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ON THE STABILITY OF HEPATITIS B VIRUS-HEPATITIS D VIRUS (HBV-HDV) CO-INFECTION WITH CONTROLS IN A DYNAMIC POPULATION

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ABSTRACT. In this paper, the stability analysis of Hepatitis B virus - Hepatitis D virus (HBV-HDV) Co-infection with controls in a dynamic population was investigated using Jacobian method. The Jacobian matrix formed was evaluated numerically. The result showed that the equilibrium point of the solution is unstable which implies that the disease existence is unstable, this indicates that any minor increase in the infection can cause epidemic in the population.

1 Introduction

Hepatitis B is a serious viral condition that causes inflammation of the liver and affects how well the liver functions. Viral hepatitis is very infectious; Infectious diseases are the second leading cause of death among humans worldwide, but number one cause of death in developing countries [22].

Hepatitis D, also known as the delta virus, is an infection that causes liver to swell. Hepatitis D Virus (HDV) is an RNA defective virus which has no independent existence; it requires the HBV for replication and has the same sources and modes of spread as HBV. HDV can infect individuals at the same time with HBV (co-infection),

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or it can super-infect those who are already chronic carriers of HBV. Co-infections give rise to acute Hepatitis which is often severe but is limited by recovery from the HBV infection [11]. Both super-infection by, and co-infection with, HDV in patients also infected with HBV results in worst outcomes than infection with HBV alone. There is a higher rate of liver failure in acute infections and a greater likelihood of developing liver cancer in chronic infection [27]. Fulminant hepatitis may develop in 20-30 % of patients coinfected with both HBV and HDV but only 2% of patients infected with isolated HBV might experience such complication [14]. Hepatitis delta antigen (HDAg) was first detected in hepatocyte nuclei in some Hepatitis B virus (HBV) carriers [20]. This antigen was subsequently shown to be an internal antigen of Hepatitis delta virus (HDV), a small defective RNA virus which is dependent on co-infection with HBV for its replication and expression [18 and 21]. HDV has a world-wide distribution; it is endemic in parts of the Mediterranean basin, Africa and South America where transmission is mainly by close personal contact, and occasionally by vertical transmission from mothers who also carry the Hepatitis B virus [11]. An HDV infection absolutely requires an associated HBV infection. The outcome of disease largely depends on whether the two viruses infect simultaneously (co-infection), or whether the newly HDV-infected person is a chronically infected HBV carrier (super-infection) [10 and 19]. Co-infection of HBV and HDV (simultaneous infection with the two viruses) results in both acute type B and acute type D hepatitis. The incubation period depends on the HBV titre of the infecting inoculum. Depending on the relative titres of HBV and HDV, a single bout or two bouts of hepatitis may be seen. Co-infections of HBV and HDV are usually acute, self-limited infections. The chronic form of hepatitis D is seen in less than 5% of HBV - HDV co-infected patient [10 and 19]. Acute hepatitis D occurs after an incubation period of 3 - 7 weeks, and a preicteric phase begins with symptoms of fatigue, lethargy, anorexia and nausea, lasting usually 3 to 7 days. During this phase, ALT and AST activities become abnormal. The appearance of jaundice is typical at the onset of the icteric phase. Fatigue and nausea persist, clay-colored stools and dark urine appear, and serum bilirubin levels become abnormal. In patients with acute, self-limiting infection, convalescence begins with the disappearance of clinical symptoms. Fatigue may persist for longer periods of time [17 and 19]. An antigen-antibody system termed the delta antigen (delta-Ag) and antibody (anti-delta) is detected in some HBV infections. The antigen is found within certain Hepatitis B surface antigen (HBsAg) particles. In blood, HDV (delta agent) contains delta-Ag (HDAg) surrounded by an HBsAg envelope. The genome of HDV consists of RNA; No homology exists with the HBV genome. HDAg is coded for by HDV RNA and is distinct from the antigenic determinants of HBV. For this reason, HDV is a defective virus that requires an HBsAg coat for transmission [6]. However, mathematical models have not been used to study the dynamic of Hepatitis B Virus -Hepatitis D Virus (HBV-HDV) Co-infection with controls (incorporating enlightenment, use of condom and therapy at the same time) in a population. The aim of this paper is therefore to develop a mathematical model for the HBV-HDV Co-infection with controls (enlightenment, use of condom and therapy). We shall further study the stability of the model using Jacobian method classification of the equilibrium of the solution in order to investigate the existence of the disease in the population. This will help give an insight on how best to tackle enormous problems associated with HBV-HDV Co-infection in a dynamic population.

2 Model formulation

Assumptions of the Model:

The model is based on the following assumptions:

1. The individuals that make up the population can be grouped into different compartments or groups according to their epidemiological state.
2. The population size in a compartment varies with respect to time.
3. The population mixes homogeneously. That is, all susceptible individuals are equally likely to be infected by infectious individuals if they come in contact with one another.
4. The infection does not confer immunity to the recovered individuals and so they can go back to the susceptible class at any given time.
5. The individuals in each compartment have equal natural death rate given as μ.
6. The gain in the infectious class is at a rate proportional to the number of infectious and susceptible individuals. That is, βSI where $\beta > 0$ is a contact parameter (effective contact rate).The susceptible are lost at the same rate.
7. The rate of removal of infectious to the recovered or removed class is proportional to the number of infectious individuals.

