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A FRACTIONAL ORDER MODEL OF HEPATITIS B TRANSMISSION UNDER THE EFFECT OF VACCINATION

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Abstract. In this paper we present a fractional order mathematical model to explain the spread of Hepatitis B Virus (HBV) in a non-constant population. The model we propose includes both vertical and horizontal transmission of the infection and also vaccination at birth and vaccination of the susceptible class. We also use a frequency dependent transmission rate in the model. We give results on existence of equilibrium points of the model and analyze the stability of the disease-free equilibrium. Finally, numerical simulations of the model are presented.

1. Introduction

Hepatitis B is a serious liver infection caused by Hepatitis B Virus (HBV). According to World Health Organization (WHO), an estimated 296 million people are living with HBV infection and in 2019 almost 820000 people died due to HBV related liver diseases [33]. However, immunization of newborns and susceptible individuals is a very effective strategy to control the transmission of the disease [34].

There are basically two different transmission types for HBV. When blood, semen or another body fluid from a person infected with HBV enters to the body of a non-infected person, horizontal transmission occurs. The virus can also be vertically transmitted [33]. Vertical transmission is the transmission of the virus from an infected mother to the baby at birth. Most of the infected individuals recover from the disease and gain immunity, however some develop chronic HBV infection. Chronic HBV infection can lead some life-threatening diseases like cirrhosis and liver cancer. The incubation period for HBV is an average of 120 days [21]. Once an individual is diagnosed with HBV, the infection is considered as acute infection for 6 months but if the infection lasts more than 6 months, it is considered as

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chronic infection [21]. For adults, recovery rate from acute infection with immunity is 95% while for infants and children, this rate is dramatically low [7].

In early 1980's a general dynamical model considering immunization, composed of partial differential equations is proposed and the idea of suitability of the given model for HBV transmission was put forward for the first time [1]. In 1994, the first differential equation model specifically for transmission of HBV infection including vaccination is proposed [16]. Since then, many researchers studied on models with vaccination (See [12]).

Medley et al. introduced a compartment epidemic model for HBV infection with immunization of children born to carrier mothers and newborn babies [22]. In this study population in the absence of disease is assumed to be constant. Zou et al. modified the model given in [22] considering the lifelong immunity gained after recovery and waning vaccine-induced immunity in a non-constant population by assuming only horizontal transmission of the disease [35]. In both of these models, transmission rate is assumed to be density dependent and also transmission occurs only through carriers ans acute infectious individual. However, HBV may transmit during its incubation period [33].

In recent years many mathematicians studied on fractional order epidemic models ([3], [17], [18]). Ullah et al. introduced a fractional order epidemic model for HBV transmission with density dependent transmission rate using Caputo-Fabrizio derivative in which only the immunization of children born to carrier mothers is considered [29]. Farman et al. analyzed an epidemic model for HBV infection consists of differential equations in Caputo sense. In this model, the population is assumed to be constant in the absence of the disease [6]. In this study we propose a more general model using fractional differential equations of Caputo sense considering newborn vaccination and also vaccination of susceptible individuals regardless of age. The reason for using fractional differential equations is to reflect the memory effect in the spread of the disease to the mathematical model ([4], [23]). In this model we consider both horizontal and vertical transmission of the disease. HBV infection is a long term infection so, ignoring the demographic structure of the population is not realistic. In the model we propose, we also consider the demographic properties of the population. Transmission rates used in epidemic models can be classified in two major forms: density dependent transmission rate and frequency dependent transmission rate [9]. Density dependent transmission rate is commonly assumed for smaller populations and specifically in modeling airborne transmitted diseases, nevertheless frequency dependent transmission rate is commonly assumed for large, heterogeneous populations and in modeling vector-borne or sexually transmitted diseases ([9], [8]). In all of the above mentioned models, transmission rates are assumed to be density dependent, however we assume frequency dependent transmission rate. We first introduce the model then analyze the equilibrium points of the model and finally we give the numerical simulations for the constructed model.

