ORIGINAL PAPER

STUDYING THE TRANSMISSION OF HEPATITIS-B VIRUS THROUGH SENSITIVITY ANALYSIS

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Abstract. *This paper presents the sensitivity analysis of an epidemiological model, SEIR, describing the transmission of Hepatitis B Virus. The classical sensitivities, the system sensitivity and the sensitivity norms of the model have been found. The sensitivities show that the susceptible individuals are majorly affected by the birth rate, contact rate, the rate at which the exposed individuals become infected and the fraction of the infected individuals in the population. System sensitivity describes the sensitivity of the whole model output with respect to all the parameters. The results of the classical sensitivities of the parameters are in agreement with the results given by the system sensitivities. The contact rate, β has the largest sensitivity norm and the exposed infected fraction of the population, t_1 has the least sensitivity norm. The qualitative and the quantitative sensitivity studies of the SEIR model reaffirm each other.*

Keywords: *Hepatitis-B; SEIR model; sensitivity functions; sensitivity norms*

1. INTRODUCTION

Hepatitis is the aggravation of the liver. It is commonly added about by the viral diseases acknowledged as the hepatitis infection. The hepatitis contamination consists of a sequence of five different pathogens, known as hepatitis A, B, C, D and E [1]. Hepatitis A, hepatitis B and hepatitis C, are a group of dangerous viral diseases influencing the liver. They have a range of warning signs and medications. Laboratory assessments determine the sorts of hepatitis. The Australia antigen causes hepatitis B; which was discovered in 1967. Dr. Blumberg acquired the Nobel Prize in Medicine for his discovery of the hepatitis B virus in 1976.

Hepatitis B brings both the acute and the chronic diseases. Hepatitis B is potentially a life-threatening liver contamination spread across by the hepatitis B virus. The HBV is a silent killer causing sickness of the liver with many contaminated no longer understanding that they possess the virus [2]. According to the World Health Organization (WHO), inside the first 12 months of infection over 90% of the contaminated adults recover naturally and some of them no longer show the signs and symptoms of the infection or ailment [3]. *Six lac* people die due to hepatitis B per annum [4]. The occurrence of HBV contamination varies in different geographical areas of the world as well as in particular populace subgroups [5].

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Developing countries of the world in Asia and Africa have the highest rate of HBV incidence In Pakistan, 9 million human beings are contaminated with HBV and the rate of its contamination is growing progressively [6]. The considerable chance factors for contracting HBV infection in Pakistan are non-standardized therapeutic, infusions, injections and barbering practices. Viral hepatitis is a main public health threat in Pakistan with accelerated morbidity and mortality. According to WHO, Pakistan falls beneath the endemic place with 3% HBV population. Dynamic epidemiological models have performed fundamental functions to examine and manipulate infectious diseases. These models are used to model the spread of the infectious disease since they interpret the changes in the disease after sometimes [7]. These models also referred to as the compartmental fashions are necessary theoretical epidemiology methods used to discover about the transmission dynamics of HBV. These are used to predict, apprehend and graph best intervention packages to manage hepatitis B and other epidemics. There are different types of mathematical models in analysis of epidemic diseases for modeling HBV.

In the early 1980s, the mathematical models model was first used to study the transmission dynamics of hepatitis B and the effectiveness of control. Nowak et al. delivered the first Ordinary Differential Equations (ODEs) model of HBV infection in 1995 [8]. His model was further studied by Tsiang et al. [9]. It represented the drug efficiency. After their models, numerous ODEs models consisting of three, four, five and six compartments in the forms of SIR, SIS, SIRS, SEIS, SEVIR, MSIR, etc., have been used to describe the transmission of HBV. Four, five and six compartmental models are the most common tools in modeling the transmission dynamics of Hepatitis. Sensitivity analysis is extremely important for the overall study of mathematical models. It analyzes the sensitivity of the output to the parameters [10]. It decides which parameters are sensitive, which are not sensitive. It helps to estimate the parameters present in the model. It is a valuable device to evaluate [9] output changes because of input changes. The modeler considers the sensitivity analysis an important tool to pick up the sensitive parameters for his model. The sensitive parameters mirror which section of the system is vital to be considered in the model [11]. Most sensitive parameters are easily estimated as a small change in this parameter brings a reasonable change in the outputs. Insensitive parameters do not require to be considered in the model. The sensitive parameters are also vital for the model evaluation due to the fact they remain steady during the progression of the time [12].

