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Mathematical modeling of co-infections of hepatitis A viral disease and typhoid fever with optimal control strategies

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Abstract

In this study, a mathematical model with optimal control measures was used to investigate the transmission dynamics of co-infection of hepatitis A virus and typhoid fever. A deterministic compartmental model was used and an analysis of the effect of various control measures was compared. The pathogen fitness that represents the epidemic indicator is obtained by using the next-generation matrix. We have shown the existence of two equilibrium states: the disease-free steady state in which there are no populations that are infected by the co-infection of hepatitis A virus and typhoid fever, the endemic state in which a co-infected population exists and is capable of transmitting the disease. The local and global stability conditions of the endemic equilibrium points were also proved. Further, it was proved that the co-infection of the model exhibited a backward bifurcation. Finally, a numerical simulation of the model was made and it reveals that prevention has a significant impact in reducing the transmission of the co-infection and applying all the control measures can successfully eliminate co-infection of hepatitis virus and typhoid fever from the community.

Keywords: Mathematical model, co-infections, hepatitis A virus, typhoid fever, Basic reproduction number
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1 Introduction

Typhoid disease is caused by the bacterium, Salmonella enterica serovar typhi (S. Typhi) and it remains the main cause of enteric disease in developing countries. Salmonella enterica serovar typhi is a gram-negative bacterium that invades the body via the small intestines and colonizes macrophages in the reticuloendothelial system, where it is shed into the bloodstream [2]. The symptoms of the disease include prolonged fever, headache, depression, and loss of appetite, sometimes accompanied by abdominal pain and, in harsh cases, intestinal perforation and neurological complications [6]. Typhoid disease results in an estimated 216,000 up to 600,000 deaths per year, mainly in children of school-age. Human being will be infected with typhoid fever by eating or drinking food or water contaminated with Salmonella Typhi bacteria.

Hepatitis, plural hepatitides, is a soreness of liver characterized by the presence of inflammatory cells or tissue [1]. It is most commonly caused by the viruses: hepatitides A, B, C, D and E. This infection is associated with poor sanitation and hygiene and is transmitted by the ingestion of contaminated food or water or by direct contact with an infected person. Peoples who are living in a group, both within and outside shelters, increases the risk for disease

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transmission, which can result in outbreaks [9]. International travelers to the areas of hepatitis A virus endemic areas, men who have sex with men and persons with chronic liver disease are more susceptible to the disease [13].

Typhoid fever is one of the causes of serious illness in children and adults in developing countries. Hepatitis A disease also continues to be an important cause of illness and acute liver failure in developing countries where congregate living conditions exits, sanitation and food hygiene are not optimal. In Africa where typhoid fever and hepatitis A are endemic, peoples can be infected by either or both of the disease. To alleviate this problem continuous research into the prevention and control of the disease is vital. Thus, mathematical modeling can address and describe the dynamics of the co-infections of the disease in the community. For example in [17] studied a mathematical model to investigate typhoid fever outbreak and optimal control with cost-effective strategies in a community with varying population. Some of other studies include; Steady, et al, (2014) used a deterministic model to assess the dynamics of typhoid disease in malaria endemic settings. The result of his study indicated that a typhoid fever outbreak in malaria endemic settings may results in higher population of dually infected individuals showing clinical symptoms of both infections than the singly infected population displaying clinical symptoms of the diseases.

Hepatitis A and typhoid fever are prevalent in many parts of the world particularly in developing countries. These disease shares a common mode of transmission via ingestion of food or water associated with poor hygiene [3]. In typhoid, involvement of liver is a consistent feature [7]. Various organs including the liver involves in the course of enteric fever, resulting in a wide array of presentations [10]. Abnormalities of liver biochemical tests are commonly found in patients with typhoid fever [12]. However, a picture of hepatitis with fever and frank jaundice characterizes the course of a small subset of a patients infected by Salmonella typhi [16]. Different mathematical models have been used to study the dynamics of either typhoid or HAV as well as the impact of some intervention strategies. So far hardly any case control studies have been undertaken to study the co-infections of these diseases. Thus, this study aimed to address mathematical modeling of the co-infection of typhoid and HAV disease using some control measures.

2 Description and Formulation of Model

In this study we used a model consisting; seven compartments of human populations and one compartment of bacterial populations. The human population consists of susceptible S(t) that is used to represent the number of individuals who are prone to the disease at time t. $I_t(t)$ denotes typhoid infected and infectious population. $I_h(t)$ denotes hepatitis A virus infected peoples and capable of infecting others. $I_{th}(t)$ denotes hepatitis A -typhoid co-infected population. $R_t(t)$ denotes peoples recovered from typhoid. $R_h(t)$ denotes population recovered from hepatitis A virus. R(t) denotes population recovered from the co infection of typhoid-hepatitis a virus. B(t) denotes salmonella bacteria population. Some populations enter susceptible class by birth or emigration at a rate of Λ or from typhoid recovered sub-class by losing temporary immunity with α rate. Susceptible individuals acquire typhoid infection at per capita rate $\lambda_1 = \frac{\nu B}{K+B}$ and enter into typhoid infected sub-class $I_t(t)$ or acquire HAV disease at a per capita rate $\lambda_2 = \frac{\gamma(I_h(t)+\vartheta I_{th}(t))}{N}$ and enter HAV infected sub-class $I_h(t)$. If $\vartheta \geq 1$ then, co-infected may infect susceptible more likely than HAV infected. $\vartheta = 1$, then both co-infected and HAV infective have equal chance to infect the susceptible, but if $\vartheta \leq 1$ then HAV infectious will have better chance to infect susceptible than co-infected. γ denotes the infectious rate of HAV, ν is the rate of ingestion of typhoid causing bacteria, K is concentration of bacteria in foods and water. The size of the co infected sub- class is increases from HAV infected group by acquiring typhoid disease with a rate of θ_2 due to the force of infection λ_1 and also from typhoid infected sub-class by acquiring HAV disease with a rate of θ_1 due to the force of infection λ_2. The HAV infected population will recover at a rate β_2 due to natural immunity and join to HAV recovered sub-class R_h or die due to disease induced death rate d_2. The typhoid fever infected population also will recover at a rate β_1 due to natural immunity and join typhoid recovered sub-class R_t dies from disease induced death rate d_1. The HAV- typhoid co infected sub class removes with a rate of δ and acquire temporary immunity either from both disease or HAV only or typhoid only and join the co infected recovered sub-class R with probability of $(1-a)(1-b)$ or HAV recovered sub-class R_h with probability of $a(1-b)$ or typhoid disease recovered sub-class R_t with probability of $b\delta$. Moreover, individuals in the co infected sub-class dies either from the co-infections or HAV or typhoid causing death with a rate of d_3. In all the human population classes µ denotes natural mortality rate. The salmonella bacteria population B grows exponentially at a growth rate of r in contaminated food or drinks. The bacteria population increases due to typhoid infected individuals and the co infected individuals with a rate of ε_1 and ε_2 respectively.

The above model description can be written in eight system of differential equation below.

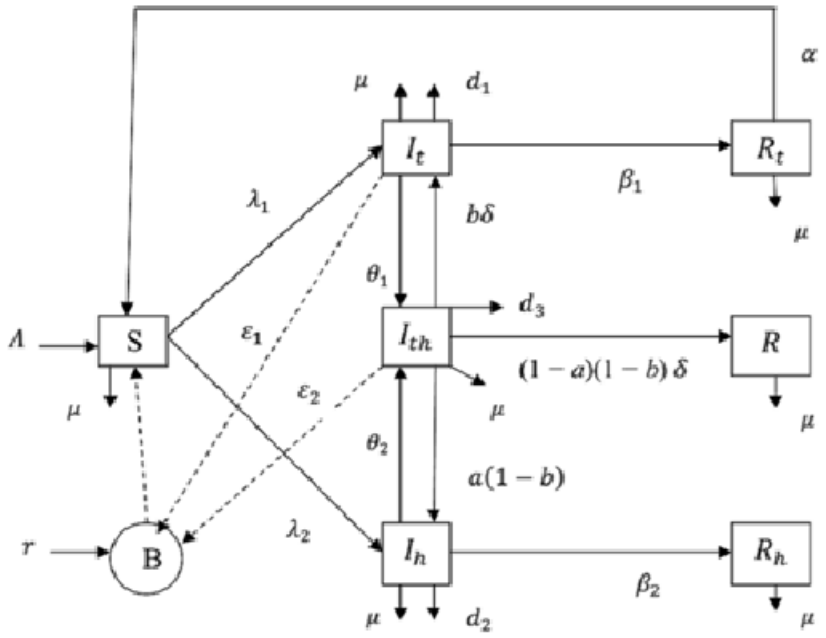

Figure 1: Flow diagram of the model

$$\frac{dS}{dt} = \Lambda + \alpha R_t - (\lambda_1 + \lambda_2 + \mu)S \tag{2.1}$$

$$\frac{dI_t}{dt} = \lambda_1 S + b\delta\ I_{th} - (\beta_1 + \theta_1 + \varepsilon_1 + d_1 + \mu)I_t \tag{2.2}$$

$$\frac{dI_h}{dt} = \lambda_2 S + a(1-b)\delta\ I_{th} - (\beta_2 + \theta_2 + d_2 + \mu)I_h \tag{2.3}$$

$$\frac{dI_{th}}{dt} = \theta_1 I_t + \theta_2 I_h - (\delta + \varepsilon_3 + d_3 + \mu)I_{th} \tag{2.4}$$

$$\frac{dR_t}{dt} = \beta_1 I_t - (\alpha + \mu)R_t \tag{2.5}$$

$$\frac{dR_h}{dt} = \beta_2 I_h - \mu R_h \tag{2.6}$$

$$\frac{dR}{dt} = (1-a)(1-b)\delta\ I_{th} - \mu R \tag{2.7}$$

$$\frac{dB}{dt} = rB + \varepsilon_1 I_t + \varepsilon_2 I_{th}, \tag{2.8}$$

where $\lambda_1 = \frac{\nu B}{K+B}$ and $\lambda_2 = \frac{\gamma(I_h(t)+\vartheta I_{th}(t))}{N}$ are force of infections of typhoid fever and HAV disease respectively. With initial conditions $S(0) = S_0, I_t(0) = I_{t0}, I_h(0) = I_{h0}, I_{th}(0) = I_{th0}, R_t(0) = R_{t0}, R_h(0) = R_{h0}, R(0) = R_0, and B(0) = B_0$.

3 The Model Analysis

3.1 HAV Only model

The HAV only model is obtained from the system $(2.1 - 2.8)$ by setting $I_t = I_{th} = R_t = R = B = \lambda_1 = \varepsilon_1 = \varepsilon_2 = \theta_1 = \alpha = 0$

$$\begin{cases} \frac{dS}{dt} = \Lambda - (\lambda_2 + \mu)S \\ \frac{dI_h}{dt} = \lambda_2 S - (\beta_2 + \theta_2 + d_2 + \mu)I_h \\ \frac{dR_h}{dt} = \beta_2 I_h - \mu R_h \end{cases} \tag{3.1}$$

3.1.1 Invariant Region

The invariant region in which the solution of the system (3.1) is bounded is shown as follows. For the model in (3.1) let the total population be

$$N_1 = S + I_h + R_h \tag{3.2}$$

Taking the time derivative on both sides in (3.2) and using the system (3.1) we get

$$\frac{dN_1}{dt} = \Lambda - \mu N_1 - d_2 I_h \tag{3.3}$$

In the absence of death due to HAV i.e., $d_2 = 0$ equation (3.3) becomes

$$\frac{dN_1}{dt} \leq \Lambda - \mu N_1 \tag{3.4}$$

Rearranging and evaluating the differential inequality in (3.4) as $t \to \infty$ we obtain

$$D_1 = \left\{ (S, I_h, R_h) \in \Re_+^3 : 0 \leq N_1 \leq \frac{\Lambda}{\mu} \right\}.$$

Therefore, the solution of the system in (3.1) is bounded in D_1.