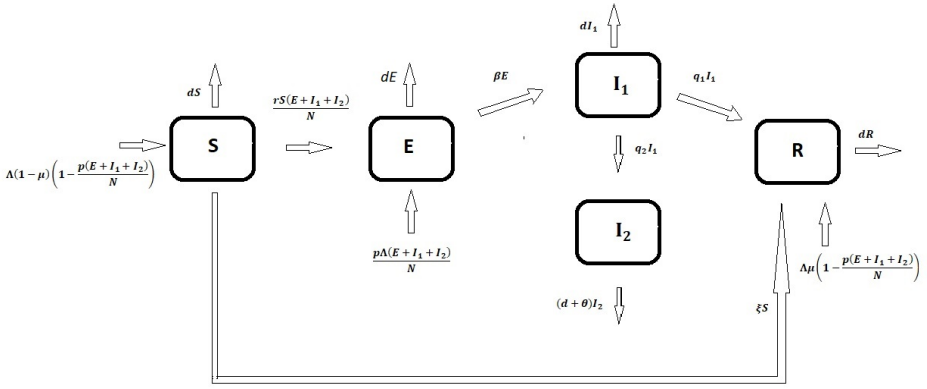

FIGURE 1. The schematic diagram of the proposed model.

2. Model Derivation

Definitions of fractional order integral and fractional order derivative in Caputo sense [19] are presented in the Appendix. Due to its nature, Caputo fractional derivative is widely used in mathematical modeling of real life problems. We also use Caputo derivative in our model. The main reason for using fractional derivative rather than the integer order derivative is the memory effect that is considered in the fractional order differential equations. Like most of the biological dynamics, dynamics of the transmission of epidemic diseases have a short memory effect [23].

The schematic diagram of the proposed epidemic model to explain the spread of HBV infection is given in Figure 1. The total population, $N(t)$, is partitioned into five classes namely susceptible, exposed, acute infectious, chronic infectious and recovered classes denoted by $S(t), E(t), I_1(t), I_2(t)$ and $R(t)$, respectively. The individuals in susceptible class are healthy individuals who are candidates for contracting the disease. The individuals in $E(t)$ class are infected individuals for whom the virus is in its incubation period. In the model there are two more infectious classes. After the symptoms are seen in an infectious individual, he/she is assumed to pass to the acute infectious class. If an acute infectious person cannot recover from the disease in a specific time interval which depends on the structure of the disease, he/she is assumed to be chronic infectious. Acute and chronic infectious compartments are denoted with $I_1(t)$ and $I_2(t)$, respectively. d is the natural death rate of the population and θ is the death rate related to the fatal diseases caused by the infection. Particularly for HBV infection, secondary fatal liver related diseases arise for the chronic infectious individuals that enhances the death rate. We assume that vaccination rate at birth is μ and the rate of vaccination of susceptible class is ξ. Also vaccinated individuals gain immunity and pass to the recovered class. Since, HBV is a virus that can be vertically transmitted which means an infected

TABLE 1. Variables and parameters used in the model.

$S(t)$:	Number of susceptible individuals at time t
$E(t)$:	Number of exposed individuals at time t
$I_1(t)$:	Number of acute infectious individuals at time t
$I_2(t)$:	Number of chronic infectious individuals at time t
$R(t)$:	Number of recovered individuals with immunity at time t
μ :	Immunization rate by vaccination at birth
Λ :	Number of recruits per unit time
d :	Natural death rate
p :	Probability of having an exposed baby for exposed and infectious classes
r :	Transmission coefficient (both exposed and infectious individuals can transmit the disease)
ξ :	Immunization rate of susceptible class
q_1:	Recovery rate from acute HBV infection
q_2:	Rate of developing chronic disease after acute Hepatitis B infection.
θ :	Disease related death rate
β :	The rate at which exposed individuals pass to acute infectious class

individual (we only consider the vertical transmission from mother) may transmit the disease to its babies before birth, the parameter p is defined as the probability of having an exposed baby for the infected individuals. All of the parameters used in the model are explained in Table 1 .