Model Variables: The following variables are used in this study, thus:

S: The number of susceptible individuals

E_{HB}: The number of individuals who are exposed to HBV

E_{THB}: The number of individuals who are exposed to HBV and are being treated.

I_{HB}: The number of individuals who are infectious of HBV.

I_{NHB}: The number of individuals who are infectious of HBV and not being treated.

I_{THB}: The number of individuals who are infected with HBV and are being treated.

R_{HB}: The number of individuals who have been treated of HBV and have recovered.

E_{HBD}: The number of individuals who are infectious of HBV and latently infected with HDV (exposed of HDV).

E_{THBD}: The number of individuals who are infectious of HBV and now exposed to HDV and being treated.

I_{HBD}: The number of individuals who are infected with HBV and HDV at the same time.

I_{NHBD}: The number of individuals who are infected with HBV and HDV and not being treated of any.

I_{THB}: The number of individuals who are infected with HBV and HDV and are being treated of both.

R_{HBD}: The number of individuals who have recovered from HBV-HDV Co infection after they have been treated.

Parameters of the Model:

We shall also use the following parameters in this model, thus:

π: The number of people that enter the population (the number of individuals that enter into the susceptible class).

β_1: Contact rate for I_{HB} with susceptible individuals (S). i.e., the rate at which susceptible individuals who had

contact with HBV infectious person become exposed to HBV.

β_2: Contact rate for I_{HBD} with susceptible classes E_{HB}, I_{NHB} and I_{THB}

τ: The rate at which individuals who are exposed to HBV become infectious of HBV.

ω: The rate at which individuals who are exposed to HBV enter into exposed and being treated compartment or class E_{THB}

ρ_2: The rate at which individuals who are infectious of HBV enter into infectious and being treated HBV class (I_{THB})

ρ_1: The rate at which individuals who are infectious of HBV enter into infectious and not being treated of HBV (I_{NHB}).

γ_1: The rate at which individuals that are infectious and being treated of HBV goes back to exposed HBV class.

γ_2: The rate at which individuals who are infectious and being treated of HBV recover from HBV.

α: The rate at which individuals who are exposed and being treated of HBV recover.

ϕ_1:: The rate at which individuals who recovered from HBV goes back to susceptible class.

φ: The rate at which individuals that are infectious and being treated of HBV become exposed to HDV, that is E_{HBD}.

ψ: The rate at which individuals who are infectious of HBV and not being treated become exposed to HDV, that is E_{HBD}.

$\beta_2[1-(c_1+c_2)]$: : The rate at which individuals who are exposed of HBV become exposed to HDV E_{HBD}

ς: The rate at which HBV infectious individuals who are exposed to HDV enter into exposed HDV being treated class E_{THBD} that is the rate at which individuals who are exposed of HBV-HDV co-infection enter into exposed HBV-HDV being treated class E_{THBD}.

κ: The rate at which HBV infectious individuals who are exposed to HDV become infectious of HBV-HDV.

ε_1: The rate at which individuals who are infectious of HBV-HDV enter into infectious HBV- HDV not being treated class I_{NHBD}.

ε_2: The rate at which individuals who are infectious of HBV-HDV enter into infectious HBV- HDV being treated class I_{THBD}.

η: The rate at which individuals that are infectious of HBV-HDV and are being treated recover

ϵ: The rate at which HBV infectious individuals who are exposed to HDV and then being treated become infectious of HBV-HDV.

$\theta(1+c)$: The rate at which HBV infectious individuals that are exposed to HDV and are being treated recover.

ϕ_2: The rate at which individuals who recovered from HBV-HDV goes back to susceptible class again.

μ: The natural mortality/death rate.

δ:HBV-induced mortality/death rate for people infectious of HBV treated class

δ_1: HBV-induced mortality/death rate for people infectious of HBV but not being treated class.

δ_2: HDV-induced mortality/death rate for HBV infectious individuals who are exposed and being treated of HDV.

δ_3: HBV-HDV-induced mortality/death rate for HBV infectious individuals who are infectious of HBV-HDV and are being treated.

δ_4: HBV-HDV-induced mortality/death rate for individuals who are infectious of HBV-HDV and are not being

treated.

θ: Cure rate

$\left.\begin{matrix} c \\ c_1 \\ c_2 \end{matrix}\right\}$:Infectivity controls; where c_1 is enlightenment, c_2 is condom use and c is drug efficacy(therapy).