3.1.2 Positivity of Solution

It is assumed that the initial condition of the model is non-negative, the solution of the model is also positive for non-negative initial conditions.

Theorem 3.1. Let $D_1 = \{(S, I_h, R_h) \in \Re_+^3 : S_0 > 0, I_{h0} > 0, R_{h0} > 0\}$ then the solutions $\{S, I_h, R_h\}$ are positive for future time.

Proof . Let t_1 be defined as shown below

$$t_1 = Sup\{t > 0 : S(\tau) > 0, I_h(\tau) > 0, R_h(\tau) > 0 \quad \text{for all} \quad \tau \in [0, t]\}.$$

Since $S_0 > 0, I_{h0} > 0, R_{h0} > 0$, $t_1 > 0$. If $t_1 < \infty$, then necessarily S or I_h or R_h is zero at $t_1 < \infty$. From the system (3.1) taking the first equation

$$\frac{dS}{dt} = \Lambda - (\lambda_2 + \mu)S. \tag{3.5}$$

Now using variation of constant formula the solution of (3.5) at $t_1$is obtained as

$$S(t_1) = S_0 exp[-\int_0^{t_1} (\lambda_2 + \mu) S dS] + \int_0^{t_1} \Lambda exp[-\int_0^{t_1} (\lambda_2 + \mu)\tau d\tau] dS.$$

Since all the variable are positive in $[0, t_1]$, we have $S(t_1) > 0$. Similarly, it can be shown that $I_h(t_1) > 0$ and $R_h(t_1) > 0$ which is a contradiction. Hence, $t_1 = \infty$. Therefore, all the solutions are positive for future time. □

3.1.3 Disease Free Equilibrium

The disease free equilibrium point of the model in (3.1) is obtained at $I_h = R_h = 0$. Thus, $E_{0h} = (\frac{\Lambda}{\mu}, 0, 0)$.

3.1.4 Basic reproduction number $\Re_{0h}$

The basic reproduction number $\Re_{0h}$ is obtained by using the next generation matrix method as shown below. Using the second equation of the system (3.1) we have

$$\frac{dI_h}{dt} = \lambda_2 S - (\beta_2 + \theta_2 + d_2 + \mu)I_h, \quad \text{here } \lambda_2 = \frac{\gamma I_h}{N}.$$

Then

$$\frac{dI_h}{dt} = \frac{\gamma I_h}{N} S - (\beta_2 + \theta_2 + d_2 + \mu)I_h.$$

Now, set $f = (\frac{\gamma I_h}{N} S)$ and $v = (\beta_2 + \theta_2 + d_2 + \mu)I_h)$, then

$$F = (\gamma) \quad \text{and} \quad V^{-1} = \frac{1}{\beta_2 + \theta_2 + d_2 + \mu}.$$

This implies that

$$FV^{-1} = \frac{\gamma}{\beta_2 + \theta_2 + d_2 + \mu}.$$

Therefore, the pathogen fitness or the basic reproduction number $\Re_{0h}$ is given by

$$\Re_{0h} = \frac{\gamma}{\beta_2 + \theta_2 + d_2 + \mu}.$$

3.1.5 Local Stability of Disease Free Equilibrium

Theorem 3.2. The disease free equilibrium E_{0h} is locally asymptotically stable if $\Re_{0h} < 1$ and unstable if $\Re_{0h} > 1$.

Proof . Taking the second equation of the system (3.1), that is

$$\frac{dI_h}{dt} = \lambda_2 S - (\beta_2 + \theta_2 + d_2 + \mu)I_h.$$

Setting $g = \lambda_2 S - (\beta_2 + \theta_2 + d_2 + \mu)I_h = \frac{\gamma I_h}{N} S - (\beta_2 + \theta_2 + d_2 + \mu)I_h$. Now taking the partial derivative of g with respect to I_h at DFE E_{0h} implies that

$$\frac{\partial g}{\partial I_h} = \gamma - (\beta_2 + \theta_2 + d_2 + \mu) < 0.$$

Then

$$(\beta_2 + \theta_2 + d_2 + \mu)(\frac{\gamma}{\beta_2 + \theta_2 + d_2 + \mu} - 1) < 0.$$

So, $(\beta_2 + \theta_2 + d_2 + \mu)(\Re_{0h} - 1) < 0$. This means that $\Re_{0h} < 1$. Therefore, the disease free equilibrium is locally asymptotically stable if $\Re_{0h} < 1$ and unstable if $\Re_{0h} > 1$. □

3.1.6 Global Stability of Disease Free Equilibrium Point

Theorem 3.3. The disease free equilibrium point E_{0h} is globally asymptotically stable if $\Re_{0h} < 1$.

Proof . To proof this theorem the Lyapunove function is constructed and is defined as follows

$$L = \frac{1}{\beta_2 + \theta_2 + d_2 + \mu} I_h.$$

Then

$$\begin{aligned}
\frac{dL}{dt} &= \frac{1}{\beta_2 + \theta_2 + d_2 + \mu} \frac{dI_h}{dt} \\
&= \frac{1}{\beta_2 + \theta_2 + d_2 + \mu} \left[\frac{\gamma I_h}{N} S - (\beta_2 + \theta_2 + d_2 + \mu)I_h \right] \\
&\leq (\frac{\gamma}{\beta_2 + \theta_2 + d_2 + \mu} - 1)I_h = (\Re_{0h} - 1)I_h \\
&\leq (\Re_{0h} - 1)I_h.
\end{aligned}$$

So $\frac{dL}{dt} \leq 0$ if and only if $\Re_{0h} \leq 1$. Furthermore, $\frac{dL}{dt} = 0$ if $I_h = 0$ or $\Re_{0h} = 1$. From this, we observe that E_{0h} is the only singleton in $D_1 = \{(S, I_h, R_h) \in \Re^3_+ : \frac{dL}{dt} = 0\}$. Therefore, by the principle in [11] the disease free equilibrium E_{0h} is globally asymptotically stable if $\Re_{0h} < 1$. □

3.1.7 Endemic Equilibrium Point

To find the endemic equilibrium point $E^*_h = (S^*, I^*_h, R^*_h)$ we considered the steady state of the system (3.1) for all state variables. The endemic equilibrium occurs when the disease persists in a population. The followings are the endemic equilibrium:

$$\begin{aligned} S^* &= \frac{\Lambda}{\mu \Re_{0h}} \\ I^*_h &= \frac{\Lambda}{\gamma}(\Re_{0h} - 1) \\ R^*_h &= \frac{\Lambda \beta_2}{\mu \gamma}(\Re_{0h} - 1). \end{aligned}$$

From this we can infer that the endemic equilibrium exists if $\Re_{0h} > 1$.

3.1.8 Global Stability of Endemic Equilibrium Point

Theorem 3.4. If $\Re_{0h} > 1$, then endemic equilibrium point E^*_h the system (3.1) is globally asymptotically stable.

Proof . To prove the global stability condition of the endemic equilibrium point E^*_h we construct a Lypunov function L as shown below

$$L = \left(S - S^* - S^* \ln \frac{S^*}{S}\right) + \left(I_h - I^*_h - I^*_h \ln \frac{I^*_h}{I_h}\right) + \left(R_h - R^*_h - R^*_h \ln \frac{R^*_h}{R_h}\right). \tag{3.6}$$

Differentiating (3.6) on both sides with respect to time results

$$\frac{dL}{dt} = \left(\frac{S - S^*}{S}\right)\frac{dS}{dt} + \left(\frac{I_h - I^*_h}{I_h}\right)\frac{dI_h}{dt} + \left(\frac{R_h - R^*_h}{R_h}\right)\frac{dR_h}{dt}. \tag{3.7}$$

Now substituting (3.1) into (3.7) we obtain that $\frac{dL}{dt} = A - B$. Here

$$A = \Lambda + (\lambda_2 + \mu)S^* + \lambda_2 S + \beta_2 I_h + (\beta_2 + \theta_2 + d_2 + \mu)I^*_h + \beta_2 I_h + \mu R^*_h$$

and

$$B = (\lambda_2 + \mu)S + \Lambda_2 \frac{S^*}{S} + (\beta_2 + \theta_2 + d_2 + \mu)I_h + \lambda_2 S \frac{I^*_h}{I_h} + \mu R_h + \beta_2 I_h \frac{R^*_h}{R_h}.$$

Thus, if $A < B$, then $\frac{dL}{dt} \leq 0$ and $\frac{dL}{dt} = 0$ if and only if $S = S^*, Ih = I^*_h, Rh = R^*_h$. From this we observe that $E^*_h = (S = S^*, I_h = I^*_h, R_h = R^*_h)$ is the largest compact invariant singleton set in $D_1 = \{(S^*, I^*_h, R^*_h) \in \Re^3_+ : \frac{dL}{dt} = 0\}$. Therefore, by the principle in [11] the endemic equilibrium point E^*_h is globally asymptotically stable in the invariant region if $A < B$. □

3.2 Typhoid fever model

The typhoid only model (3.7) is obtained from the system $(2.1 - 2.8)$ by setting $I_h = I_{th} = R_h = R = \lambda_2 = \varepsilon_2 = \theta_2 = \delta = 0$. Then it is obtained

$$\begin{cases} \frac{dS}{dt} = \Lambda + \alpha R_t - (\lambda_1 + \mu)S \\ \frac{dI_t}{dt} = \lambda_1 S - (\beta_1 + \theta_1 + \varepsilon_1 + d_1 + \mu)I_h \\ \frac{dR_t}{dt} = \beta_1 I_t - (\alpha + \mu)R_t \\ \frac{dB}{dt} = rB + \varepsilon I_t \end{cases} \tag{3.8}$$

where $\lambda_1 = \frac{\nu B}{K+B}$ is the force of infections of typhoid fever. With initial conditions $S(0) = S_0, I_t(0) = I_{t0}, R_t(0) = R_{t0}, B(0) = B_0$.

3.2.1 Invariant Region

The invariant region where the solution of the system (3.7) is bounded. For the model in (3.1) let the total population be

$$N_2 = S + I_t + R_t \tag{3.9}$$

Taking the time derivative on both sides in (3.8) and using the system (3.7) we get

$$\frac{dN_2}{dt} = \Lambda - \mu N_2 - d_1 I_t \tag{3.10}$$

In the absence of death due to HAV i.e., $d_1 = 0$ equation (3.9) becomes

$$\frac{dN_2}{dt} \leq \Lambda - \mu N_2 \tag{3.11}$$

Rearranging and evaluating the differential inequality in (3.11) as $t \to \infty$, we obtain

$$D_2 = \left\{ (S, I_t, R_t) \in \Re_+^3 : 0 \leq N_2 \leq \frac{\Lambda}{\mu} \right\}.$$

Therefore, the solution of the system in (3.7) is bounded in D_2.

3.2.2 Positivity of Solution

It is assumed that the initial condition of the model is non-negative, the solution of the model is also positive for non-negative initial conditions.

Theorem 3.5. Let $D_2 = \{(S, I_t, R_t, B_t) \in \Re_+^4 : S_0 > 0, I_{h0} > 0, R_{h0} > 0, B_0 > 0\}$ then the solutions $\{S, I_h, R_h, B > 0\}$ are positive for future time.