These assumptions lead to the following system of differential equations with $0 < \alpha < 1$,

$$\begin{aligned} &D^{\alpha}S = (1-\mu)\,\Lambda\left(1-\tfrac{p(E+I_1+I_2)}{N}\right) - S\left(\tfrac{r(E+I_1+I_2)}{N}+d+\xi\right),\\ &D^{\alpha}E = (rS+p\Lambda)\,\tfrac{(E+I_1+I_2)}{N} - (\beta+d)\,E,\\ &D^{\alpha}I_1 = \beta E - (q_1+q_2+d)I_1,\\ &D^{\alpha}I_2 = q_2 I_1 - (\theta+d)\,I_2,\\ &D^{\alpha}R = q_1 I_1 + \mu\Lambda\left(1-\tfrac{p(E+I_1+I_2)}{N}\right) + \xi S - dR \end{aligned} \tag{1}$$

and the initial conditions

$$S(0) = S_0,\ E(0) = E_0,\ I_1(0) = I_{10},\ I_2(0) = I_{20},\ R(0) = R_0, \tag{2}$$

where $N(t) = S(t) + E(t) + I_1(t) + I_2(t) + R(t)$ and $(S, E, I_1, I_2, R) \in R_+^5$. Using system (1), we obtain

$$D^{\alpha}N(t) = \Lambda - dN - \theta I_2. \tag{3}$$

Theorem 1. *The initial value problem (1)-(2) has a unique solution and the solution remains in* R_+^5.

Proof. The existence and uniqueness of the solution of (1)-(2) in $(0,\infty)$ can be shown by using [13]. We now show the positive invariance of the domain R_+^5.

Since,

$$\begin{aligned}
D^{\alpha}S \quad | \quad _{S=0} &= \Lambda(1-\mu)\left(1-\frac{p\left(E+I_1+I_2\right)}{N}\right)\geq 0,\\
D^{\alpha}E \quad | \quad _{E=0} &= \frac{rS(I_1+I_2)}{S+I_1+I_2+R}+\frac{p\Lambda(I_1+I_2)}{S+I_1+I_2+R}\geq 0,\\
D^{\alpha}I_1 \quad | \quad _{I_1=0} &= \beta E\geq 0,\\
D^{\alpha}I_2 \quad | \quad _{I_2=0} &= q_2 I_1\geq 0,\\
D^{\alpha}R \quad | \quad _{R=0} &= q_1 I_1+\mu\Lambda\left(1-\frac{p\left(E+I_1+I_2\right)}{S+E+I_1+I_2}\right)+\xi S\geq 0,
\end{aligned}$$

on every hyperplane bounding the nonnegative orthant, the vector field points into R_+^5.

□

It is clear that $N\left(t\right)$ also remains nonnegative.
Let $\Omega=\left\{\left(S\left(t\right),E\left(t\right),I_1\left(t\right),I_2\left(t\right),R\left(t\right)\right)\in R_+^5 : 1\leq N\left(t\right)\leq \Lambda/d\right\}$.

Lemma 1. *The set Ω is positively invariant with respect to system (1).*

Proof. (3) implies that

$$\begin{aligned}
D^{\alpha}N(t) &\leq -dN\left(t\right)+\Lambda,\\
0 &< \alpha<1.
\end{aligned}$$

So,

$$N\left(t\right) \leq \left(N_0-\frac{\Lambda}{d}\right)E_{\alpha}\left(-dt^{\alpha}\right)+\frac{\Lambda}{d}.$$

Consequently, $N\left(t\right)\leq\frac{\Lambda}{d}$, if $N_0\leq\frac{\Lambda}{d}$.

□

For the sake of simplicity in calculations, we use the system

$$\begin{aligned}
&D^{\alpha}S=\left(1-\mu\right)\Lambda\left(1-\tfrac{p(E+I_1+I_2)}{N}\right)-S\left(\tfrac{r(E+I_1+I_2)}{N}+d+\xi\right),\\
&D^{\alpha}E=\left(rS+p\Lambda\right)\tfrac{(E+I_1+I_2)}{N}-\left(\beta+d\right)E,\\
&D^{\alpha}I_1=\beta E-(q_1+q_2+d)I_1,\\
&D^{\alpha}I_2=q_2I_1-\left(\theta+d\right)I_2,\\
&D^{\alpha}N(t)=\Lambda-dN-\theta I_2
\end{aligned} \tag{4}$$

that can be obtained by (1) and (3) with the initial conditions

$$S\left(0\right)=S_0,\ E\left(0\right)=E_0,\ I_1\left(0\right)=I_{10},\ I_2\left(0\right)=I_{20},\ N\left(0\right)=N_0.$$

