Modelling the Transmission Dynamics of HIV and HBV Co-epidemics: Analysis and Simulation.

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Abstract

The prevalence of Hepatitis B Virus (HBV) and Human immunodeficiency virus (HIV) co-infection have been on the increase. Moreover, none of these two diseases has a cure for now while both diseases are very deadly. However, the mode of transmission of these diseases are closely related and this highly predisposes individuals to co-infection. There is, therefore, the need to initiate effective control measures that would forestall the co-epidemic of the two diseases in our society, considering the grave implications of such situation. Consequently, a deterministic model for HIV and HBV co-epidemic which unveils measures that should be implemented to avoid the menace associated with the co-epidemic is considered. The model is qualitatively analyzed and the model basic reproduction number is derived. The criteria for the stability of each of the model equilibria are established. The model is numerically solved and simulated for the different scenarios of the co-epidemic. The findings from the simulations are discussed.

Keywords: Hepatitis B Virus, Human immunodeficiency virus, Co-epidemic, Disease prevalence, Equilibrium solution, Stability analysis

1   INTRODUCTION

Human immunodeficiency virus (HIV) and Hepatitis B Virus (HBV) disease co-infection is common globally due to similar mode of

transmission [6, 3]. It is estimated by the Joint United Nations Program on HIV/HBV that 10% of 33 million HIV-infected patients are concurrent infected with chronic HBV [11]. Aside, there are more than 350 million people currently infected with HBV while 75% of these carriers reside in Asia [4, 18]. In Nigeria, the prevalence of HIV/HBV co-infection ranges between 10% − 70% of the population in each of the geopolitical zones. The variation across these zones is about the widest observed in any country in the world [16]. Co-infection of HBV and HIV occur when individuals who are HIV positive are concurrently infected with HBV. Getting infected with HBV is not automatic for HIV infected individuals unless they have sufficient contact (devoid of precautionary measures) with infectious HBV individuals. Similarly, individuals infected with HBV do not get infected with HIV unless they are sufficiently exposed to the (HIV) virus without effective protection.

It is worthy to note that HIV infection modifies the course of HBV infection by increasing rates of chronicity, prolonging HBV viremia, and increasing liver diseases associated deaths. This calls for concern because, apart from increasing the toxicity to antiretroviral medications, patients with HIV/HBV co-infection have increased levels of HBV replication, decreased rates of spontaneous resolution of the HBV infection, and more risk of reactivation of previous infections. Thus, individuals with co-infection of both diseases have higher tendency of developing cirrhosis of the liver. Although, HBV and HIV possess similar features like transmission using a reverse transcriptase enzyme during replication, likelihood to develop chronic infections, and high probability of mutation in their genome occasionally resulting into resistance to widely used anti-viral agents [16]. The medical profile of an acute HBV infected patient may change in the presence of HIV infection with the exhibition of fewer cases of icteric illness and reduced spontaneous clearance of HBV [8].

Moreover, individuals that are infected with both HIV and chronic HBV have higher levels of HBV DNA and reduced rates of clearance of the hepatitis B e-antigen (HBeAg). According to some medical professionals, serum transaminase levels may be lower in HIV/HBV co-infected patients when compared to patients infected with only HBV, but normal transaminase levels should not be taking as an indication that there is no underlying hepatic fibrosis [13]. In recent times, diseases associated with liver infection are the top killer diseases, with the exception of HIV/AIDS, particularly in parts of the world with wide coverage for the antiretroviral therapy (ART) administration. Worse still, some cohort studies also show that the risk of liver-associated disease induced deaths is 2-3 times higher in HIV/HBV co-infected patients than in patients infected with only HIV disease (14% *vs* 6%) [13]. Equally, HIV/HBV co-infection could result into more frequent flares of hepatic transaminase which may trigger immune reconstitution inflammatory syndrome (IRIS) due to ART, interruption of HIV/HBV treatment, or the development of resistance to HIV/HBV therapy .

In the field of epidemiology, mathematical modeling has provided valuable insights into the spread of infectious diseases among humans while it has also helped inform health policies which could be implemented to address serious epidemiological issues. Thus, there have been series of modelling research works on infectious diseases. Some of these works provide general framework for modelling infectious diseases which exhibits some features without focusing on a particular disease (see [10, 22, 21]). On the other hand, there are other research works that are centered on the dynamics of a particular disease and how it can be successfully controlled and possibly eradicated. For instance, Yusuf et al, Waziri et al, and Nsuami considered models for the spread, treatment, and control of HIV/AIDS [15, 19, 20]. Similarly, Hsin-Yun et al, Ijalana et al, Medley et al, and Zhang et al worked on models for the spread and control of HBV [6, 7, 14, 22]. However, there are quite a few works on modelling co-infection of two infectious diseases (See [1, 2, 3, 5, 17]). Research

works on co-infection are important because such works are central in discerning the interrelationship between these diseases. Equally, such studies help in determining how prevention and treatment efforts can be most effective in such circumstance. In this research work, a model for HIV/HBV co-epidemics will be considered. This is justifiable because only few works has been done in the area while the issues poses a serious threat in places where the prevalence of both diseases is very high.

This paper is structured as follows: In section 2, an epidemiological model for HIV and HBV co-epidemic is proposed. The model will be shown to be epidemiologically well-posed while the basic reproduction number (R_0) for the model will be presented. In section 3, the equilibrium solutions of the model and its different sub-models will be determined. In addition, the criteria for the local and global stability of each of these equilibria will be established. In section 4, the sensitivity analysis of R_0 with respect to each of the model parameters are carried out and the model will be solved numerically. The numerical results are simulated for different scenarios of the co-epidemics while finding from the simulations are discussed. In the last section, the conclusions from the study are given.

2   PROPOSED MATHEMATICAL MODEL

A mathematical model which divides the human population into four mutually exclusive compartments is considered. The compartments are the Susceptible class $S(t)$, the HBV only infected class $I_B(t)$, HIV only infected class $I_H(t)$, and the HIV/HBV co-infected class $I_C(t)$. The schematic diagram for the disease transmission dynamics is presented in Figure 2.1 while the model representing the dynamics of HIV/HBV co-epidemics is given as a system of nonlinear ordinary differential equations afterwards:
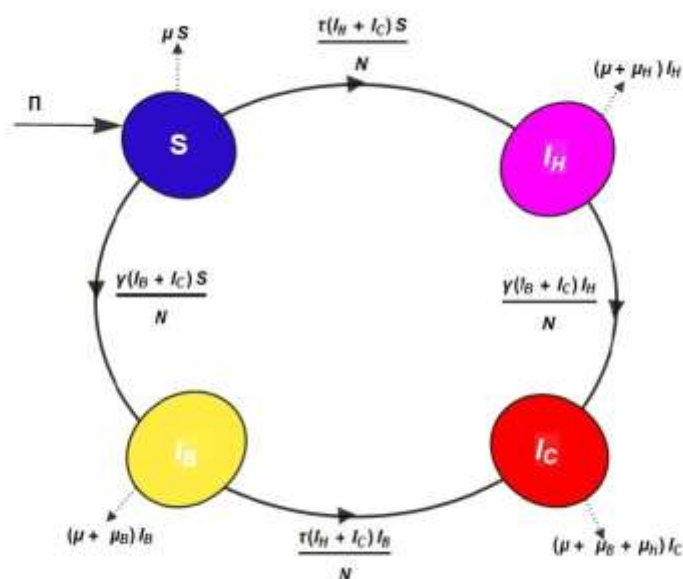
Figure 2.1: Diagrammatic Representation of the Model Dynamics

Basic Model Assumptions

Taking a cue from Kalu et al [9] and Long et al [5], we constructed our proposed model using the assumptions below:

- Individuals in the population of interest are classified into different compartments based on their infection status with respect to each of the two diseases.

- The compartments in the model are mutually exclusive while the population dynamics of each of the compartment is purely deterministic.

- Individuals in the different compartments mix freely, without segregation, irrespective of individual's infection status.

- The natural death rate for individuals in the various compartments is the same, since there is no immunity to death whether one is sick or healthy.

- No individual gets infected with both diseases at once, rather they get infected with one of the two diseases first while they contact the second afterwards.

- The model parameters are all non-negative and each take same numerical value for individuals infected with either or both diseases.