Proof . Let t_1 be defined as shown below

$$t_1 = \sup\{t > 0 : S(\tau) > 0, I_t(\tau) > 0, R_t(\tau) > 0, B(\tau) > 0 \quad \text{for all} \quad \tau \in [0, t]\}.$$

Since $S_0 > 0, I_{t0} > 0, R_{t0} > 0, B_0 > 0$, $t_1 > 0$. If $t_1 < \infty$, then necessarily S or I_t or R_t or B is zero at $t_1 < \infty$. From the system (3.7) taking the first equation

$$\frac{dS}{dt} = \Lambda - (\lambda_1 + \mu)S. \tag{3.12}$$

Now using variation of constant formula the solution of (3.12) at t_1 is obtained as

$$S(t_1) = S_0 \exp\left[- \int_0^{t_1} (\lambda_1 + \mu) S ds \right] + \int_0^{t_1} (\Lambda \exp\left[- \int_0^{t_1} (\lambda_1 + \mu)\tau d\tau \right] dS.$$

Since all the variable are positive in $[0, t_1]$, we have $S(t_1) > 0$. Similarly it can be shown that $I_t(t_1) > 0$, $R_t(t_1) > 0$ and $B(t_1) > 0$ which is a contradiction. Hence, $t_1 = \infty$. Therefore, all the solutions are positive for future time. □

3.2.3 Disease Free Equilibrium

The disease free equilibrium point of the model in (3.7) is obtained at $I_t = R_t = B = 0$. Thus, $E_{0t} = (\frac{\Lambda}{\mu}, 0, 0, 0)$.

3.2.4 Basic reproduction number $\Re_t$

The basic reproduction number $\Re_t$ is obtained by using the next generation matrix method as shown below. Using the second and third equation of the system (3.7) we have

$$\frac{dI_t}{dt} = \lambda_1 S - (\beta_1 + \theta_1 + \varepsilon_1 + d_1 + \mu) I_t$$

and

$$\frac{dB}{dt} = rB + \varepsilon I_t.$$

By the principle of next generation matrix, we have

$$g = \begin{bmatrix} (\beta_1 + \theta_1 + \varepsilon_1 + d_1 + \mu)I_t \\ -rB - \varepsilon_1 I_t \end{bmatrix}$$

Then

$$F = \begin{bmatrix} 0 & \frac{\Lambda\nu}{\mu K} \\ 0 & 0 \end{bmatrix} \quad \text{and} \quad G^{-1} = \begin{bmatrix} \frac{1}{\beta_1+\theta_1+\varepsilon_1+d_1+\mu} & 0 \\ \frac{-\varepsilon_1}{r(\beta_1+\theta_1+\varepsilon_1+d_1+\mu)} & -r \end{bmatrix}$$

So,

$$FG^{-1} = \begin{bmatrix} \frac{\varepsilon_1\Lambda\nu}{r\mu K(\beta_1+\theta_1+\varepsilon_1+d_1+\mu)} & \frac{-r\Lambda\nu}{\mu K} \\ 0 & 0 \end{bmatrix}$$

The eigne values of FG^{-1} are 0 and $\frac{\varepsilon_1\Lambda\nu}{r\mu K(\beta_1+\theta_1+\varepsilon_1+d_1+\mu)}$. Therefore, the basic reproduction number $\Re_t$ is given by

$$\Re_t = \frac{\varepsilon_1\Lambda\nu}{r\mu K(\beta_1 + \theta_1 + \varepsilon_1 + d_1 + \mu)}.$$

3.2.5 Local Stability of Disease Free Equilibrium

Theorem 3.6. The disease free equilibrium point E_{0t} is locally asymptotically stable if $\Re_t < 1$ and unstable if $\Re_t > 1$.

Proof . To prove the theorem the Jacobean matrix of (3.7) at disease free equilibrium point E_{0t} is constructed as follows:

$$J_{E_{0t}} = \begin{bmatrix} 0 & 0 & \alpha & -\frac{\Lambda\nu}{\mu K} \\ 0 & -(\beta_1 + \theta_1 + \varepsilon_1 + d_1 + \mu) & 0 & \frac{\Lambda\nu}{\mu K} \\ 0 & \beta_1 & -(\alpha + \mu) & 0 \\ 0 & \varepsilon_1 & 0 & r \end{bmatrix} \tag{3.13}$$

The characteristic polynomial of (3.13) is

$$(-\mu - \lambda_*)[-(\alpha + \mu) - \lambda_*][\lambda^{*2} + (\beta_1 + \theta_1 + \varepsilon_1 + d_1 + \mu)\lambda^* - \frac{\Lambda\nu}{\mu K}(\frac{-1}{\Re_t} + 1)] = 0.$$

This implies $\lambda_1^* = -\mu$, $\lambda_2^* = -(\alpha+\mu)$ and $\lambda^{*2} + (\beta_1 + \theta_1 + \varepsilon_1 + d_1 + \mu)\lambda^* - \frac{\Lambda\nu}{\mu K}(\frac{-1}{\Re_t} + 1) = 0$. By the Routh-Huarth criteria the roots of the above quadratic equation will be negative provided that the coefficients are positive i.e.,

$$(\beta_1 + \theta_1 + \varepsilon_1 + d_1 + \mu) > 0 \quad \text{and} \quad -\frac{\Lambda\nu}{\mu K}(\frac{-1}{\Re_t} + 1) > 0.$$

This implies $\Re_t < 1$. Therefore, the disease free equilibrium E_{0t} is locally asymptotically stable if $\Re_t < 1$ and unstable if $\Re_t > 1$. □

3.2.6 Global Stability of Disease Free Equilibrium point E_{0t}

Theorem 3.7. The disease free equilibrium point E_{0t} is globally asymptotically stable if $\Re_t < 1$ and unstable if $\Re_t > 1$.

Proof . For typhoid only model since the Metzler conditions do not met the disease free equilibrium point is not globally asymptotically stable. □

3.2.7 Endemic Equilibrium Point

The endemic equilibrium point $E_t^* = (S^*, I_t^*, R_t^*, B^*)$ exists and it occurs when the disease persists in the community. It can be obtained when we solve the system (3.7) at a steady state as follows:

$$\Lambda + \alpha R_t^* - (\lambda_1 + \mu)S^* = 0 \tag{3.14}$$

$$\lambda_1 S^* - (\beta_1 + \theta_1 + \varepsilon_1 + d_1 + \mu)I_t^* = 0 \tag{3.15}$$

$$\beta_1 I_t^* - (\alpha + \mu)R_t^* = 0 \tag{3.16}$$

$$rB^* + \varepsilon I_t^* = 0. \tag{3.17}$$

Thus, we have the following results

$$S^* = \frac{r}{\varepsilon_1}(\beta_1 + \theta_1 + \varepsilon_1 + d_1 + \mu)(K + B^*) \tag{3.18}$$

$$I_t^* = \frac{r\varepsilon_1\Lambda + \mu K r^2(\beta_1 + \theta_1 + \varepsilon_1 + d_1 + \mu)}{\varepsilon_1[-\alpha\beta_1 r + (\nu + \mu)(\beta_1 + \theta_1 + \varepsilon_1 + d_1 + \mu)]} \tag{3.19}$$

$$R_t^* = \frac{\beta_1 I_t^*}{\alpha + \mu} \tag{3.20}$$

$$B^* = \frac{\varepsilon_1\Lambda + \mu K r(\beta_1 + \theta_1 + \varepsilon_1 + d_1 + \mu)}{\alpha\beta_1 r - (\nu + \mu)(\beta_1 + \theta_1 + \varepsilon_1 + d_1 + \mu)} \tag{3.21}$$

3.2.8 Global Stability of Endemic Equilibrium

Theorem 3.8. If $\Re_t > 1$, then the endemic equilibrium point E_t^* of the model (3.7) is globally asymptotically stable.

Proof . To prove the global stability condition of the endemic equilibrium point E_t^* we construct a Lypunov function L as shown below.

$$L = \left(S - S^* + S^* \ln \frac{S^*}{S}\right) + \left(I_t - I_t^* + I_t^* \ln \frac{I_t^*}{I_t}\right) + \left(R_t - R_t^* + R_t^* \ln \frac{R_t^*}{R_t}\right) + \left(B - B^* + B^* \ln \frac{B^*}{B}\right). \tag{3.22}$$

Differentiating (3.22) on both sides with respect to time results

$$\frac{dL}{dt} = \left(\frac{S - S^*}{S}\right)\frac{dS}{dt} + \left(\frac{I_t - I_t^*}{I_t}\right)\frac{dI_t}{dt} + \left(\frac{R_t - R_t^*}{R_t}\right)\frac{dR_t}{dt} + \left(\frac{B - B^*}{B}\right)\frac{dB}{dt}. \tag{3.23}$$

Now substituting (3.7) into (3.23) we obtained that $\frac{dL}{dt} = X - Y$, where

$$X = \Lambda + \alpha R_t^* - (\lambda_1 + \mu)S^* + \lambda_1 S + (\beta_1 + \theta_1 + \varepsilon_1 + d_1 + \mu)I_t^* + \beta_1 I_t + (\alpha + \mu)R_t^* + rB + \varepsilon_1 I_t$$

and

$$Y = (\lambda_1 + \mu)S + \Lambda\frac{S^*}{S} + \alpha R_t\frac{S^*}{S} + \lambda_1 S\frac{I_t^*}{I_t} + (\beta_1 + \theta_1 + \varepsilon_1 + d_1 + \mu)I_t + \beta_1 I_t\frac{R_t^*}{R_t} + (\alpha + \mu)R_t + rB^* + \varepsilon_1 I_t\frac{B^*}{B}.$$

Thus, if $X < Y$, then $\frac{dL}{dt} \leq 0$ and $\frac{dL}{dt} = 0$ if and only if $S = S^*$, $I_t = I_t^*$, $R_t = R_t^*$, $B = B^*$. From this, we observe that $E_t^* = (S^*, I_t^*, R_t^*, B^*)$ is the largest compact invariant singleton set in $D_2 = \{(S^*, I_t^*, R_t^*, B^*) \in \Re_+^4 : \frac{dL}{dt} = 0\}$. Therefore, by the principle in [11] the endemic equilibrium point E_t^* is globally asymptotically stable in the invariant region if $X < Y$. □

3.3 HAV-Typhoid Co-infection model

The HAV-typhoid co-infection model is given in the following eight systems of non-linear differential equations.

$$\begin{cases} \frac{dS}{dt} = \Lambda + \alpha R_t - (\lambda_1 + \lambda_2 + \mu)S \\ \frac{dI_t}{dt} = \lambda_1 S + b\delta\ I_{th} - (\beta_1 + \theta_1 + \varepsilon_1 + d_1 + \mu)I_t \\ \frac{dI_h}{dt} = \lambda_2 S + a(1-b)\delta\ I_{th} - (\beta_2 + \theta_2 + d_2 + \mu)I_h \\ \frac{dI_{th}}{dt} = \theta_1 I_t + \theta_2 I_h - (\delta + \varepsilon_3 + d_3 + \mu)I_{th} \\ \frac{dR_t}{dt} = \beta_1 I_t - (\alpha + \mu)R_t \\ \frac{dR_h}{dt} = \beta_2 I_h - \mu R_h \\ \frac{dR}{dt} = (1-a)(1-b)\delta\ I_{th} - \mu R \\ \frac{dB}{dt} = rB + \varepsilon_1 I_t + \varepsilon_2 I_{th} \end{cases} \tag{3.24}$$

where $\lambda_1 = \frac{\nu B}{K+B}$ and $\lambda_2 = \frac{\gamma(I_h(t)+\vartheta I_{th}(t))}{N}$ are force of infections of typhoid fever and HAV disease respectively. With initial conditions $S(0) = S_0, I_t(0) = I_{t0}, I_h(0) = I_{h0}, I_{th}(0) = I_{th0}, R_t(0) = R_{t0}, R_h(0) = R_{h0}, R(0) = R_0$, and $B(0) = B_0$.

3.3.1 The Invariant Region

The invariant region in which the solution of the system (3.24) is bounded. Let total population for the given model is N

$$N = S + I_t + I_h + I_{th} + R_t + R_h + R. \tag{3.25}$$

Taking the time derivative on both sides in (3.25) and using the system (3.24), we get

$$\frac{dN}{dt} = \Lambda - \mu N - (d_1 I_t + d_2 I_h + d_3 I_{th}). \tag{3.26}$$

In the absence of death due to typhoid fever or HVA or both i.e., $d_1 = d_2 = d_3 = 0$ equation (3.27) becomes

$$\frac{dN}{dt} \leq \Lambda - \mu N. \tag{3.27}$$

Rearranging and evaluating the differential inequality in (3.28) as $t \to \infty$ we obtain

$$D = \left\{ (S, I_t, I_h, I_{th}, R_t, R_h, R) \in \Re_+^7 : 0 \leq N \leq \frac{\Lambda}{\mu} \right\}.$$

Therefore, the solution of the system in (3.24) is bounded in D.