3. Equilibrium Points and Stability

System (4) has a disease free equilibrium (DFE) at $H_0 = \left(\frac{\Lambda(1-\mu)}{d+\xi}, 0, 0, 0, \frac{\Lambda}{d}\right)$. The positive equilibrium appears at $H_1 = (S^*, E^*, I_1^*, I_2^*, N^*)$ where

$$\begin{aligned} S^* &= \left(\frac{N^* A_0 A_1}{A_0 A_1 + A_0 + 1} - p\Lambda\right)\frac{1}{r}, \\ E^* &= A_0 A_1 I_2^*, \\ I_1^* &= A_0 I_2^* \\ N^* &= \frac{\Lambda - \theta I_2^*}{d} \end{aligned}$$

and

$$\begin{aligned} A_0 &= \frac{d+\theta}{q_2}, \\ A_1 &= \frac{(d+q_1+q_2)}{\beta}, \end{aligned}$$

if the condition

$$\frac{A_0 A_1 (d+\xi)}{r(1-\mu)d(A_0 A_1 + A_0 + 1)} > 1, \qquad \mu < 1$$

holds true.

Basic reproduction number, denoted by R_0^*, for an infection is the number of secondary infections caused by one infected individual introduced to a totally susceptible population. Therefore, it is assumed to be a treshold value for the infection to persist. Jacobian method is commonly used to determine the value of R_0^* in epidemic models. However, it is not easy to overcome the algebraic work needed to apply Jacobian method to models with multiple infectious compartments. Next generation matrix (NGM) method is an alternative method to find the value of R_0^*. The details of the NGM method can be found in [2], [30], [31] and [32]. We first give the outline of the NGM method and apply it to the model given by (4).

Consider the system given with

$$\frac{dX}{dt} = G(X).$$

Let $X = (x_1, x_2, ..., x_n)^T$ be the number of individuals in each compartment of the epidemic model and let the first m compartments ($m < n$) are composed of infected individuals. Consider the equations represented in the form

$$\frac{dx_i}{dt} = \mathcal{F}_i(X) - \mathcal{V}_i(X), \qquad i = 1, 2, ..., m \tag{5}$$

where $\mathcal{F}_i(X)$ is the rate of appearance of new infections in compartment i and $\mathcal{V}_i(X)$ is the rate of transitions between the infected compartments. Here $\mathcal{F}_i$ and

$\mathcal{V}_i$ are assumed to be in $\mathcal{C}^2$. FV^{-1} is called the next generation matrix where

$$F = \left[\frac{\partial \mathcal{F}_i\left(X^*\right)}{\partial x_j}\right] \text{ and } V = \left[\frac{\partial \mathcal{V}_i\left(X^*\right)}{\partial x_j}\right], \qquad 1 \leq i, j \leq m$$

and the spectral radius of the NGM is the basic reproduction number.

Theorem 2. *([32]) If X_0 is a disease free equilibrium of the system $\frac{dx_i}{dt} = \mathcal{F}_i\left(X\right) - \mathcal{V}_i\left(X\right)$ then X_0 is locally asymptotically stable if $R_0^* = \rho\left(FV^{-1}\right) < 1$, but unstable if $R_0^* > 1$.*

Remark 1. *Consider an epidemic model given by the integer order system*

$$\frac{dX}{dt} = G\left(X\right) \tag{6}$$

and its fractional order counterpart

$$\frac{d^\alpha X}{dt^\alpha} = G\left(X\right). \tag{7}$$

Systems (6) and (7) have the same equilibrium points. Let X^* be the disease free equilibrium point for both models. If X^* is stable for (6), then it is also stable for (7). But the converse is not always true. Therefore, Theorem 1 gives only a sufficient condition for the stability of X^* for (7).

We now consider the system consisting of three infected compartments of the model (4),

$$\begin{array}{l} D^\alpha E = \left(rS + p\Lambda\right)\frac{\left(E+I_1+I_2\right)}{N} - \left(\beta + d\right)E \\ D^\alpha I_1 = \beta E - \left(q_1 + q_2 + d\right)I_1 \\ D^\alpha I_2 = q_2 I_1 - \left(\theta + d\right)I_2 \end{array} \tag{8}$$

and split the system in the form (5).