- New recruits (i.e. new entries) into the population are all susceptible and they come into the population at a constant rate Π

- The transmission of diseases among individuals in the different compartments occur through random mixing of the individuals.

Sequel to the above listed assumptions, the proposed model subdivides the total population at time t denoted as $N(t)$ into four epidemiological classes representing the susceptible $S(t)$, HBV infected $I_B(t)$, HIV infected $I_H(t)$ and the co-infected $I_C(t)$. Thus,

$$N(t) = S(t) + I_B(t) + I_H(t) + I_C(t)$$

Individuals enter the susceptible population either by birth or immigration at the constant rate Π. The susceptible populationclass decreases due to infection of susceptibles by the HBV or HIV infected individuals at constant rates of γ and τ respectively. The susceptible class population is further reduced due to natural death at a constant rate μ. Thus,

$$\frac{dS}{dt} = \Pi - \gamma(I_B + I_C)\frac{S}{N} - \tau(I_H + I_C)\frac{S}{N} - \mu S, \qquad (2.1)$$

With sufficient contact of susceptible individual with either HBV infected or HIV/HBV co-infected individuals, the susceptible individual becomes a member of the HBV (I_B) class at a constant rate of γ. Individuals in HBV class could progress to the co-infected class I_C if he/she have a sufficient contact with either HIV individual or co-infected individual at the rate of τ. HBV infected population is reduced by death due to disease or by natural death rate denoted as μ_B or μ. Hence,

$$\frac{dI_B}{dt} = \gamma(I_B + I_C)\frac{S}{N} - \tau(I_H + I_C)\frac{I_B}{N} - (\mu + \mu_B)I_B \qquad (2.2)$$

Similarly, susceptible individuals who had sufficient contact with either HIV or HIV/HBV co-infected individuals become a member of HIV class (I_H) at constant rate of τ. Individuals in HIV class could become HIV/HBV co-infected if they are exposed (without adequate protection) to HBV infection through contact with either HBV-infected individuals or HIV/HBV co-infected individuals at the rate of γ. HIV-infected class population is reduced by HIV disease death at constant rate μ_H or by natural death at constant rate denoted as μ. Thus,

$$\frac{dI_H}{dt} = \tau(I_H + I_C)\frac{S}{N} - \gamma(I_B + I_C)\frac{I_H}{N} - (\mu + \mu_H)I_H \qquad (2.3)$$

The population of the HIV/HBV co-infected class increased due as a result of individuals who have been co-infected from HBV compartment at constant rate τ and those that has been co-infected from HIV compartment at constant rate of γ while individuals in this compartment die either due to natural death at the rate μ, HBV induced death at the μ_B or HIV induced death at rate μ_H. Hence,

$$\frac{dI_C}{dt} = \gamma(I_B + I_C)\frac{I_H}{N} + \tau(I_H + I_C)\frac{I_B}{N} - (\mu + \mu_B + \mu_H)I_C \qquad (2.4)$$

Thus, the model for the dynamics of the HIV/HBV co-epidemics is as presented below:

$$\begin{aligned}
\frac{dS}{dt} &= \Pi - \gamma(I_B + I_C)\frac{S}{N} - \tau(I_H + I_C)\frac{S}{N} - \mu S, \\
\frac{dI_B}{dt} &= \gamma(I_B + I_C)\frac{S}{N} - \tau(I_H + I_C)\frac{I_B}{N} - (\mu + \mu_B)I_B, \\
\frac{dI_H}{dt} &= \tau(I_H + I_C)\frac{S}{N} - \gamma(I_B + I_C)\frac{I_H}{N} - (\mu + \mu_H)I_H, \\
\frac{dI_C}{dt} &= \gamma(I_B + I_C)\frac{I_H}{N} + \tau(I_H + I_C)\frac{I_B}{N} - (\mu + \mu_B + \mu_H)I_C
\end{aligned} \qquad (2.5)$$

In addition, the total population is given by:

$$N(t) = S(t) + I_B(t) + I_H(t) + I_C(t)$$

Therefore, the rate of change of the total population $N(t)$ is obtained as below:

$$\frac{dN}{dt} = \Pi - \mu S - (\mu - \mu_B)I_B - (\mu - \mu_H)I_H - (\mu - \mu_B - \mu_H)I_C$$

$$\frac{dN}{dt} = \Pi - \mu(S + I_B + I_H + I_C) - \mu I_B - \mu I_H - (\mu_B + \mu_H)I_C$$

$$\frac{dN}{dt} = \Pi - \mu N - \mu_B I_B - \mu_H I_H - (\mu_B + \mu_H)I_C \qquad (2.6)$$

It is imperative to note that $\lim_{t \to \infty} N(t) \to \frac{\Pi}{\mu}$. However, there is the need to show that the region Θ defined by

$$\Theta = \left\{ (S, I_B, I_H, I_C) \in \mathbb{R}_+^4 \mid S(t) + I_B(t) + I_H(t) + I_C(t) \leq \frac{\Pi}{\mu} \right\} \qquad (2.7)$$

is positively invariant.

For the model to be biological meaningful, it is important to ensure that the system of equations (2.5) are epidemiologically well posed. In order to show this, it suffices to prove that the system is positive invariant. This implies that the model predicts a positive value for each of the compartment at any time $t \geq 0$ and this can be established using the following Lemma.

Lemma 1 *The region Θ is an attractor and it attracts all solutions starting in the interior of the positive orthant* $\mathbb{R}_+^4$

Proof

Given that each of the model state variables and parameters are non-negative, it follows from equation (2.6) that

$$(2.8) \quad \frac{dN}{dt} \leq \Pi - \mu N$$

$$\frac{dN}{dt} + \mu N \leq \Pi$$

$$\qquad (2.9)$$

On integration of equation (2.9) and necessary simplification, we have

$$N(t) = \frac{\Pi}{\mu} + c e^{-\mu t} \qquad (2.10)$$

Using the initial condition that at $t = 0$, $N(0) = N_0$ gives:

$$N(t) \leq \frac{\Pi}{\mu} + \left(N_0 - \frac{\Pi}{\mu}\right) \exp^{-\mu t} \qquad (2.11)$$

Therefore as $t \to \infty$, the human population N approaches $K = \frac{\mu}{\mu}$; where the parameter $K = \frac{\mu}{\mu}$ is called the carrying capacity. Hence, all feasible solutions of the human population of the model equation (2.5) enter the region:

$\Theta = \{(S, I_B, I_H, I_C) \in\, <\mathrm{R}^4 : S > 0, \quad I_B \geq 0 \quad I_H \geq 0, \quad I_C \geq 0, \quad N \leq \frac{\Pi}{N}\}$

Thus, the trajectoriesstarting Θ remains in Θ all through time. Consequently, Θ is positive invariant and the proposed model is mathematically and epidemiologically well posed.

2.1   HBV Sub-model

In the absence of HIV (i.e. $I_H = 0$, $I_C = 0$), the model reduces to the HBV sub-model given by:

$$\frac{dS}{dt} = \Pi - \gamma I_B \frac{S}{S + I_B} - \mu S, \qquad (2.12)$$

$$\frac{dI_B}{dt} = \gamma I_B \frac{S}{S + I_B} - (\mu + \mu_B) I_B \qquad (2.13)$$

However, the basic reproduction number R_0 was derived using the next generation matrix approach as

$$\mathcal{R}_B = \frac{\gamma}{\mu + \mu_B} \qquad (2.14)$$

2.2   HIV Sub-model

Similarly, in the absence of HBV where $I_B = 0$ and $I_C = 0$, the model reduces to the HIV sub-model given by:

$$\frac{dS}{dt} = \Pi - \tau I_H \frac{S}{S + I_H} - \mu S, \qquad (2.15)$$

$$\frac{dI_H}{dt} = \gamma I_H \frac{S}{S + I_H} - (\mu + \mu_H) I_H \qquad (2.16)$$

Using same approach as done for the HBV sub-model, the basic reproduction number to the model was obtained as:

$$\mathcal{R}_H = \frac{\tau}{\mu + \mu_H} \qquad (2.17)$$

Therefore, R_B and R_H in equations (2.14 & 2.17) are important threshold quantities required to determine whether the situation under consideration is an endemic one or not. The basic reproduction number R_0 for system (2.5) equals the maximum of R_B and R_H That is,

$$\mathcal{R}_0 = \max\left\{\frac{\gamma}{\mu + \mu_B}, \frac{\tau}{\mu + \mu_H}\right\}$$

So, the co-epidemic will persist in the society if this threshold quantity is greater than unity

3   QUALITATIVE ANALYSIS

In this section, a qualitative analysis of the modelled system will be carried out in order to discern the long term behaviour of the system. In achieving this, the dynamics of HBV sub-model and HIV sub-model will be thoroughly studied to provide insight towards understanding the full co-epidemic model dynamics

3.1   Disease-free equilibrium

The disease free equilibrium is a situation where there is no individual that is infected with either or both diseases in society. Mathematically, this is determined by setting the derivatives in the model equations to zeros and solving simultaneously for the dependent variables. Thus, the disease-free equilibria are $\varepsilon_{0B} = \left(\frac{\Pi}{\mu}, 0\right)$ for the HBV Sub-model, $\varepsilon_{0H} = \left(\frac{\Pi}{\mu}, 0\right)$ for the HIV Sub-model, and $\varepsilon_0 = \left(\frac{\Pi}{\mu}, 0, 0, 0\right)$ for the full model respectively.