3.3.2 Positivity of Solution

It is assumed that the initial condition of the model (3.24) is non-negative, and can be shown that the solution of the model is also positive.

Theorem 3.9. Let

$$D = \{(S, I_t, I_h, I_{th}, R_t, R_h, R) \in \Re_+^7 : S_0 > 0, I_{t0} > 0, R_{t0} > 0\}.$$

Then the solutions $\{S, I_t, I_h, I_{th}, R_t, R_h, R\}$ are positive for future time.

Proof . Let t_3 be defined as shown below

$$t_3 = \sup\{t > 0 : S(\tau) > 0, I_t(\tau) > 0, I_h(\tau) > 0, I_{th}(\tau) > 0, R_t(\tau) > 0, R_h(\tau) > 0, R(\tau) > 0 \quad \text{for all} \quad \tau \in [0, t]\}.$$

Since $S_0 > 0, I_{t0} > 0, I_{h0} > 0, I_{th0} > 0, R_{t0} > 0, R_{h0} > 0, R_0 > 0$, we have $t_3 > 0$. If $t_3 < \infty$, then necessarily S or I_t or I_h or I_{th} or R_t or R_h or R is zero at $t_3 < \infty$. From the system (3.24) taking the first equation

$$\frac{dS}{dt} = \Lambda + \alpha R_t - (\lambda_1 + \lambda_2 + \mu)S. \tag{3.28}$$

Now using variation of constant formula the solution of (3.29) at $t_3$is obtained as

$$S(t_3) = S_0 \exp\left[-\int_0^{t_3}(\lambda_1+\lambda_2+\mu)Sds\right] + \int_0^{t_3}(\Lambda+\alpha R_t)\exp\left[-\int_0^{t_3}(\lambda_1+\lambda_2+\mu)\tau d\tau\right]dS.$$

Since all the variable are positive in $[0, t_3]$, we have $S(t_3) > 0$. Similarly, it can be shown that $I_t(t_3) > 0$, $I_h(t_3) > 0$, $I_{th}(t_3) > 0$, $R_t(t_3) > 0$, $R_h(t_3) > 0$ and $R(t_3) > 0$ which is a contradiction. Hence, $t_3 = \infty$ Therefore, all the solutions are positive for future time. □

3.3.3 Disease Free Equilibrium

The disease free equilibrium point of the co-infection model in (3.24) is obtained at $I_t = I_h = I_{th} = R_t = R_h = R = B = 0$. Thus, $E_0 = (\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0, 0, 0)$.

3.3.4 Basic reproduction number $\Re_0$

To obtain the basic reproduction number $\Re_0$ of the model (3.24) we used the next generation matrix method as shown below.

$$\begin{aligned}
\frac{dI_t}{dt} &= \lambda_1 S + b\delta\ I_{th} - (\beta_1+\theta_1+\varepsilon_1+d_1+\mu)I_t\\
\frac{dI_h}{dt} &= \lambda_2 S + a(1-b)\delta I_{th} - (\beta_2+\theta_2+d_2+\mu)I_h\\
\frac{dI_{th}}{dt} &= \theta_1 I_t + \theta_2 I_h - (\delta+\varepsilon_3+d_3+\mu)I_{th}\\
\frac{dB}{dt} &= rB + \varepsilon_1 I_t + \varepsilon_2 I_{th}.
\end{aligned}$$

Then by the principle of next generation matrix, we have

$$f = \begin{bmatrix} \frac{\nu B}{K+B}S \\ \frac{\gamma(I_h(t)+\vartheta I_{th}(t))}{N}S \end{bmatrix} \quad \text{and} \quad v = \begin{bmatrix} (\beta_1+\theta_1+\varepsilon_1+d_1+\mu)I_t - b\delta\ I_{th} \\ (\beta_2+\theta_2+d_2+\mu)I_h - a(1-b)\delta I_{th} \\ (\delta+\varepsilon_2+d_3+\mu)I_{th} - (\theta_1 I_t+\theta_2 I_h) \\ -rB-\varepsilon_1 I_t-\varepsilon_2 I_{th} \end{bmatrix}$$

Then

$$F = \begin{bmatrix} 0 & 0 & \alpha & \frac{\Lambda\nu}{\mu K} \\ 0 & \frac{\Lambda\gamma}{\mu} & \frac{\Lambda\gamma\vartheta}{\mu} & \frac{\Lambda\nu}{\mu K} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \quad \text{and} \quad V = \begin{bmatrix} l_1 & 0 & -b\delta & 0 \\ 0 & l_2 & l_3 & 0 \\ -\theta_1 & -\theta_2 & l_4 & 0 \\ -\varepsilon_1 & 0 & -\varepsilon_2 & -r \end{bmatrix}$$

where $l_1 = \beta_1+\theta_1+\varepsilon_1+d_1+\mu$, $l_2 = \beta_2+\theta_2+d_2+\mu$, $l_3 = -a(1-b)\delta$ and $l_4 = \delta+\varepsilon_2+d_3+\mu$. Then

$$FV^{-1} = \begin{bmatrix} \frac{\Lambda\nu\varepsilon_1[l_2(\theta_1+l_4)-\theta_2 l_3]}{K\mu det(V)} & \frac{\Lambda\nu(\theta_2\varepsilon_1 l_1 - b\delta\theta_2\varepsilon_1)}{K\mu det(V)} & \frac{\Lambda\nu c_{34}}{K\mu det(V)} & \frac{\Lambda\nu c_{44}}{K\mu det(V)} \\ \frac{\Lambda\gamma\theta_1(-l_3 r+br l_2\varphi)}{\mu det(V)} & \frac{\Lambda\gamma(c_{22}+\varphi c_{23})}{\mu det(V)} & \frac{\Lambda\gamma c_{33}(1+\varphi)}{\mu det(V)} & \frac{\Lambda\gamma(c_{42}+\varphi c_{43})}{\mu det(V)} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

where $c_{22} = r(l_1 l_4 - b\delta\theta_1)$, $c_{23} = \theta_2 l_1 r$, $c_{32} = -l_1 l_3 r$, $c_{33} = l_1 l_2 r$, $c_{34} = \varepsilon_2(l_1 l_2 - b\delta\varepsilon_1 l_2)$, $c_{44} = l_1(l_2 l_4 - \theta_2 l_3) - b\delta\theta_1\theta_2$, $c_{42} = c_{43} = 0$, and $\det(V) = r(l_1 l_2 l_4 + l_1 l_2\theta_2 - b\delta\theta_1 l_2)$. The eigne values of FV^{-1} are $\lambda_1^* = \lambda_2^* = 0, \lambda_3^* = \frac{\varepsilon_1\nu\Lambda}{\mu K l_1 r} = \Re_{t0}$ and $\lambda_4^* = \frac{\gamma}{l_2} = \Re_{h0}$. Therefore, the basic reproduction number is $\Re_0$ is given by $\Re_0 = \max\{\Re_{t0}, \Re_{h0}\}$.

3.3.5 Local Stability of Disease Free Equilibrium

Theorem 3.10. The disease free equilibrium point E_0 is locally asymptotically stable if $\Re_0 < 1$ and unstable if $\Re_0 > 1$.

Proof . To prove the theorem the Jacobean matrix of (3.24) at disease free equilibrium point E_0 is constructed as follows:

$$J_{E_0} = \begin{bmatrix} -\mu & 0 & -\gamma & -\gamma\varphi & \alpha & 0 & 0 & -\frac{\Lambda\nu}{\mu K} \\ 0 & A_1 & 0 & b\delta & 0 & 0 & 0 & \frac{\Lambda\nu}{\mu K} \\ 0 & 0 & A_2 & A_3 & 0 & 0 & 0 & 0 \\ 0 & \theta_1 & \theta_2 & A_4 & 0 & 0 & 0 & 0 \\ 0 & \beta_1 & 0 & 0 & A_5 & 0 & 0 & 0 \\ 0 & 0 & \beta_2 & 0 & 0 & -\mu & 0 & 0 \\ 0 & 0 & 0 & A_6 & 0 & 0 & -\mu & 0 \\ 0 & \varepsilon_1 & 0 & \varepsilon_2 & 0 & 0 & 0 & r \end{bmatrix} \tag{3.29}$$

where $A_1 = -(\beta_1+\theta_1+\varepsilon_1+d_1+\mu)$, $A_2 = -(\beta_2+\theta_2+d_2+\mu)$, $A_3 = a(1-b)\delta$, $A_4 = -(\delta+\varepsilon_2+d_3+\mu)$, $A_5 = -(\alpha+\mu)$ and $A_6 = (1-a)(1-b)\delta$. The characteristic polynomial of (3.31) is

$$(-\mu-\lambda^*)(-\mu-\lambda^*)(-\mu-\lambda^*)(-r-\lambda^*)(-A_5-\lambda^*)(-A_6-\lambda^*)(\lambda^{*2} - rb\delta A_1\lambda^* - r\theta_2\varepsilon_1 A_5) = 0.$$

This implies $\lambda_1^* = -\mu, \lambda_2^* = -\mu, \lambda_3^* = -\mu, \lambda_4^* = -r, \lambda_5^* = A_5, \lambda_6^* = A_2$ and $\lambda^{*2} - rb\delta A_1\lambda^* - r\theta_2\varepsilon_1 A_5 = 0$. By the Routh-Huarth criteria the roots of the above quadratic equation will be negative provided that $\Re_{0t} < 1$ and if $\Re_{0h} < 1$. Therefore, the disease free equilibrium point E_0 is locally asymptotically stable if $\Re_0 < 1$ and unstable if $\Re_0 > 1$. □

3.3.6 Global Stability of Disease Free Equilibrium point

In this section, the global stability of the disease free equilibrium point is analyzed by using the techniques used in [18]. The system in (3.24) can be written in the form:

$$\begin{cases} \frac{dX_S}{dt} = A(X_S - X_{DFE,S}) + A_1X_i \\ \frac{dX_i}{dt} = A_2X_i \end{cases} \tag{3.30}$$

Here X_S is the vector representing the non-transmitting compartment and X_i is the vector representing the transmitting compartments. The disease free equilibrium point E_0 is globally asymptotically stable if matrix A has only negative eigne values and A_2 is Metzler (i.e. the off-diagonal elements of A_2 are non-negative).

For the model equation (3.24), we have:

$$X_S = (S, R_t, R_h, R)^T \quad \text{and} \quad X_i = (I_t, I_h, I_{th}, B)^T,$$

where the superscript T refers to a transpose of the matrix. We need to check whether a matrix A for non-transmitting compartments has real negative eigne values and that A_2 is Metzler matrix. From the equation for non-transmitting compartments in the model it is obtained:

$$A = \begin{bmatrix} -(\lambda_1+\lambda_2+\mu) & \alpha & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & -\mu & 0 \\ 0 & 0 & 0 & -\mu \end{bmatrix}, \qquad A_1 = \begin{bmatrix} 0 & 0 & 0 & 0 \\ \beta_1 & \theta_2 & 0 & 0 \\ 0 & \beta_2 & 0 & 0 \\ 0 & 0 & (1-a)(1-b)\delta & 0 \end{bmatrix}$$

and

$$A_2 = \begin{bmatrix} -(\beta_1+\theta_1+\varepsilon_1+d_1+\mu) & 0 & b\delta & \frac{\nu S}{K+B} \\ 0 & -(\beta_2+\theta_2+d_2+\mu) & a(1-b)\delta & 0 \\ \theta_1 & \theta_2 & -(\delta+\varepsilon_2+d_3+\mu) & 0 \\ \varepsilon_1 & 0 & \varepsilon_2 & r \end{bmatrix}$$

From the matrix A it can be checked that all the eigne values are real and negative. Moreover, all the off-diagonal elements of A_2 are non-negative. Therefore, the disease free equilibrium point is globally asymptotically stable.

