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ANALYSIS OF A MODEL ON THE TRANSMISSION DYNAMICS (WITH PREVENTION AND CONTROL) OF HEPATITIS B

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Abstract. In this paper, the fractional order model for Hepatitis B was introduced that describes the transmission dynamics of the virus which also displays the suitable control and preventive measures that restrains the spread of the virus. The basic reproduction number was computed for the model using the next generation matrix approach. The critical point of the model was obtained by equating the derivative of the states variables to zero. The disease free equilibrium points were obtained. The endemic equilibrium point was also obtained for the model and their stability analyzed using Jacobian transformation. More over the numerical solution of the model was obtained using the Adams- type Predictor corrector method with the aid of MATLAB. The Simulation results conclusively indicate that the combination of vaccination and treatment as well as reduction of contact rates through creation of awareness is the most effective way to curb the spread of the virus.

1. Introduction

Hepatitis, derived from the Greek word hepar meaning "liver" and "itis" meaning "inflammation", simply means the inflammation of the liver[1]. It is caused by viruses, continuous exposure to alcohol, drugs or toxic chemicals (such as those contained in paint thinners and aerosol sprays) and bacterial infections[2]. The painful red swelling that occurs when body tissues become infected or injured is known as inflammation. Inflammation most time causes organs not to function properly. Thus Hepatitis reduces the liver's ability to perform certain life-preserving functions[3]. When viral Hepatitis is spoken of by medical experts, they are referring to Hepatitis caused by a few specific viruses that attacks the liver. Interestingly there are several viral hepatitis and they are types A, B, C, D, E, F (even though unconfirmed) and G[4].The alphabetical list may grow longer as the knowledge of Hepatitis viruses increases[5]. Types A, B and C are the most common types of viral Hepatitis[6]. However hepatitis B, C and D happens to be the most serious types of Hepatitis in the world[7]. In this paper, the case study is Hepatitis B which happens to be a potentially life threatening liver infection that is caused by the hepatitis B virus (HBV)[3]. It has two stages of infection namely: Acute and

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Chronic. The World Health Organization reported that more than one-third of the world's population is actively infected with Hepatitis B virus. Also, more than three hundred and fifty million of these have chronic infections and sadly twenty five to forty percent of them die of liver Cirrhosis (scarring of the liver) or primary Hepatocellular carcinoma (a type of liver cancer characterized by abnormal harmful growth(s) in the liver)[8]. Hepatitis B is the tenth leading cause of death worldwide[9]. Hepatocellular cancer (HCC) is the third most common cause of cancer death worldwide since it accounts for more than five hundred per year[10]. The prevalence of the disease ranges from over 10% in Asia to under 0.5% in the United States and Europe[11] . Ways in which people get infected include vertical transmission (through child birth), early life horizontal transmission (such as through bites and sanitary habits) and adult horizontal transmission (mainly sexual intercourse and intravenous drug use)[12]. The primary method by which HBV is transmitted is an important factor that determines the prevalence of chronic HBV in a given area. For instance, in low prevalence areas such as the United States and Western Europe, intravenous drug use and unprotected sexual intercourse are the primary methods of transmission. Meanwhile in moderate prevalence areas such as Japan and Russia where two to seven percent of the population is chronically infected, the disease is mostly spread among children. In areas of high prevalence such as Africa and China, transmission during child birth is most common. At least 8% of the population in areas of high endemicity is chronically infected[12]. Mathematical modeling of infectious diseases using integer order system of differential equations has gained a lot of attention over the past years[9, 13]. However, epidemiological models and other models in science and engineering have successfully been formulated and analyzed using fractional derivatives and integrals[14, 15]. Fractional derivatives are nonlocal as opposed to the local behavior of integer derivatives. This implies that the next state of a fractional system does not only depend on its current state but also upon all of its historical states [16]. The main objective of this thesis is to formulate an epidemiological model (Hepatitis B in this case) using fractional order derivatives which has an advantage over the classical integer order models owing to its memory effect feature. Qualitative stability analysis will be carried out on the model and numerical simulations will be performed.

2. Fractional Order Calculus

Fractional order models have been the focus of many studies due to their frequent appearance in various applications in several scientific fields. We first give the definition of fractional-order integration and fractional order differentiation. For the concept of fractional derivative, we will consider Caputo's definition. It has an advantage of dealing properly with initial value problem.