Consideration of stability for disease free equilibrium provides certain conditions under which HIV or HBV will die out or persist in the population.

3.1.1   Local Stability of Disease Equilibria

Theorem 1 *The disease free equilibrium* E_{0B} *for the HBV sub-model is locally asymptotically stable if* $R_B < 1$*; otherwise it is unstable.*

Proof

For the HBV sub-model, The Jacobian matrix of the system of equations (2.12–2.13) is given by:

$$J_B = \begin{pmatrix} -\frac{\gamma I_B}{S+I_B} + \frac{\gamma S I_B}{(S+I_B)^2} - \mu & \frac{-\gamma S}{S+I_B} + \frac{\gamma S I_B}{(S+I_B)^2} \\ \frac{\gamma I_B}{S+I_B} - \frac{\gamma S I_B}{(S+I_B)^2} & \frac{\gamma S}{S+I_B} - \frac{\gamma S I_B}{(S+I_B)^2} - \mu - \mu_B \end{pmatrix}$$

Evaluating matrix J_B at disease free equilibrium gives:

$$J_{(0B)} = \begin{pmatrix} -\mu & \frac{-\gamma S}{S} \\ 0 & \frac{\gamma S}{S} - \mu - \mu_1 \end{pmatrix} = \begin{pmatrix} -\mu & -\gamma \\ 0 & \gamma - \mu - \mu_1 \end{pmatrix} \qquad (3.1)$$

Matrix $J_{(0B)}$ has the following eigenvalues of

$$\lambda_1 = -\mu \qquad \lambda_2 = (R_B - 1)(\mu + \mu_1) \qquad (3.2)$$

Since the all the eigenvalues of the Jacobian matrix evaluated at E_{0B} have negative real parts whenever $R_B < 1$, then E_{0B} is locally asymptotically stable. Therefore, the disease free equilibrium E_{0B} for the HBV sub-model is locally asymptotically stable if $R_B < 1$ while it is unstable otherwise.

Theorem 2 *The disease free equilibrium* E_{0H} *for the HBV sub-model is locally asymptotically stable if* $R_H < 1$*; otherwise it is unstable.*

Similarly, the Jacobian matrix for the HIV sub-model in equations (2.12–2.13) is:

$$J_H = \begin{pmatrix} \frac{-\tau I_H}{S+I_H} + \frac{\tau S I_H}{(S+I_H)^2} - \mu & \frac{-\tau S}{S+I_H} + \frac{\tau S I_H}{(S+I_H)^2} \\ \frac{\tau I_H}{S+I_H} - \frac{\tau S I_H}{(S+I_H)^2} & \frac{\tau S}{S+I_H} - \frac{\tau S I_H}{(S+I_H)^2} - \mu - \mu_H \end{pmatrix}$$

Evaluating matrix J_H at disease free equilibrium gives:

$$J_{0H} = \begin{pmatrix} -\mu & \frac{-\tau S}{S} \\ 0 & \frac{\tau S}{S} - \mu - \mu_H \end{pmatrix} = \begin{pmatrix} -\mu & -\tau \\ 0 & \tau - \mu - \mu_H \end{pmatrix} \qquad (3.3)$$

The matrix J_H has eigenvalues as

$$\lambda_2 = -\mu \qquad \lambda_3 = (R_H - 1)(\mu + \mu_2) \quad (3.4)$$

Equally, all the eigenvalues of the Jacobian matrix evaluated at E_{0H} have negative real parts whenever $R_H < 1$, then E_{0H} is locally asymptotically stable. Therefore, the disease free equilibrium E_{0H} for the HBV sub-model is locally asymptotically stable if $R_B < 1$; otherwise it is unstable.

Theorem 3 *The disease free equilibrium* E_0 *for the full HIV/HBV co-epidemic model is locally asymptotically stable if* $R_0 < 1$; *otherwise it is unstable.*

The Jacobian matrix *J* for the HIV/HBV co-epidemic model in (2.5) takes the form:

$$
\begin{pmatrix}
-\frac{\gamma(I_B+I_C)}{\rho} + \frac{\gamma S(I_B+I_C)}{(\rho)^2} & -\frac{\gamma S}{\rho} + \frac{\gamma S(I_B+I_C)}{(\rho)^2} & -\frac{\gamma S}{\rho} + \frac{\gamma S(I_B+I_C)}{(\rho)^2} & \frac{\gamma S(I_B+I_C)}{(\rho)^2} - \frac{\tau S}{\rho} \\
-\frac{\tau(I_H+I_C)}{\rho} + \frac{\tau S(I_H+I_C)}{(\rho)^2} - \mu & +\frac{\tau S(I_H+I_C)}{(\rho)^2} & \frac{\tau S}{\rho} + \frac{\tau S(I_H+I_C)}{(\rho)^2} & +\frac{\tau S(I_H+I_C)}{(\rho)^2} \\
\\
\frac{\gamma(I_B+I_C)}{\rho} - \frac{\gamma S(I_B+I_C)}{(\rho)^2} & \frac{\gamma S}{\rho} - \frac{\gamma S(I_B+I_C)}{\rho^2} - \frac{\tau(I_H+I_C)}{\rho} & \frac{\gamma S}{\rho} - \frac{\gamma S(I_B+I_C)}{\rho^2} & -\frac{\gamma S(I_B+I_C)}{\rho^2} - \frac{\tau I_B}{(\rho} \\
+\frac{\tau I_B(I_H+I_C)}{(\rho)^2} & +\frac{\tau I_B(I_H+I_C)}{(\rho)^2} - \mu - \mu_B & -\frac{\tau I_B}{rho} + \frac{\tau I_B(I_H+I_C)}{(\rho)^2} & +\frac{\tau I_B(I_H+I_C)}{(\rho)^2} \\
\\
\frac{\tau(I_H+I_C)}{\rho} - \frac{\tau S(I_H+I_C)}{(\rho)^2} & -\frac{\tau S(I_H+I_C)}{\rho^2} - \frac{\gamma I_H}{\rho} & \frac{\tau S}{\rho} - \frac{\tau S(I_H+I_C)}{\rho^2} & \frac{\tau S}{\rho} - \frac{\tau S(I_H+I_C)}{\rho^2} - \frac{\gamma(I_B+I_C)}{\rho} \\
+\frac{\gamma I_H(I_B+I_C)}{\rho^2} & +\frac{\gamma I_H(I_B+I_C)}{(\rho)^2} & +\frac{\gamma I_H}{\rho} + \frac{\gamma I_H(I_B+I_C)}{\rho^2} & +\frac{\gamma I_H(I_B+I_C)}{\rho^2} - \mu - \mu_H \\
\\
-\frac{\gamma I_H(I_B+I_C)}{\rho^2} & \frac{\gamma I_H}{\rho} - \frac{\gamma I_H(I_B+I_C)}{\rho^2} & \frac{\gamma I_H}{\rho} - \frac{\gamma I_H(I_B+I_C)}{(\rho)^2} & \frac{\gamma(I_B+I_C)}{\rho} - \frac{\gamma I_H(I_B+I_C)}{\rho^2} \\
-\frac{\tau I_B(I_H+I_C)}{\rho^2} & +\frac{\tau(I_H+I_C)}{\rho} - \frac{\tau I_B(I_H+I_C)}{\rho^2} & +\frac{\tau I_B}{\rho} - \frac{\tau I_B(I_H+I_C)}{(\rho)^2} & +\frac{\tau I_B}{\rho} - \frac{\tau I_B(I_H+I_C)}{\rho^2} \\
& & -\mu - \mu_B - \mu_H &
\end{pmatrix}
$$