Let $X = (S, E, I_1, I_2, N)$ and define

$$\begin{aligned} \mathcal{F}_1\left(X\right) &= \frac{\left(r + p\Lambda\right)S\left(E + I_1 + I_2\right)}{N}, \\ \mathcal{F}_2\left(X\right) &= 0, \\ \mathcal{F}_3\left(X\right) &= 0, \\ \mathcal{V}_1\left(X\right) &= \left(\beta + d\right)E, \\ \mathcal{V}_2\left(X\right) &= -\beta E + \left(d + q_1 + q_2\right)I_1, \\ \mathcal{V}_3\left(X\right) &= \left(d + \theta\right)I_2 - q_1 I_1. \end{aligned}$$

So,

$$F\mid_{H_0} = \begin{bmatrix} \frac{rd(1-\mu)}{d+\xi} + pd & \frac{rd(1-\mu)}{d+\xi} + pd & \frac{rd(1-\mu)}{d+\xi} + pd \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix},$$

$$V\mid_{H_0}=\begin{bmatrix}(\beta+d) & 0 & 0\\ -\beta & d+q_1+q_2 & 0\\ 0 & -q_2 & d+\theta\end{bmatrix}$$

and

$$R_0^*=\rho\left(FV^{-1}\right)=\frac{dp\,(d+\xi)+d\,(1-\mu)\,r}{(\beta+d)\,(d+\xi)}.$$

Theorem 3. *DFE of system (4) is locally asymptotically stable, if $R_0^*<1$ and unstable if $R_0^*>1$.*

Proof. The first part of the theorem is a direct consequence of NGM method and Remark 1. In order to prove the unstability condition, we apply the Jacobian method. The characteristic equations of system (4) for the DFE is

$$(-d-\xi-\lambda)\,(-d-\lambda)\,P_3\,(\lambda)=0$$

where $P_3\,(\lambda)=-\lambda^3+a_2\lambda^2+a_1\lambda+a_0$ with

$$\begin{aligned}a_2 &= (d+\beta)\,(R_0^*-1)-(A_1\beta+A_0q_2)\\ a_1 &= (A_1\beta+A_0q_2)\,(d+\beta)\,(R_0^*-1)-A_0A_1\beta q_2+(d+\beta)\,R_0^*\beta\\ a_0 &= (d+\beta)\,\beta q_2\,(A_0A_1\,(R_0^*-1)+R_0^*\,(A_0+1)).\end{aligned}$$

If $R_0^*>1$ then $a_0>0$. Applying Descartes' rule of signs, we see that P_3 has at least one positive root, that is DFE is unstable. □

Theorem 4. *DFE of the system (4) is globally asymptotically stable in Ω if $R_0^*<1$ and the following condition holds:*

$$\frac{(q_1+q_2+d)\,[(\beta+d)\,(\theta+d)+q_2\,(r+p)]}{(r+p)\,(q_1+q_2+d+\beta)\,(\theta+d+R_0^*q_2)}\geq 1. \tag{9}$$

Proof. Consider the Lyapunov function

$$L=A_1E+A_2I_1+A_3I_2,$$

where

$$\begin{aligned}A_1 &= (q_1+q_2+d)\,(\theta+d)\,R_0^*,\\ A_2 &= (r+p)\,(\theta+d+R_0^*q_2)\,,\\ A_3 &= (r+p)\,(q_1+q_2+d)\,R_0^*.\end{aligned} \tag{10}$$

Using system (4), we have

$$\begin{aligned}D^\alpha L \leq\ & E\,[A_1\,(r+p)-A_1\,(\beta+d)+A_2\beta]\\ & +I_1\,[A_1\,(r+p)-A_2\,(q_1+q_2+d)+A_3q_2]\\ & +I_2\,[A_1\,(r+p)-A_3\,(\theta+d)]\,.\end{aligned}$$