Definition 1 The Caputo Fractional derivative of order α of a function $f : \Re^+ \to \Re$ is given by

$$D_t^\alpha f(t) = \frac{1}{\Gamma(\alpha - n)} \int_\alpha^t \frac{f^{(n)}(\tau) d\tau}{(t-\tau)^{\alpha+1-n}} \qquad (n-1 < \alpha \leq n) \tag{1}$$

Definition 2 The formular for the Laplace transform of the Caputo derivative is

given by

$$\int_0^\infty e^{-pt}\{D_t^\alpha f(t)\}dt = p^\alpha F(p) - \sum_{k=0}^{n-1} p^{\alpha-k-1} f^{(k)}(0), \qquad (n-1 < \alpha \leq n) \quad (2)$$

Definition 3 The Fractional integral of order α of a function $f : \Re^+ \to \Re$ is given by

$$J^\alpha(f(x)) = \frac{1}{\Gamma(\alpha)} \int_0^x (x-t)^{\alpha-1} f(t)dt, \qquad \alpha > 0, x > 0 \quad (3)$$

Definition 4 The fractional integral of the Caputo Fractional derivative of order α of a function $f : \Re^+ \to \Re$ is given by

$$J^\alpha\{D^\alpha f(t)\} = f(t) - \sum_{k=0}^{n-1} f^{(k)}(0)\frac{t^k}{k!}, \qquad t > 0 \quad (4)$$

Definition 5 A two-parameter function of the Mittag-Leffler type is defined by the series expansion

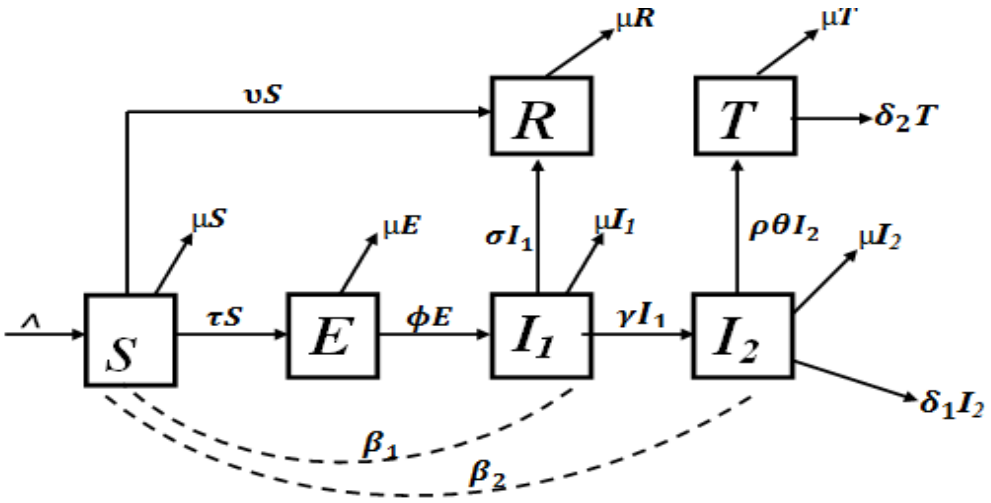
$$E_{\alpha,\beta}(z) = \sum_{k=0}^{\infty} \frac{z^k}{\Gamma(\alpha k + \beta)}, \qquad (\alpha, \beta > 0) \quad (5)$$

3. Model Formulation

In applying the SEITR model, we have succeeded in dividing the population into six classes namely; The Susceptible class (S); The Exposed class (E); The Acutely infectious class (I_1); The Chronically infectious class (I_2); The class undergoing treatment (T) The Removed class (R);The Susceptible class S consists of individuals that are yet to come in contact with the virus but are still capable of contracting the disease. The Exposed class E consists of individuals that are in their latent period of infection. This implies that they are the ones that have been infected with the virus but are incapable of spreading the virus. The Acutely infectious class I_1 contains individuals who have tested positive to the Hepatitis B virus within the duration of six months or less and are capable of infecting the susceptible class. The Chronically infectious class I_2 consists of individuals who have tested positive to the Hepatitis B virus for more than six months. The T compartment contains individuals who are undergoing treatment. The Removed R are those individuals that are permanently immune to the disease (either as a result of vaccine or recovery while at the acute stage of the illness) We assumed that population considered is non-constant;Any individual who recovers completely from the disease or who has been vaccinated receives a lifelong immunity from the disease;the Susceptible classes comprise of people of all age group who are equally likely to be infected by infectious individuals;The proportion of people that moves from the susceptible to the removed class directly is assumed to have received the required three doses of Hepatitis B vaccine;the treated class consists of people who are undergoing treatment to remain stable;the rate at which people die of the disease in the treated class is lesser than the rate at which people die of the disease in the chronically infectious class,that means δ_2 is lesser than δ_1;the contact rate between the chronically infectious class is greater than the contact rate between the acutely infectious class,this means thatβ_2 is greater than β_1;the acutely and chronically infectious classes ($I_1 and I_2$respectively) are capable of infecting the susceptible