Model Description:

Based on the standard SEIR model, the population is partitioned into thirteen compartments or classes namely: Susceptible(S), Exposed to HBV(E_{HB}), Exposed to HBV and Treated(E_{THB}), Infectious of HBV(I_{HB}), Infectious of HBV and Treated(I_{THB}), Infectious of HBV and not Treated(I_{NHB}), Recovered of HBV(R_{HB}), HBV infectious now Exposed to HDV(E_{HBD}),HBV infectious now Exposed to HDV and treated(E_{THBD}), Infectious of HBV-HDV Co infection(I_{HBD}), Infectious of HBV-HDV Co infection and treated(I_{THBD}), Infectious of HBV-HDV Co infection and not treated(I_{NHBD}), Recovered of HBV-HDV Co infection(R_{HBD}) Compartments.

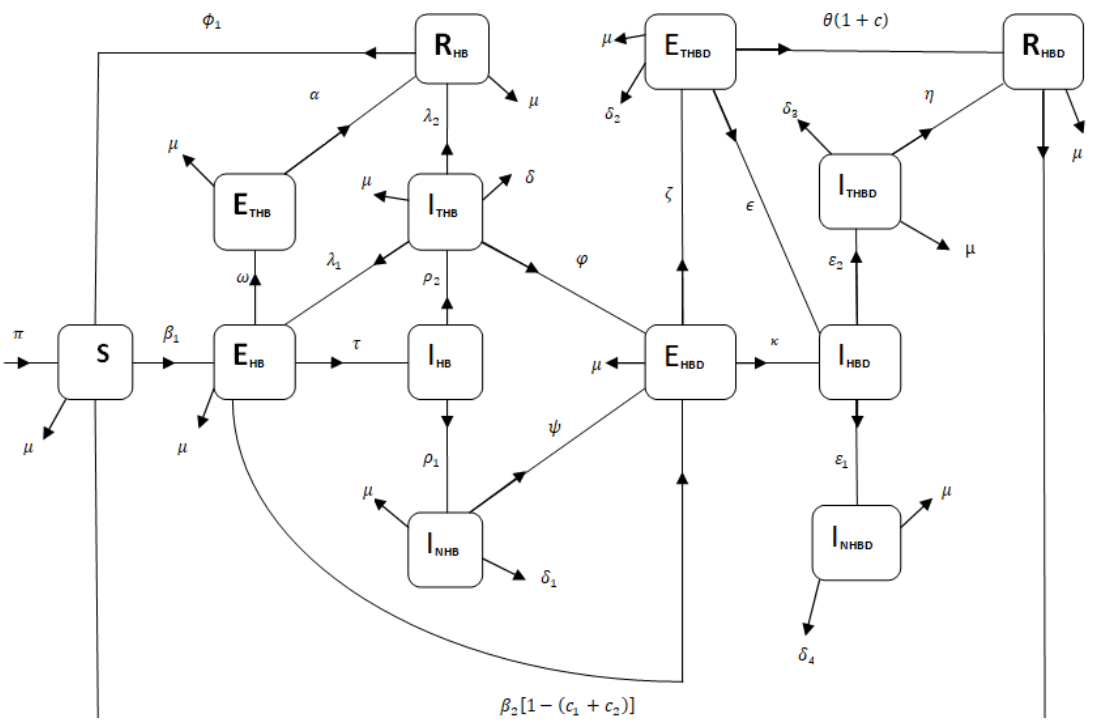

Figure 1: Flow Diagram of HBV-HDV Co-infection Transmission with controls

Model Equations of HBV-HDV Co-infection:

$$\frac{ds}{dt} = \pi + \phi_1 R_{HB} + \phi_2 R_{HBD} - \beta_1 S I_{HB} - \mu S \tag{1}$$

$$\frac{dE_{HB}}{dt} = \beta_1 S I_{HB} - \beta_2[1-(c_1+c_2)]E_{HB} I_{HBD} + \gamma_1 I_{THB} - \omega E_{HB} - \tau E_{HB} - \mu E_{HB} \tag{2}$$

$$\frac{dE_{THB}}{dt} = \omega E_{HB} - \mu E_{THB} - \alpha E_{THB} \tag{3}$$

$$\frac{dI_{HB}}{dt} = \tau E_{HB} - \rho_1 I_{HB} - \rho_2 I_{HB} \tag{4}$$

$$\frac{dI_{NHB}}{dt} = \rho_1 I_{HB} - \psi I_{NHB} I_{HBD} - \mu I_{NHB} - \delta_1 I_{NHB} \tag{5}$$

$$\frac{dI_{NHB}}{dt} = \rho_2 I_{HB} - \varphi I_{THB} - \lambda_1 I_{THB} - \lambda_2 I_{THB} - \mu I_{THB} - \delta I_{THB} \tag{6}$$

$$\frac{dR_{HB}}{dt} = \lambda_2 I_{THB} + \alpha E_{THB} - \phi_1 R_{HB} - \mu R_{HB} \tag{7}$$

$$\frac{dE_{HBD}}{dt} = \beta_2 E_{HB} I_{HBD} + \psi I_{NHB} I_{HBD} + \varphi I_{THB} E_{HBD} - kE_{HBD} - \varsigma E_{HBD} - \mu E_{HBD} \tag{8}$$

