International Journal of Advanced Research in Engineering and Applied Sciences
ISSN: 2278-6252
Impact Factor: 7.388

HEPATITIS B VIRUS – INFECTIOUS IN DEBRE BERHAN TOWN, ETHIOPIA ANALYZED BY MATHEMATICAL MODELING CONCEPTS

Birhanu Baye Terefe, Department of Mathematics, Debre Berhan University, Ethiopia
Temesgen Tibebu Mekonen, Department of Mathematics, Debre Berhan University, Ethiopia

Abstract: *In this work, we consider a non-linear mathematical model to study the dynamics of Hepatitis B in the case of Debre Berhan town, Ethiopia. We found the basic reproduction number of the dynamical system is* $R_0 = \frac{\lambda_1\beta_2+\beta_1(\mu+\gamma_2+\lambda_2)}{(\mu+\gamma_1+\lambda_1)(\mu+\gamma_2+\lambda_2)}$ *which depends on seven parameters. We also found that the numerical value of the basic reproduction number based on the real data collected from Debre Berhan town community is* $R_0 = 1.134979926 > 1$. *This in principle shows that Hepatitis B virus is spreads in the community. We also found that the disease free equilibrium point is unstable and the endemic equilibrium point is stable. To control the disease, we identify the control parameter. The basic control parameter that can inhibit the spread of the disease is unaware contact rate* $\beta_1 = 0.041405984$. *Therefore to be the reproduction number is less than one the parameter* β_1 *must be less than* 0.041405984. *The effect of other control parameters that can decrease the basic reproduction number are discussed in detail in their subsections.*

Keywords: Communicable disease, contagious infectious disease, chronic stage, Tribal ceremonies, Pentavalent Combination vaccine

1. INTRODUCTION

Infectious diseases are caused by pathogens that are transmitted either directly between persons or indirectly via a vector or the environment, called communicable diseases, because their transmission relies on some form of contact between individuals of a population. The fact that the transmission occurs makes the epidemiology of infectious diseases different from the epidemiology of non – communicable diseases for the important reason that the risk of contracting the disease depends on t prevalence in the population [6]

Hepatitis B is the contagious infectious disease that is characterized by the inflammation of the liver and is caused by the Hepatitis B virus (HBV), which is a Double – Standard DNA virus belonging to the family of Hepadnaviruses; include duck Hepatitis virus, woodchuck

Hepatitis virus and ground squirrel Hepatitis virus. Hepadnaviruses have a strong preference for infecting liver cells, but small amounts of hepadnaviral DNA can be found in kidney, pancreas and mononuclear cells [4, 14, 7]

Infections of HBV occur only if the virus is able to enter the blood stream and reach the liver. Once in the liver, the virus reproduces and releases large numbers of new viruses into the blood [1, 10]. It can be either acute or chronic stage, the acute form is a short – term illness that occurs within the first 6 months after a person is exposed toHBV. In the chronic stage HBV occurs more than 6 months after a person exposed to HBV, although this does not happen and particularly in the case of HBV, the likelihood of chronicity depends on a person's age at the time of infection. Most people infected with HBV are not aware that they have been infected until they have symptoms of cirrhosis or a type of liver cancer, like Hepatocellur Carcinoma (HCC), many years later, about 65% of the infected population is unaware that they are infected with HBV [7]

Ethiopia is one of the developing countries in the world, in developing countries, the main routes of transmission are: prenatal with HBV carrier mother infecting her infant usually during birth or soon after birth following close contract, transfer of HBV via cuts, sexual transmission, transfusion of infected blood or bloods products, needle stick injury, re – use of HBV contaminated needles, syringes, lancets and instruments including those used in tribal ceremonies, possible blood sucking insects and bed bugs [11]. Even HBV is present in the blood, saliva, semen vaginal secretions, menstrual blood, and to a lesser extent, perspiration, breast milk, tears, and urine of infected individuals. A highly resilient virus, HBV is resistant to breakdown, can survive outside the body, and is easily transmitted through contact with infected body fluids [2] HBV vaccine is now one of the most widely used vaccines in the world and is part of the routine vaccination schedule for many of the world's infants and children. It is the world's first cancer prevention vaccine and the first vaccine to prevent the transmitted disease [8]. Among those developing countries, Ethiopia has successfully introduced HBV vaccine in the form of pentavalent combination vaccine into the routine schedule in 2007. HBV infections among apparently healthy mothers in Ethiopia are studied in [12]. Seroprevalence and predictors of HBV infection among pregnant women attending routine antenatal care in South Ethiopia is studied in [3], a cross – sectional study among blood donors in Ethiopia are studied in [13]. In this article we proposed an improvement of the model [9] that a non linear mathematical model studied using SITR model in which birth rates

and death rates of population are equal and total population is constant, which divided into four compartments. But in our article we extended the model.

1.1. Study Area in Ethiopia

Data collected in Ethiopia central city Debre Berhan is located in the North Shewa Zone, Amhara Region. The town has latitude of $9°41'N$ and longitude of $39°32' E$, with an elevation of 2, 840 meters and its estimated population size of 103, 450 out of those 56, 672 (54.9%) are female and 46, 778 (45.22%) are male.

1.2. Statements of Research Problem

This research is based on deterministic mathematical model with numerical simulation investigation that has raised the following research questions:

a. What are the control parameters in the spread and control of HBV?
b. What is the reproduction number of HBV?
c. What is the role of screening for unaware infectious?

1.3. Methodology

We use deterministic model of epidemiology described by using ordinary differential equations (ODE). We classified ODE's equilibrium point as disease free equilibrium point and endemic equilibrium point and analyzing their stability by using Routh Hurwitz Criteria. We also use different data collection methods to get the relevant data finally the gathered data will be analyzed and interpreted.

1.4. Basic Concepts – Definitions Needed for our Research:

1.4.1. Differential Equation

It is an equation for unknown function that contains not only the function but also its derivatives. Here we take differential equations for a function of a single real variable (ODE) and it has the general form

$F\left(t, x(x), x'(t), \dots, x^{(n)}(t)\right) = 0$ *where* F, x' *and* $x^{(n)}$, they are given function, first derivative and nth derivative respectively.

1.4.2. System of ODE

A system of simultaneous first order ODE is an equation that contains two or more ODE which has the general form

$$\frac{dx_i}{dt} = f_i(t, x_1, \dots, x_n),\ i = 1, 2, \dots, n$$

1.4.3. System of autonomous ODE

A system of ODE is not depended on time $(i.e.)$ $\frac{dx_i}{dt} = f_i(x_1, \dots, x_n),\ i = 1, 2, \dots, n$

1.4.4. Equilibrium point or steady state

Suppose that $x_0 \in \mathbb{R}^n$, it is the equilibrium point of the first order ODE $\frac{dx_i}{dt} = f(X)$ $where$ $X = (x_1, \dots, x_n)^T$, it is obtained by making $\frac{dx_i(t)}{dt} = 0, i = 1, 2, \dots, n$ and $f(x_0) = (0, \dots, 0)$

1.4.5. Stability of equilibrium points

In the function or mapping $f: \mathbb{R}^n \longrightarrow \mathbb{R}^n, x \in \mathbb{R}^n$, defined by $f(x) = 0$, and then$x$, it is called an equilibrium point for the $\frac{dx_i}{dt} = f_i(x_i(t)),\ i = 1, \dots, n,$ and the linear part of f at x denoted by $Df(x)$ $where$ D, it is the partial derivative of x , and then for any $y \in \mathbb{R}^n$, write