Where $\qquad \rho = S + I_B + I_H + I_C$

Evaluating the stability of disease free equilibrium at $S = \frac{\Pi}{\mu}, I_B = I_H = I_C = 0$ andwriting in term of the basic reproduction number R_0

$$
J_0 = \begin{pmatrix}
-\mu & -\gamma & -\tau & -\gamma-\tau \\
0 & \tau-\mu-\mu_B & 0 & \gamma \\
0 & 0 & \tau-\mu-\mu_H & \tau \\
0 & 0 & 0 & -\mu-\mu_B-\mu_H
\end{pmatrix} = 0 \qquad (3.5)
$$

The eigenvalues of J_0 are obtained as follows:

$$
\begin{aligned}
\lambda_1 &= -\mu, \quad \lambda_2 = -\mu - \mu_B - \mu_H, \\
\lambda_3 &= (\mathcal{R}_H - 1)(\mu + \mu_H) \leq (\mathcal{R}_0 - 1)(\mu + \mu_H), \\
\lambda_4 &= (\mathcal{R}_B - 1)(\mu + \mu_B) \leq (\mathcal{R}_0 - 1)(\mu + \mu_H).
\end{aligned}
\tag{3.6}
$$

Note that the first two eigenvalues are negative while the remaining other two eigenvalues require that $R_0 < 1$ in order to be strictly negative. Hence, the disease free equilibrium E_0 is locally asymptomatically stable if the basic reproduction number is less than unity($R_0 < 1$); otherwise it is unstable.

3.1.2   Global Stability of Disease Equilibria

The global stability for the disease free equilibria will be established using Lyapunov function approach on the sub-models equations (2.12–2.13) and (2.15–2.16).

Theorem 4 *The disease free equilibria $\mathcal{E}_{0B} = (\frac{\mu}{\mu}, 0)$ and $\mathcal{E}_{0H} = (\frac{\mu}{\mu}, 0)$ are respectively globally asymptotically stable, whenever* $R_B < 1$ *and* $R_H < 1$.

Applying Lyapunov function below on the HBV sub-model equations (2.15–2.16):

$$
V(S, I_B) = \delta I_B \qquad , \delta > 0 \tag{3.7}
$$

Differentiating $V(S, I_B)$ with respect to time $\dot{v}$ yields $\dot{V} = \delta I_B$, while substituting the model equation into (3.7) and solving gives:

$$
\begin{aligned}
\dot{V} &= \delta \left[\frac{\gamma I_B S}{N} - (\mu + \mu_B) I_B \right] \\
&= \delta \left[\frac{\gamma S}{N} - (\mu + \mu_B) \right] I_B; \text{ taking } \quad N = S = \frac{\mu}{\mu}, \quad \text{we have:}
\end{aligned}
$$

$$
\begin{aligned}
\dot{V} &\leq \delta \left[\gamma - (\mu + \mu_B) \right] I_B \tag{3.8} \\
&\leq \delta [(R_B - 1)(\mu + \mu_B)] I_B, \quad \text{choosing} \quad \delta = \frac{1}{(\mu + \mu_B)} \\
&\leq (R_B - 1) I_B
\end{aligned}
$$

$$\therefore \ \dot{V} \leq 0.$$

Similarly, applying lyapunov function on HIV sub-model equation (2.15–2.16)

$$V(S, I_H) = \delta I_H \quad , \delta > 0 \qquad (3.9)$$

Differentiating $V(S, I_H)$ with respect to time yields $\dot{v} = \delta \dot{i}_H$ substituting the model equations into (3.10) and solving gives:

$$\dot{V} = \delta \left[\frac{\tau I_H S}{N} - (\mu + \mu_H) I_H \right]$$

$$= \delta \left[\frac{\tau S}{N} - (\mu + \mu_H) \right] I_H; \quad \text{taking } N = S = \frac{\mu}{\mu} \quad \text{we have:}$$

$$\dot{v} \leq \delta [\tau - (\mu + \mu_H)] I_H \qquad (3.10)$$

$$\leq \delta [(R_H - 1)(\mu + \mu_H)] I_H, \qquad \text{choosing } \delta = \frac{1}{(\mu + \mu_H)}$$

$$\leq (R_H - 1) I_H$$

$$\therefore \quad \dot{v} \leq 0$$

It is important to know that, $\dot{v} = 0$ provided $I_B = 0$ and $I_H = 0$ in equation (3.8 and 3.10). Therefore, the global stability of E_0 whenever $R_B < 1$ and $R_H < 1$ follows from LaSalles invariance principle [12].

Theorem 5 *The disease free equilibrium* $\mathcal{E}_0 = (\frac{\mu}{\mu}, 0, 0, 0)$ *whenever* $R_0 < 1$. *is globally asymptotically stable,*
Proof
Let us consider a Lyapunov function of the form.

$$V(S, I_B, I_H, I_C) = \alpha_1 I_B + \alpha_2 I_H + I_C \qquad (3.11)$$

Differentiating $V(S, I_B, I_H, I_C)$ with respect to time gives:

$$\dot{V}(S, I_B, I_H, I_C) = \alpha_1 \dot{I}_B + \alpha_2 \dot{I}_H + \dot{I}_C \qquad (3.12)$$

Substituting for $\dot{I}_B, \dot{I}_H$, and $\dot{I}_C$ in equation (3.12) yields

$$\dot{V}(S, I_B, I_H, I_C) = \alpha_1 \left[\gamma(I_B + I_C)\frac{S}{N} - \tau(I_H + I_C)\frac{I_B}{N} - (\mu + \mu_B)I_B \right]$$
$$+ \alpha_2 \left[\tau(I_H + I_C)\frac{S}{N} - \gamma(I_B + I_C)\frac{I_H}{N} - (\mu + \mu_H)I_H \right] \quad (3.13)$$
$$+ \left[\gamma(I_B + I_C)\frac{I_H}{N} + \tau(I_H + I_C)\frac{I_B}{N} - (\mu + \mu_B + \mu_H)I_C \right]$$

At the disease free equilibrium $\mathcal{E}_0 = \left[\frac{\Pi}{\mu}, 0, 0, 0 \right]$ with $\mathcal{R}_0 = max[\mathcal{R}_B, \mathcal{R}_H]$, $\frac{\gamma}{\mu+\mu_B+\mu_H} < \frac{\gamma}{\mu+\mu_B}$,

and $\frac{\gamma}{\mu+\mu_B+\mu_H} < \frac{\gamma}{\mu+\mu_H}$; equation (3.13) can be simplified as below :

$$\dot{V}(S, I_B, I_H, I_C) \leq \alpha_1 \left[\gamma I_B + \gamma I_C - (\mu + \mu_B)I_B \right]$$
$$+ \alpha_2 \left[\tau I_H + \tau I_C - (\mu + \mu_H)I_H \right]$$
$$- \left[\mu + \mu_B + \mu_H \right] I_C$$
$$= \alpha_1 \left[\gamma - (\mu + \mu_B) \right] I_B + \alpha_2 \left[\tau - (\mu + \mu_H) \right] I_H$$
$$+ \left[\alpha_1 \gamma + \alpha_2 \tau - (\mu + \mu_B + \mu_H) \right] I_C$$
$$= \frac{\alpha_1}{\mu+\mu_B} \left[\mathcal{R}_B - 1 \right] I_B + \frac{\alpha_2}{\mu+\mu_H} \left[\mathcal{R}_H - 1 \right] I_H$$
$$\frac{1}{\mu+\mu_B+\mu_H} \left[\frac{\alpha_1 \gamma}{\mu+\mu_B+\mu_H} + \frac{\alpha_2 \tau}{\mu+\mu_B+\mu_H} - 1 \right] I_H \quad (3.14)$$
$$\leq \frac{\alpha_1}{\mu+\mu_B} \left[\mathcal{R}_B - 1 \right] I_B + \frac{\alpha_2}{\mu+\mu_H} \left[\mathcal{R}_H - 1 \right] I_H$$
$$+ \frac{1}{\mu+\mu_B+\mu_H} \left[\alpha_1 \mathcal{R}_B + \alpha_2 \mathcal{R}_H - 1 \right] I_C$$
$$\leq \frac{\alpha_1}{\mu+\mu_B} \left[\mathcal{R}_0 - 1 \right] I_B + \frac{\alpha_2}{\mu+\mu_H} \left[\mathcal{R}_0 - 1 \right] I_H$$
$$+ \frac{1}{\mu+\mu_B+\mu_H} \left[\alpha_1 \mathcal{R}_0 + \alpha_2 \mathcal{R}_0 - 1 \right] I_C$$

