\begin{aligned} \frac{dE}{dt} &= \beta(A + kC)S - \delta E + \delta\pi\eta C - \gamma_1 E - \xi E + \mu_1 M \\ \frac{dA}{dt} &= \gamma_1 E - (\delta + \gamma_2)A + \mu_2 M \\ \frac{dC}{dt} &= q\gamma_2 A - (\delta + \alpha_0 + \gamma_3)C \\ \frac{dM}{dt} &= \xi E - (\mu_1 + \mu_2 + \delta + \alpha)M \\ \frac{dS}{dt} &= \delta\pi(1 - \eta C) - \delta S - \beta(A + kC)S + \delta_0(1 - S - E - A - C - M) - pS + \alpha M \end{aligned} \tag{2.7}$$

From the first to fourth equation of (2.7), we have the new infective and transfer from one compartment to another given as

$$f = \begin{pmatrix} \beta(A + KC)S \\ 0 \\ 0 \\ 0 \end{pmatrix} \tag{2.8}$$

and

$$V = \begin{pmatrix} (\delta + \xi + \gamma_1)E - \delta\pi\eta C - \mu_1 M \\ (\delta + \gamma_2)A - \mu_2 M - \gamma_1 E \\ (\delta + \alpha_0 + \gamma_3)C - q\gamma_2 A \\ (\mu_1 + \mu_2 + \alpha + \delta)M - \xi E \end{pmatrix} \tag{2.9}$$

Now,

$$V^- = \begin{pmatrix} (\delta + \xi + \gamma_1)E \\ (\delta + \gamma_2)A \\ (\delta + \alpha_0 + \gamma_3)C \\ (\mu_1 + \mu_2 + \alpha + \delta)M \end{pmatrix} \text{ and } V^+ = \begin{pmatrix} \delta\pi\eta C + \mu_1 M \\ \mu_2 M + \gamma_1 E \\ q\gamma_2 A \\ \xi E \end{pmatrix}$$

Where $V = V^- - V^+$

Therefore, taking the partial derivatives of (2.8) with respect to (E, A, C, M) at disease free equilibrium $X_0 = S^0$, we obtain

$$G = Df(X_0) = \begin{pmatrix} 0 & \beta \left(\frac{\delta\pi + \delta_0}{\delta + \delta_0 + P} \right) & \beta K \left(\frac{\delta\pi + \delta_0}{\delta + \delta_0 + P} \right) & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \tag{2.10}$$

Similarly, the partial derivatives of (2.9) with respect to (E, A, C, M) at disease free equilibrium X_0 give

$$U = DV(X_0) = \begin{pmatrix} \delta + \xi + \gamma_1 & 0 & -\delta\pi\eta & -\mu_1 \\ -\gamma_1 & \delta + \gamma_2 & 0 & -\mu_2 \\ 0 & -q\gamma_2 & \delta + \alpha_0 + \gamma_3 & 0 \\ -\xi & 0 & 0 & \alpha + \delta + \mu_1 + \mu_2 \end{pmatrix} \tag{2.11}$$

Therefore, the determinant of (2.11) is

$$|V| = \begin{vmatrix} \delta + \xi + \gamma_1 & 0 & -\delta\pi\eta & -\mu_1 \\ -\gamma_1 & \delta + \gamma_2 & 0 & -\mu_2 \\ 0 & -q\gamma_2 & \delta + \alpha_0 + \gamma_3 & 0 \\ -\xi & 0 & 0 & \alpha + \delta + \mu_1 + \mu_2 \end{vmatrix}$$

Let,

$$a = (\alpha + \delta + \mu_1 + \mu_2), b = (\delta + \gamma_2), c = (\delta + \alpha_0 + \gamma_3), d = (\delta + \xi + \gamma_1),$$

Therefore,

$$|V| = \left(\left(d \begin{vmatrix} b & 0 & -\mu_2 \\ -qy_2 & c & 0 \\ 0 & 0 & a \end{vmatrix} - \delta\pi\eta \begin{vmatrix} -y_1 & b & -\mu_2 \\ 0 & -qy_2 & 0 \\ -\xi & 0 & a \end{vmatrix} + (\mu_1) \begin{vmatrix} -y_1 & b & 0 \\ 0 & -qy_2 & c \\ -\xi & 0 & 0 \end{vmatrix} \right) \right)$$