$f(y) = (f_1(y), \dots, f_n(y))^T$ $where$ f_i, called the components of f, and define

$Df(x) = \begin{bmatrix} \frac{\partial f_1(x)}{\partial y_1} & \dots & \frac{\partial f_1(x)}{\partial y_n} \\ \vdots & \ddots & \vdots \\ \frac{\partial f_n(x)}{\partial y_1} & \dots & \frac{\partial f_n(x)}{\partial y_n} \end{bmatrix} = J$, where$J$, it is called Jacobean matrix and the stability of nonlinear system obtained by solving characteristic polynomial equation $|Df(x) - \lambda I| = 0$

Where λ, a constant and I, an $n \times n$ identity matrix, the solution of polynomial equations they are $\lambda_1, \dots, \lambda_n$, called eigenvalues of Jacobean matrix and if all $\lambda_1, \dots, \lambda_n$, they are distinct with$|J| \neq 0$, then

a. The equilibrium point is asymptotically stable if all eigenvalues have negative real part
b. The equilibrium point is unstable if all eigenvalues have positive real part

2. BASIC REPRODUCTION NUMBER (BRN)

It is denoted by R_0, it is one of the important concepts in the field of infectious diseases epidemiology and defined as the average number of secondary infectious caused by one infectious individual placed in a population consisting entirely of susceptible [5], it is also called basic reproductive rate, basic reproductive ratio of an infection is the expected number of cases generated over the course of its infectious period by an factious.

2.1.Method for Calculating the BRN

We shall compute BRN of the present model using the next generation method. It is a threshold quantity used to study the spread of infection disease in epidemiological modeling and it is the spectral radius (i.e. the dominant eigenvalues) of the next generation matrix.

Assume that there are$n$ compartments of which$m$compartments are infected. So define the vector

$\boldsymbol{x} = (x_i),\ i = 1, \dots, n\ \ and\ \ x_i$ Denotes the number or proportion of individual in the ith compartment

Let $f_i(x)$, it is the rate of transfer of individual into the compartment$i$at time $t\ and\ v_i^-$ it is the rate of transfer of individual out of the compartment$i$at time$t$by any means. Note that $f_i(x)$, it should include only infections that are newly arising, but does not include terms which describe the transfer of infectious individuals form one infected compartment to another

Assumed that each function $f_i(x), i = 1, \dots, n$ is continuously differentiable at least twice in each variable, the model of infectious disease dynamics can be formulated as follows:

$\frac{dx_i}{dt} = f_i(x) - v_i(x), i = 1, \dots n; v_i = v_i^- - v_i^+$

Ifx_0, it is the free equilibrium and $f_i(x)$ satisfy those technical assumption, then derivatives $Df_i(x_0)\ and\ Dv_i(x_0)$, they can be partitioned as $\begin{bmatrix} F & 0 \\ 0 & 0 \end{bmatrix} and \begin{bmatrix} v & 0 \\ 0 & J_p \end{bmatrix}, wherFandv$ they are$m \times m$ matrices defined by $F = \left(\frac{\partial f_i(x)}{\partial x_i}(x_0)\right) andv = \left(\frac{\partial f_i(x)}{\partial v_j}(x_0)\right), 1 \le i, j \le m,$ moreover F, it is non - negative and V, it is invertible with eigenvalues whose real parts are positive and all eigenvalues of J_p have positive real parts and p, it is the number of compartments .

Suppose that the infected individual introduced into compartment$k$ of disease – free population. Then the (j, k) entry of $(v_i)^{-1}$, it is the mean length of time and this individual spends in compartment$j$ during its life time, assume that the population remains near the disease free equilibrium and barring re – infection. Then the (i, j) entry of$F$, it is rate at which infected individuals in compartment$j$produce new infections in compartment$i$produced by the infected individuals originally introduced into compartment$k$. The matrix Fv^{-1}, it is usually referred the next generation matrix for the model. Now we have $R_0 = \rho Fv^{-1}\ where\ \rho$, denotes the spectral radius of matrix Fv^{-1} (eigenvalues with the maximum absolute value).We also used Concepts of van den Driesch and Warmouth (2002) stated that "R_0" it is a threshold parameter for local stability of the disease free equilibrium, the disease transmission model given by $f_i(x)$, and x_0, it is the disease free equilibrium of the model, thenx_0, it is the locally asymptotically stable when $R_0 < 1$, and unstable when $R_0 > 1$"

2.2.Compartment Model in Epidemiology

In this article we will use the basic epidemiology model of the deterministic models known as compartmental models, which attempt to describe and explain what happens on the average at

the population scale. It categorizes individuals into different compartments or subgroups and used to describe transport of material in a biological system, exchange materials with each compartment contains well mixed material.

2.3.We extended the previous research [9] as shown below initial model flow chart:

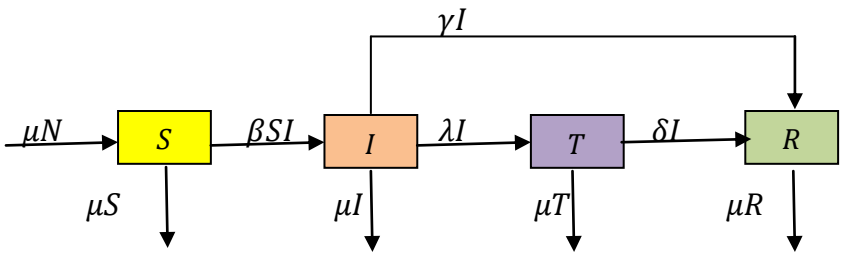

Figure 1: Initial Modeling – Source [9]

2.4. Using State variables and parameters appearing in the dynamical system (Initial and Extended Model) shown below: in Table – 1 and Table – 2:

Table – 1 – Stable Variables

State Variables	Description
S	Susceptible population
I	Hepatitis B infected population
I_1	Unaware infected populations
I_2	Aware Infected population
T	Treated population
R	Removed population
N	Total number of population

Table – 2 – Parameters

Parameters	Description
β	Infectious rate of HBV
λ	The recruitment rate of treated class from infected class
γ	The recruitment rate of recovered class from infected individual
δ	The recruitment rate of recovered class from treated individual (The rate of treated individuals are recruited into the removed class)
β_1	The recruitment rate into the unaware infected class by due to the interaction of unaware infected and susceptible class
β_2	The recruitment rate into the unaware infected class by due to the interaction of aware infected and susceptible class
μ	Natural birth and death rate
λ_1	The rates of recruitment into the aware infected class from the unaware of infected class due to screening process (screening rate)
λ_2	The rates of recruitment into the treated class from the aware infected class
γ_1	The rate of unaware infected individuals are recruited in the removed class
γ_2	The rate of aware infected individuals are recruited in the removed class
R_0	Basic Reproduction Number (BRN)

2.5. Assumption in our Extended Model

- The Population is Constant, heterogeneously mixing, and is divided into five compartments
- The death occurred due to natural mortality in each class
- The new born children are susceptible
- Birth rate = Death rate
- Unaware HBV infected is an infectious, but they don't know whether they are infectious or not?
- The individuals once unaware infected become aware infected and the remaining unaware infected is removed
- Treated individuals are an infected and who are medically treating
- There is no immigration and migration in the population