Taking $\alpha_1 = \alpha_2 = \frac{1}{2}$, we have

$$\dot{V}(S, I_B, I_H, I_C) \leq \frac{1}{2(\mu+\mu_B)} \left[\mathcal{R}_0 - 1 \right] I_B + \frac{1}{2(\mu+\mu_H)} \left[\mathcal{R}_0 - 1 \right] I_H$$
$$+ \frac{1}{\mu+\mu_B+\mu_H} \left[\mathcal{R}_0 - 1 \right] I_C \quad (3.15)$$
$$\leq 0$$

It is important to note that $\dot{V}(S, I_B, I_H, I_C) = 0$ only at the disease-free equilibrium E_0, otherwise it is negative. Therefore, it follows from Lasalle's invariance principle that all solutions of the model equations converges to the E_0 as $t \to \infty$ whenever $R_0 < 1$. Hence, E_0 is globally asymptotically stable whenever $R_0 < 1$

3.2   Endemic Equilibrium Solution

The endemic equilibrium is the steady state in which the disease compartments have positive values. This indicates a situation where HIV, HBV and HIV/HBV co-infection is always present in the society. The endemic equilibria were obtained based on each of the sub-models (HBV-Model, HIV- Model and Co-infection model) which implies that $I_B \geq 0, I_H \geq 0, I_C \geq 0, S > 0$

.

Thus, the endemic equilibrium solution for the HBV-sub model (2.12–2.13) is:

$$\mathcal{E}_B^* = \left[S^* = \frac{\Pi}{\gamma - \mu_B} \quad and \quad I_B^* = \frac{\Pi(\mathcal{R}_B - 1)}{(\gamma - \mu_B)} \right] \tag{3.16}$$

Also, the endemic equilibrium solution for the HIV-sub model (2.15–2.16) is:

$$\mathcal{E}_H^* = \left[S^* = \frac{\Pi}{\tau - \mu_B} \quad and \quad I_H^* = \frac{\Pi(\mathcal{R}_H - 1)}{(\tau - \mu_H)} \right] \tag{3.17}$$

However, the endemic equilibrium solution for the full co-infected model (2.1–2.4) is computationally laborious to obtain, hence μ_B, μ_H are set to zeros to obtain a close estimate to the equilibrium:

$$\mathcal{E}^* = \left[S^* = \frac{\Pi}{\gamma + \tau - \mu}, \, I_B^* = \frac{\Pi(\gamma - \mu)}{\tau(\gamma + \tau - \mu)}, \, I_H^* = \frac{\Pi(\tau - \mu)}{\gamma(\gamma + \tau - \mu)}, \, I_C^* = \frac{\Pi(\tau - \mu)(\gamma - \mu)(\gamma + \tau)}{\gamma \tau \mu(\gamma + \tau - \mu)} \right]$$
$$\tag{3.18}$$

3.2.1   Local Stability of the Endemic Equilibria:

Theorem 6 *The endemic equilibrium* E_B^**for the HBV sub-model is locally asymptotically stable if* $R_B > 1$ *while the endemic equilibrium* E_H^**for the HIV sub-model is locally asymptotically stable if* $R_H > 1$.

Proof.

(i)   The HBV sub-model is linearized using Jacobian Matrix approach and the resulting matrix is evaluated at the endemic equilibrium $(\mathcal{E}_B^*)$ to obtain :

$$J_B = \begin{pmatrix} -\dfrac{\gamma\Pi(\gamma-\mu-\mu_B)}{(\gamma-\mu_B)(\mu+\mu_B)\left(\frac{\Pi}{\gamma-\mu_B}+\frac{\Pi(\gamma-\mu-\mu_B)}{(\gamma-\mu_B)(\mu+\mu_B)}\right)} \\ +\dfrac{\gamma\Pi(\gamma-\mu-\mu_B)\Pi}{(\gamma-\mu_B)^2(\mu+\mu_B)\left(\frac{\Pi}{\gamma-\mu_B}+\frac{\Pi(\gamma-\mu-\mu_B)}{(\gamma-\mu_B)(\mu+\mu_B)}\right)^2}-\mu & -\dfrac{\gamma\Pi}{(\gamma-\mu_B)\left(\frac{\Pi}{\gamma-\mu_B}+\frac{\Pi(\gamma-\mu-\mu_B)}{(\gamma-\mu_B)(\mu+\mu_B)}\right)} \\ +\dfrac{\gamma\Pi(\gamma-\mu-\mu_B)\Pi}{(\gamma-\mu_B)^2(\mu+\mu_B)\left(\frac{\Pi}{\gamma-\mu_B}+\frac{\Pi(\gamma-\mu-\mu_B)}{(\gamma-\mu_B)(\mu+\mu_B)}\right)^2} \\[4em] \dfrac{\gamma\Pi(\gamma-\mu-\mu_B)}{(\gamma-\mu_B)(\mu+\mu_B)\left(\frac{\Pi}{\gamma-\mu_B}+\frac{\Pi(\gamma-\mu-\mu_B)}{(\gamma-\mu_B)(\mu+\mu_B)}\right)} \\ +\dfrac{\gamma\Pi(\gamma-\mu-\mu_B)\Pi}{(\gamma-\mu_B)^2(\mu+\mu_B)\left(\frac{\Pi}{\gamma-\mu_B}-\frac{\Pi(\gamma-\mu-\mu_B)}{(\gamma-\mu_B)(\mu+\mu_B)}\right)^2} & \dfrac{\gamma\Pi}{(\gamma-\mu_B)\left(\frac{\Pi}{\gamma-\mu_B}+\frac{\Pi(\gamma-\mu-\mu_B)}{(\gamma-\mu_B)(\mu+\mu_B)}\right)} \\ +\dfrac{\gamma\Pi(\gamma-\mu-\mu_B)\Pi}{(\gamma-\mu_B)^2(\mu+\mu_B)\left(\frac{\Pi}{\gamma-\mu_B}-\frac{\Pi(\gamma-\mu-\mu_B)}{(\gamma-\mu_B)(\mu+\mu_B)}\right)^2}-\mu-\mu_B \end{pmatrix}$$

$$(3.19)$$

Based on Routh-Hurwitz criteria for a 2×2 matrix, the endemic equilibrium is locally asymptotically stable, if the matrix Trace is negative and its Determinant is positive. So, the Trace and Determinant of matrix J_B is given as:

$$\text{Trace } (J_B) = -\gamma + \mu_B = -(R_B - 1) - \mu$$

$$(3.20)$$

$$\text{Det } (J_B) = \frac{\mu+\mu_B}{\gamma}(\gamma-\mu_B)(\gamma-\mu-\mu_B) \quad = \frac{1}{\gamma}(\gamma-\mu_B)(\mathcal{R}_B-1)$$

From the foregoing, the endemic equilibrium $\mathcal{E}_B^*$ is locally asymptotically stable if $R_B > 1$ provided $\gamma > \mu_B$.