3.3.7 The Endemic Equilibrium point

The endemic equilibrium point E^* for the co-infection model (3.24) occurs when both diseases persists in a community. To obtain it we evaluate the system (3.24) at its steady state and we obtained the following result:
$S^* = \frac{\Lambda+\alpha R_t^*}{\lambda_1+\lambda_2}$

Table 1: Parameter values for typhoid model

Parameters	Descriptions	values	source
α	Proportion of typhoid recovered groups who are joining susceptible subclass	0.8	[12]
μ	Natural mortality rate	0.02	Estimated
d_1	Typhoid induced mortality rate	0.005	Assumed
d_2	HAV induced mortality rate	0.002	Assumed
d_3	HAV and typhoid induced mortality rate	0.1	Assumed
γ	Infectious rate of HAV	0.01	Assumed
β_1	Recovery rate of typhoid by natural immunity	0.071	Estimated
β_2	Recovery rate of HAV by natural immunity	0.034	Estimated
θ_1	Rate of typhoid infected class joining the co-infection class	0.002	Assumed
θ_2	Rate of HAV infected class joining the co-infection class	0.003	Assumed
δ	Rate of removal of HAV-typhoid co-infection class	0.4	Assumed
r	Rate of growth of salmonella bacteria	7	Assumed
ν	Ingestion rate of salmonella bacteria	0.6	Assumed
K	Concentration of salmonella bacteria	100,000	Assumed
ε_1	Discharge rate of salmonella bacteria from typhoid infected class	0.7	Assumed
ε_2	Discharge rate of salmonella bacteria from HAV-typhoid co- infected class	0.5	Assumed

$I_t^* = \frac{c_4 R_t^*}{\beta_1}$
$I_h^* = \frac{\mu R_h^*}{\beta_2}$
$I_{th}^* = \frac{\beta_2\theta_1 c_4 R_t^* + \beta_1\theta_2\mu R_h^*}{\beta_1\beta_2 c_3}$
$R_t^* = \frac{\Lambda\beta_1(\beta_1\lambda_1 + c_3\lambda_2)}{\beta_1 c_1 c_4(\lambda_1+\lambda_2) - [\theta_1 c_4(\lambda_1+\lambda_2) + \alpha\lambda_2\beta_1 c_4 + b\delta\theta_1\beta_1 c_4(\lambda_1+\lambda_2) + \alpha\lambda_1\beta_1^2]}$
$R_h^* = \frac{R_t^*[c_1 c_4(\lambda_1+\lambda_2) - b\delta\theta_1(\lambda_1+\lambda_2) - \beta_1\alpha\lambda_1] - \Lambda\lambda_1\beta_1}{b\delta\mu\theta_2\beta_1(\lambda_1+\lambda_2)}$
$R* = \frac{(1-a)(1-b)\delta\beta_2\theta_1 c_4 R_t^* + \beta_1\theta_2\mu R_h^*}{\mu\beta_1\beta_2 c_3}$
$B* = \frac{\varepsilon_1 I_t^* + \varepsilon_2 I_{th}^*}{r}$
where $c_1 = \beta_1 + \theta_1 + \varepsilon_1 + d_1 + \mu$, $c_2 = \beta_2 + \theta_2 + d_2 + \mu$, $c_3 = \delta + \varepsilon_2 + d_3 + \mu$, $c_4 = \alpha + \mu$.

3.3.8 Impact of Typhoid fever on HAV

In this section the impact of typhoid fever on HAV disease and vice versa is determined. To see the impact of typhoid fever on HAV infected individual the following techniques are used:

$$\Re_h = \frac{\gamma}{\beta_2 + \theta_2 + d_2 + \mu} \tag{3.31}$$

and

$$\Re_t = \frac{\varepsilon_1\Lambda\nu}{r\mu K(\beta_1 + \theta_1 + \varepsilon_1 + d_1 + \mu)}. \tag{3.32}$$

From (3.33) we get

$$\mu = \frac{\gamma}{\Re_h} - (\beta_2 + \theta_2 + d_2). \tag{3.33}$$

Substituting (3.35) into (3.34), we get

$$\Re_t = \frac{\varepsilon_1\Lambda\nu}{[\frac{\gamma}{\Re_h} - (\beta_2 + \theta_2 + d_2)][\beta_1 + \theta_1 + \varepsilon_1 + d_1 + \frac{\gamma}{\Re_h} - (\beta_2 + \theta_2 + d_2)]Kr}. \tag{3.34}$$

To determine the impact of typhoid over HAV and vice-versa we take the partial derivative of $\Re_h$ or $\Re_t$ with respect to each other as follows

$$\frac{\partial\Re_t}{\partial\Re_h} = \frac{\varepsilon_1\Lambda\nu}{Kr\mu^2(\beta_1 + \theta_1 + \varepsilon_1 + d_1 + \mu)^2} > 0 \tag{3.35}$$

From (3.35) it is possible to conclude HAV disease increases the burden of typhoid cases and similarly it is possible to show typhoid fever increases the burden of HAV cases.

3.3.9 Existence of backward bifurcation

The existence of a backward bifurcation can be proved by applying the centre manifold theorem on system (3.24). Consider the ingestion rate ν and μ as bifurcation parameters so that $\Re_t = 1$ and $\Re_h = 1$ if and only if

$$\nu = \nu^* = \frac{r\mu K(\beta_1 + \theta_1 + \varepsilon_1 + d_1 + \mu)}{\varepsilon_1 \Lambda} \quad \text{and} \quad \gamma = \gamma^* = \beta_2 + \theta_2 + d_2 + \mu.$$

Now we use the following change of variables: $S = x_1, I_t = x_2, I_h = x_3, I_{th} = x_4, R_t = x_5, R_h = x_6, R = x_7, B = x_8$ and $N = x_1 + x_2 + x_3 + x_4 + x_5 + x_6 + x_7 + x_8$. Using vector notation $\overrightarrow{x} = (x_1, x_2, x_3, x_4, x_5, x_6, x_7, x_8)^T$, HAV-Typhoid co-infection model can be expressed in vector notation as $\overrightarrow{x'} = F(\overrightarrow{x})$

$$\begin{cases} x_1 = \Lambda + \alpha x_5 - (\lambda_1 + \lambda_2 + \mu)x_1 \\ x_2 = \lambda_1 x_1 + b\delta\ x_4 - (\beta_1 + \theta_1 + \varepsilon_1 + d_1 + \mu)x_2 \\ x_3 = \lambda_2 x_1 + a(1-b)\delta\ x_4 - (\beta_2 + \theta_2 + d_2 + \mu)x_3 \\ x_4 = \theta_1 x_2 + \theta_2 x_3 - (\delta + \varepsilon_3 + d_3 + \mu)x_4 \\ x_5 = \beta_1 x_2 - (\alpha + \mu)x_5 \\ x_6 = \beta_2 x_3 - \mu x_6 \\ x_7 = (1-a)(1-b)\delta\ I_{th} - \mu x_7 \\ x_8 = r x_8 + \varepsilon_1 x_2 + \varepsilon_2 x_4 \end{cases} \tag{3.36}$$

where $\lambda_1 = \frac{\nu x_8}{K + x_8}$ and $\lambda_2 = \frac{\gamma(x_3 + \vartheta x_4)}{N}$. Then we use the Jacobean matrix at disease free equilibrium as follows

$$J_{E_0} = \begin{bmatrix} -\mu & 0 & -\gamma & -\gamma\varphi & \alpha & 0 & 0 & -\frac{\Lambda\nu}{\mu K} \\ 0 & A_1 & 0 & b\delta & 0 & 0 & 0 & \frac{\Lambda\nu}{\mu K} \\ 0 & 0 & A_2 & A_3 & 0 & 0 & 0 & 0 \\ 0 & \theta_1 & \theta_2 & A_4 & 0 & 0 & 0 & 0 \\ 0 & \beta_1 & 0 & 0 & A_5 & 0 & 0 & 0 \\ 0 & 0 & \beta_2 & 0 & 0 & -\mu & 0 & 0 \\ 0 & 0 & 0 & A_6 & 0 & 0 & -\mu & 0 \\ 0 & \varepsilon_1 & 0 & \varepsilon_2 & 0 & 0 & 0 & r \end{bmatrix} \tag{3.37}$$

where $A_1 = -(\beta_1 + \theta_1 + \varepsilon_1 + d_1 + \mu)$, $A_2 = -(\beta_2 + \theta_2 + d_2 + \mu)$, $A_3 = a(1-b)\delta$, $A_4 = -(\delta + \varepsilon_2 + d_3 + \mu)$, $A_5 = -(\alpha + \mu)$, $A_6 = (1-a)(1-b)\delta$. J_{E_0} has a simple zero eigen value, together with other eigenvalues having negative real parts. Hence the centre manifold theorem [5] can be applied.

By calculating the right and the left eigenvectors of J_{E_0} denoted by $\overrightarrow{w} = (w_1, w_2, w_3, w_4, w_5, w_6, w_7, w_8)^T$ and $\overrightarrow{v} = (v_1, v_2, v_3, v_4, v_5, v_6, v_7, v_8)^T$ respectively. We obtained
$w_1 = (-\frac{\gamma}{\mu} + \frac{l_1\gamma\varphi}{l_3\mu})w_3 - \frac{\alpha}{\mu}w_5 - \frac{\Lambda\nu}{\mu K}w_8$, $w_2 = \frac{\mu}{\varepsilon_1}w_8 + \frac{\varepsilon_2 l_2}{l_3}w_3$, $w_4 = -\frac{l_3}{l_2}w_3$, $w_6 = \frac{l_3}{l_2}w_3$, $w_7 = -\frac{\mu l_2}{l_3 l_6}w_3$, $v_1 = v_5 = v_6 = v_7 = 0$, $v_2 = \frac{\mu^2 K}{\Lambda\nu}v_8$, $v_3 = -\frac{b\delta\mu^2 K}{\Lambda\nu}v_8 + \frac{\theta_2}{theta_1 l_2}(\frac{\mu^2 l_1 K}{\Lambda\nu} + \varepsilon_1)v_8$, and $v_4 = -\frac{1}{\theta_1 l_2}(\frac{\mu^2 l_1 K}{\Lambda\nu} + \varepsilon_1)v_8$.

To compute a and b we use the following formula

$$a = \sum_{k,j,i=1}^{n} v_k w_i w_j \frac{\partial^2 f}{\partial x_i \partial x_j}(S_0, 0, 0, 0, 0, 0, 0, 0) \quad \text{and} \quad b = \sum_{k,j,i=1}^{n} v_k w_i \frac{\partial^2 f}{\partial x_i \partial v^*}(S_0, 0, 0, 0, 0, 0, 0, 0).$$

After some rigorous computations, we obtained that

$$a = v_2 w_1 w_8 \frac{\nu}{K} + v_2 w_1 w_3 \frac{\gamma}{\Lambda}(1 - \frac{l_2\varphi}{l_3}) \quad \text{and} \quad b = v_1 w_1 \frac{\mu\varphi}{\Lambda}.$$

Whenever the coefficient b is positive, it follows from [5] that we have the following lemma.