2.6. Our Extended Modified Model from Initial Model

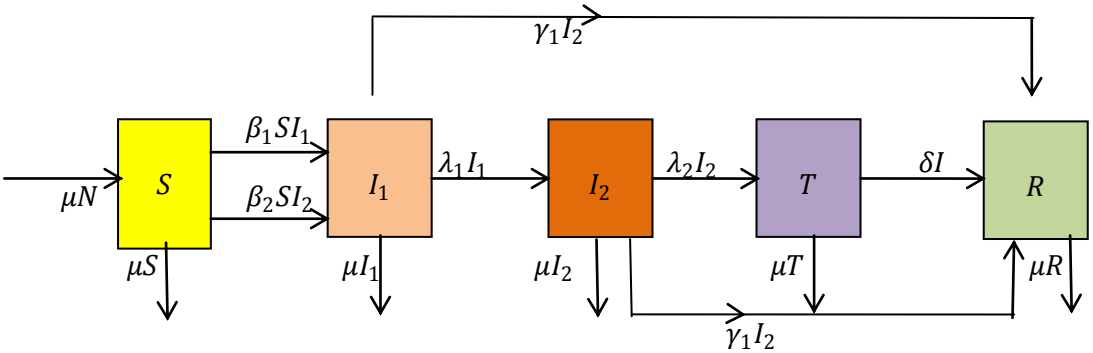

Figure 2: Extended modified modeling – Source (own)

Here we divided Compartment in two parts and parameters like as$\beta, I, \gamma and \lambda$) are also divided in two parts

By the extended modified modeling, the dynamical system of Hepatitis B is governed by the system of nonlinear equations subject to nonnegative initial conditions are:

$$\frac{dS}{dt} = \mu N - \left(\frac{\beta_1 SI_1}{N} + \frac{\beta_2 SI_2}{N} + \mu S\right) \quad (1)$$

$$\frac{dS}{dI_1} = \left(\frac{\beta_1 SI_1}{N} + \frac{\beta_2 SI_2}{N}\right) - (\mu I_1 + \gamma_1 I_1 + \lambda_1 I_1) \quad (2)$$

$$\frac{dS}{dI_2} = \lambda_1 I_1 - (\lambda_2 I_2 + \mu I_2 + \gamma_2 I_2) \quad (3)$$

$$\frac{dS}{dt} = \lambda_2 I_2 - (\delta I + \mu T) \quad (4)$$

$$\frac{dS}{dt} = (\gamma_1 I_1 + \gamma_2 I_2 + \delta T) - \mu R \quad (5)$$

With initial conditions $S(0) = S_0 > 0;\ I_1(0) = I_{01} > 0; I_2(0) = I_{02} > 0;\ T(0) = T_0 > 0\ ; and$

$R(0) = R_0 > 0\ \ and\ \ all\ \ parameters\ \ \beta_1, \beta_2, \gamma_1, \gamma_2, \lambda_1, \lambda_2, \mu\ \ and\ \ \delta > 0$

2.7. Observingthe class of the population from the flow chart and corresponding dynamical system

- The new born population into the susceptible is represented by μN
- The removed population from the susceptible, unaware infected, aware infected, treated and then removed class due to natural mortality rate represented by $(-\mu S, -\mu I_1, -\mu I_2, -\mu T, -\mu R)\ \ respectively$
- The population moved away from the susceptible class and entered into the unaware infected class due to the transmission rate are represented by $\beta_1 S I_1 + \beta_2 S I_2$
- The population moved from the unaware infected class and entered into the aware infected class due to the screening rateλ_1, represented by $\lambda_1 I_1$
- The population moved from the unaware infected class and entered into the recovered class without any medical treatment represented by $\lambda_2 I_2$
- The population moved from the aware infected class and entered into the treated class without any medical treatment represented by $\gamma_1 I_1$
- The population moved from the aware infected class and entered into the recovered class without any medical treatment represented by $\gamma_2 I_1$
- The population moved from the treated class and entered into the recovered class after they take medical treatment represented by δT

2.8. Variable Proportion

In our model the total population$N$splitted into five compartments such as susceptible, unaware infectedaware infected, treated and removed classes with their density denoted by $S(t), I_1(t), I_2(t), T(t)\ \ and\ \ R(t)$, respectively, and then we have

$N(t) = S(t) + I_1(t) + I_2(t) + T(t) + R(t)$

The rate of those compartments are represented by the dynamical system eqn. 1 to 5 with initial conditions as mention above in (2.6), we represented for calculation purposes as:

$$s(t) + i_1(t) + i_2(t) + z(t) + r(t) = \frac{S(t) + I_1(t) + I_2(t) + T(t) + R(t)}{N(t)} = \frac{N(t)}{N(t)} \qquad (6)$$

$\Longrightarrow s(t) + i_1(t) + i_2(t) + z(t) + r(t) = 1$, and then we have

$s(t) = \frac{S(t)}{N(t)} \Longrightarrow \frac{dS}{dt} = \frac{1}{N^2}\left[N\frac{dS}{dt} - S\frac{dN}{dt}\right] = \frac{1}{N}\frac{dS}{dt}$ (Since N it is a constant)

Similarly we get $i_1(t) = \frac{1}{N}\frac{dI_1}{dt}; i_2(t) = \frac{1}{N}\frac{dI_2}{dt}; \frac{1}{N}\frac{dT}{dt}$ and $\frac{1}{N}\frac{dR}{dt}$,

These values substituted in eqn. (1 to 5), we have

$$\frac{ds}{dt} = \mu - (\beta_1 s i_1 + \beta_2 s i_2 + \mu s) \quad (7)$$

$$\frac{di_1}{dt} = (\beta_1 s i_1 + \beta_2 s i_2) - (\mu i_1 + \gamma_1 i_1 + \lambda_1 i_1) \quad (8)$$

$$\frac{di_2}{dt} = \lambda_1 i_1 - (\lambda_2 i_2 + \mu i_2 + \gamma_2 i_2) \quad (9)$$

$$\frac{dz}{dt} = \lambda_2 i_2 - (\delta I + \mu z) \quad (10)$$

$$\frac{dr}{dt} = (\gamma_1 i_1 + \gamma_2 i_2 + \delta z) - \mu r \quad (11)$$

Since $s(t) + i_1(t) + i_2(t) + z(t) + r(t) = 1 \Longrightarrow r(t) = 1 - s(t) - i_1(t) - i_2(t) - z(t)$, and then ignore eqn. (11) and the reduced dynamical model have only equations (7 to 10)

2.9. Positivity of the Solution

A dynamical system of a model is important to show all solutions the state variables with nonnegative conditions are nonnegative. To prove that we can find the solutions of eqn. (7 to 10)

For example

From equation (7) we have $\frac{ds}{dt} = \mu - (\beta_1 s i_1 + \beta_2 s i_2 + \mu s)$, we can rewrite as