(ii)   Similarly, the Jacobian Matrix of HIV sub-model was obtained and evaluated at the endemic equilibrium (E_H^*) as given below :

$$J_H = \begin{pmatrix} -\dfrac{\tau\Pi(\tau-\mu-\mu_H)}{(\tau-\mu_H)(\mu+\mu_H)\left(\frac{\Pi}{\tau-\mu_H}+\frac{\Pi(\tau-\mu-\mu_H)}{(\tau-\mu_H)(\mu+\mu_H)}\right)} \\ +\dfrac{\tau\Pi(\tau-\mu-\mu_H)\Pi}{(\tau-\mu_H)^2(\mu+\mu_H)\left(\frac{\Pi}{\tau-\mu_H}+\frac{\Pi(\tau-\mu-\mu_H)}{(\tau-\mu_H)(\mu+\mu_H)}\right)^2}-\mu & -\dfrac{\tau\Pi}{(\tau-\mu_H)\left(\frac{\Pi}{\tau-\mu_H}+\frac{\Pi(\tau-\mu-\mu_H)}{(\tau-\mu_H)(\mu+\mu_H)}\right)} \\ +\dfrac{\tau\Pi(\tau-\mu-\mu_H)\Pi}{(\tau-\mu_H)^2(\mu+\mu_H)\left(\frac{\Pi}{\tau-\mu_H}+\frac{\Pi(\tau-\mu-\mu_H)}{(\tau-\mu_H)(\mu+\mu_H)}\right)^2} \\[4em] \dfrac{\tau\Pi(\tau-\mu-\mu_H)}{(\tau-\mu_H)(\mu+\mu_H)\left(\frac{\Pi}{\tau-\mu_H}+\frac{\Pi(\tau-\mu-\mu_H)}{(\tau-\mu_H)(\mu+\mu_H)}\right)} \\ +\dfrac{\tau\Pi(\tau-\mu-\mu_H)\Pi}{(\tau-\mu_H)^2(\mu+\mu_H)\left(\frac{\Pi}{\tau-\mu_H}-\frac{\Pi(\tau-\mu-\mu_H)}{(\tau-\mu_H)(\mu+\mu_H)}\right)^2} & \dfrac{\tau\Pi}{(\tau-\mu_H)\left(\frac{\Pi}{\tau-\mu_H}+\frac{\Pi(\tau-\mu-\mu_H)}{(\tau-\mu_H)(\mu+\mu_H)}\right)} \\ +\dfrac{\tau\Pi(\tau-\mu-\mu_H)\Pi}{(\tau-\mu_H)^2(\mu+\mu_H)\left(\frac{\Pi}{\tau-\mu_H}-\frac{\Pi(\tau-\mu-\mu_H)}{(\tau-\mu_H)(\mu+\mu_H)}\right)^2}-\mu-\mu_H \end{pmatrix}$$

$$(3.21)$$

$$\text{Trace } (J_H) = -\tau + \mu_H \qquad = -(R_H - 1) - \mu$$

$$(3.22)$$

$$\text{Det } (J_H) = \frac{\mu+\mu_H}{\tau}(\tau-\mu_H)(\tau-\mu-\mu_H) \quad = \frac{1}{\tau}(\tau-\mu_H)(\mathcal{R}_H-1)$$

Just as in the HBV sub-model, the endemic equilibrium $\mathcal{E}_H^*$ for the HIV-sub-model is locally asymptotically stable if $R_H > 1$, provided $\tau > \mu_H$.

3.2.2   Global stability of the Endemic Equilibria

Theorem 7 *If $R_B > 1$, then there exist an endemic equilibrium E_B^*(in addition to the disease free equilibrium) and it is globally asymptotically stable.*

Proof:

Given that $R_B > 1$, then the existence of the equilibrium is guaranteed considering a Lyapunov function.

$$V(S, I_B) = \omega_1(S - S^*)^2 + \omega_2(I_B - I_B^*)^2, \quad \omega_1 \geq 0, \qquad \omega_2 \geq 0 \quad (3.23)$$

Differentiating $V(S, I_B)$ with respect to time gives:

$$
\begin{aligned}
\dot{V}(S, I_H) &= 2\omega_1(S - S^*)\dot{S} + 2\omega_2(I_B - I_B^*)\dot{I}_B \\
&= 2\omega_1(S - S^*)(\Pi - \gamma I_B \tfrac{S}{N} - \mu S) \\
&\quad + 2\omega_2(I_B - I_B^*)(\gamma I_B \tfrac{S}{N} - (\mu + \mu_B)I_B)
\end{aligned}
\quad (3.24)
$$

Substituting $\Pi = \gamma I_B^* \tfrac{S^*}{N} + \mu S^*)$ and $\mu + \mu_B = \gamma \tfrac{S^*}{N}$ with $N \approx N^*$ in the preceding equation yields:

$$
\begin{aligned}
\dot{V}(S, I_H) &\leq 2\omega_1(S - S^*)(\gamma I_B^* \tfrac{S^*}{N} + \mu S^* - \gamma I_B \tfrac{S}{N} - \mu S) \\
&\quad + 2\omega_2(I_B - I_B^*)(\gamma I_B \tfrac{S}{N} - \gamma I_B \tfrac{S^*}{N}) \\
&\leq 2\omega_1(S - S^*)(\mu(S^* - S) + \tfrac{\gamma}{N}(I_B^* S - I_B S)) \\
&\quad + 2\omega_2(I_B - I_B^*)(\tfrac{\gamma}{N}(I_B S - I_B S^*)) \\
&\leq 2\omega_1(S - S^*)(\mu(S^* - S) + \tfrac{\gamma}{N}(I_B^* S^* - I_B S^* + I_B S^* - I_B S)) \\
&\quad + 2\omega_2(I_B - I_B^*)(\tfrac{\gamma}{N}(I_B S - I_B S^*)) \\
&= -2\omega_1\mu(S - S^*)^2 + 2\omega_1\gamma\tfrac{S^*}{N}(I_B^* - I_B)(S - S^*) \\
&\quad - 2\omega_1\gamma\tfrac{I_B}{N}(S - S^*)^2 - 2\omega_2\tfrac{\gamma I_B}{N}(I_B^* - I_B)((S - S^*)) \\
&= -2\omega_1\mu(S - S^*)^2 - 2\omega_1\gamma\tfrac{I_B}{N}(S - S^*)^2 \\
&\quad + \tfrac{2\gamma}{N}(\omega_1 S^* - \omega_2 I_B)(I_B^* - I_B)(S - S^*) \\
&\leq 0 \qquad \omega_1, \omega_2 \in < R^+ \text{ choosing such that } I_B \geq \tfrac{\omega_1 S^*}{\omega_2} \text{ while } S \geq S^*, I_B \leq I_B^*
\end{aligned}
$$

$$(3.25)$$

Thus, $\dot{V}(S, I_H) \leq 0$ while it only vanishes at the endemic equilibrium E_B^*. Based on Lasalle's invariance principle, all the model solutions

approaches $\mathcal{E}_B^*$ as $t \to \infty$ whenever $R_B > 1$. Hence, $\mathcal{E}_B^*$ exists and it is globally asymptotically stable in Θ whenever $R_B > 1$.

It is imperative to mention here that the proof for the global stability of the endemic equilibrium E_H* follows the same approach with substitution of I_H for I_B and $R_H > 1$ for $R_B > 1$.

4   NUMERICAL RESULTS AND DISCUSSION

In this section, sensitivity analysis of the basic reproduction number with respect to each of the model parameters will be carried out and the model will be solved numerically using Runge-Kutta Fourth Order Scheme. The numerical results will be simulated using computer programs that will be executed with MATLAB mathematical software.

4.1   Model Variables Initial Conditions and Parameter Values

Considering the Nigerian Demographic Population Data, the country estimated population for the year 2016 is 186 million (United Nations, 2016). In addition, Nigeria has the second largest HIV epidemic in the world with a total estimate of 3.4 million people living with HIV. Furthermore, Nigeria has one of the highest prevalence of Hepatitis B infection in the world with a national prevalence of 10% while 0.3% of the population are co-infected with HIV and HBV. Based on these information, the model variables initial conditions is taking as

$S(0) = \frac{88N}{100} = 163.68 \, million, \quad I_B(0) = \frac{10N}{100} = 18.60 \, million,$

$I_H(0) = \frac{1.7N}{100} = 3.16 \, million, \quad and \, I_C(0) = \frac{0.3N}{100} = 0.56 \, million.$

Also, the model parametervalues are as given in the table below:

Table 4.1: The model parameter description and their corresponding values

Parameter	Definition	Value	Reference
Π	Recruitment rate into S	$0.22 \times N$	[5]
μ	Natural death rate	0.012 yr^{-1}	[3, 20]
μ_B	HBV induced death rate	$0.11\ yr^{-1}$	Estimated and [3]
μ_H	HIV induced death rate	$0.09\ yr^{-1}$	Estimated and [20]
γ	Transmission rate of HBV	0.125	Estimated
τ	Transmission rate of HIV	0.041	Estimated