Keeping in view the magnitude of the sensitivity evaluation for the model evaluation of the HBV transmission, we have chosen one of the widely studied four-compartmental model referred to as the SEIR model initially presented by Li et al. [13]. We have divided our work of this article into six sections. We describe the SEIR model of Hepatitis B Virus in Section 2. We develop the theoretical frame-work necessary to perform the sensitivity analysis of the model in the Section 3. The numerical implementation of the theory developed is in Section 3 to find the sensitivities of the hepatitis model will be given in Section 4. The results of our work will be given in Section 5. In Section 6, we present the conclusion of the work.

2. THE SEIR MODEL OF HEPATITIS B

The $SEIR$ model of the transmission of Hepatitis B Virus comprises of a population which is further sub-divided into four mutually disjoint classes; the susceptible individuals, the exposed, the infected and the recovered individuals. The number of the individuals in

these four classes are respectively given by S, E, I and R. The total population is given by $N = S + E + I + R$. The state variables are described below:

1. S is the number of susceptible individuals in the population that is, the uninfected and new individuals who have not come into contact with the HBV.
2. E is the number of exposed individuals in the population, those individuals who have had contact with the virus; but do not spread it.
3. I is the number of infected individuals in the population; the ones who spread HBV in the population.
4. R is the number of recovered individuals in the population; the virus-free individuals having immunity.

Let $S(t)$, $E(t)$, $I(t)$, $R(t)$ denote the corresponding numbers of individuals at time t, without ambiguity; if they are abbreviated by S, E, I, R, respectively, then the $SEIR$ model is presented by the following system of four non-linear Ordinary Differential Equations(ODEs) [14]:

$$\begin{aligned} \frac{dS}{dt} &= \mu - \beta SI - t_1\mu E - t_2\mu I - \mu S \\ \frac{dE}{dt} &= \beta SI + t_1\mu E + t_2\mu I - (\psi + \mu)E \\ \frac{dI}{dt} &= \psi E - (\delta_1 + \mu)I \\ \frac{dR}{dt} &= \delta_1 I - \mu R \end{aligned} \tag{1}$$

The initial conditions are given by:

$$S(0) \geq 0, E(0) \geq 0, I(0) \geq 0, R(0) \geq 0 \tag{2}$$

The assumptions on the model are that it is a constant-population model where the *natural birth rate* equals the *death rate* (μ) as is shown in the diagrammatic representation of the model, Figure (1). Every individual in the population is susceptible to the virus. The exposed individuals E become infected I with a *constant rate* (ψ), and infected individuals I recover with rate (δ_1). (β) is assumed to be the *contact rate* between the susceptible S and the infective I. The model assumes that a fraction of the offspring of the exposed E and infected individuals I are infected with HBV at birth and so enters the exposed compartment E, resulting in the vertical transmission of the disease. Thus, a fraction t_1 of the offsprings from the exposed individuals E and a fraction t_2 of the offspring from the infective individuals I are born into the exposed class.

The parameters used in the model are described in the Table 1 along with their assumed values [13-14] which we shall use to solve the model numerically in our onward course of work:

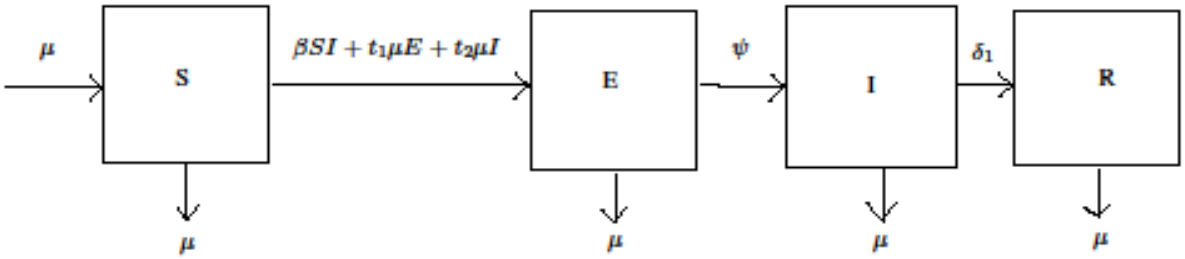

Figure 1. Representation of SEIR Model.

Table 1. Description of parameters of the Hepatitis B Model.