Where $e = (\delta\pi\eta qy_2)$ we have,

$$|V| = \{dbca - [e(y_1a + \xi\mu_2)] - \xi\mu_1bc\}$$

Therefore, by taking the transpose of the matrix of co factors and dividing by its determinant, we have,

$$|U^{-1}| = |A_0 \ B_0|$$

Where

$$A_0 = \begin{vmatrix} \frac{abc}{|V|} & \frac{-ea}{|V|} \\ \frac{+c[\xi\mu_2 + y_1a]}{|V|} & \frac{-c[da - \mu_1\xi]}{|V|} \\ \frac{+qy_2[y_1a + \mu_2\xi]}{|V|} & \frac{qy_2[da - \mu_1\xi]}{|V|} \\ \frac{\xi bc}{|V|} & \frac{\xi e}{|V|} \end{vmatrix}$$

and

$$B_0 = \begin{vmatrix} \frac{ab(\delta\pi\eta)}{|V|} & \frac{e\mu_2 - cb\mu_1}{|V|} \\ \frac{-\delta\pi\eta[\mu_2\xi + ay_1]}{|V|} & \frac{c[d\mu_2 + y_1\mu_1]}{|V|} \\ \frac{b[da - \mu_1\xi]}{|V|} & \frac{-qy_2[d\mu_2 + y_1\mu_1]}{|V|} \\ \frac{\xi(\delta\pi\eta)b}{|V|} & \frac{dbc + ey_1}{|V|} \end{vmatrix}$$

$$GU^{-1} = \begin{bmatrix} 0 & \beta S^o & \beta KS^o & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} |A_0 \ B_0|$$

$$|GU^{-1} - \lambda I| = \begin{bmatrix} w - \lambda & x & y & 0 \\ 0 & 0 - \lambda & 0 & 0 \\ 0 & 0 & 0 & 0 - \lambda \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

Where,

$$w = \left\{ \beta S^o c \frac{[e\mu_2 + y_1a]}{|V|} + \beta ks^o qy_2 \frac{(y_1a + \mu_2\xi)}{|V|} \right\}, x = -\beta S^o C \frac{[da - \mu_1\xi]}{|V|} + \beta ks^o y_2 \frac{[da - \mu_1\xi]}{|V|},$$

$$y = -\beta S^o \delta\pi\eta \frac{[\mu_2\xi + ay_1]}{|V|} + \beta ks^o \frac{b[da - \mu_1\xi]}{|V|}, z = \beta S^o c \frac{[d\mu_2 + y_1\mu_1]}{|V|} + \beta ks^o - qy_2 \frac{[d\mu_2 + y_1\mu_1]}{|V|}$$

Or

$$\left(\frac{\beta S^o [c(\xi\mu_2 + y_1a) + Kqy_2(y_1a + \mu_2\xi)]}{|V|} - \lambda \right) - \lambda^3 = 0$$

$$\lambda_1 = \beta S^o \frac{[c[\xi\mu_2 + y_1a] + Kqy_2[y_1a + \mu_2\xi]]}{|V|}, \lambda_2 = \lambda_3 = \lambda_4 = 0$$

Where, $\lambda_1 = Re$

$$Re = \frac{\beta S^o [(c + Kqy_2)(\mu_2\xi + y_1a)]}{dbca - \xi\mu_1bc - e[y_1a + \xi\mu_2]} \tag{2.12}$$

Given that

$$dbca > [e[y_1a + \xi\mu_2] + \xi\mu_1bc]$$

Where,

$$a = (\alpha + \delta + \mu_1 + \mu_2), b = (\delta + y_2), c = (\delta + \alpha_0 + y_3), d = (\delta + \xi + y_1), e = (\delta\pi\eta qy_2)$$

$$\text{and } S^0 = \frac{\delta\pi + \delta_0}{\delta + \delta_0 + p}$$

3.3 Existence of Endemic Equilibrium state

At endemic equilibrium the first equation of system (2.5) gives

$$S^* = \frac{E^*(\delta + y_1 + \xi) - \delta\pi\eta C^* - \mu_1 M^*}{\beta(A^* + KC^*)} \tag{2.13}$$