$$\frac{dE_{THBD}}{dt} = \varsigma E_{HBD} - \theta(1+c) E_{THBD} - \epsilon E_{THBD} - \mu E_{THBD} - \delta_2 E_{THBD} \tag{9}$$

$$\frac{dI_{HBD}}{dt} = kE_{HBD} + \epsilon E_{THBD} - \varepsilon_1 I_{HBD} - \varepsilon_2 I_{HBD} \tag{10}$$

$$\frac{dI_{NHBD}}{dt} = \varepsilon_1 I_{HBD} - \mu I_{NHBD} - \delta_4 I_{NHBD} \tag{11}$$

$$\frac{dI_{THBD}}{dt} = \varepsilon_2 I_{HBD} - \eta I_{THBD} - \mu I_{THBD} - \delta_3 I_{THBD} \tag{12}$$

$$\frac{dR_{HBD}}{dt} = \theta(1+c) E_{THBD} - \eta I_{THBD} - \mu R_{HBD} - \phi_2 R_{HBD} \tag{13}$$

$$N = S + E_{HB} + E_{THB} + I_{NHB} + I_{THB} + R_{HB} + E_{HBD} + E_{THBD} + I_{NHBD} + I_{THBD} + R_{HBD} \tag{14}$$

Susceptible individuals acquire HBV infection following effective contact with individuals infected with HBV (i.e., those in the E_{HB}, I_{NHB} and I_{THB} classes) at a rate β_1, given by $\beta_1 = \frac{\theta_B(E_{HB}+\mu_3 I_{NHB}+\mu_4 I_{THB})}{N}$; $N = S + E_{HB} + I_{NHB} + I_{THB}$,

where θ_B is the effective contact rate for HBV transmission[23]. Further, the modification parameters $\mu_3 \geq 1$ and $\mu_4 < 1$ account for the relative infectiousness of individuals in the I_{NHB} and I_{THB} classes in comparison to those in the E_{HB} class. That is individuals in I_{NHB} are more infectious than those individuals in the E_{HB} class, likewise, I_{THB} are less infectious than those in the I_{NHB} class (because the use of treatment significantly reduces the viral load in those treated). Similarly, individuals in the susceptible classes (E_{HB}, I_{NHB} and I_{THB}) acquire HBD, following effective contact with individuals infected with HBD.

(i.e., those in the $E_{HBD}, I_{NHBD}, I_{THBD}$) at a rate β_2, given by

$$\beta_2 = \frac{\theta_{BD}(E_{HBD} + \mu_5 I_{NHBD} + \mu_6 I_{THBD})}{N};\ N = S + E_{HBD} + I_{NHBD} + I_{THBD}$$

where θ_{BD} is the effective contact rate for HBD transmission[23]. Further, the modification parameters $\mu_5 \geq 1$ and $\mu_6 < 1$ account for the relative infectiousness of individuals in the I_{NHBD} and I_{THBD} classes in comparison to those in the E_{HBD} class. That is, individuals in the I_{NHBD} class are more infectious than those in the E_{HBD} class, and likewise, I_{THBD} are less infectious than those in I_{NHBD} class (because the use of treatment significantly reduces the viral load in those treated).

3 Analysis of the Model

Equilibrium Solutions: Let $E : (S, E_{HB}, E_{THB}, I_{HB}, I_{NHB}, I_{THB}, R_{HB}, E_{HBD}, E_{THBD}, I_{HBD}, I_{NHBD}, I_{THBD}, R_{HBD})$ be the equilibrium point of the system described by the equations (2.1) (2.14).

At the equilibrium state, we have that;

$$\dot{S} = \dot{E}_{HB} = \dot{E}_{THB} = \dot{I}_{HB} = \dot{I}_{NHB} = \dot{I}_{THB} = \dot{R}_{HB} = \dot{E}_{HBD} = \dot{E}_{THBD} = \dot{I}_{HBD} = \dot{I}_{NHBD} = \dot{I}_{THBD} = \dot{R}_{HBD} = 0.$$

i.e.,

$$\pi + \phi_1 R_{HB} + \phi_2 R_{HBD} - \beta_1 S I_{HB} - \mu S = 0 \tag{15}$$

$$\beta_1 S I_{HB} - \beta_2 [1 - (c_1 + c_2)] E_{HB} I_{HBD} + \gamma_1 I_{THB} - \omega E_{HB} - \tau E_{HB} - \mu E_{HB} = 0 \tag{16}$$

$$\omega E_{HB} - \mu E_{THB} - \alpha E_{THB} = 0 \tag{17}$$

$$\tau E_{HB} - \rho_1 I_{HB} - \rho_2 I_{HB} = 0 \tag{18}$$

$$\rho_1 I_{HB} - \psi I_{NHB} I_{HBD} - \mu I_{NHB} - \delta_1 I_{NHB} = 0 \tag{19}$$