$\frac{ds}{dt} + (\beta_1 s i_1 + \beta_2 s i_2 + \mu s) = \mu$, it is the first order ODE and whose integrating factor is $e^{\int_0^t (\beta_1 i_1 + \beta_2 i_2 + \mu) d\tau}$, and its solution is given by

$$s(t) = e^{-\int_0^t (\beta_1 i_1 + \beta_2 i_2 + \mu) d\tau} \int_o^t \mu e^{\int_0^t (\beta_1 i_1 + \beta_2 i_2 + \mu) d\tau} d\tau$$

Clearly in this solution all parameters are positive and the range of exponential function is also positive$\Longrightarrow s(t) = e^{-\int_0^t (\beta_1 i_1 + \beta_2 i_2 + \mu) d\tau} \int_o^t \mu e^{\int_0^t (\beta_1 i_1 + \beta_2 i_2 + \mu) d\tau} d\tau$>0

Similarly from eqn. (8), we have $i_1(t) = e^{-\int_0^t (\mu + \gamma_1 + \lambda_1) d\tau} \int_o^t \beta_2 s e^{\int_0^t (\mu + \gamma_1 + \lambda_1) d\tau} d\tau > 0$

From eqn. (9), we have $i_2(t) = e^{-\int_0^t (\mu + \gamma_2 + \lambda_2) d\tau} \int_o^t \lambda_1 i_1 e^{\int_0^t (\mu + \gamma_2 + \lambda_2) d\tau} d\tau > 0$

From eqn. (10), we have $z(t) = e^{-\int_0^t (\delta + \mu) d\tau} \int_o^t \lambda_2 i_2 e^{\int_0^t (\delta + \mu) d\tau} d\tau > 0$

Even though we ignore eqn. (11), it also has solution as

$$r(t) = e^{-\int_0^t (\mu) d\tau} \int_o^t (\gamma_1 i_1 + \gamma_2 i_2 + \delta z) e^{\int_0^t (\mu) d\tau} d\tau > 0$$

We conclude now all state variables, they are existing in our dynamical systems, are positive.

2.10. Boundedness of the Solution

Since $N(t) = S(t) + I_1(t) + I_2(t) + T(t) + R(t)$, differentiate both sides with respect to t, we get

$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dI_1}{dt} + \frac{dI_2}{dt} + \frac{dT}{dt} + \frac{dR}{dt}$, by taking their value, we have

$$\frac{dN}{dt} = \begin{Bmatrix} \mu N - (\beta_1 S I_1 + \beta_2 S I i_2 + \mu S) + (\beta_1 S I_1 + \beta_2 S I_2) + \lambda_1 I_1 - (\lambda_2 I_2 + \mu I_2 + \gamma_2 I_2) \\ + \lambda_2 I_2 - (\delta I + \mu T) + (\gamma_1 I_1 + \gamma_2 I_2 + \delta T) - \mu R \end{Bmatrix}$$

$$\Longrightarrow \frac{dN}{dt} = \mu N - \mu(S + I_1 + I_2 + T + R) = \mu N - \mu N = 0$$

Since $\frac{dN}{dt}$, it is the first order separable ODE so we get after integrating both sides

$N(t) = c, where\ c$, it is an integrating constant that is $N(0) = N_0 = c$, so that we get bounded condition as $0 < N(t) \leq N_0$

$\Longrightarrow$The solution is bounded in

$$\mathbb{R} = \{(S, I_1, I_2, T, R) | N(t) = S(t) + I_1(t) + I_2(t) + T(t) + R(t),\ 0 < N(t) \leq N_0\}$$

2.11. Equilibrium Point of the Model

To determine the equilibrium point of eqn. (7 to 10) simply solve $\frac{ds}{dt} = \frac{di_1}{dt} = \frac{di_2}{dt} = \frac{dz}{dt} = 0$

By solving above four first orders ODE, by substituting $i_1 = 0$, in eqn. (9) we get $i_2 = 0$, by simple calculation, similarly, from (7) we get $s = 1$, from eqn. (10) we get $z = 0$, and therefore the disease free equilibrium point is $(s, i_1, i_2, z) = (1, \quad 0, \quad 0, \quad 0)$

2.12. Endemic Equilibrium Point

In this case assume that$i_1 \neq 0$, and using eqns. (7 to 10) by simple calculations we get the endemic point is

$(s, i_1, i_2, z) =$

$$\begin{pmatrix} \frac{(\mu+\gamma_1+\lambda_1)(\mu+\gamma_2+\lambda_2)}{(\lambda_1\beta_2+\beta_1(\mu+\gamma_2+\lambda_2))}, & \frac{\mu(\mu+\gamma_2+\lambda_2)}{(\lambda_1\beta_2+\beta_1(\mu+\gamma_2+\lambda_2))}\left(\frac{\lambda_1\beta_2+\beta_1(\mu+\gamma_2+\lambda_2)}{(\mu+\gamma_1+\lambda_1)(\mu+\gamma_2+\lambda_2)} - 1\right), \\ \frac{\mu\lambda_1}{\lambda_1\beta_2+\beta_1(\mu+\gamma_2+\lambda_2)}\left(\frac{\lambda_1\beta_2+\beta_1(\mu+\gamma_2+\lambda_2)}{(\mu+\gamma_1+\lambda_1)(\mu+\gamma_2+\lambda_2)} - 1\right), & \frac{\mu\lambda_1\lambda_2}{(\delta+\mu)(\lambda_1\beta_2+\beta_1(\mu+\gamma_2+\lambda_2))}\left(\frac{\lambda_1\beta_2+\beta_1(\mu+\gamma_2+\lambda_2)}{(\mu+\gamma_1+\lambda_1)(\mu+\gamma_2+\lambda_2)} - 1\right) \end{pmatrix}$$

2.13. Basic Reproduction Number

Since $\frac{dx_i}{dt} = f_i(x) - v_i(x),\ where\ v_i(x) = v_i^-(x) - v_i^+(x)$, and also we have

$f(x) = [f_1(x), \quad \cdots, \quad f_n(x)]^T\ and\ v(x) = [v_1(x), \quad \cdots, \quad v_n(x)]^T$

Letx_0, it is the disease free equilibrium point and the value of the Jacobean matrices $f(x), v(x)$, by the part 2.1 (Method of calculating BRN) we have four compartments that is why we have $J_p = J_4$

Then, in our model we have $N = S + I_1 + I_2 + T + R$, and also the system have three infected state variables$I_1, I_2, and\ T$, using all these concepts we have

$$f_i = \begin{bmatrix}(\beta_1 I_1 + \beta_2 I_2)s \\ 0\end{bmatrix} \Longrightarrow f = \begin{bmatrix}\beta_1 & \beta_2 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0\end{bmatrix};\ and$$

$$v_i^+(x) = \begin{bmatrix}0 \\ \lambda_1 I_1 \\ \lambda_2 I_2\end{bmatrix}, v_i^-(x) = \begin{bmatrix}(\mu+\gamma_1+\lambda_1)I_1 \\ (\mu+\gamma_2+\lambda_2)I_2 \\ (\delta+\mu)T\end{bmatrix} \Longrightarrow v_i = \begin{bmatrix}(\mu+\gamma_1+\lambda_1)I_1 \\ (\mu+\gamma_2+\lambda_2)I_2 - \lambda_1 I_1 \\ (\delta+\mu)T - \lambda_2 I_2\end{bmatrix}$$