Lemma 3.11. Suppose that $b > 0$. Then we have the following result:

1. System (3.24) will undergo a backward bifurcation if the coefficient $v_2 w_1 w_8 \frac{\nu}{K} + v_2 w_1 w_3 \frac{\gamma}{\Lambda}(1 - \frac{l_2\varphi}{l_3}) > 0$.
2. System (3.24) will undergo transcritical bifurcation if the coefficient

$v_2w_1w_8\frac{\nu}{K} + v_2w_1w_3\frac{\gamma}{\Lambda}(1 - \frac{l_2\varphi}{l_3}) < 0.$

Notice: If a is positive then the disease free equilibrium is locally asymptotically stable but not globally stable. This implies the disease persist even if the basic reproduction number is reduced below unity. If a is negative then the disease free equilibrium may be globally stable.

4 Sensitivity Analysis

In this section sensitivity analysis of the basic parameters of the model is evaluated based on the parameter values given in table 1. Sensitivity analysis on typhoid fever

$$\nu^{\Re_t} = \frac{\partial \Re_t}{\partial \nu} \times \frac{\nu}{\Re_t} = 1 > 0$$
$$r^{\Re_t} = \frac{\partial \Re_t}{\partial r} \times \frac{r}{\Re_t} = 1 > 0.$$

Using similarly approach, we obtain $\varepsilon_1^{\Re_t} > 0$,$\beta_1^{\Re_t} < 0$, $d_1^{\Re_t} < 0$, $K^{\Re_t} > 0$ and $\mu^{\Re_t} < 0$.

Sensitivity analysis on HAV disease are as follow

$$\gamma^{\Re_h} = \frac{\partial \Re_h}{\partial \gamma} \times \frac{\gamma}{\Re_h} = 1 > 0$$
$$\Lambda^{\Re_h} = \frac{\partial \Re_h}{\partial \Lambda} \times \frac{\Lambda}{\Re_h} = 1 > 0$$

Similarly, the sensitivity of each parameters are summarized in table 2 below

Table 2: Table2. Sensitivity index table.

Parameters	Descriptions	Sensitivity index
ν	Ingestion rate	+ve
r	Growth rate of salmonella bacteria	+ve
K	Concentration of salmonella bacteria	+ve
ε_1	Discharge rate of salmonella bacteria from typhoid infected individuals	+ve
μ	Natural mortality rate	-ve
d_1	Typhoid induced mortality rate	-ve
β_1	Recovery rate of typhoid by natural immunity	-ve
γ	The infectious rate of HAV	+ve
θ_1	Rate of typhoid infected class joining the co-infection class	+ve
β_2	Recovery rate of HAV by natural immunity	-ve
d_2	HAV induced mortality rate	-ve

The sensitivity index in Table 2 shows that increasing the value of the parameters K, ν, γ, r and ε_1 have an impact in increasing the burden of typhoid fever while the remaining parameters remains constant. The parameters β_1, β_2, d_1 and μ decreases the burden of typhoid fever while the remaining parameter values remain constant.

5 Extension into an Optimal control

In this section, we applied different control methods for the system (3.24) by using [8]. The optimal control model is an extension of HAV-typhoid model by incorporating the following five controls strategies mentioned below.

1. u_1 is the prevention effort of HAV disease, that protect susceptible from contracting HAV disease by using personal needles and proper hygiene.
2. u_2 is the prevention effort of typhoid disease, that protect susceptible from contracting the disease by using proper hygiene.
3. u_3 is the treatment effort of HAV infected individuals.

4. u_4 is the treatment effort of typhoid infected individuals.
5. u_5 is the effort used to eliminate Salmonella bacteria from the environment and providing pure water.

After incorporating u_1, u_2, u_3, u_4 and u_5 in co-infections of HAV-typhoid model (3.24), we get the following optimal model of co-infection of HAV-Typhoid disease.

$$\begin{cases} \frac{dS}{dt} = \Lambda + \alpha R_t - [(1-u_2)\lambda_1 + (1-u_1)\lambda_2 + \mu]S \\ \frac{dI_t}{dt} = (1-u_2)\lambda_1 S + (b\delta + u_4)I_{th} - (\beta_1 + u_2)I_t - (\theta_1 + \varepsilon_1 + d_1 + \mu)I_t \\ \frac{dI_h}{dt} = (1-u_1)\lambda_2 S + (a(1-b)\delta + u_4)I_{th} - (\beta_2 + u_3)I_h - (\theta_2 + d_2 + \mu)I_h \\ \frac{dI_{th}}{dt} = \theta_1 I_t + \theta_2 I_h - (\delta + u_4)I_{th} - (\varepsilon_3 + d_3 + \mu)I_{th} \\ \frac{dR_t}{dt} = (\beta_1 + u_2)I_t - (\alpha + \mu)R_t \\ \frac{dR_h}{dt} = (\beta_2 + u_3)I_h - \mu R_h \\ \frac{dR}{dt} = ((1-a)(1-b)\delta + u_4)I_{th} - \mu R \\ \frac{dB}{dt} = (r - u_5)B + \varepsilon_1 I_t + \varepsilon_2 I_{th} \end{cases} \tag{5.1}$$

where $\lambda_1 = \frac{\nu B}{K+B}$ and $\lambda_2 = \frac{\gamma(I_h(t)+\vartheta I_{th}(t))}{N}$ are force of infections of typhoid fever and HAV disease respectively. With initial conditions $S(0) = S_0, I_t(0) = I_{t0}, I_h(0) = I_{h0}, I_{th}(0) = I_{th0}, R_t(0) = R_{t0}, R_h(0) = R_{h0}, R(0) = R_0$, and $B(0) = B_0$.

The control functions, $u_1(t), u_2(t), u_3(t), u_4(t)$ and $u_5(t)$ are bounded, Lebesgue integrable functions, which are defined as

$$U = \{(u_1(t), u_2(t), u_3(t), u_4(t), u_5(t)) : 0 \leq u_i(t) < 1 for i = 1, 2...5, \text{ and } 0 \leq t \leq T\}.$$

We need to obtain a control $U, S, I_t, I_h, I_{th}, R_t, R_h, R$ and B associated with state variables that can minimize the proposed objective function J and the form of objective functional is taken in line with the literature on epidemic model [17], given by:

$$J = \min_{u_1,u_2,u_3,,u_4,,u_5} \int_0^{t_f} (a_1 I_t + a_2 I_t + a_3 I_{th} + \frac{1}{2}\sum_{i=1}^{5} w_i u_i^2)dt \tag{5.2}$$

where a_1, a_2, a_3 and w_i are positive. The expression $\frac{1}{2}w_i u_i^2$ represents costs which are associated with the controls u_i and t_f is the final time. Now we want to find the controls $u_1^*, u_2^*, u_3^*, u_4^*, u_5^*$, such that

$$J(u_1^*, u_2^*, u_3^*, u_4^*, u_5^*) = \min\{J(u_1, u_2, u_3, u_4, u_5) : u_1, u_2, u_3, u_4, u_5 \in U\}$$

where $U = \{J(u_1, u_2, u_3, u_4, u_5)\}$ is a measurable set and $t \in [0, t_f]$ for the control set.

5.1 Hamiltonian and Optimality System

The necessary condition for the optimal pair is obtained using the principle in [14]. Therefore, using this principle we get a Hamiltonian which is defined as:

$$\begin{aligned} H(S, I_t, I_h, I_{th}, R_t, R_h, R, B, t) =& L(I_t, I_h, I_{th}, u_1, u_2, u_3 + u_4 + u_5) + h_1\frac{dS}{dt} + h_2\frac{dI_t}{dt} + h_3\frac{dI_h}{dt} \\ &+ h_4\frac{dI_{th}}{dt} + h_5\frac{dR_t}{dt} + h_6\frac{dR_h}{dt} + h_7\frac{dR}{dt} + h_8\frac{dB}{dt} \end{aligned}$$

where

$$L(I_t, I_h, I_{th}, u_1, u_2, u_3 + u_4 + u_5) = a_1 I_t + a_2 I_t + a_3 I_{th} + \frac{1}{2}\sum_{i=1}^{5} w_i u_i^2$$

and h_i is an adjoint variable to be determined using Pontryagin's Maximum Principle.

Theorem 5.1. For an optimal control sets u_1, u_2, u_3, u_4 and u_5 that minimizes J over U, there are adjoint variables

$h_1, h_2, ...h_8$ such that:

$$\begin{cases} \frac{dh_1}{dt} = [(1-u_2)\lambda_1 + (1-u_1)\lambda_2 + \mu]h_1 - \lambda_1(1-u_1)h_2\lambda_2(1-u_1)h_3 \\ \frac{dh_2}{dt} = -a_1 - h_2(\beta_1 + u_2 + \theta_1 + \varepsilon_1 + d_1 + \mu) - h_4\theta_1 - (\beta_1 + u_2)h_5 - \varepsilon_1 h_8 \\ \frac{dh_3}{dt} = -a_2 - h_1(1-u_1)\gamma S - h_3[(1-u_1)\gamma S - (\beta_2 + u_3 + \theta_2 + d_2 + \mu)] - h_4\theta_2 - (\beta_2 + u_3)h_6 \\ \frac{dh_4}{dt} = -a_3 - h_1(1-u_1)\gamma\varphi S - h_2(b\delta + u_4) - h_3[a(1-b)\delta + u_4] \\ ... + h_4(\delta + d_3 + \varepsilon_1 + \mu) - h_7[(1-b)(1-b)\delta + u_4] - \varepsilon_2 h_8 \\ \frac{dh_5}{dt} = -h_1\alpha + h_5(\alpha + \mu) \\ \frac{dh_6}{dt} = h_6\mu \\ \frac{dh_7}{dt} = h_7\mu \\ \frac{dh_8}{dt} = h_1(1-u_1)\frac{\nu BS}{(K+B)^2} - h_2(1-u_2)\frac{\nu BS}{(K+B)^2} - h_8(r-u_5) \end{cases} \tag{5.3}$$

with transversality conditions, $\lambda_i(t_f) = 0$ for $i = 1, 2, ...8$. Furthermore, we obtained the control set $(u_1^*, u_2^*, u_3^*, u_4^*, u_5^*)$ characterized by $\frac{\partial H}{\partial u_i^*} = 0$ for $i = 1, 2, ..., 8$. Hence, we obtained

$$u_1^*(t) = \max\{0, \min(1, \sigma_1)\}$$

$$u_2^*(t) = \max\{0, \min(0.85, \sigma_2)\}$$

$$u_3^*(t) = \max\{0, \min(1, \sigma_3)\}$$

$$u_4^*(t) = \max\{0, \min(1, \sigma_4)\}$$

$$u_5^*(t) = \max\{0, \min(1, \sigma_5)\}$$

where $\sigma_1 = \frac{(h_3-h_1)(I_t+\varphi I_{th})}{Nw_1}$, $\sigma_2 = \frac{(h_2-h_1)\nu BS}{(K+B)w_2} + \frac{(h_2-h_5)I_t}{w_2}$, $\sigma_3 = \frac{(h_3-h_6)I_h}{w_3}$, $\sigma_4 = \frac{(h_4-h_2-h_3-h_7)I_{th}}{w_4}$ and $\sigma_5 = \frac{(h_8 B}{w_5}$.