Parameter	Parameter Name	Estimated Value
μ	birth rate	0.00004
β	contact rate	0.009
Ψ	rate at which the exposed becomes infected	0.0385
δ_1	recovery rate	0.002
t_1	exposed infected fraction	0.0002
t_2	fraction of the infected	0.0003

3. SENSITIVITY ANALYSIS

The compartmental models of a dynamical system described by the system of the Ordinary Differential Equations (ODEs), as in our article, are also multiple-output system with the measurable outputs. We describe a general mathematical procedure to find the sensitivity equations with respect to the parameter θ. The mathematical models are generally represented in the vectorial forms as:

$$\begin{aligned} \frac{dx}{dt}(t) &= F(x,\theta), \\ x(0) &= x_0 \end{aligned} \tag{3}$$

where:

$x(t) = (x_1(t), x_2(t), \ldots, x_n(t))^T$ is the state variable,
$x_0 = (x_1(0), x_2(0), \ldots, x_n(0))^T$ is the initial condition vector and
$\theta = (\theta_1, \theta_2, \ldots, \theta_p)^T$ is the vector of parameters.
$F = (f_1, f_2, \ldots, f_m)^T$ is the vector function
$F: \mathbb{R}^n \times \mathbb{R}^p \longrightarrow \mathbb{R}^m$ defined by the first equation of the System (3) [15].

Sensitivities of the state variables $x_j(t)$; $j = 1, \ldots, n$ are their normalized partial derivatives with respect to the parameter components θ_i; $i = 1,2,3, \ldots, p$ [16]. This is done by finding the ODE systems of the sensitivities of the solution vector $x(t)$ with respect to the parameter vector θ. So, vectorially differentiating the ODEs System (3) with respect to the vector θ, we obtain

$$\begin{aligned} \frac{d}{d\theta}\frac{dx}{dt}(t) = \frac{d}{dt}\frac{dx}{d\theta}(t) &= \frac{d}{d\theta}F(x,\theta), \\ \frac{d}{d\theta}x(0) &= \frac{d}{d\theta}x_0. \end{aligned} \tag{4}$$

which gives the ODE systems of the sensitivities of the solution vector $x(t)$ with respect to the parameter vector θ as below:

$$\begin{aligned} \frac{dw}{dt}(t) &= F_x(x,\theta)w(t) + F_\theta(x,\theta), \\ w(0) &= 0, \end{aligned} \tag{5}$$

where

$$w = \frac{dx}{dt}(t) = \left(\frac{\partial x_i}{\partial \theta_j}\right)_{n\times p}, \quad i = 1, \ldots, n, \quad j = 1, \ldots, p,$$

$$F_x = \frac{dF}{dx}(t) = \left(\frac{\partial f_l}{\partial x_i}\right)_{m\times n}, \quad l = 1,\dots,m, \quad i = 1,\dots,n.$$

and

$$F_\theta = \frac{dF}{d\theta}(t) = \left(\frac{\partial f_l}{\partial \theta_1}\right)_{m\times p}, \quad l = 1,\dots,m, \quad j = 1,\dots,p. \tag{6}$$

Equation(6) is called the *Sensitivity Matrix* [17], and is given by

$$F_\theta = \begin{pmatrix} \frac{\partial f_1}{\partial \theta_1} & \frac{\partial f_1}{\partial \theta_2} & \cdots & \frac{\partial f_1}{\partial \theta_p} \\ \frac{\partial f_2}{\partial \theta_1} & \frac{\partial f_2}{\partial \theta_2} & \cdots & \frac{\partial f_2}{\partial \theta_p} \\ \cdot & \cdot & \cdots & \cdot \\ \cdot & \cdot & \cdots & \cdot \\ \frac{\partial f_n}{\partial \theta_1} & \frac{\partial f_n}{\partial \theta_2} & \cdots & \frac{\partial f_n}{\partial \theta_p} \end{pmatrix} \tag{7}$$

3.1. SENSITIVITY FUNCTIONS

A single output of the model is by

$$x(t,\theta) = \big(f_1(t,\theta),\dots,f_m(t,\theta)\big), \quad 0 \le t \le T, \quad \theta \in U, \tag{8}$$

where $T > 0$ is a fixed time instant and U^p is an open set consisting of parameters θ [18, 19]. The sensitivity or sensitivity functions of the single output $f_i(t,\theta)$ with regard to a parameter component θ_ϕ, being the normalized partial derivative at $t \in [0,T]$, is defined by [20, 21]

$$S_{\frac{f_i}{\theta_\phi}}(t) = \frac{\partial f_i(t,\theta)}{\partial \theta_\phi}.\frac{\theta_\phi}{f_i(t,\theta)}, \phi = 1,\dots,p, \quad i = 1,\dots,m. \tag{9}$$

Here both θ_ϕ, $\phi = 1,\dots,p$ and $f_i(t,\theta), i = 1,\dots m$ are assumed to be non-zero.