$$\rho_2 I_{HB} - \varphi I_{THB} - \lambda_1 I_{THB} - \lambda_2 I_{THB} - \mu I_{THB} - \delta I_{THB} = 0 \tag{20}$$

$$\lambda_2 I_{THB} + \alpha E_{THB} - \phi_1 R_{HB} - \mu R_{HB} = 0 \tag{21}$$

$$\beta_2 E_{HB} I_{HBD} + \psi I_{NHB} I_{HBD} + \varphi I_{THB} E_{HBD} - k E_{HBD} - \varsigma E_{HBD} - \mu E_{HBD} = 0 \tag{22}$$

$$\varsigma E_{HBD} - \theta(1 + c) E_{THBD} - \epsilon E_{THBD} - \mu E_{THBD} - \delta_2 E_{THBD} = 0 \tag{23}$$

$$k E_{HBD} + \epsilon E_{THBD} - \varepsilon_1 I_{HBD} - \varepsilon_2 I_{HBD} = 0 \tag{24}$$

$$\varepsilon_1 I_{HBD} - \mu I_{NHBD} - \delta_4 I_{NHBD} = 0 \tag{25}$$

$$\varepsilon_2 I_{HBD} - \eta I_{THBD} - \mu I_{THBD} - \delta_3 I_{THBD} = 0 \tag{26}$$

$$\theta(1 + c) E_{THBD} - \eta I_{THBD} - \mu R_{HBD} - \phi_2 R_{HBD} = 0 \tag{27}$$

In order to obtain the disease-free equilibrium state, we shall solve equations (3.1) (3.13) simultaneously.

The Disease-free Equilibrium State (DFE):

The disease-free equilibrium state is the state of total absence of the disease.

Let $E_* : (S_*, E_{HB*}, E_{THB*}, I_{HB*}, I_{NHB*}, I_{THB*}, R_{HB*}, E_{HBD*}, E_{THBD*}, I_{HBD*}, I_{NHBD*}, I_{THBD*}, R_{HBD*})$ be the disease-free equilibrium state. At the disease-free equilibrium state, we have that

$$E_{HB} = E_{THB} = I_{HB} = I_{NHB} = I_{THB} = R_{HB} = E_{HBD} = E_{THBD} = I_{HBD} = I_{NHBD} = I_{THBD} = R_{HBD} = 0 \tag{28}$$

Now by substituting the values of equation (3.14) into equations (3.1) (3.13) and solving simultaneously, we obtain the following results;

Equation (3.1) reduces to:

$$\pi + \phi_1 R_{HB} + \phi_2 R_{HBD} - \mu S = 0 \tag{29}$$

Equation (3.7) reduces to:

$$-\phi_1 R_{HB} - \mu R_{HB} = 0 \tag{30}$$

Equation (3.13) reduces to:

$$-\mu R_{HBD} - \phi_2 R_{HBD} = 0 \tag{31}$$

From Equation (3.16), we get

$$-\phi_1 R_{HB} - \mu R_{HB} = 0 \Rightarrow -\phi_1 R_{HB} = \mu R_{HB}$$

Hence $(\mu - \phi_1)R_{HB} = 0 \Rightarrow R_{HB} = 0$

Also from equation (3.17),

$$-\mu R_{HBD} - \phi_2 R_{HBD} = 0 \Rightarrow -\mu R_{HBD} = \phi_2 R_{HBD}$$

Therefore, $(\mu - \phi_2)R_{HBD} = 0 \Rightarrow R_{HBD} = 0$.

Now substituting the values of $R_{HB} = 0$ and $R_{HBD} = 0$ into equation (3.15) we obtain;

$$\pi - \mu S = 0 \Rightarrow \mu S = \pi$$

Therefore, $S = \frac{\pi}{\mu}$. Therefore the disease-free equilibrium state for the model (HBV-HDV Co-infection) is thus;

Let

$$E_* : (S_*, E_{HB*}, E_{THB*}, I_{HB*}, I_{NHB*}, I_{THB*}, R_{HB*}, E_{HBD*}, E_{THBD*}, I_{HBD*}, I_{NHBD*}, I_{THBD*}, R_{HBD*}) = (\frac{\pi}{\mu}, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0) \in \mathbb{R}^{13} \tag{32}$$

Stability Analysis: To determine the stability or otherwise of the disease-free equilibrium state E_* we shall examine the behavior of the model population near this equilibrium solution. We shall determine the condition(s) that must be met for the disease-free equilibrium state to be stable. Hence, we shall determine the condition(s) that must be met if the disease is to be totally absent in the population.