$$\Longrightarrow v = \begin{bmatrix}\frac{\partial v_1}{\partial I_1} & \frac{\partial v_1}{\partial I_2} & \frac{\partial v_1}{\partial T} \\ \frac{\partial v_2}{\partial I_1} & \frac{\partial v_2}{\partial I_2} & \frac{\partial v_2}{\partial T} \\ \frac{\partial v_3}{\partial I_2} & \frac{\partial v_3}{\partial I_2} & \frac{\partial v_3}{\partial T}\end{bmatrix} = \begin{bmatrix}(\mu+\gamma_1+\lambda_1) & 0 & 0 \\ -\lambda_1 & (\mu+\gamma_2+\lambda_2) & 0 \\ 0 & -\lambda_2 & (\delta+\mu)\end{bmatrix}$$

$$\Longrightarrow v^{-1} = \begin{bmatrix}\frac{1}{(\mu+\gamma_1+\lambda_1)} & 0 & 0 \\ \frac{\lambda_1}{(\mu+\gamma_1+\lambda_1)(\mu+\gamma_2+\lambda_2)} & \frac{1}{(\mu+\gamma_2+\lambda_2)} & 0 \\ \frac{\lambda_1\lambda_2}{(\mu+\gamma_1+\lambda_1)(\mu+\gamma_2+\lambda_2)(\delta+\mu)} & \frac{\lambda_2}{(\mu+\gamma_2+\lambda_2)(\delta+\mu)} & \frac{1}{(\delta+\mu)}\end{bmatrix}$$

$$\Longrightarrow fv^{-1} = \begin{bmatrix}\beta_1 & \beta_2 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0\end{bmatrix}\begin{bmatrix}\frac{1}{(\mu+\gamma_1+\lambda_1)} & 0 & 0 \\ \frac{\lambda_1}{(\mu+\gamma_1+\lambda_1)(\mu+\gamma_2+\lambda_2)} & \frac{1}{(\mu+\gamma_2+\lambda_2)} & 0 \\ \frac{\lambda_1\lambda_2}{(\mu+\gamma_1+\lambda_1)(\mu+\gamma_2+\lambda_2)(\delta+\mu)} & \frac{\lambda_2}{(\mu+\gamma_2+\lambda_2)(\delta+\mu)} & \frac{1}{(\delta+\mu)}\end{bmatrix}$$

$$\Longrightarrow fv^{-1} = \begin{bmatrix}\frac{\beta_1}{(\mu+\gamma_1+\lambda_1)} + \frac{\lambda_1\beta_2}{(\mu+\gamma_1+\lambda_1)(\mu+\gamma_2+\lambda_2)} & \frac{\beta_2}{(\mu+\gamma_2+\lambda_2)} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0\end{bmatrix}$$

Then the eigenvalues of the matrix (fv^{-1}), it is the reproduction number $R_0 = \frac{\lambda_1\beta_2+\beta_1(\mu+\gamma_2+\lambda_2)}{(\mu+\gamma_1+\lambda_1)(\mu+\gamma_2+\lambda_2)}$

2.14. The endemic equilibrium point in terms of BRN

The endemic equilibrium point in terms of R_0 as

$(s, i_1, i_2, z) =$

$$\left(\frac{1}{R_0},\ \frac{\mu(\mu+\gamma_2+\lambda_2)}{(\lambda_1\beta_2+\beta_1(\mu+\gamma_2+\lambda_2))}(R_0-1)\ \ \frac{\lambda_1\mu}{(\lambda_1\beta_2+\beta_1(\mu+\gamma_2+\lambda_2))}(R_0-1),\ \ \frac{\lambda_1\lambda_2\mu}{(\delta+\mu)(\lambda_1\beta_2+\beta_1(\mu+\gamma_2+\lambda_2))}(R_0-1)\right)$$

2.15. Stability Analysis Approach

Here, to determine the stability of the equilibrium point, use the linearization approach for eqns.

(7 to 10) as following manner:

$$f(s, i_1, i_2, z) = \mu - (\beta_1 s i_1 + \beta_2 s i_2 + \mu s) \quad (12)$$

$$g(s, i_1, i_2, z) = (\beta_1 s i_1 + \beta_2 s i_2) - (\mu i_1 + \gamma_1 i_1 + \lambda_1 i_1) \quad (13)$$

$$h(s,i_1,i_2,z)=\lambda_1 i_1-(\lambda_2 i_2+\mu i_2+\gamma_2 i_2) \quad (14)$$

$$l(s,i_1,i_2,z)=\lambda_2 i_2-(\delta I+\mu z) \quad (15)$$

Then the Jacobean matrix $J(s,i_1,i_2,z)=\begin{bmatrix}\frac{\partial f}{\partial s} & \frac{\partial f}{\partial i_1} & \frac{\partial f}{\partial i_2} & \frac{\partial f}{\partial z}\\ \frac{\partial g}{\partial s} & \frac{\partial g}{\partial i_1} & \frac{\partial g}{\partial i_2} & \frac{\partial g}{\partial z}\\ \frac{\partial h}{\partial s} & \frac{\partial h}{\partial i_1} & \frac{\partial h}{\partial i_2} & \frac{\partial h}{\partial z}\\ \frac{\partial l}{\partial s} & \frac{\partial l}{\partial i_1} & \frac{\partial l}{\partial i_2} & \frac{\partial l}{\partial z}\end{bmatrix}$

$$\Longrightarrow J(s,i_1,i_2,z)=\begin{bmatrix}-(\beta_1 i_1+\beta_2 i_2+\mu) & -\beta_1 s & -\beta_2 s & 0\\ (\beta_1 i_1+\beta_2 i_2) & \beta_1 s-(\mu+\gamma_1+\lambda_1) & \beta_2 s & 0\\ 0 & \lambda_1 & -(\mu+\gamma_1+\lambda_1) & 0\\ 0 & 0 & 0 & (\delta+\mu)\end{bmatrix}$$

2.16. Stability Analysis of Disease Free Equilibrium Point

The Jacobean matrix at the free equilibrium point $(s,i_1,i_2,z)=(1,\ 0,\ 0,\ 0)$ is

$$J(1,\ 0,\ 0,\ 0,)=\begin{bmatrix}-\mu & -\beta_1 & -\beta_2 & 0\\ 0 & \beta_1-(\mu+\gamma_1+\lambda_1) & \beta_2 & 0\\ 0 & \lambda_1 & -(\mu+\gamma_2+\lambda_2) & 0\\ 0 & 0 & 0 & (\delta+\mu)\end{bmatrix}$$

Now we can find the eigenvalues of $J(1,\ 0,\ 0,\ 0)$, and assume that τ, it is one of the eigenvalues, from characteristic polynomial equation we get $\tau=-\mu$, and the remaining eigenvalues also obtained from characteristic equation like as quadratic equation in terms of τ as:

$a_2\tau^2+a_1\tau+a_0=0, where$

$a_2=1$

$a_1=\left[\left(-\beta_1-(\mu+\gamma_1+\lambda_1)\right)-(\mu+\gamma_2+\lambda_2)\right]$

$a_0=\left[\left(-\beta_1-(\mu+\gamma_1+\lambda_1)\right)(\mu+\gamma_2+\lambda_2)+\beta_2\lambda_1\right]$

By using Routh Hurwitz criteria to determine the sign of the (eigenvalues) roots that is

$$\begin{array}{cc|cc}\tau^2 & 1 & a_0 & 0\\ \tau^1 & a_1 & 0 & \\ \tau^0 & b_1 & & \end{array}$$