The sensitivity functions $S_{\frac{f_i}{\theta_\phi}}(t)$ quantify the effects of the changes in the parameters on the outputs of the model at a particular time instant t. They describe to which parameter the model output is the most or the least sensitive in a particular time interval $[0,T]$. They describe the local behavior of the change of the output with respect to the change in the parameter. The sensitivities of the parameters of the model help in their identifiability studies[23]. The global behavior of the model output due the change in the parameter is given by the system sensitivity.

Definition 1. *The system sensitivity with respect to a component of the parameter vector at any time instant t in $[0,T]$ combining the individual sensitivities of all model outputs $f_i, i = 1,\dots,m$ is defined by [20]*

$$S_{\theta_\phi}(t) = \left(\sum_{i=1}^{m} \left(S_{\frac{fi}{\theta_\phi}}(t) \right)^2 \right)^{\frac{1}{2}}, \qquad \phi = 1, \ldots, p \tag{10}$$

In order to have an idea of the measure of the *system sensitivity*, we can also take different *norms* of the *system sensitivity*, however they have a limited use due to the local character of the sensitivity functions depending upon t and θ as explained earlier. These norms give us a global picture of the sensitivity of the parameters. The norms quantify numerical changes index of a parameter with respect to its sensitivity over the whole model. To obtain a measure that validates the sensitivities, the Euclidean norms and absolute value norms are used frequently [17]. We collect the following definitions from [17, 20].

Definition 2. *The Euclidean norm of the sensitivity functions of the model output is defined by*

$$\| S_{\theta_\phi} \|_2 = \left(\sum_{j=1}^{N} |S_{\theta_\phi}(t_j)|^2 \right)^{\frac{1}{2}}, \tag{11}$$

where $\phi = 1, \ldots, p$ and N is the number of the subdivision points of the interval $[0, T]$.

Definition 3. *The absolute value norm of sensitivity functions of the model output is given by*

$$\| S_{\theta_\phi} \|_1 = \sum_{j=1}^{N} \left| S_{\theta_\phi}(t_j) \right|, \tag{12}$$

where $\phi = 1, \ldots, p$ and N is the number of the subdivision points of the interval $[0, T]$.

4. NUMERICAL IMPLEMENTATION

Following the theory developed in Section 3 to do the sensitivity analysis of a mathematical model given by a system of ODEs, we take

$$\theta = (\mu, \beta, \psi, \delta_1, t_1, t_2),$$

and

$$F = (f_1, f_2, \ldots, f_m)^T,$$

with its components given by:

1. $f_1(t, \theta) = \mu - \beta SI - t_1 \mu E - t_2 \mu I - \mu S,$
2. $f_2(t, \theta) = \beta SI + t_1 \mu E + t_2 \mu I - (\psi + \mu) E,$
3. $f_3(t, \theta) = \psi E - (\delta_1 + \mu) I,$
4. $f_4(t, \theta) = \delta_1 I - \mu R.$

We take the values of parameters as shown in the Table 1 and the initial conditions $S(0) = 950$, $E(0) = 10$, $I(0) = 3$ and $R(0) = 2$, [14] for Model (1). We then develop the ODEs system of the sensitivity equations in accordance with Equation (5) for our model. We

take $x = (S, E, I, R)$ as the state vector consisting of the variables S, E, I and R. We partially differentiate equations of the model (1) successively with respect to μ,β, ψ, δ_1, t_1, and t_2). We partially differentiate Equations (1) with respect to μ and use the results:

$$\frac{d}{d\mu}\frac{dS}{dt} = \frac{d}{dt}\left(\frac{dS}{d\mu}\right)$$
$$\frac{d}{d\mu}\frac{dE}{dt} = \frac{d}{dt}\left(\frac{dE}{d\mu}\right)$$
$$\frac{d}{d\mu}\frac{dI}{dt} = \frac{d}{dt}\left(\frac{dI}{d\mu}\right)$$

and

$$\frac{\boldsymbol{d}}{\boldsymbol{d\mu}}\frac{\boldsymbol{dR}}{\boldsymbol{dt}} = \frac{\boldsymbol{d}}{\boldsymbol{dt}}\left(\frac{\boldsymbol{dR}}{\boldsymbol{d\mu}}\right)$$