Proof . The adjoint variables and transversality conditions are standard results of Pontryagin's maximum principle'. To obtain the adjoint equations we differentiate the Hamiltonian H with respect to the state variables $S, I_t, I_h, I_{th}, R_t, R_h, R$ and B respectively and then we obtain:

$$\begin{aligned} \frac{dh_1}{dt} &= -\frac{\partial H}{\partial S} = [(1-u_2)\lambda_1 + (1-u_1)\lambda_2 + \mu]h_1 - \lambda_1(1-u_1)h_2\lambda_2(1-u_1)h_3 \\ \frac{dh_2}{dt} &= -\frac{\partial H}{\partial I_t} = -a_1 - h_2(\beta_1 + u_2 + \theta_1 + \varepsilon_1 + d_1 + \mu) - h_4\theta_1 - (\beta_1 + u_2)h_5 - \varepsilon_1 h_8 \\ \frac{dh_3}{dt} &= -\frac{\partial H}{\partial I_h} = -a_2 - h_1(1-u_1)\gamma S - h_3[(1-u_1)\gamma S - (\beta_2 + u_3 + \theta_2 + d_2 + \mu)] - h_4\theta_2 - (\beta_2 + u_3)h_6 \\ \frac{dh_4}{dt} &= -\frac{\partial H}{\partial I_{th}} = -a_3 - h_1(1-u_1)\gamma\varphi S - h_2(b\delta + u_4) - h_3[a(1-b)\delta + u_4] + \cdots \\ &\quad + h_4(\delta + d_3 + \varepsilon_1 + \mu) - h_7[(1-b)(1-b)\delta + u_4] - \varepsilon_2 h_8 \\ \frac{dh_5}{dt} &= -\frac{\partial H}{\partial R_t} = -h_1\alpha + h_5(\alpha + \mu) \\ \frac{dh_6}{dt} &= -\frac{\partial H}{\partial R_h} = h_6\mu \\ \frac{dh_7}{dt} &= -\frac{\partial H}{\partial R} = h_7\mu \\ \frac{dh_8}{dt} &= -\frac{\partial H}{\partial B} = h_1(1-u_1)\frac{\nu BS}{(K+B)^2} - h_2(1-u_2)\frac{\nu BS}{(K+B)^2} - h_8(r-u_5). \end{aligned}$$

Again using the method of (Pontryagin et.al, 1986), we obtain the controls by solving $\frac{\partial H}{\partial u_i^*} = 0$ for $i = 1, 2, ..., 8$, Then

$$
\begin{aligned}
u_1^* &= \frac{(h_3 - h_1)(I_t + \varphi I_{th})}{N w_1} \\
u_2^* &= \frac{(h_2 - h_1)\nu BS}{(K+B)w_2} + \frac{(h_2 - h_5)I_t}{w_2} \\
u_3^* &= \frac{(h_3 - h_6)I_h}{w_3} \\
u_4^* &= \frac{(h_4 - h_2 - h_3 - h_7)I_{th}}{w_4} \\
u_5^* &= \frac{h_8 B}{w_5}.
\end{aligned}
$$

Thus, writing $u_1^*, u_2^*, u_3^*, u_4^*$ and u_5^* using standard control arguments involving the bounds on the controls, we obtained:

$$
u_1^* = \begin{cases} \sigma_1, & \text{if } 0 < \sigma_1 < 1; \\ 0, & \text{if } \sigma_1 \leq 0; \\ 1, & \text{if } \sigma_1 \geq 1 \end{cases}, \quad u_2^* = \begin{cases} \sigma_2, & \text{if } 0 < \sigma_2 < 1; \\ 0, & \text{if } \sigma_2 \leq 0; \\ 1, & \text{if } \sigma_2 \geq 1 \end{cases}
$$

$$
u_3^* = \begin{cases} \sigma_3, & \text{if } 0 < \sigma_3 < 1; \\ 0, & \text{if } \sigma_3 \leq 0; \\ 1, & \text{if } \sigma_3 \geq 1 \end{cases} \quad u_4^* = \begin{cases} \sigma_4, & \text{if } 0 < \sigma_4 < 1; \\ 0, & \text{if } \sigma_4 \leq 0; \\ 1, & \text{if } \sigma_4 \geq 1 \end{cases} \quad u_5^* = \begin{cases} \sigma_5, & \text{if } 0 < \sigma_5 < 1; \\ 0, & \text{if } \sigma_5 \leq 0; \\ 1, & \text{if } \sigma_5 \geq 1 \end{cases}
$$

Hence, the following optimality system is constructed

$$
\begin{cases}
\frac{dS}{dt} = \Lambda + \alpha R_t - [(1-u_2)\lambda_1 + (1-u_1)\lambda_2 + \mu]S \\
\frac{dI_t}{dt} = (1-u_2)\lambda_1 S + (b\delta + u_4)I_{th} - (\beta_1 + u_2)I_t - (\theta_1 + \varepsilon_1 + d_1 + \mu)I_t \\
\frac{dI_h}{dt} = (1-u_1)\lambda_2 S + (a(1-b)\delta + u_4)I_{th} - (\beta_2 + u_3)I_h - (\theta_2 + d_2 + \mu)I_h \\
\frac{dI_{th}}{dt} = \theta_1 I_t + \theta_2 I_h - (\delta + u_4)I_{th} - (\varepsilon_3 + d_3 + \mu)I_{th} \\
\frac{dR_t}{dt} = (\beta_1 + u_2)I_t - (\alpha + \mu)R_t \\
\frac{dR_h}{dt} = (\beta_2 + u_3)I_h - \mu R_h \\
\frac{dR}{dt} = ((1-a)(1-b)\delta + u_4)I_{th} - \mu R \\
\frac{dB}{dt} = (r - u_5)B + \varepsilon_1 I_t + \varepsilon_2 I_{th} \\
\frac{dh_1}{dt} = [(1-u_2)\lambda_1 + (1-u_1)\lambda_2 + \mu]h_1 - \lambda_1(1-u_1)h_2\lambda_2(1-u_1)h_3 \\
\frac{dh_2}{dt} = -a_1 - h_2(\beta_1 + u_2 + \theta_1 + \varepsilon_1 + d_1 + \mu) - h_4\theta_1 - (\beta_1 + u_2)h_5 - \varepsilon_1 h_8 \\
\frac{dh_3}{dt} = -a_2 - h_1(1-u_1)\gamma S - h_3[(1-u_1)\gamma S - (\beta_2 + u_3 + \theta_2 + d_2 + \mu)] - h_4\theta_2 - (\beta_2 + u_3)h_6 \\
\frac{dh_4}{dt} = -a_3 - h_1(1-u_1)\gamma\varphi S - h_2(b\delta + u_4) - h_3[a(1-b)\delta + u_4] \\
... + h_4(\delta + d_3 + \varepsilon_1 + \mu) - h_7[(1-b)(1-b)\delta + u_4] - \varepsilon_2 h_8 \\
\frac{dh_5}{dt} = -h_1\alpha + h_5(\alpha + \mu) \\
\frac{dh_6}{dt} = h_6\mu \\
\frac{dh_7}{dt} = h_7\mu \\
\frac{dh_8}{dt} = h_1(1-u_1)\frac{\nu BS}{(K+B)^2} - h_2(1-u_2)\frac{\nu BS}{(K+B)^2} - h_8(r - u_5)
\end{cases} \tag{5.4}
$$

with the initial conditions $S(0) = S_0, I_t(0) = I_{t0}, I_h(0) = I_{h0}, I_{th}(0) = I_{th0}, R_t(0) = R_{t0}, R_h(0) = R_{h0}, R(0) = R_0$, $B(0) = B_0$ and transversality conditions $\lambda_i(t_f) = 0$, for $i = 1, 2, ...8$. □

6 Numerical Simulations

In this section, we have applied an epidemic model with various control measures. We applied a Pontryagin's Maximum Principle to determine the necessary conditions for the optimal control of hepatitis-A and typhoid fever co-infection. Numerical simulations was carried out to show the impacts of various control measures in minimizing

the co-infections of hepatitis-A and typhoid disease. We used the following parameter values with varying control measures for simulation purpose. Letting $\alpha = 0.8$, $\mu = 0.02$, $d_1 = 0.005$, $d_2 = 0.002$, $d_3 = 0.1$, $\beta_1 = 0.071$, $\beta_2 = 0.037$, $\theta_1 = 0.002$, $\theta_2 = 0.003$, $\sigma = 0.4$, $\nu = 0.6$, $r = 7$, $\varepsilon_1 = 0.7$, $\varepsilon_2 = 0.5$, $\gamma = 0.36$, $K = 100,000$, $T = 3$, $a_1 = 2$, $a_2 = 1$, $a_3 = 3$, $w_1 = 2$, $w_2 = 1$, $w_3 = 2$, $w_4 = 3$, $w_5 = 4$, and initial conditions $S(0) = 5,000$, $I_t(0) = 800$, $I_h(0) = 300$, $I_{th}(0) = 500$, $R_t(0) = 400$, $R_h(0) = 200$, $R(0) = 300, and B(0) = 15,000$.

The time dependent control solution is obtained by solving the optimality system (5.2), which consists of the state system, the adjoint system and transversality condition. Based on the parameter values given above we analyzed and interpreted the numerical solutions of the optimality system and the corresponding results for various control values. We anticipated the following four strategies for numerical simulation of the co-infection model:

1. The prevention effort of HAV and typhoid disease ($u_1 \neq 0, u_2 \neq 0, u_3 = 0, u_4 = 0, u_5 = 0$).
2. The prevention effort of HAV and treatment of typhoid disease ($u_1 \neq 0, u_2 = 0, u_3 = 0, u_4 \neq 0, u_5 = 0$).
3. The prevention effort of typhoid fever and treatment of HAV ($u_1 = 0, u_2 \neq 0, u_3 \neq 0, u_4 = 0, u_5 = 0$).
4. Using all intervention efforts($u_1 \neq 0, u_2 \neq 0, u_3 \neq 0, u_4 \neq 0, u_5 \neq 0$).

6.1 Control with prevention only

The simulation diagram in figure 2 and 3 shows the control profile of the prevention effort on HAV and typhoid disease while the other controls are set to zero. From the simulation diagram we conclude that an optimized prevention has a significant impact in eradicating the co infection from the community in specified time. Therefore, a good hygiene practice can leads to the eradication of the co-infection of HAV and typhoid fever disease from the community. This result agrees with the guideline in [15].

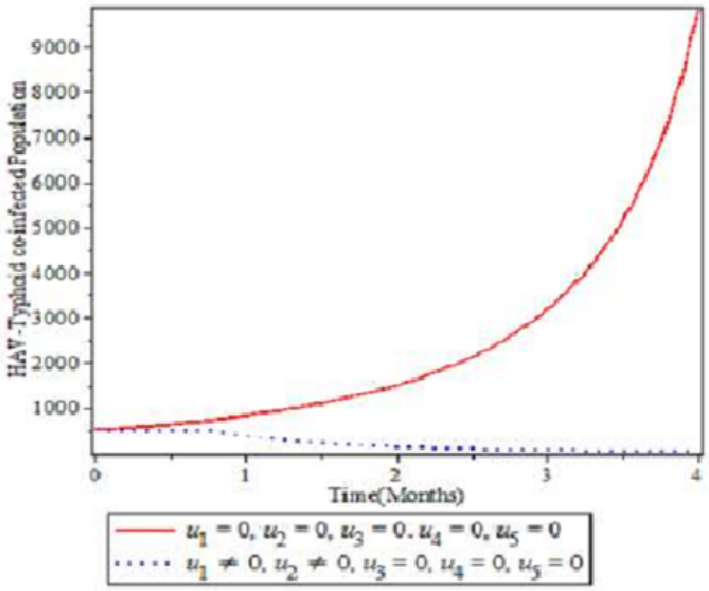

Figure 2: Simulations of the HAV-typhoid model showing the effect of prevention of the co-infections of the diseases

6.2 Control with prevention effort of HAV and treatment of typhoid disease

The simulation diagram in figure 4 and 5 shows the control profile of the prevention effort on HAV and treatment of typhoid disease. From the simulation diagram we observe that an optimized prevention of HAV and treatment of typhoid disease has an impact in minimizing the burden the co infection from the community.

6.3 Control with prevention effort of typhoid fever and treatment of HAV

We next examined the effect of the prevention effort of typhoid disease and supportive treatments used for HAV infected population. The simulation diagram in figure 6 and 7 shows applying these strategies has a significant effect in minimizing the burden of the disease as compared to the case without control.