The second equation of the model system (2.5) becomes

$$E^* = \frac{(\delta + y_2)A^* - \mu_2 M^*}{y_1} \tag{2.14}$$

Also, the third equation of the model (2.5) gives

$$C^* = \frac{qy_2 A^*}{\delta + \alpha_0 + y_3} \tag{2.15}$$

and the fourth equation of the model (2.5) result to;

$$M^* = \frac{\xi E^*}{\mu_1 + \mu_2 + \delta + \alpha} \tag{2.16}$$

Substitute equation (2.14) into (2.16), we have

$$M^* = \frac{\xi(\delta + y_2)A^*}{\xi\mu_2 + y_1(\mu_1 + \mu_2 + \delta + \alpha)} \tag{2.17}$$

Substitute (2.17) in equation (2.14) we have,

$$E^* = \frac{(\delta + y_2)A^* - \frac{\xi\mu_2(\delta + y_2)A^*}{(\xi\mu_2 + y_1(\mu_1 + \mu_2 + \delta + \alpha))}}{y_1}$$

$$E^* = \frac{(\delta + y_2)(\mu_1 + \mu_2 + \delta + \alpha)A^*}{(\xi\mu_2 + y_1(\mu_1 + \mu_2 + \delta + \alpha))} \tag{2.18}$$

Substituting equation (2.15), (2.17) and (2.18) into (2.13)

$$S^* = \frac{\frac{(\delta + y_2)(\mu_1 + \mu_2 + \alpha + \delta)(\delta + \xi + y_1)A^*}{\xi\mu_2 + y_1(\mu_1 + \mu_2 + \alpha + \delta)} - \frac{\delta\pi\eta qy_2 A^*}{\delta + \alpha_0 + y_3} - \frac{\mu_1 \xi (\delta + y_2) A^*}{\xi\mu_2 + y_1(\mu_1 + \mu_2 + \alpha + \delta)}}{\beta \left(A^* + \frac{kqy_2 A^*}{\delta + \alpha_0 + y_3} \right)}$$

Let,

$$a = (\alpha + \delta + \mu_1 + \mu_2), b = (\delta + y_2), c = (\delta + \alpha_0 + y_3), d = (\delta + \xi + y_1), e = \delta\pi\eta qy_2$$

Therefore

$$S^* = \frac{\frac{badA^*}{\xi\mu_2 + y_1a} - \frac{eA^*}{c} - \frac{\mu_1 \xi bA^*}{\xi\mu_2 + y_1a}}{\beta \left(A^* + \frac{kqy_2 A^*}{c} \right)}$$

$$S^* = \frac{cb(ad - \mu_1 \xi)}{\beta(c + kqy_2)(\xi\mu_2 + y_1a)} - \frac{eA^*(\xi\mu_2 + y_1a)}{\beta A^*(c + kqy_2)(\xi\mu_2 + y_1a)}$$

$$S^* = \frac{dbca - [e(\xi\mu_2 + y_1a) + \xi\mu_1 bc]}{\beta(c + kqy_2)(\xi\mu_2 + y_1a)} \tag{2.19}$$

Where, $a = (\alpha + \delta + \mu_1 + \mu_2), b = (\delta + y_2), c = (\delta + \alpha_0 + y_3), d = (\delta + \xi + y_1), e = \delta\pi\eta qy_2$

At endemic equilibrium equation (2.17) results to

$$0 = \delta\pi(1 - \eta C^*) - S^* \beta A^* - S^*(\delta + \beta k C^* + \delta_0 + p) - \delta_0 A^* + \delta_0(1 - E^* - C^* - M^*) + \alpha M^*$$

$$(S^* \beta + \delta_0)A^* + \delta\pi\eta C^* + S^* \beta k C^* + \delta_0(E^* + C^*) = \delta\pi - S^*(\delta + \delta_0 + p) + \delta_0(1 - M) + \alpha M^*$$

$$\left\{ \left[(S^* \beta + \delta_0) + \frac{(e + S^* \beta k q y_2)}{c} + \delta_0 \left(\frac{bac + qy_2(\xi\mu_2 + y_1a)}{c(\xi\mu_2 + y_1a)} \right) + \frac{\xi b(\delta_0 - \alpha)}{\xi\mu_2 + y_1a} \right] A^* \right.$$

$$\left. = \delta\pi + \delta_0 - S^*(\delta + \delta_0 + p) \right\}$$

From which we obtain

$$A^* K = \delta\pi + \delta_0 - S^*(\delta + \delta_0 + p)$$

$$A^* = \frac{(\delta + \delta_0 + p) S^* \left(\frac{S^0}{S^*} - 1 \right)}{K}$$