This gives the sensitivity equations of the model outputs S,E, I and R with respect to the parameter μ as given below:

$$\begin{aligned}
\frac{d}{dt}\left(\frac{dS}{d\mu}\right) &= 1 - \beta\left(S\frac{\partial I}{\partial \mu} + I\frac{\partial S}{\partial \mu}\right) - t_1\mu\left(\frac{\partial E}{\partial \mu}\right) - t_1 E - t_2\mu\left(\frac{\partial I}{\partial \mu}\right) - \mu\left(\frac{\partial S}{\partial \mu}\right) - S \\
\frac{d}{dt}\left(\frac{dE}{d\mu}\right) &= \beta\left(S\frac{\partial I}{\partial \mu} + I\frac{\partial S}{\partial \mu}\right) + t_1\mu\left(\frac{\partial E}{\partial \mu}\right) + t_1 E + t_2\mu\left(\frac{\partial I}{\partial \mu}\right) - \psi\left(\frac{\partial E}{\partial \mu}\right) - \mu\left(\frac{\partial E}{\partial \mu}\right) - E \\
\frac{d}{dt}\left(\frac{dI}{d\mu}\right) &= \psi\left(\frac{\partial E}{\partial \mu}\right) - \delta_1\left(\frac{\partial I}{\partial \mu}\right) - \mu\left(\frac{\partial I}{\partial \mu}\right) - I \\
\frac{d}{dt}\left(\frac{dR}{d\mu}\right) &= \delta_1\left(\frac{\partial I}{\partial \mu}\right) - \mu\left(\frac{\partial R}{\partial \mu}\right) - R
\end{aligned} \tag{13}$$

In a similar way, we differentiate partially Model (1) w.r.t $\beta, \psi, \delta_1, t_1, t_2$ to get their respective sensitivity equations. Combining these equations along with Model (1), we get an ODEs system of 28 equations. Using Matlab solver ode45 over the time interval [0, 100], we solve this system. We discover the sensitivities of the states S, E, I and R w.r.to $\mu, \beta, \psi, \delta_1, t_1, t_2$. The system sensitivity given by Equation (10) and sensitivity norms given by Equations (11) and (12) are also evaluated. The Results are described below:

5. RESULTS

The results obtained from the sensitivity analysis of the model are given:

5.1. NUMERICAL SOLUTION

The closed-form solution (see [22]) of Model (1) does not exist. The numerical solution, depicting the dynamical behavior of the susceptible S, the exposed E, the infected I, and the recovered R individuals of the population N respectively over the time interval [0, 100] (in years), is drawn in Fig. 2. The initial population size for the susceptible, the exposed, the infected, and the recovered individuals are taken to be S(0) = 950, E(0) = 10, I(0) = 3 and R(0) = 2 respectively. The susceptible individuals decrease sharply in the first ten years until all the susceptible population is infected with the disease and leaves no susceptible individual. The exposed individuals increase sharply in the first nine years; then decrease sharply for the remaining years. The infective individuals increase highly and maintain its equilibrium for the

rest of the years. The simulations of the model show that the susceptible individuals decrease sharply up to 10 years, then remains constant throughout, the exposed individuals increase rapidly at the beginning up to 10 years and decrease rapidly for the rest of the time, the infected individuals increase sharply throughout the time with the exception at the beginning where they increase slowly. The recovered individuals increase slowly after 15 years, as shown in Fig. 2. The results on the sensitivity studies of the $SEIR$ model are given in the following paragraphs.

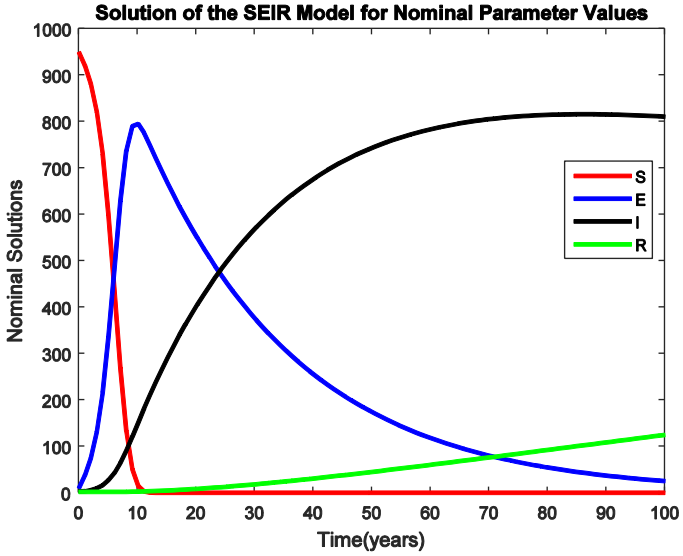

Figure 2. Numerical Solution of the SEIR Model of Hepatitis B Virus

5.2. SENSITIVITIES OF SEIR MODEL

The sensitivities of the model outputs S, E, I and R with respect to the parameters μ, β, ψ, δ_1, t_1 and t_2 are drawn in Figure 3

5.2.1. Sensitivities of S

Fig. 3 illustrates that the model output S is not sensitive to the parameter μ up to 14 years. Then its sensitivity increases sharply up to 19 years. Beyond 19 years, its sensitivity remain constant. It means that the birth rate, μ, of the off-springs in the populations affects the susceptible population mainly from 14 to 19 years. Sensitivity of μ in the time interval [16-18] years, then it remains constant. The susceptible individuals are sensitive to the parameter β up to 20 years.