Recall that at the equilibrium state, we have the following set of equations:

$$\pi + \phi_1 R_{HB} + \phi_2 R_{HBD} - \beta_1 S I_{HB} - \mu S = 0$$

$$\beta_1 S I_{HB} - \beta_2 [1 - (c_1 + c_2)] E_{HB} I_{HBD} + \gamma_1 I_{THB} - \omega E_{HB} - \tau E_{HB} - \mu E_{HB} = 0$$

$$\omega E_{HB} - \mu E_{THB} - \alpha E_{THB} = 0$$

$$\tau E_{HB} - \rho_1 I_{HB} - \rho_2 I_{HB} = 0$$

$$\rho_1 I_{HB} - \psi I_{NHB} I_{HBD} - \mu I_{NHB} - \delta_1 I_{NHB} = 0$$

$$\rho_2 I_{HB} - \varphi I_{THB} - \lambda_1 I_{THB} - \lambda_2 I_{THB} - \mu I_{THB} - \delta I_{THB} = 0$$

$$\lambda_2 I_{THB} + \alpha E_{THB} - \phi_1 R_{HB} - \mu R_{HB} = 0$$

$$\beta_2 E_{HB} I_{HBD} + \psi I_{NHB} I_{HBD} + \varphi I_{THB} E_{HBD} - k E_{HBD} - \varsigma E_{HBD} - \mu E_{HBD} = 0$$

$$\varsigma E_{HBD} - \theta(1 + c) E_{THBD} - \epsilon E_{THBD} - \mu E_{THBD} - \delta_2 E_{THBD} = 0$$

$$k E_{HBD} + \epsilon E_{THBD} - \varepsilon_1 I_{HBD} - \varepsilon_2 I_{HBD} = 0$$

$$\varepsilon_1 I_{HBD} - \mu I_{NHBD} - \delta_4 I_{NHBD} = 0$$

$$\varepsilon_2 I_{HBD} - \eta I_{THBD} - \mu I_{THBD} - \delta_3 I_{THBD} = 0$$

$$\theta(1 + c) E_{THBD} - \eta I_{THBD} - \mu R_{HBD} - \phi_2 R_{HBD} = 0$$

We now linearize the system of equations to get the Jacobian Matrix J.

Now the determinant of the entries of the Jacobian Matrix evaluated at Disease-free equilibrium is as shown below;

$J^* =$

$$\begin{bmatrix} -\omega-\tau-\mu-X & 0 & \beta_1\frac{\pi}{\mu} & \lambda_1 & 0 & 0 & 0 & 0 & 0 & 0 \\ \omega & -\mu-\alpha-X & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \tau & 0 & -\rho_1-\rho_2-X & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \rho_2 & -\Phi-\lambda_1-\lambda_2-\mu-\delta-X & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \alpha & 0 & \lambda_2 & -\phi_1-\mu-X & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -\kappa-\zeta-\mu-X & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \xi & -\theta(1+c)-\varepsilon-\mu-\delta_2-X & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \kappa & \varepsilon & -\varepsilon_1-\varepsilon_2-X & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \varepsilon_2 & -\eta-\mu-\delta_3-X & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \theta(1+c) & 0 & \eta & -\mu-\phi_2-X \end{bmatrix}$$

Let $F := -\omega-\tau-\mu$; $G := -\mu-\alpha$; $H := -\rho_1-\rho_2$; $R := -\Phi-\lambda_1-\lambda_2-\mu-\delta$; $s : -\phi_1-\mu$
$T := -k-\zeta-\mu$; $U := \theta(1+c)-\varepsilon-\mu-\delta_2$; $V := -\varepsilon_1-\varepsilon_2$; $w := -\eta-\mu-\delta_3$; $z := -\mu-\phi_2$
Therefore, it reduces to;

$$J^* = \begin{bmatrix} F-X & 0 & \beta_1\frac{\pi}{\mu} & \lambda_1 & 0 & 0 & 0 & 0 & 0 & 0 \\ \omega & G-X & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \tau & 0 & H-X & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \rho_2 & R-X & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \alpha & 0 & \lambda_2 & s-X & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & T-X & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \xi & u-X & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & k & \varepsilon & v-X & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \varepsilon_2 & w-X & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \theta(1+c) & 0 & \eta & z-X \end{bmatrix}$$

$$\frac{(G-X)\cdot(S-X)\cdot(T-X)\cdot(U-X)\cdot(V-X)\cdot(W-X)\cdot(Z-X)\left[-\mu X^3+(F\cdot\mu+H\cdot\mu+R\cdot\mu)X^2+\left(\pi\cdot\tau\cdot\beta_1-F\cdot H\cdot\mu-F\cdot R\cdot\mu-H\cdot R\cdot\mu\right)X+\left(F\cdot H\cdot R\cdot\mu-\pi\cdot R\cdot\tau\cdot\beta_1+\mu\cdot\tau\cdot\rho_2\lambda_1\right)\right]}{\mu}=0$$