4.2   Sensitivity Indices of R_0

The sensitivity of R_0 with respect to each of the model parameters are obtained as follows:

$$
\begin{aligned}
\Gamma_\Pi &= \frac{\partial R_0}{\partial \Pi} \times \frac{\Pi}{R_0} = 0 \\[4pt]
\Gamma_\gamma &= \frac{\partial R_0}{\partial \gamma} \times \frac{\gamma}{R_0} = \frac{1}{\mu+\mu_B} \times \frac{\gamma(\mu+\mu_B)}{\gamma} = 1 \\[4pt]
\Gamma_\mu &= \frac{\partial R_0}{\partial \mu} \times \frac{\mu}{R_0} = -\frac{\gamma}{(\mu+\mu_B)^2} \times \frac{\mu(\mu+\mu_B)}{\gamma} = -\frac{\mu}{\mu+\mu_B} \\[4pt]
\Gamma_{\mu_B} &= \frac{\partial R_0}{\partial \mu_B} \times \frac{\mu_B}{R_0} = -\frac{\gamma}{(\mu+\mu_B)^2} \times \frac{\mu_B(\mu+\mu_B)}{\gamma} = -\frac{\mu_B}{\mu+\mu_B} \\[4pt]
\Gamma_\tau &= \frac{\partial R_0}{\partial \tau} \times \frac{\tau}{R_0} = \frac{1}{\mu+\mu_H} \times \frac{\tau(\mu+\mu_H)}{\tau} = 1 \\[4pt]
\Gamma_\mu &= \frac{\partial R_0}{\partial \mu} \times \frac{\mu}{R_0} = -\frac{\tau}{(\mu+\mu_H)^2} \times \frac{\mu(\mu+\mu_H)}{\tau} = -\frac{\mu}{\mu+\mu_H} \\[4pt]
\Gamma_{\mu_H} &= \frac{\partial R_0}{\partial \mu_H} \times \frac{\mu_H}{R_0} = -\frac{\tau}{(\mu+\mu_H)^2} \times \frac{\mu_H(\mu+\mu_H)}{\tau} = -\frac{\mu_H}{\mu+\mu_H}
\end{aligned}
\tag{4.1}
$$

Based on the parameter values stated in Table 4.1, the sensitivity indices of R_0 with respect to each of the parameters are displayed in the table below:

Table 4.2: Sensitivity analysis for basic reproduction number

Sensitive Index	Value
Γ_γ	1
Γ_μ	-0.0983
$\Gamma\mu B$	-0.9016
Γ_τ	1
Γ_μ	-0.117
$\Gamma\mu H$	-0.8823

The sign in front of each of the values in Tables 4.2 shows what will happen to R_0 if the parameter is increased or decreased. R_0 increases when sensitivity indices with positive signs increase, while R_0 decreases when sensitivity indices with negative signs increase and vice versa. The most sensitive parameters to R_B and R_H are found to be τ and γ respectively. Sensitivity indices $\tau = 1$ and $\gamma = 1$ mean that R_B or R_H approximately decreases by 1% when either τ or γ is decreased by 1%. This implies that any control measure that can be put in place to reduce γ - HBV transmission rate and τ - HIV transmission rate would be effective in controlling the spread of HBV and HIV respectively. Moreover, R_B and R_H is also remarkably sensitive to μ_B - HBV-induced death rate and μ_H - HIV-induced death rate. The indices show that asthese disease death rates increase, R_B and R_H decrease, thus implying reduction in the spread of the two diseases. However, the natural death rate (μ) is the least sensitive to the basic reproduction numbers, though it affects them adversely.

4.3   Numerical Simulations and Discussion

Using the set initial conditions and parameter values in Table 4.1, the model system of equations is solved numerically with graphical results presented as follows:
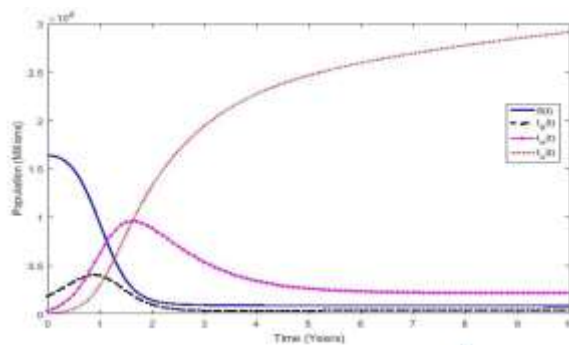

Figure 4.1: Population Profile for $S(t)$, $I_B(t)$, $I_H(t)$, and $I_C(t)$ when R_0 >1 with $\tau = 3.50,$ $\gamma = 1.60,$ $\mu = 0.012,$ $\mu_B = 0.011, \mu_H = 0.090$

.

Figure 4.1 shows the population dynamics of each of the model compartments over time. The population profile of the susceptible class S(t) which has the largest population of the four compartments at initial time with a total population of 163.68 million individuals falls drastically to a level below 20 million within two years while the population in the co-infected class $I_C(t)$ rises logistically to as high as 180 million in about half a decade. However, the $I_B(t)$ and $I_H(t)$ rise slowly to different peaks, after which they both started falling and stabilizes at different population levels with the final population levelof the $I_H(t)$ class remarkably higher than that of $I_B(t)$ class. It is important to note that the scenario depicted in Figure 4.1 is what would have happened if no control measures have been put in place to curtail the alarming spread of each of the two diseases and their co-infection.
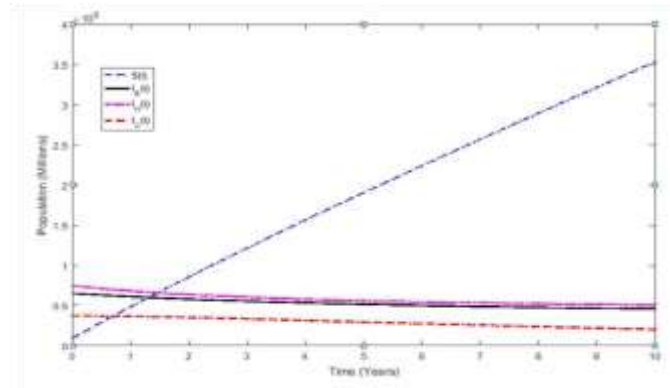
Figure 4.2: Population Profile when $R_0 < 1$ with $\tau = 0.084$, $\gamma = 0.015$, $\mu = 0.012$, $\mu_B = 0.011, \mu_H = 0.090$

.

On the contrary, Figure 4.2 depicts a scenario where there are effective control measures to forestall the spread of each of the diseases and the co-infection by both diseases. This is actually the case when R_0 is less than unity. As can be seen, Figure 4.2 shows that the population in the susceptible class S(t) continues to increase over time while the population in each of the infected classes $I_B(t)$, $I_H(t)$, and $I_C(t)$ continue to fall. Thus, it can be inferred that any control measures that can effectively reduce R_0 below unity would be useful in curtailing the spread of each of the diseases and their co-infection.
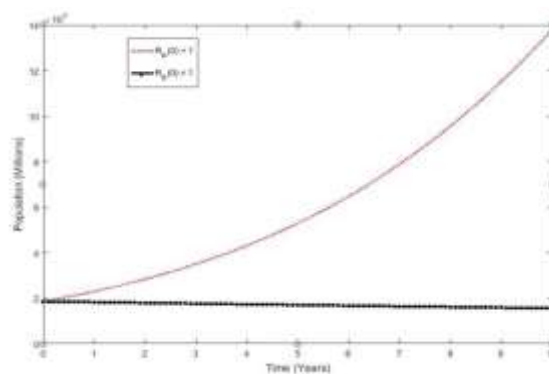

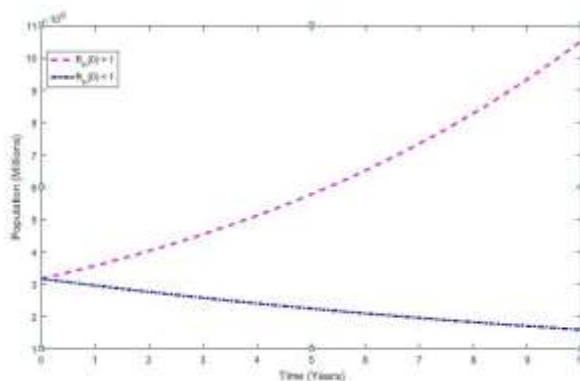Figure 4.3: Population profile of HBV when $R_B = 1.8525 > 1$ and $R_B = 0.0459 < 1$.