Where $b_1=-\frac{1}{a_1}\begin{vmatrix}a_2 & a_0\\ a_1 & 0\end{vmatrix}=-\frac{1}{a_1}(-a_0a_1)=a_0$

We have two cases they are

Case – 1:

If $a_1>0\ and\ a_0>0$, then the first column of the Routh Hurwitz array have no sign change then the roots of the characteristic polynomial equation is negative

$\Longrightarrow J(s, i_1, i_2, z) = J(1, \quad 0, \quad 0, \quad 0)$, the disease free equilibrium point is stable

Case – 2:

If $a_1 < 0$ and $a_0 < 0$, then the first column of the Routh Hurwitz array have sign change then the roots of the characteristic polynomial equation is positive

$\Longrightarrow J(s, i_1, i_2, z) = J(1, \quad 0, \quad 0, \quad 0)$, the disease free equilibrium point is unstable

3. REAL PARAMETRIC ESTIMATIONS AND NUMERICAL SIMULATIONS

3.1. Introduction

In this article we analyzed a non – linear (SI_1I_2TR) mathematical model of HBV with sexual, horizontal and blood donation transmission using the secondary data from the City Debre berhan in Ethiopia.

3.2. Method of Collection of Data

We use Secondary data, which are obtained from the individuals indirectly. According to the nature of our research we select secondary data because it has an important role in terms of increasing the level of research validity, accuracy and reliability.

3.3. Collection of Secondary Data

The required data collected from Debre Berhan city about the population as given in table 3:

Table – 3: Population in Debre Berhan

Description	Notation	Values
Total Number of Women	W	56, 672
Total Number of Male	M	46, 7798
Total Population	N	103, 450

Table – 4: The required Secondary Data collected from Debre Berhan city in Ethiopia about the population and newly given from 10th January 2018 to 10th April 2018

Description	**Notation**	**Values**
Susceptible	S	10,2800
Unaware Hepatitis B infected	I_1	330
Aware Hepatitis B infected	I_2	200
Treated population	T	90
Recovered population	R	30
The number of population who are recovered from unaware infected by unknown cause		6
The number of population who are recovered from aware infected by unknown cause		20
The number of population moves from unaware to aware infected		7
The number of population moves from aware infected to treated class		90
The number of individual who are recovered after taking treatment		19

Table – 5: Descriptions, Symbol and Values of the Variables and Parameters of Formula of Model using in BRN(R_0)

Description	Symbol	Formula	Values
Fraction of susceptible individual	s_0	$\frac{Number\ of\ initial\ susceptable\ population}{Total\ number\ of\ population}$	0.993716771
Fraction of unaware infected individual	i_{10}	$\frac{Number\ of\ initial\ unaware\ in\ infected\ population}{Total\ number\ of\ population}$	0.003189946
Fraction of aware infected individual	i_{20}	$\frac{Number\ of\ initial\ aware\ in\ infected\ population}{Total\ number\ of\ population}$	0.001933301
Fraction of treated individual	z_0	$\frac{Number\ of\ initial\ treated\ population}{Total\ number\ of\ population}$	0.00869985
Fraction of recovered individual	r_0	$\frac{Number\ of\ initial\ recovered\ population}{Total\ number\ of\ population}$	0.000289995
The effective unaware contact rate leads to infection	β_1	$\frac{Unaware\ effective\ contact}{Total\ number\ of\ contact}$	0.047142857
The effective aware contact rate	β_2	$\frac{Aware\ effective\ contact}{Total\ number\ of\ contact}$	0.0285714285
Natural death rate	μ_1	$\frac{Number\ of\ population\ dies\ by\ natural\ cause}{Total\ number\ of\ population}$	0.00038666
Natural birth rate	μ_2	$\frac{Number\ of\ new\ born\ babies}{Total\ number\ of\ population}$	0.005828902
The average of natural birth and death rate	μ	$\frac{\mu_1+\mu_2}{2}$	0.003107781
The rate of aware Hepatitis B infection	λ_1	$\frac{Number\ of\ population\ moves\ from\ unaware\ to\ aware\ infected}{Number\ of\ unaware\ Hepetitis\ B\ infected\ population}$	0.0212121212
The recruitment rate of treated class (Treatment rate)	λ_2	$\frac{Number\ of\ population\ moves\ from\ aware\ \ infected\ to\ treated}{Number\ of\ aware\ Hepetitis\ B\ infected\ population}$	0.4500000000
The recruitment rate of recovered class from unaware infected class	γ_1	$\frac{Number\ of\ population\ moves\ from\ unaware\ \ to\ removed\ class}{Number\ of\ unaware\ Hepetitis\ B\ infected\ population}$	0.018181818
The recruitment rate of recovered class from aware infected class	γ_2	$\frac{Number\ of\ population\ moves\ from\ aware\ \ to\ removed\ class}{Number\ of\ unaware\ Hepetitis\ B\ infected\ population}$	0.010000000
The recruitment rate of recovered class from treated class	δ	$\frac{Number\ of\ population\ moves\ from\ trested\ to\ removed\ class}{Number\ of\ \ Hepetitis\ B\ treated\ population}$	0.211111111

Note: The shaded (Colored) rows in the table – 5, needed for our numerical simulation of BRN (R_0)

3.4. Numerical Simulations

In our model, we consider BRN of nonlinear (SI_1I_2RT) −Mathematical Model

$R_0 = \frac{\lambda_1\beta_2+\beta_1(\mu+\gamma_1+\lambda_2)}{(\mu+\gamma_1+\lambda_1)(\mu+\gamma_2+\lambda_2)}$, it depends on seven parameters namely, namely

The effective unaware contact rate $\beta_1 = 0.47142857$ leads to infection

The effective aware contact rate $\beta_2 = 0.0285714285$leads to infection

The recruitment rate of aware Hepatitis B infection $\lambda_1 = 0.0212121212$

The recruitment rate of treated (treatment) class $\lambda_2 = 0.45$

The rate of movement from unaware infected class to the recovered class $\gamma_1 = 0.018181818$

The rate of movement from aware infected class to the recovered class$\gamma_2 = 0.1$

The natural death rate $\mu = 0.003107781$

(All numerical values taken from the Table – 5)

We can verify and find the BRNR_0, by using from seven parameters one unknown and remaining other six parameters are constant

Case – 1:

β_1, it is unknown and remaining parameters values are as above mentioned then we can find R_0

For example:

$$R_0 = \frac{\lambda_1\beta_2+\beta_1(\mu+\gamma_1+\lambda_2)}{(\mu+\gamma_1+\lambda_1)(\mu+\gamma_2+\lambda_2)} = \frac{0.0212121212 \times 0.0285714285 + \beta_1(0.003107781 + 0.018181818 + 0.45)}{(0.003107781 + 0.018181818 + 0.0212121212)\left((0.003107781 + 0.018181818 + 0.45)\right)}$$

$$\Longrightarrow R_0 = 23.52845955\beta_1 + 0.025780975$$

Case – 2:

β_2, it is unknown and remaining parameters values are as above mentioned then we can find R_0, i.e.