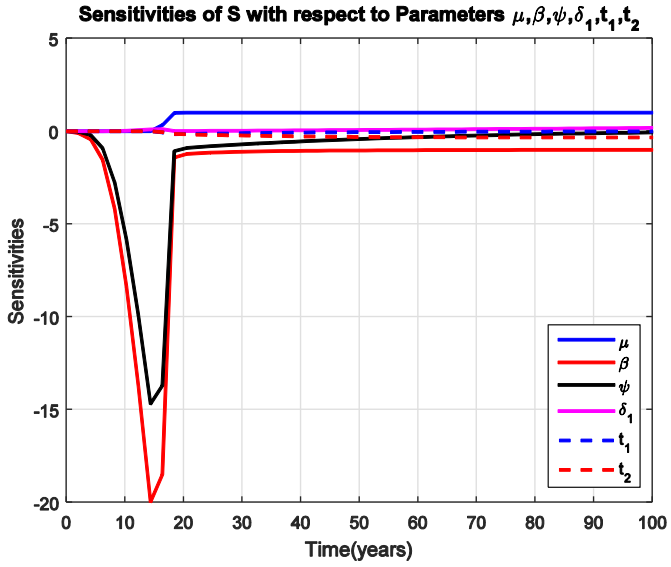

Figure 3. Sensitivity of S with respect to parameters μ, β, ψ, δ_1, t_1 and t_2

First decreasing, then their sensitivity increases very slowly up to to 18 years. Beyond 18 years, their sensitivity remains constant. That is, the contact rate, β, affects the susceptible population mainly up to 20 years. The susceptible individuals are very sensitive to the parameter ψ up to 20 years. Then their sensitivity increases slowly. This describes that the rate at which the exposed individuals become infected affect the susceptible population enormously during the first 20 years. The model output S is least sensitive to the parameters δ_1 and t_1 and ts sensitivity to t_2 is also not so enormous. The susceptible individuals will mostly be affected by the birth rate, contact rate and the rate at which exposed becomes infected. β and ψ show more sensitivity than μ and t_2. That the infected fraction of the population affects the susceptible populations beyond fourteen years.

5.2.2. Sensitivities of *E*

The model outputs E is sensitive with respect to β and ψ during the first 13 years as is shown in the Fig. 4. Beyond 13 years E still remains very sensitive to the parameter ψ, however, it remains almost insensitive to the parameter β. That is, the exposed individual remain sensitive to the contact rate, β up to 13 years, and to the rate at which exposed becomes infected throughout the time interval [0,100]. The exposed individuals E remain almost insensitive to the parameters μ, δ_1, t_1 and t_2.

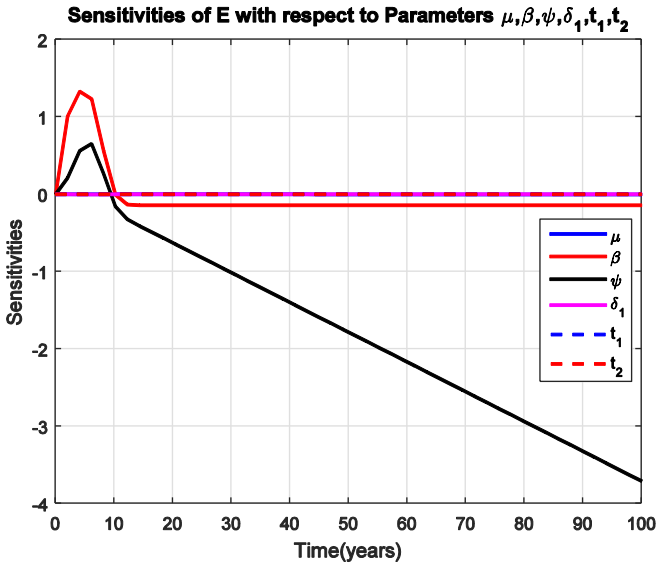

Figure 4. Sensitivity of *E* with respect to parameters μ, β, ψ, δ_1, t_1 and t_2

5.2.3. Sensitivities of *I*

The output I remains very sensitive with respect to ψ, rate at which the exposed becomes infected; β, contact rate, and δ_1, the recovery rate as shown in Fig. 5. I is sensitive for the first half of the whole time interval with respect to these three parameters. The parameter ψaffects the outputs, I throughout the transmission period [0, 100]. The parameter β affects I up to [0, 80]. The parameter δ_1 affects I moderately throughout the transmission period.