Since $R_e = \frac{S^0}{S^*}$

Where

$$K = (S^* \beta + \delta_0) + \frac{(e + S^* \beta k q y_2)}{c} + \delta_0 \left(\frac{bac + qy_2(\xi\mu_2 + y_1a)}{c(\xi\mu_2 + y_1a)} \right) + \frac{\xi b(\delta_0 - \alpha)}{\xi\mu_2 + y_1a}, \quad k > 0$$

It follows that

$$A^* = \frac{(\delta + \delta_0 + p)S^*}{K}(R_e - 1), \quad R_e > 1 \tag{2.20}$$

Where,

$$a = (\alpha + \delta + \mu_1 + \mu_2), b = (\delta + y_2), c = (\delta + \alpha_0 + y_3), d = (\delta + \xi + y_1), e = \delta\pi\eta qy_2$$

Therefore, at $X_1 = (S^*, E^*, A^*, C^*, M^*)$ the endemic equilibrium state of the system (2.5) are given by equation ((2.19, 2.18, 2.20, 2.15 and 2.17,)) respectively.

Thus, the following result (2.19, 2.18, 2.20, 2.15 and 2.17,) is established

Proposition 5: The endemic equilibrium state exists whenever $R_e > 1$

3.4 Local Stability of the Endemic equilibrium state

In this section, we determine the local stability of (2.5) at endemic equilibrium.

Theorem 1: For $R_e > 1$, the model system (2.5) is locally asymptotically stable around the endemic equilibrium state J^* , when the vaccination and treatment rates are kept below 0.6, otherwise, it is unstable.

Proof: The Jacobian matrix J^* computed at X_1 is given by

$$J^* = \begin{pmatrix} -g_1 - \lambda & -\delta_0 & -g_2 & -g_3 & g_4 \\ g_5 & -g_6 - \lambda & g_7 & g_8 & \mu_1 \\ 0 & \gamma_1 & -g_9 - \lambda & 0 & \mu_2 \\ 0 & 0 & g_{10} & -g_{11} - \lambda & 0 \\ 0 & \xi & 0 & 0 & -g_{12} - \lambda \end{pmatrix}$$

Where $g_1 = (\delta + \rho + \delta_0) + \beta(A^* + KC^*)$, $g_2 = (\beta S + \delta_0)$, $g_3 = (\delta\pi\eta + \beta KS + \delta_0)$, $g_4 = \alpha_0 - \delta_0$, $g_5 = \beta(A^* + KC^*)$, $g_6 = (\delta + y_1 + \xi)$, $g_7 = \beta S^*$, $g_8 = \delta\pi\eta + \beta KS^*$, $g_9 = \delta + y_2$, $g_{10} = qy_2$, $g_{11} = \delta + \alpha_0 + y_3$, $g_{12} = \alpha + \delta + \mu_1 + \mu_2$