Substituting $A_1,\ A_2$ and A_3 as given in (10), we obtain

$$\begin{aligned}D^\alpha L \leq\ & (E+I_1)\,(R_0^*-1)\,(q_1+q_2+d)\,(r+p)\,(\theta+d)\\ & +E[(\beta+q_1+q_2+d)\,(r+p)\,(\theta+d+R_0^*q_2)\end{aligned}$$

$$\begin{aligned} & -(q_1+q_2+d)\,R_0^*\,((\theta+d)\,(\beta+d)+q_2\,(r+p))] \\ \leq\ & 0, \end{aligned}$$

if $R_0^* < 1$ and (9) holds. Consequently, using LaSalle's invariance principle, we conclude that DFE is globally stable in Ω. □

4. Numerical Solutions of the Model Using Data of Turkey

Hepatitis B virus infection is a serious public health issue in Turkey as well as the rest of the world. There are two phases of the infection namely acute and chronic. Once a person is diagnosed with chronic HBV infection he/she may develop new HBV related fatal diseases like cirrhosis and liver carcinoma. A traditional SIR model is performed for explaining HBV transmission in Turkey and transmission coefficient for this model is estimated for two different values for birth and natural death rate of the population [10]. We also simulate our model using data of Turkey.

According to the data provided by Turkish Statistical Institution (TUIK), the average number of people born in Turkey every year is 1303000 and the average death rate in Turkey is 0.00521 between the years 2010 and 2020 [28].

The most effective method to control the spread of HBV is the immunization of the individuals in the population. In our model there are two parameters related to the immunization. The first one is μ that represents the efficient immunization rate of the newborns. In Turkey since 1997, every baby born in hospitals is being vaccinated after birth. The immunity is gained after three doses of vaccine with 95% [20]. In Turkey nearly 94% of the births take place in hospitals and the newborns receive the first dose after birth but only 75% percent of them take three doses of vaccine ([24]). For the parameter that represents the efficient vaccination rate at birth, μ, we use the estimated value 0.66975 that is the product of 0.95, 0.94 and 0.75.

Vertical transmission of HBV is important for the models explaining the dynamics of the spread of HBV because the rate of developing chronic Hepatitis B is $70\% - 90\%$ for the babies who are born infected ([25]). The rate of having an exposed baby for the infected mothers is known to be almost 90% and according to TUIK ([28]), the rate of giving birth for the population is 1.7% in Turkey. So, we set the parameter $p = 0.0153$. β is assumed to be the the rate at which the exposed individuals pass to the acute infectious compartment, that is closely related with the incubation period of the virus. The incubation period of HBV is known to be $60 - 180$ days and for the simulations we assume it to be 120 days and set $\beta = 360/120 = 3$.

The average recovery rates from acute infection for adults, children and babies are 95%, 50% and 10%, respectively. Using the demographic data of Turkey we use the weighted average for the recovery rate for Hepatitis B as 3.5008 considering the average recovery duration 90 days. We also use the value 0.2496 for the parameter q_2, that is the rate of developing chronic HBV infection for the acute infectious compartment. This value is calculated by $q_2 = 2(1 - q_1/4)$.

TABLE 2. Initial values for system (4).

$N(0)$	$74724.269(\times 10^3)$
Hepatitis B prevalence ([26])	4.57%
Number of HBV infectious people	$3414.899(\times 10^3)$
$I_1(0)$ ([5])	$406.372(\times 10^3)$
$I_2(0)$	$3008.526(\times 10^3)$
$E(0)$ (assumed)	$100(\times 10^3)$
$R(0)$ ([27])	$23837.041(\times 10^3)$
$S(0)$	$47372.33(\times 10^3)$

Chronic HBV infection causes liver related fatal diseases and chronic HBV related deaths are due to liver cancer with 55% and cirrhosis and other liver diseases with 45% ([15]). Disease related death rate, θ, is estimated to be 2.2×10^{-5} ([14]). We also assume that the vaccination rate for the susceptible compartment is 0.0001.

Transmission coefficient of the disease does not only dependent on the type of the virus but also depends on the social structure of the population we work on. So, we simulate the model for different values of transmission coefficient, r ($r = 0.8, 1$).