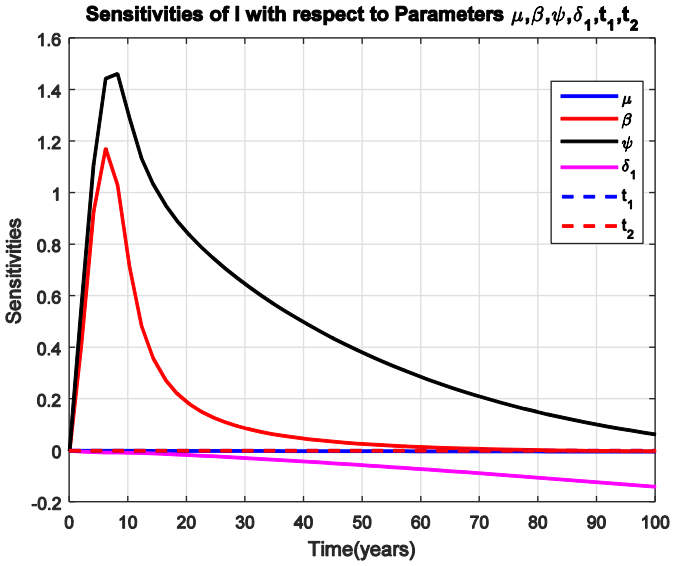

Figure 5. Sensitivity of *I* with respect to parameters μ, β, ψ, δ_1, t_1 and t_2

The outputs I remains almost insensitive to the parameters μ, t_1 and t_2 throughout the dynamic period. That is, the infected population will be affected by mainly by the rate at which the exposed becomes infected, contact rate and the recovery rate.

5.2.4. Sensitivities of R

The last compartment R shows sensitivity with respect to the parameter β, ψ and δ_1 in whole time period. The parameters μ, t_1 and t_2 are insensitive to this compartment. That R remains sensitive with respect to the birth rate through the time interval of the transmission dynamics of the HBV. However, the sensitivity of R with respect to these parameters is high during the initial phases of the time interval. These parameters affect R through the transmission period [0; 100]. The recovered individuals are affected sharply by the parameter δ_1 during the first half and beyond that their sensitivity changes slowly. R also remain sensitive with respect to t_1 throughout the dynamic period.

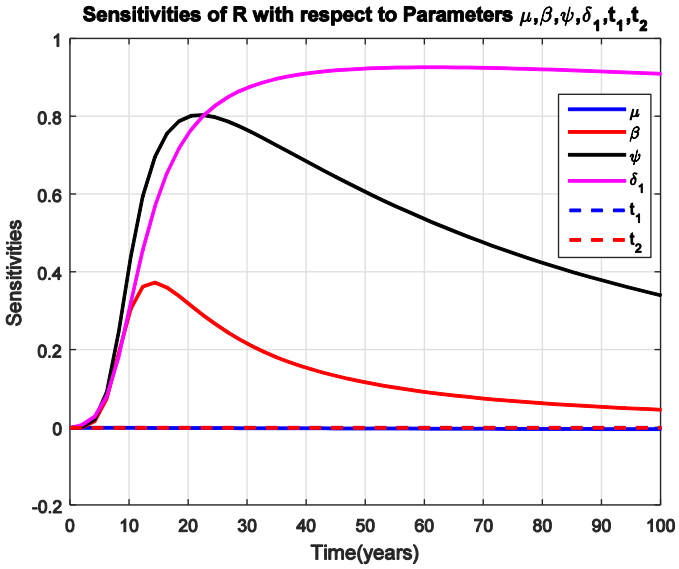

Figure 6. Sensitivity of R with respect to parameters μ, β, ψ, δ_1, t_1 and t_2

5.3. SYSTEM SENSIITIVITIES

System sensitivities of the parameters combine the effects of the sensitivities of all the outputs of the SEIR model. They also depend on the number of the measurements points. By taking the mesh points as the measurement points, the system sensitivities for the model are given in the Fig. 7. The information given by the time courses of the system sensitivities are more or less similar to the information given by their individual sensitivities. The system sensitivities indicate that the model output $X = (S, E, I, R)$ is most sensitive with respect to the parameter β, then with respect to the parameter $\boldsymbol{\psi}$, then is with respect to $\boldsymbol{\delta_1}$, then μ and then t_2.The model output is least sensitive with respect to the parameter t_1.