$$R_0 = 0.902335048\beta_2 + 1.109198804$$

For these two cases (1 and 2) the graphical representation of basic reproduction numbers in $(R_0, \beta_1)\ and\ (R_0, \beta_2)$ −planes shown below in figure – 3 and figure – 4 respectively

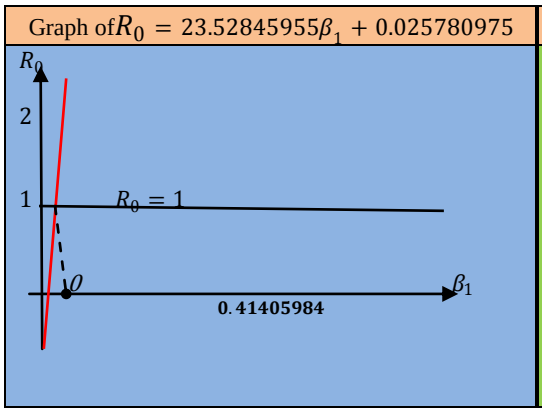

Figure – 3

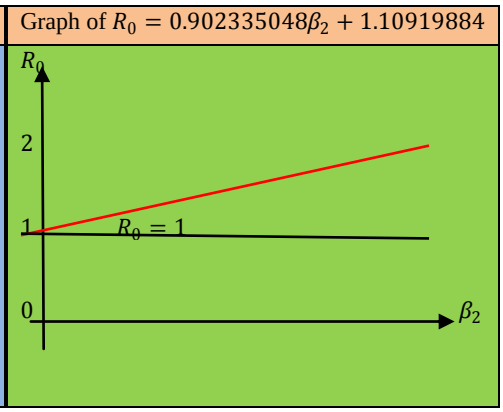

Figure – 4

Explanation of Graphs:

In figure – 3: The graph shows that the BRN

$R_0 < 1 \ when \ \beta_1 < 0.47142857$, and also $R_0 > 1 \ when \ \beta_1 > 0.47142857$

In figure – 4:The graph shows that the BRN

$R_0 \geq 1 \ when \ \beta_2 \geq 0.0285714285$(Always)

Case – 3:

The recruitment rate of aware Hepatitis B infectionλ_1, it is unknown and remaining parameters are constant, in this case we have

$$R_0 = \frac{0.051656168\,\lambda_1 + 0.047142857}{0.021289599 + \lambda_1}$$

Case – 4:

The recruitment rate of treated (treatment) classλ_2,it is unknown and remaining parameters are constant, in this case we have

$$R_0 = \frac{0.014259658}{0.103107781 + \lambda_2} + 1.109198804$$

For these two cases (3 and 4) the graphical representation of basic reproduction numbers in $(R_0, \lambda_1) \ and \ (R_0, \lambda_2)$ −planes shown below in figure – 3 and figure – 4 respectively

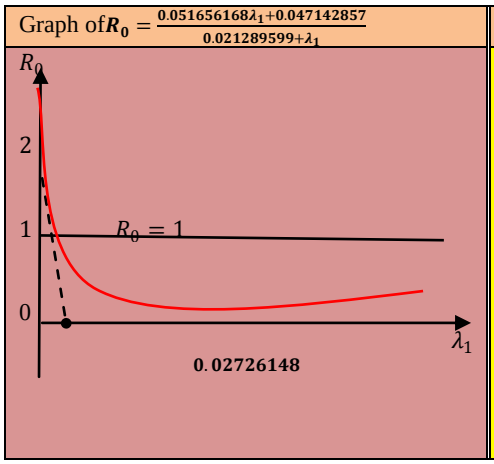

Figure – 5

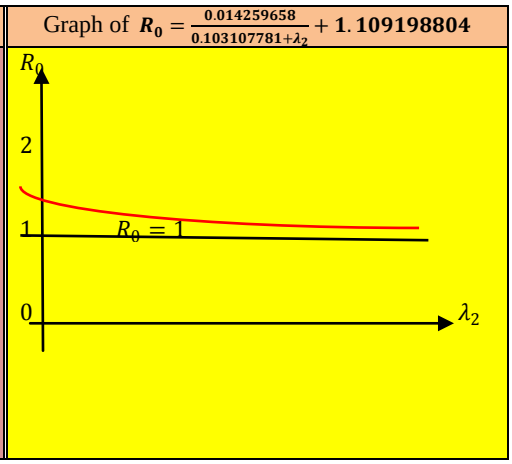

Figure – 6

Explanation of Graphs:

In figure – 5: The graph shows that the BRN

$R_0 < 1 \ when \ \lambda_1 > 0.02726148$, and also $R_0 > 1 \ when \ \lambda_1 < 0.02726148$

In figure – 6: The graph shows that the BRN $R_0 \geq 1 \ when \ \lambda_1 \geq or < 0.02726148$ (Always)

Case – 5:

The recruitment rate of aware Hepatitis B infectionλ_1, it is unknown and remaining parameters are constant, in this case we have

$$R_0 = \frac{0.051656168\,\lambda_1 + 0.047142857}{0.021289599 + \lambda_1}$$

Case – 6:

The recruitment rate of treated (treatment) class λ_2,it is unknown and remaining parameters are constant, in this case we have

$$R_0 = \frac{0.014259658}{0.103107781 + \lambda_2} + 1.109198804$$

For these two cases (3 and 4) the graphical representation of basic reproduction numbers in$(R_0, \gamma_1) \ and \ (R_0, \gamma)$ −planes shown below in figure – 3 and figure – 4 respectively

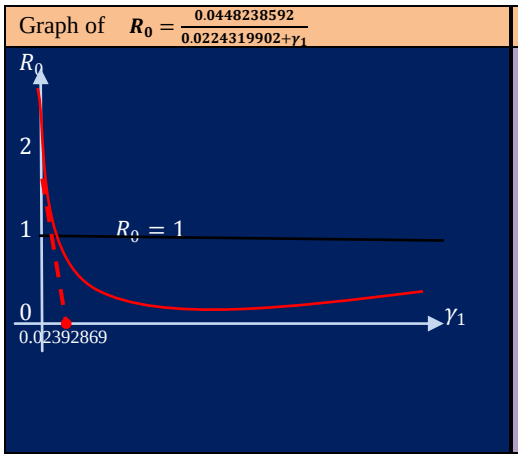

Figure – 7

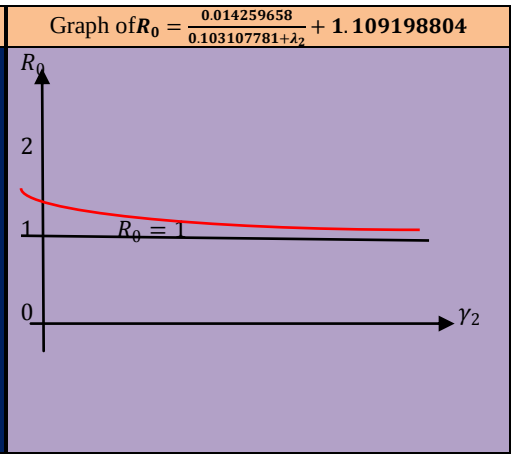

Figure – 8

Explanation of Graphs:

In figure – 7: The graph shows that the BRN

$R_0 < 1 \ when \ \gamma_1 > 0.018181818$, and also $R_0 > 1 \ when \ \gamma_1 < 0.018181818$