We start the simulation from 2011, when the prevalence of HBV in Turkey was 4.57% ([26]). According to the Annual Epidemiological Report (2010-2014) on Hepatitis B of European Center for Disease Prevention and Control (ECDC), 11.9% of reported Hepatitis B cases are acute ([5]). Also the rate of anti-HBs positivity which is a marker for gained immunity rate for Turkey is 31.9% ([27]). We use the values given in Table 2 to determine the initial values of system (4).

Basic reproduction numbers are calculated as 0.0862849 and 0.107849 for $r = 0.8$ and $r = 1$, respectively. The solutions of the proposed model using the above mentioned parameters for different values of α are represented in the figures (2)-(5).

5. Conclusion

Epidemic diseases and their health and economic consequences are one of the major problems in the world. The first step to control the spread of a disease is to understand its dynamics. Mathematical models are very convenient tools to understand how a disease spread. Although statistical analysis of the data about the spread of a disease gives a foresight about the future, it generally ignores the dynamical feature of the process. Also, collecting appropriate data needs a long time and also it is too expensive. In this paper we propose an epidemic model to explain the spread of Hepatitis B. Hepatitis B epidemic is a long term epidemic unlike the seasonal diseases. So, the population in the model is assumed to be non-constant. Also, due to the nature of HBV both vertical and horizontal transmissions are considered in the model. We also use a fractional order system to reflect the memory

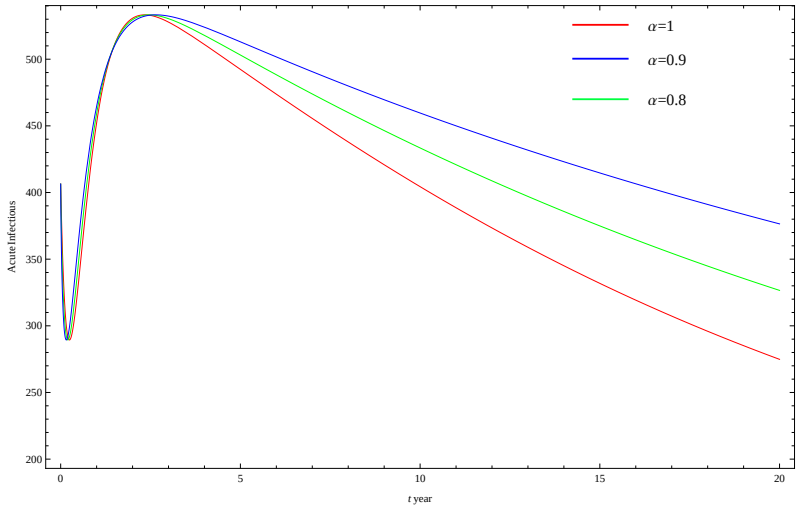

FIGURE 2. Acute infectious compartment for $r = 0.8$.

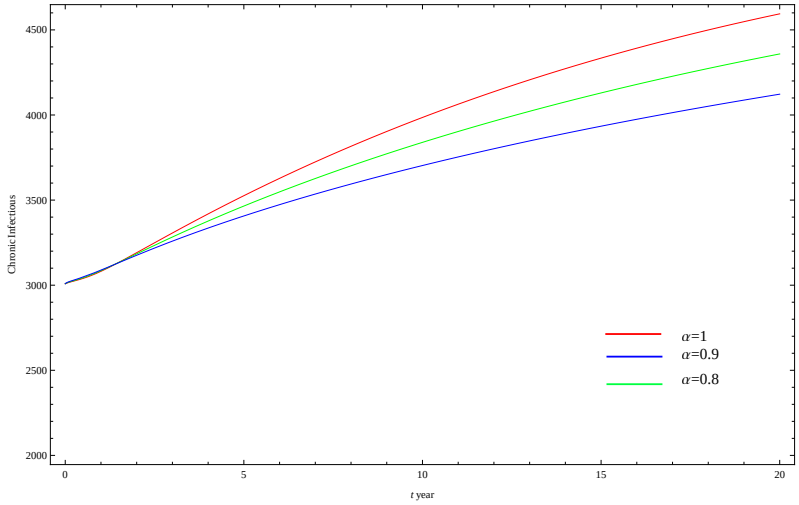

FIGURE 3. Chronic infectious compartment for $r = 0.8$.