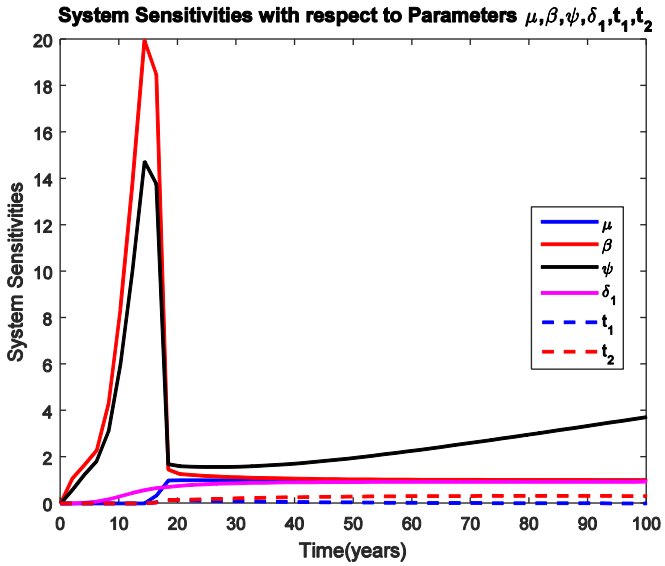

Figure 7. System Sensitivity.

5.4 SENSITIVITY NORMS

The numerical results in the Table 2 give different norms of the system sensitivities and in terms of them, we can say that the whole system of transmission of HBV is least sensitive to parameters t_1 and t_2. This is also in agreement with the information about these two parameters given by their individual sensitivities. The parameters in descending order of their system sensitivities in terms of the norms $\| S_{\theta_i} \|_2$ and $\| S_{\theta_i} \|_1$ are β, ψ, μ, δ_1, t_2 and t_1.

Table 2. Different norms of system sensitivities of the parameters of the SEIR model.

Parameter	L_2 Norm	L_1 Norm
μ	6.4319	41.781
β	32.8	133.79
ψ	28.477	203.64
δ_1	5.9375	46.564
t_1	0.41444	2.0586
t_2	1.877	11.862

6. CONCLUSIONS

The sensitivity functions describe the effects of changes in measurements on the outputs of the mathematical models. We have evaluated the sensitivity functions of the four model outputs S, E, I and R with respect to the six parameters μ, β, ψ, δ_1 ,t_1, t_2 of the model. In our selected model $SEIR$ of the Hepatitis transmission, we observed that all the model outputs are sensitive enough with respect to all parameters mainly in the time interval [0-20]. The case for the susceptible individuals i.e., output S is more evident in this interval. This means that all the parameters can be identified by collecting data from this region during the process of parameter estimation. The parameter μ which describes the birth rate is most sensitive in the compartments E, I and R, but with small magnitude and it is sensitive in S in time interval [14-19] years. The sensitivities of the parameters β and ψ in $SEIR$ model shows that these two parameters are more or less sensitive for any output S or I or R or together. So, one can suggest on this basis that that this model can better describe the virus dynamics if other parameter or even a single parameter can be included in it.

The sensitivity studies of $SEIR$ model describes that the parameter t_1 is least sensitive for all measurements taken from S, E, I or R or together. This suggests that this parameter cannot be identified correctly through a parameter estimation process. However, it can be identified a priori. The parameter μ, β, ψ, δ_1 and t_2 are highly sensitive where as the parameters t_1 are least sensitive in $SEIR$ model. System sensitivity which describes the sensitivity of the whole output of the model with respect to different parameters depicts a global character as against the local character of the classical sensitivity of the model outputs. Our results of the classical sensitivities of the parameters are in agreement with the results given by the system sensitivities.

The classical sensitivities and system sensitivities are considered the qualitative measures of the effects of the changes of the parameters over the model outputs, however, norms of the system sensitivities of the parameters present this relation quantitatively. The norms of all parameters are given in the Table 2. So, we can say that the parameter β has the largest sensitivity norm and the parameter t_1 has the least sensitivity norm. The qualitative and the quantitative sensitivity studies of the $SEIR$ reaffirm each other.

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