In figure – 8:The graph shows that the BRN

$R_0 \geq 1 \ when \ \gamma_2 \geq 0.1 \ or \ \gamma_2 < 0.1$ (Always)

Case – 7:

The natural death rate μ,it is unknown and remaining parameters are constant, in this case we have

$$R_0 = \frac{0.00060606}{(0.039393939+\mu)(\mu+0.55)} + \frac{0.047142857}{(0.039393939+\mu)}$$

For the case (7) the graphical representation of basic reproduction numbers in(R_0, μ) −plane shown below in figure – 9

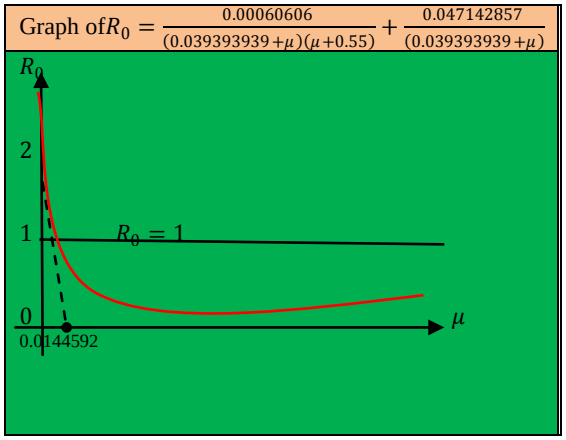

Figure – 9:

Explanation of Graph:

In figure – 9: The graph shows that the BRN

$R_0 < 1 \ when \ \mu > 0.0144592$, and also $R_0 > 1 \ when \ \mu < 0.0144592$

3.5. Results and Discussion

Due to our Extended Modified Model by using BRN $R_0 = \frac{\lambda_1\beta_2+\beta_1(\mu+\gamma_1+\lambda_2)}{(\mu+\gamma_1+\lambda_1)(\mu+\gamma_2+\lambda_2)}$, from this we can observe that BRN R_0 depends on seven parameters $(\beta_1, \beta_2, \lambda_1, \lambda_2, \gamma_1, \gamma_2, and \ \mu)$ and also we have

1. From the graph (figure 3) R_0, affected by β_1 that is if the effective unaware contact rate β_1 increases then R_0, also increase, this means that the rate of conversion from susceptible class to unaware infected class is increased by due to the contact of unaware infected class with the susceptible class, then the number of unaware infected is increased.
2. From the graph (figure 4) R_0, affected by β_2 that is if the effective aware contact rate β_2 increases then R_0, also increase.
3. From the graph (figure 5) R_0, affected by recruitment rate λ_1 of aware HBV infection: In this case the recruitment rate λ_1 of aware HBV then R_0, decrease that is the rate of conversion from unaware infected class to aware infected class is increased by screening their blood, and then the number of unaware infected is decrease
4. From the graph (figure 6) R_0, affected by recruitment rate λ_2 of treated class , here if λ_2 increases then R_0, decreases, that is the rate of conversion from aware infected class to aware infected class is increased by taking HB vaccination, then the number of treated class is increased

5. From the graph (figure 7) R_0, affected by the rate of movement from unaware infected class to the recovered class γ_1 , here if γ_1 increases then R_0, decreases, that is the rate of conversion from unaware infected class to recovered class is increased when the unaware HBV infected is in adult stage,, then the recovered class is increased
6. From the graph (figure 8) R_0, affected the rate of movement from aware infected class to the recovered class γ_2 , here ifγ_2 increases then R_0, decreases, that is the rate of conversion from aware infected class to recovered class is increased when the aware HBV infected is in adult stage,, then the recovered class is increased
7. From the graph (figure 9) R_0, affected the natural death rate μ, here if μ increases then R_0, decreases, that is the natural death is increased then the unaware HBV infected class, aware HBV infected class and HBV treated class are decreased

3.6. Conclusion – Recommendations – Future Research In this Field

Based on collecting real data in Debre Berhan city in Ethiopia, we got from our extended modified mathematical model from initial model [9] BRN $R_0 = 1.134979926$. This shows that HBV generation number is greater than 1 means that HBV infectious in Debre berhan city in Ethiopia community is increase.

Based on our finding the current research results we recommend

- To decrease the transmission of disease, the value of our control parameter

$\beta_1 < 0.04140584$

- To decrease the transmission of disease, the value of our control parameter

$\lambda_1 > 0.02726148$

- To decrease the transmission of disease, the value of our control parameter

$\gamma_1 < 0.02726148$

In our research we consider only Sexual transmission, Horizontal transmission, Transfer of HBV via cuts, Transmission of infected blood or Blood products and Re – use of HBV contaminated sharp material. But HBV can be transmitted by Vertical transmission, therefore for the coming researchers will better to consider this limitation in order to more modified the new model and to control the spread of HBV.

REFERENCES

1. Akbari, R., et al. "*Stability analysis of the transmission dynamics of an HBV model*." International Journal of Industrial Mathematics 8.2 (2016): 119-129.

2. Boldin, Barbara. "*Deterministic structured population epidemic models*."Textr book, Pearson edition limited, published, 2004.
3. Chitins, Nakul. "*Einführung in die MathematischeEpidemiologie*: *Introduction to Mathematical Epidemiology: The Basic Reproductive Number.*" (2011).
4. Ganem, Don, and Alfred M. Prince. "*Hepatitis B virus infection—natural history and clinical consequences*." New England Journal of Medicine 350.11 (2004): 1118-1129.
5. Hartemink, N. A., et al. "*The basic reproduction number for complex disease systems: Defining R 0 for tick-borne infections.*" The American Naturalist 171.6 (2008): 743-754.
6. Lavanchy, Daniel. "Hepatitis B virus epidemiology, disease burden, treatment, and current and emerging prevention and control measures." *Journal of viral hepatitis*" 11.2 (2004): 97-107.
7. Mitchell, Abigail E., and Heather M. Colvin, eds. "*Hepatitis and liver cancer: a national strategy for prevention and control of hepatitis B and C.*"National Academies Press, 2010.
8. Ott, J. J., et al. "*Global epidemiology of hepatitis B virus infection: new estimates of age-specific HBsAg seroprevalence and endemicity*." Vaccine 30.12 (2012): 2212-2219.
9. Sacrifice, Nana-Kyere, et al. "*An SITR Analysis of Treatment Model of Hepatitis B Epidemic*." 2011
10. Shepard, Colin W., et al. "*Hepatitis B virus infection: epidemiology and vaccinati*on." Epidemiologic reviews 28.1 (2006): 112-125.
11. Sylla, Bakary S., and Christopher P. Wild. "*A million Africans a year dying from cancer by 2030: what can cancer research and control offer to the continen*t?" International journal of cancer 130.2 (2012): 245-250.
12. www.who.int/mediacentre/factsheets/fs204/en/
13. Yami, Alemeshet, FissehayeAlemseged, and AlimaHassen. "*Hepatitis B and C virus infections and their association with Human Immunodeficiency virus: a cross-sectional study among blood donors in Ethiopia.*" Ethiopian journal of health sciences 21.1 (2011): 67-75.
14. Zanetti, Alessandro R., Pierre Van Damme, and Daniel Shouval. "*The global impact of vaccination against hepatitis B: a historical overview. Vaccine*" 26.49 (2008): 6266-6273.