Note: Multiply the whole determinant by; $-(\mu+X)\cdot(\mu+\delta_1+X)\cdot(\mu+\delta_4+X)$

$$\frac{\left[-(\mu+X)\cdot(\mu+\delta_1+X)\cdot(\mu+\delta_4+X)\cdot(G-X)\cdot(S-X)\cdot(T-X)\cdot(U-X)\cdot(V-X)\cdot(W-X)\cdot(Z-X)\right]\left[\mu X^3+(-F\cdot\mu-H\cdot\mu-R\cdot\mu)X^2+(F\cdot H\cdot\mu-\pi\cdot\tau\cdot\beta_1+F\cdot R\cdot\mu+H\cdot R\cdot\mu)X+(\pi\cdot R\cdot\tau\cdot\beta_1-F\cdot H\cdot R\cdot\mu-\mu\cdot\tau\cdot\rho_2\lambda_1)\right]}{\mu}=0$$

$$\frac{\left[-(\mu+X)\cdot(\mu+\delta_1+X)\cdot(\mu+\delta_4+X)\cdot(G-X)\cdot(S-X)\cdot(T-X)\cdot(U-X)\cdot(V-X)\cdot(W-X)\cdot(Z-X)\right]\cdot\left(AX^3+BX^2+CX+D\right)}{\mu}=0$$

where $A := \mu$; $B = -F\mu-H\mu-R\mu$; $C := (-\pi\tau\beta_1+FH\mu+FR\mu+HR\mu)$; $D := (-FHR\mu+\pi R\tau\beta_1-\mu\tau\rho_2\lambda_1)$.
With the numerical values of the parameters (see table 4), we got the respective values of A, B, C and D as follows

$$A = 0.02;\ B = 0.029;\ C = -184.98;\ D = -29.044$$

4 Results

Eigen value classification of stability (Eigen value of the Jacobean Matrix of the equilibrium point):

Assumption of the equilibrium:

We assumed that the equilibrium point is an isolated critical point or the zero solution or the null solution. It is upon this assumption that we discuss our result(s).

Now consider the result

$$AX^3 + BX^2 + CX + D = 0$$

Where the values of A, B, C and D are as shown above The following theorems and definitions will validate our discussion, thus

Theorem 1: Let A be a constant matrix in the system $\dot{x} = Ax$ with eigenvalues $\lambda i, i = 1, 2, ..n$. (i) If the system is stable, then $Re\{\lambda i\} \leq 0, i = 1, 2, ..., n$.

(ii) If either $Re\{\lambda i\} < 0, i = 1, 2, ..., n$; or if $Re\lambda i \leq 0, i = 1, 2, ..., n$

and there is no zero repeated eigenvalue; then the system is uniformly stable.

(iii) The system is asymptotically stable if and only if $Re\{\lambda i\} < 0, i = 1, 2, ..., n$

(and then it is also uniformly stable, by (ii)).

(iv) If $Re\{\lambda i\} > 0$ for any i, the solution is unstable. In connection with (ii), note that if there is a zero repeated Eigen value the system may be stable or unstable [4, 8 and 13].

Theorem 2: Suppose that we have a set of autonomous ordinary differential equations, written in vector form:

$$\dot{x} = f(x) \tag{33}$$

Suppose that x^* is an equilibrium point. By definition, $f(x^*) = 0$ An equilibrium point x^* of the differential equation (4.1) is stable if all the eigenvalues of J^*, the Jacobian matrix evaluated at x^*, have negative real parts. The equilibrium point is unstable if at least one of the eigenvalues has a positive real part[4, 8 and 13].

Definition 1: An equilibrium state $x = 0$ is said to be :

1. stable if for any positive scalar ε there exists a positive scalar δ such that $||x(t_0)|| < \delta$ implies $||x(t)|| < \epsilon$ for all $t \geq t_0$
2. asymptotically stable if it is stable and if in addition $x(t) \to 0$ as $t \to \infty$
3. unstable if it is not stable; that is, there exists an $\varepsilon > 0$ such that for every $\delta > 0$ there exists an $x(t_0)$ with $||x(t_0)|| < \delta, ||x(t_1)|| \geq \varepsilon$ for some $t_1 > t_0$
4. completely unstable if there exists an $\varepsilon > 0$ such that for every $\delta > 0$ and for every $x(t_0)$ with $||x(t_0)|| < \delta, ||x(t_1)|| \geq \varepsilon$ for some $t_1 > t_0$[13]. (Note: The definition (a) is often called 'stability in the sense of Lyapunov')

Definition 2: The equilibrium point q is said to be stable if given $\varepsilon > 0$ there is a $\delta > 0$ such that $||\phi(t, p) - q|| < \epsilon$ for all $t > 0$ and for all p such that $p - q < \delta$. If δ can be chosen not only so that the solution q is stable but also so that $\phi(t, p) \to q$ as $t \to \infty$, then q is said to be asymptotically stable. If q is not stable it is said to be unstable. [13].

Now considering equation (4.1).