Figure 4.4: Population profile of HIV when $R_H = 2.451 \geq 1$ and $R_H = 0.1863 \leq 1$.

In Figure 4.3, the model population dynamics was considered in the absence of HIV disease for cases with $R_B < 1$ and $R_B > 1$. It was observed that the population of HBV infected class continues to fall in the case with $R_B < 1$ while it continues to rise in the case with $R_B > 1$. Similarly, the model dynamics was considered in the absence of HBV disease for cases with $R_H < 1$ and $R_H > 1$. Just as in the case without HIV, the population of the HIV infected class continues to increase when $R_H > 1$ while it continues to fall when $R_H < 1$. Obviously, these results behaved as expected and it is an indication that the model predictions would be reasonable.
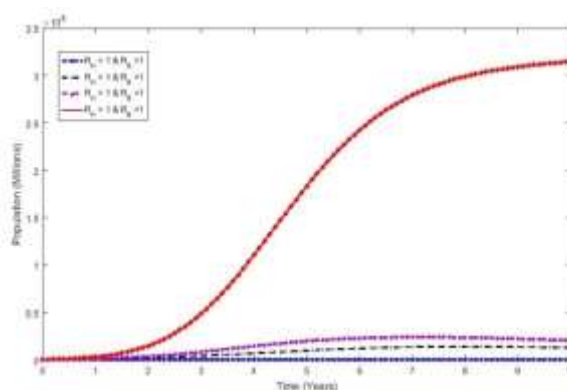

Figure 4.5: Population Profile of co-infected for four different scenarios of basic reproduction number

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In Figure 4.5, the population profile of the co-infected compartment with respect to four different scenarios were considered. These scenarios are : ($R_H < 1$, $R_B < 1$), ($R_H > 1$, $R_B < 1$), ($R_H < 1$, $R_B > 1$), and ($R_H > 1$, $R_B > 1$). Here, the co-infected population decreases over time until it reaches a level where it stabilizes when both basic reproduction numbers were less than unity (i.e. $R_H < 1$ and $R_B < 1$). However, there was gradual increase in the co-infected population when ($R_H > 1$, $R_B < 1$) and when ($R_H < 1$, $R_B > 1$) from the first year to the fourth year but this increase is not substantial when compared to the scenario where ($R_H > 1$, $R_B > 1$) which shows a drastic increase from the second year to the third year. Nevertheless, there was a slight decrease in the population from the fifth year until it reaches a level where it stabilizes over time.
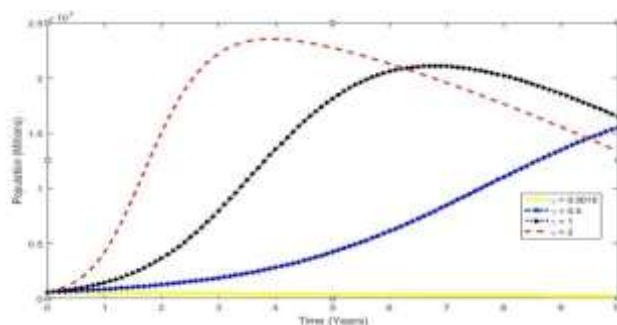

Figure 4.6: Population Profile of co-infected for different values of γ

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Figure 4.6 shows the population profile of the co-infected compartment for different values of HBV transmission rate (γ). Four different scenarios were considered with increasing HBV transmission rates (γ) whose values were 0.0015, 0.5, 1 and 2 respectively. It was observed that when $\gamma = 2$, there was a rapid growth in the population of co-infected individuals from 0.1 million to about 2 million up to the third year. Thereafter, there was a gradual decrease in the population which could be due to disease induced deaths which could outnumber the HIV/HBV co-infection incidence at such instance since the co-infected individuals are the likely majority. Equally, when $\gamma = 1$, the

co-infected individuals population rises steadily from 0.1 million to 1.67 million from the first year to the sixth year. Thereafter, there was a decline in the population of co-infected individuals as time progresses as a result of death either by HIV or HBV infections. Also, it was observed that when γ = 0.5, there *was a slow increase in the co-infected class population which takes a longer time to reach its peak as compared to when γ = 2 or 1.*

The foregoing notwithstanding, the scenario with γ = 0.0015 results in a decrease in the co-infected individuals population to a steady minimal level. This could be due to effective control measures put in place to forestall the spread of HBV disease. Some of the measures could be routine HBV vaccination with adequate coverage, early detection of the disease and its immediate treatment, awareness and educational enlightenment of susceptibles to avoid getting infected, etc.
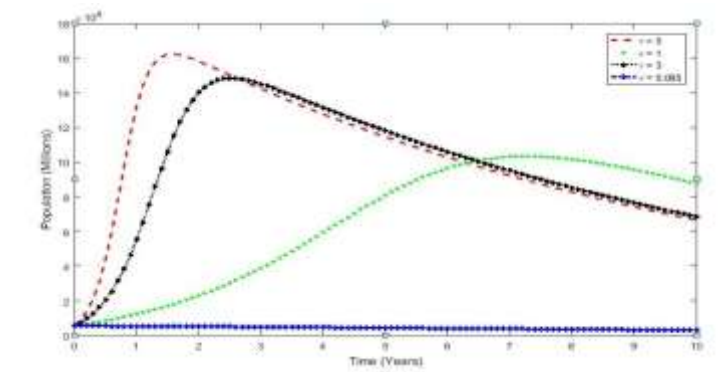

Figure 4.7: Population Profile of co-infected for different values of τ

.

Figure 4.7 shows the population profile of the co-infected compartment when the transmission rate of HIV (τ) is assigned each of the four different values τ = 5, τ = 3, τ = 1, and τ = 0.085 respectively.

In this Figure, it was observed that, when the value of τ = 5, there was a rapid growth in the population of co-infected individuals from 0.7 million to about 14 million within the first year (indicating a scenario

of high HIV incidence in the population). Thereafter, there was a gradual decrease in the population due to HIV disease-induced deaths. Moreover, a similar trend as that for $\tau = 5$ was observed when $\tau = 3$ and $\tau = 1$, though the peaks attained in the latter cases were lesser while it took a relatively longer time to get there. However, the co-infected population decline steady over time from the first year when $\tau = 0.085$. This situation could happen if effective control measures can be put in place to ensure that infected individuals do not infect any one before their eventual death.

.

5   CONCLUSION

In this paper, a simplified mathematical model consisting of four non-linear ordinary differential equations on HIV and HBV co-epidemic was considered. The model basic reproduction number R_0 was derived and it was used to establish the criteria for the stability of the model equilibria. It was shown that each of the three disease-free equilibrium E_{0B}, E_{0H}, E_0 for the respective HBV-sub model, HIV-sub model and the full model are locally asymptotically stable when $R_0 < 1$ (i.e. $R_B < 1$, $R_H < 1$). Also, the global stability analysis of HIV-sub model and HBV-sub model was accomplished using appropriate Lyapunov functions. In addition, a sensitivity analysis of R_0 with respect to each of the model parameters were carried out; it was found that R_0 was most sensitive to τ and γ. This implies that each of these two parameters should be correctly estimated in order for the model predictions to be reliable. This also indicates that control measures that reduce each of these parameters would be useful in mitigating the spread of the two diseases. Nevertheless, the proposed model was solved numerically using Runge-Kunta method of order four which was executed with MATLAB R2016a. Simulations of our numerical result corroborates the findings from our mathematical analyses. The simulations show that the co-epidemic could only be eradicated, if control measures that can drive the basic reproduction number below unity are put in place, otherwise the HIV/HBV co-epidemic would persists in such society. Thus, it is recommended that in any society where either HBV or HIV disease is endemic, proactive and effective

control measures should be taken to forestall the spread of the other disease because inability to do this could lead to an alarming co-epidemic of both diseases. This could be accomplished by initiating programs that would facilitate timely detection of infected individuals while identified infected patients should be regularly counseled and placed on immediate treatment.

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