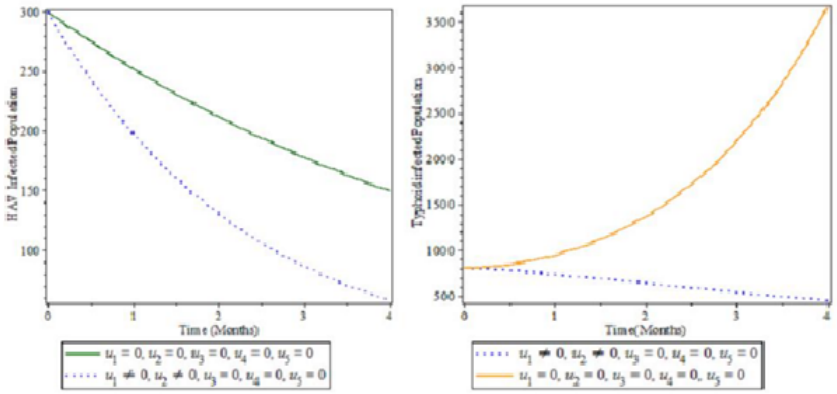

Figure 3: Simulations diagram of the prevention of HAV and prevention of typhoid fever.

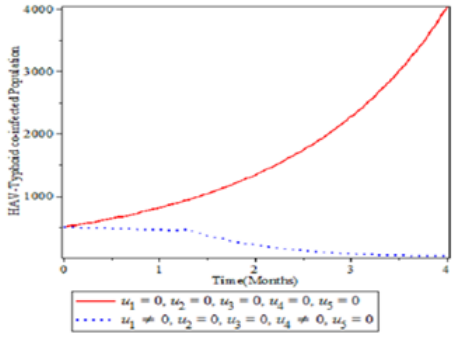

Figure 4: Simulations of the co-infection with prevention of HAV and treatment of typhoid fever

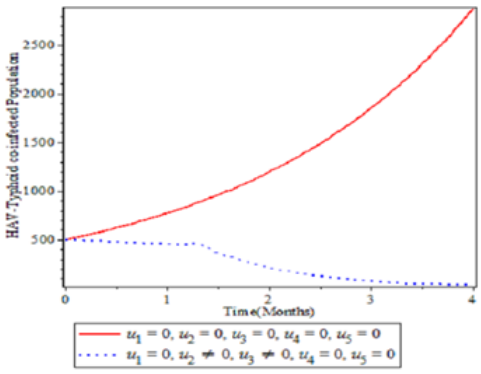

Figure 5: Simulations diagram with prevention of HAV and treatment of typhoid fever

6.4 Using all the intervention efforts

Lastly, we examined the case where all controls, including prevention of HAV and typhoid fever, treatment and mass cleaning of the environment. In this strategy all the controls $(u_1, u_2, u_3, u_4, u_5)$ are used to optimise the objective functional J.The simulation diagram in figure 8 and 9 shows applying all the intervention strategies can significantly eliminate the co infection of HAV and typhoid fever from the community in a specified time. Related to this result it is imperative to practice good hygiene, predominantly thorough hand washing before food preparation and after toilet use to prevent the disease. There are also three monovalent inactivated hepatitis A vaccines, two combined hepatitis A and hepatitis B vaccine and two combined hepatitis A and typhoid vaccines currently licensed for use [4]. Clinical trials have demonstrated that these vaccines are highly immunogenic and effective at preventing hepatitis A infection in up to 95

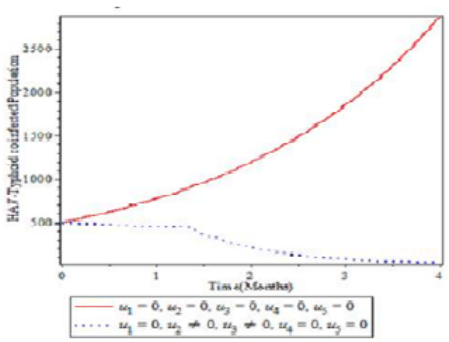

Figure 6: Simulations of the co-infection with prevention of typhoid and treatment of HAV

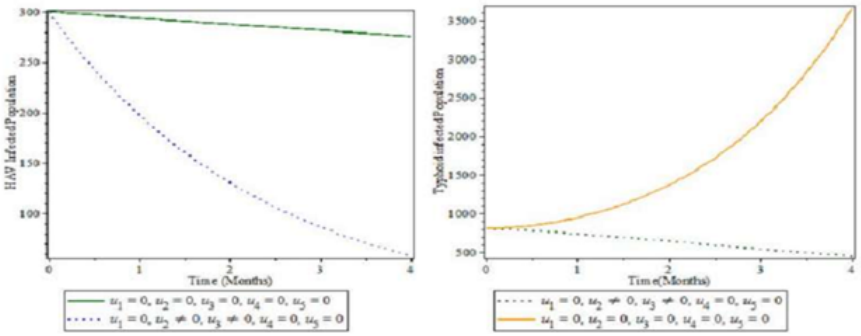

Figure 7: Simulations diagram of the prevention of typhoid fever and treatment HAV

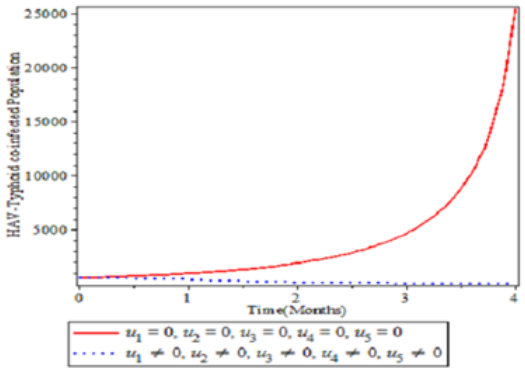

Figure 8: Simulations diagram showing the effect of all control measures on the transmission of the co-infection of HAV –typhoid diseases

7 Discussions and Conclusions

In this study, we formulated and analyzed a deterministic mathematical model for the transmission dynamics of HAV and typhoid co infection with optimal control measures. Various control measures was compared and the effectiveness of each control strategies were examined. Our choice of controls u_1, u_2, u_3, u_4 and u_5 agrees with the reports in [4]. We have shown that there exists a feasible region where the model is well posed mathematically and biologically meaningful. The basic reproduction number that represents the epidemic indicator was obtained by using the next generation matrix. It was shown that there is a unique disease free equilibrium point for each sub-model, if the pathogen fitness is less than unity. It was also proved that the model has a unique endemic equilibrium if the pathogen fitness is greater than unity. The steady state points were obtained and their local and global stability conditions were investigated. A qualitative and numerical simulation of the model was carried out and various results were obtained as it is mentioned in section 6. The sensitivity analysis of the model parameter revealed that ingestion rate (ν) and infectious rate of HAV (γ) are most sensitive in escalating the transmission of the disease. Moreover, it was proved that the co infection of the model exhibit a backward bifurcation whenever $v_2 w_1 w_8 \frac{\nu}{K} + v_2 w_1 w_3 \frac{\gamma}{\Lambda}(1 - \frac{l_2 \varphi}{l_3}) > 0$ This

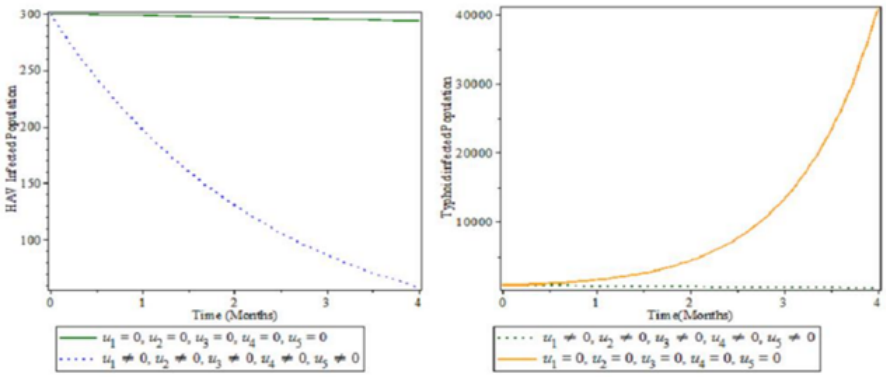

Figure 9: Simulation diagram with all control measures

implies the disease persist even if the basic reproduction number is reduced below unity.

Further, the characterization of an optimal control problem was established by using Pontryagin's maximum principle. A numerical simulation of the model was conducted and different combinations of control measures were compared. Figure 3 suggests that using a good hygiene practice can leads to the elimination of the co infection of HAV and typhoid fever from the community. Figure 5 and 7 illustrates prevention and treatment has a significant impact in controlling the transmission of the co infection as compared to the cases without control. Finally it was observed that applying all the control measures will leads to total eradication of the co infection of HAV and typhoid disease from the community.

References

[1] G.L. Armstrong and B.P. Bell *Hepatitis A virus infections in the United States: model-based estimates and implications for childhood immunization* Amer. Acad. Pediat. **109** (2002), no. 5, 839–845.

[2] M.K. Bhan, R. Bahl and S. Bhatnagar, *Typhoid and paratyphoid fever*, Lancet **366** (2005), 749—762.

[3] D. Bhat, G.S. Dhooria and H.S. Bains, *Co-infection of hepatitis A and E with Salmonella infection; A case report*, Iran. J. Pediatr. **9** (2009), no. 1, 79–81.

[4] V. Demicheli, *The effectiveness and safety of hepatitis A vaccine: A systematic review*, Vaccine **21** (2003), no. 19-20, 2242–2245.

[5] C. Castillo-Chavez and B. Song, *Dynamical model of tuberculosis and their applications*, Math. Biosci. Eng. **1** (2004), 361—404.

[6] G. Dougan and S. Baker, *Salmonella enterica serovar typhi and the pathogenesis of typhoid fever*, Annu. Rev. Microbio. **68** (2014), 317—36.

[7] H.M. El-Newihi, M.E. Alamy and T.B. Reynolds, *Salmonella hepatitis: analysis of 27 cases and comparison with acute viral hepatitis*, Hepatology **24** (1996), 516–519.

[8] W.H. Fleming and R.W. Rishel, *Deterministic and stochastic optimal control*, Springer Newyork, 1982.

[9] M. Gambatese, D. Marder, E. Begier, A. Gutkovich, R. Mos, A. Griffin, R. Zimmerman and A. Madsen, *Programmatic impact of 5 years of mortality surveillance of New York City homeless populations*, Amer. J. Public Health **103** (2013), no. S2, S193–S198.

[10] T.A. Hoffman, C.J. Ruiz, G.W. Counts, J.M. Sachs and J.L. Nitzkin, *Waterborne typhoid fever in Dade County, Florida: Clinical and therapeutic evaluations of 105 bacteremic patients*, Amer. J. Med. **59** (1975), 481–487.

[11] J.P. LaSalle, *The stability of dynamical system*, SIAM **30** (1976), 36–24.

[12] R. Morgenstern and P.C. Hayes, *The liver in typhoid fever: always affected, not just a complication*, Amer. J. Gastroenterol **86** (1991), 1235–1239.

[13] N.P. Nelson, R. Link-Gelles, M.G. Hofmeister, J.R. Romero, K.L. Moore, J.W. Ward and S.F. Schillie, Update:

Recommendations of the advisory committee on immunization practices for use of hepatitis A vaccine for post-exposure prophylaxis and for preexposure prophylaxis for international travel, MMWR Morb Mortal Wkly Rep. **67** (2018), 1216—1220.

[14] L.S. Pontryagin, *Mathematical theory of optimal processes*, Wiley Newyork, 1986.

[15] Public Health England, *Public health control and management of hepatitis A*, Guidelines, 2017.

[16] S. Ramachandran, J.J. Godfrey and M.V.F. Perera, *Typhoid hepatitis*, JAMA 230 (1974), no. 2, 236–240.

[17] G.T. Tilahun, O.D. Makinde and D. Malonza, *Modelling and optimal control of typhoid fever disease with cost-effective strategies*, Comput. Math. Meth. Med. **2017** (2017).

[18] M.S. Wameko, *Mathematical model for the transmission dynamics of hepatitus C virus with optimal control strategies*, Int. J. Math. Modell. Comput. **9** (2019), no. 3, 213–237.