This is a cubic equation, and the general formula for the roots, in terms of the coefficients of any cubic equation, is as follows:

$$X_k = -\frac{1}{3A}(B + u_k L + \frac{\Delta_0}{u_k L}), k = 1, 2, 3$$

where $u_1 = 1, u_2 = \frac{-1+i\sqrt{3}}{2}, u_3 = \frac{-1-i\sqrt{3}}{2}$ are the three cube roots of unity, and where $L = \sqrt[3]{\frac{\Delta_1+\sqrt{\Delta_1^2-4\Delta_0^3}}{2}}$ with $\Delta_0 = B^2 - 3AC$ and $\Delta_1 = 2B^3 - 9ABC + 27A^2D$.[4,5,7,8,9,12,15,24,25] and [26]

Now the three roots are: When $k = 1$, we computed X_1 as:

$X_1 = 94.46385835340232762 + 90.00203173838270501923$ Similarly, we computed X_2 and X_3 when $k = 2$ and $k = 3$ respectively and obtained: $X_2 = 93.2535985877151052190.00205063417222723027$

$X_3 = 0.17069261526515854234 0.004082372554932249 4715i$

Using Eigen value classification of stability, we shall summarise our discussion of the roots of this equation using table under the following headings: classification of the root, behaviour of the solution of the root and the nature of stability of the root as shown in table 1, table 2 and table 3 below for X_1, X_2 and X_3 respectively.

Table 1: For the first root (X_1):

Classification	Behaviour of the solution	The nature of Stability
Complex with negative real part	Spiral sink	Asymptotically stable

Table 2:For the second root (X_2):

Classification	Behaviour of the solution	The nature of Stability
Complex with positive real part	Spiral Source	Unstable

Table 3: For the Third root (X_3):

Classification	Behaviour of the solution	The nature of Stability
Complex with negative real part	Spiral sink	Asymptotically stable

Computation of the Value of the Effective Reproduction Number R_0 of HBV-HDV Co-infection by substituting the numerical values of the parameters of HBV-HDV Co-infection using Mathcad:

The effective reproduction number of HBV-HDV co-infection was calculated by [1] ; thus;

$$R_0 = \frac{\pi\tau\beta_1(\mu+\Phi+\delta+\lambda_1+\lambda_2) + \pi\sqrt{\tau^2+\delta_1^2(\mu+\Phi+\delta+\lambda_1+\lambda_2)^2}}{2\mu[\tau\lambda_1\rho_2 + (\mu+\tau+\omega)(\rho_1+\rho_2)(\mu+\Phi+\delta+\lambda_1+\lambda_2)]}$$

$$R_0 = \frac{\Pi\tau\beta_1(\mu+\phi+\Delta+\lambda_1+\lambda_2) + \Pi\sqrt{\tau^2+\delta_1^2(\mu+\phi+\Delta+\lambda_1+\lambda_2)^2}}{2\mu[\tau\lambda_1\rho_2 + (\mu+\tau+\omega)(\rho_1+\rho_2)(\mu+\phi+\Delta+\lambda_1+\lambda_2)]}$$

By substituting the numerical values of the parameters in the effective reproduction number , we will get the result as shown below;

$$R_0 = \frac{10000.500.37(0.021+0.043+0.068+0.01+0.015) + 1000\sqrt{0.50^2.0.37^2(0.021+0.043+0.068+0.01+0.015)^2}}{2.0.021[0.50.0.01.0.33 + (0.021+0.50+0.02)(0.33+0.33)(0.021+0.043+0.068+0.01+0.015)]}$$

$$R_0 = 23966.957301815542$$

$$R_0 > 1 \Rightarrow \text{Unstable}$$

Discussion: From our results displayed in tables1, 2 and 3 above; we can see that the disease is unstable, this means that any minor increase in the infection can cause epidemic in the population. Moreover, the result shows

that the disease is asymptotically stable, this implies that there are traces of the disease in the population, but it is no longer pronounced in the sense that a small control on the infected persons (individuals) can remove it completely from the population.

Conclusion: We built a mathematical model for HBV-HDV Co-infection with controls (enlightenment, condom use and therapy). Furthermore, the equilibrium solution of the model was obtained. The results of the stability analysis of HBV-HDV Co-infection was verified and discussed.

S/N	Parameter	Value	Reference
1	μ	0.021	[2] and [3]
2	π	1000	assumed
3	β_1	0.37	Assumed
4	τ	0.50	[28] and [16]
5	β_2	0.37	Assumed
6	c_1	0.08	[2]
7	c_2	0.08	[2]
8	ψ	0.047	Assumed
9	$\varphi \Rightarrow \Phi$	0.043	Assumed
10	λ_1	0.01	Assumed
11	λ_2	0.015	[2]
12	ω	0.02	Assumed
13	α	0.015	[2]
14	ρ_1	0.33	[28] and [16]
15	ρ_2	0.33	[28] and [16]
16	θ	0.08	[2]
17	c	0.08	[2]
18	ε_1	0.038	Assumed
19	ε_2	0.038	Assumed
20	η	0.028	Assumed
21	K	0.50	[28] and [16]
22	ς	0.032	Assumed
23	ϵ	0.035	Assumed
24	ϕ_1	0.92	Assumed
25	ϕ_1	0.92	Assumed
26	δ	0.068	[2]
27	δ_1	0.08	[2]
28	δ_2	0.08	[2]
29	δ_3	0.08	[2]
30	δ_4	0.08	[2]

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