$$\begin{aligned} & (-g_1 - \lambda) \begin{bmatrix} -g_6 - \lambda & g_7 & g_8 & \mu_1 \\ \gamma_1 & -g_9 - \lambda & 0 & \mu_2 \\ 0 & g_{10} & -g_{11} - \lambda & 0 \\ \xi & 0 & 0 & -g_{12} - \lambda \end{bmatrix} - g_5 \begin{bmatrix} -\delta_0 & -g_2 & -g_3 & g_4 \\ \gamma_1 & -g_9 - \lambda & 0 & \mu_2 \\ 0 & g_{10} & -g_{11} - \lambda & 0 \\ \xi & 0 & 0 & -g_{12} - \lambda \end{bmatrix} \\ & (-g_1 - \lambda) \left\{ -g_6 - \lambda \begin{bmatrix} -g_9 - \lambda & 0 & \mu_2 \\ g_{10} & -g_{11} - \lambda & 0 \\ 0 & 0 & -g_{12} - \lambda \end{bmatrix} - \gamma_1 \begin{bmatrix} g_7 & g_8 & \mu_1 \\ g_{10} & -g_{11} - \lambda & 0 \\ 0 & 0 & -g_{12} - \lambda \end{bmatrix} - \xi \begin{bmatrix} g_7 & g_8 & \mu_1 \\ -g_9 - \lambda & 0 & \mu_2 \\ g_{10} & -g_{12} - \lambda & 0 \end{bmatrix} \right\} \\ & -g_5 \left\{ -\delta_0 \begin{bmatrix} -g_9 - \lambda & 0 & \mu_2 \\ g_{10} & -g_{11} - \lambda & 0 \\ 0 & 0 & -g_{12} - \lambda \end{bmatrix} - \gamma_1 \begin{bmatrix} -g_2 & -g_3 & g_4 \\ g_{10} & -g_{11} - \lambda & 0 \\ 0 & 0 & -g_{12} - \lambda \end{bmatrix} - \xi \begin{bmatrix} -g_2 & -g_3 & g_4 \\ -g_9 - \lambda & 0 & \mu_2 \\ g_{10} & -g_{11} - \lambda & 0 \end{bmatrix} \right\} \end{aligned}$$

$$\begin{aligned} & \{ \lambda^5 + \lambda^4(g_1 + g_{11} + g_{12} + g_6 + g_9) + \lambda^3(\delta_0 g_5 + (g_{11} + g_{12} + g_6 + g_9)g_1 \\ & + g_{11}g_{12} + (g_6 + g_9)(g_{11} + g_{12}) + g_6g_9 - (\gamma_1 g_7 + \mu_1 \xi)) + \lambda^2(g_{11}g_{12}(g_6 + g_9) \\ & + g_6g_9(g_{11} + g_{12}) + g_1(g_{11}g_{12} + (g_6 + g_9)(g_{11} + g_{12}) + g_6g_9) \\ & + g_5(\delta_0 g_9 + \delta_0(g_{11} + g_{12}) + \gamma_1 g_2) - \gamma_1 g_7(g_{11} + g_{12}) \\ & + \gamma_1 g_8 g_{10} + \xi \mu_2 g_7 + \mu_1 \xi(g_4 + g_{12}) + \xi g_4 g_5 + g_7(\gamma_1 g_7 + \mu_1 \xi)) \\ & + \lambda(g_1(g_{11}g_{12}(g_6 + g_9) + g_6g_9(g_{11} + g_{12}) + g_6g_9g_{11}g_{12})) + (\delta_0 g_9(g_{11} + g_{12}) \\ & + \delta_0 g_{11}g_{12} + \gamma_1 g_3 g_{10} + \xi g_2 \mu_2 + \xi g_4(g_9 + g_{11}))g_5 - (\gamma_1 g_7(g_{11} + g_{12}) \\ & + \gamma_1 g_8 g_{10} + \xi \mu_2 g_7 + \mu_1 \xi(g_4 + g_{12}))g_1 + (\gamma_1 g_7 g_{11}g_{12} + \gamma_1 g_8 g_{10}g_{12} + \mu_2 \xi g_8 g_{10} + \mu_2 \xi g_7 g_{12} + \mu_1 \xi g_4 g_{12}) \\ & + g_7 g_6 g_9 g_{11}g_{12} + g_5(\delta_0 g_9 g_{11}g_{12} + \gamma_1 g_2(g_{11} + g_{12}) + \gamma_1 g_2 g_{11}g_{12} + \gamma_1 g_3 g_{10}g_{12} + \xi g_2 \mu_2 g_{11} \\ & + \xi g_3 \mu_2 g_{10} + \xi g_4 g_9 g_{11}) - g_1(\gamma_1 g_7 g_{11}g_{12} + \gamma_1 g_8 g_{10}g_{12} + \mu_2 \xi g_8 g_{10} + \mu_2 \xi g_7 g_{12} + \mu_1 \xi g_4 g_{12}) \} \end{aligned} \tag{2.21}$$

The characteristic equation is of the form $\lambda^5 + A\lambda^4 + B\lambda^3 + C\lambda^2 + D\lambda + E = 0$, with the constant terms of the characteristic equation $D, C, B, A > 0$. In this case, if $E > 0$, is satisfied then all eigenvalues are negative, whereas when $E < 0$, the largest eigenvalue has positive real part. Thus the stability is determined solely by the sign of the constant term of the characteristic equation [32] as is given in table 3.