effect of the epidemic. After determining the equilibrium points of the model, we give local stability analysis of the disease free equilibrium. We also give numerical simulations for the model. The parameters used in the simulations are obtained using previously published research and the numerical solutions are plotted for two different values of the transmission coefficient. The solutions are presented for

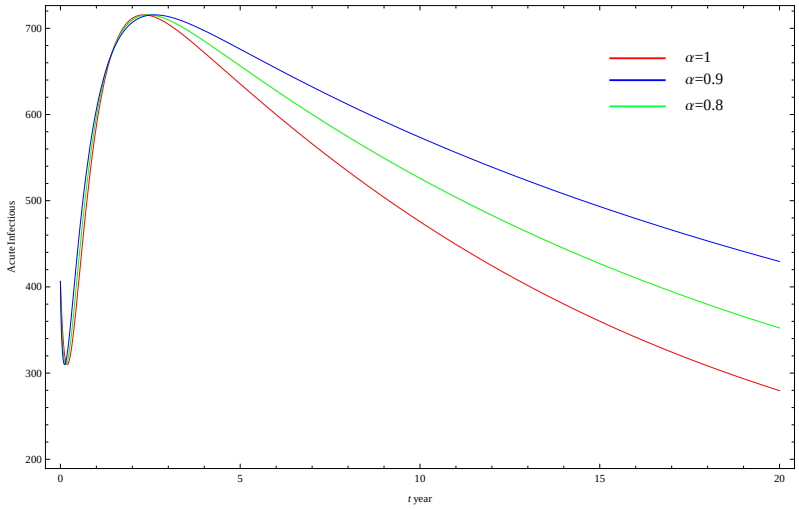

FIGURE 4. Acute infectious compartment for $r = 1$.

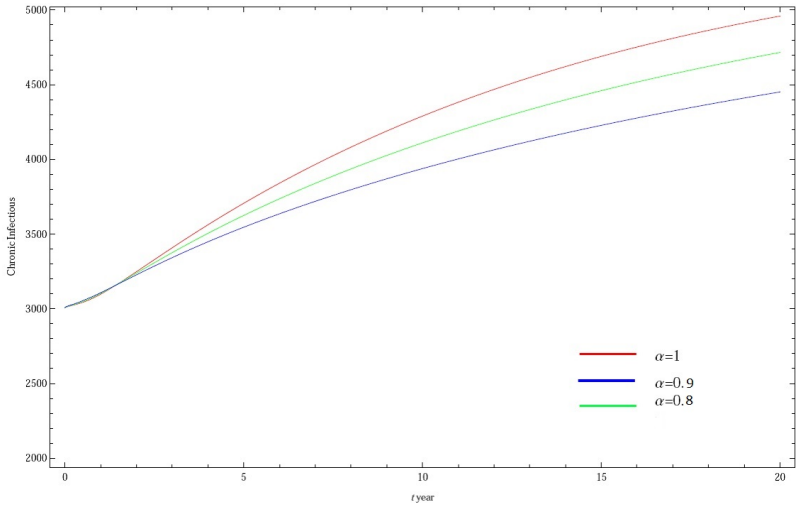

FIGURE 5. Chronic infectious compartment for $r = 1$.

$\alpha = 1, 0.9, 0.8$. Data for the incidence of the disease is easily reachable for Hepatitis B. But for the simulations of the proposed model, we need the prevalence data and the only comprehensive data for the prevalence of HBV infection in Turkey is given in 2011 ([26]). This model may give a foresight for the future of HBV infection in Turkey under the mentioned scenario.

Appendix

Definition 1. *[19] Riemann-Liouville fractional order integral of order $\alpha > 0$ for a function $f : R^+ \to R$ is defined by*

$$I^{\alpha} f(t) = \frac{1}{\Gamma(\alpha)} \int_0^t (t-\tau)^{\alpha-1} f(\tau)\, d\tau$$

and Caputo fractional order derivative of order $\alpha \in (n-1, n)$ of $f(t)$ is defined by

$$D^{\alpha} f(t) = I^{n-\alpha} D^{\alpha} f(t)$$

where $n = \lfloor \alpha \rfloor - 1$ and $D = d/dt$. Here and elsewhere Γ denotes the Gamma function.

Declaration of Competing Interests The authors declare that they have no competing interests.

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