Therefore, using the published model parameters given in table 2 below

Table 2 Parameters used in numerical simulations

Parameters	Value	Source
β	0.8	Khan <i>et al.</i> (2016)
δ	0.0143	Khan <i>et al.</i> (2016)
δ_0	0.03-0.06	Khan <i>et al.</i> (2016)
y_1	6 per year	Khan <i>et al.</i> (2016)
y_2	4 per year	Khan <i>et al.</i> (2016)
y_3	0.34	Khan <i>et al.</i> (2016)
K	0.1	Khan <i>et al.</i> (2016)
π	0.8	Khan <i>et al.</i> (2016)
η	0.7	Khan <i>et al.</i> (2016)
μ_1	0.1	Khan <i>et al.</i> (2016)
μ_2	0.1	Khan <i>et al.</i> (2016)
α	0-1	Khan <i>et al.</i> (2016)
ε	0-1	Khan <i>et al.</i> (2016)
q	0.05-0.9	WHO, 2002
P	0-1	Assumed
α_o	0-1	Assumed

To estimate A,B, C,D and E in J^* , We use mathematical software (maple) to compute the result as shown in table 3.

Table 3: Stability analysis of the endemic equilibrium state of the model using the sign of the constant term of the characteristic equation (Heffernan *et al.*, 2005)

ρ	α_0	A	B	C	D	E	NATURE OF THE EIGEN VALUE (λ)	R_e	Remarks
0.1	0.1	1.3681	0.6742	0.1374	0.0094	0.0001769	$\lambda < 0$	4.4370	stable
0.2	0.2	1.5653	0.8651	0.1897	0.0118	0.0001724	$\lambda < 0$	2.6208	stable
0.3	0.3	1.7607	1.0733	0.2505	0.0145	0.0001521	$\lambda < 0$	1.8596	stable
0.4	0.4	1.9518	1.2953	0.3186	0.0175	0.0001161	$\lambda < 0$	1.4410	stable
0.5	0.5	2.1275	1.5146	0.3888	0.0207	0.0000644	$\lambda < 0$	1.1763	stable
0.6	0.6	1.9870	1.2890	0.3167	0.0258	-0.000003	$\lambda > 0$	0.9937	unstable
0.7	0.7	2.6510	2.2661	0.6399	0.0268	-0.000086	$\lambda > 0$	0.8602	Unstable
0.8	0.8	2.8124	2.5244	0.7314	0.0307	-0.000185	$\lambda > 0$	0.7583	Unstable
0.9	0.9	3.0010	2.8426	0.8453	0.0347	-0.000299	$\lambda > 0$	0.6780	Unstable
1.0	1.0	3.1955	3.1895	0.9715	0.0389	-0.000430	$\lambda > 0$	0.6131	Unstable

Therefore, for $R_e > 1$ it follows that the system (2.5) is locally asymptotically stable around the endemic equilibrium state J^* if vaccination and treatment rates are kept below 0.6, otherwise, it is unstable. The proof is completed.

4. CONCLUDING REMARKS

In this paper, we modify the work of [28] by incorporating treatment rate of chronic carriers and redefined the vaccinated class to remove class. The model is then transformed into proportions to reduce the number of equations, in order to define the prevalence of infection, where the model is biologically and mathematically well posed. By adding this new feature, we have obtained a compartmental model that assesses the effects of vaccination and treatment on HBV transmission with infective migrants.

The disease free equilibrium state is obtained and we compute the effective reproduction number from which we establish the endemic equilibrium state of the model. The local stability of the endemic equilibrium state was analyzed using the sign of the constant terms of the characteristic equation and proved to be stable when the vaccination and treatment rates are kept below 0.6 and becomes unstable at a rate 0.6 and above. Therefore, Government and other partners should strengthen routine HBV-health program and effort should be intensified, so as to ensure high coverage with effective vaccination and treatment options.

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