population;The population in the treatment compartment will not recover from the illness;The acutely infectious individuals do not undergo any form of treatment but recover naturally from the ailment;The population undergoing treatment can still die as a result of the disease;The acutely infectious population does not die as a result of the disease. The schematic diagram of the disease on which we base our model is as follow:

FIGURE 1. Model Flow Diagram.



3.1. **Model Equation.**

$$\begin{cases} D_t^\alpha S(t) = \Lambda - \nu S - \beta_1 S I_1 - \beta_2 S I_2 - \mu S \\ D_t^\alpha E(t) = \beta_1 S I_1 + \beta_2 S I_2 - (\mu + \phi) E \\ D_t^\alpha I_1(t) = \phi E - I_1(\gamma + \mu + \sigma) \\ D_t^\alpha I_2(t) = \gamma I_1 - I_2(\mu + \delta_1 + \rho\theta) \\ D_t^\alpha T(t) = \rho\theta I_2 - (\delta_2 + \mu) T \\ D_t^\alpha R(t) = \nu S + \sigma I_1 - \mu R \end{cases} \tag{6}$$

For $0 < \alpha < 1$ with the following initial conditions: $S(0) > 0, E(0) > 0, I_1(0) > 0, I_2(0) > 0, T(0) > 0, R(0) > 0$.

3.2. **Lemma 1.** The closed set $\Omega = \{(S, E, I_1, I_2, T, R)\varepsilon R_+^6 : S + E + I_1 + I_2 + T + R \leq \frac{\Lambda}{\mu}\}$ is positively invariant with respect to model (6) Proof
The fractional derivative of the total human population, obtained by adding all the human equations of model (6), is given by

$$D^\alpha N(t) = \Lambda - \mu N(t) \tag{7}$$

Taking the Laplace transform of (7) gives:

$$S^{\alpha}N(s) - S^{\alpha-1}N(0) = \frac{\Lambda}{S} - \mu N(s)$$
$$\Rightarrow N(s) = \frac{\Lambda}{S(S^{\alpha}+\mu)} + \frac{S^{\alpha-1}}{s^{\alpha}+\mu}N(0) \tag{8}$$

Taking the inverse Laplace transform of (8), we have:

$$N(t) = N(0)E_{\alpha,1}(-\mu t^{\alpha}) + \Lambda t^{\alpha}E_{\alpha,\alpha+1}(-\mu t^{\alpha}) \tag{9}$$

where $E_{\alpha,\beta}$ is the Mittag-Leffler function. But the fact that the Mittag-Leffler functions has an asymptotic behavior[17, 18], it follows that:

$$E_{\alpha,1}N(t) = \sum_{k=0}^{\infty}\frac{N^K(t)}{\Gamma(\alpha k+1)}, \alpha > 0 \tag{10}$$

$$E_{\alpha,\alpha+1}N(t) = \sum_{k=0}^{\infty}\frac{N^K(t)}{\Gamma(\alpha k+\alpha+1)}, \alpha > 0 \tag{11}$$

Expanding (10), we have

$$E_{\alpha,1}N(t) = \frac{1}{\Gamma 1} + \frac{N(t)}{\Gamma(\alpha+1)} + \frac{N^2(t)}{\Gamma(2\alpha+1)} + ...$$

Expanding (11), we have

$$E_{\alpha,\alpha+1}N(t) = \frac{1}{\Gamma(\alpha+1)} + \frac{N(t)}{\Gamma(2\alpha+1)} + \frac{N^2(t)}{\Gamma(3\alpha+1)} + ...$$

Since Mittag-Leffler function has an asymptotic property, we have

$$N(t) = 1 + O(N)$$

Taking limit as k$\longrightarrow \infty$, we have

$$N(t) \approx 1$$

Then, it is clear that Ω is a positive invariant set.Therefore, all solutions of the model with initial conditions in Ω remain in Ω for all t > 0. Then , $\Omega = N(t) > 0$ implies that it is feasible with respect to model (6).

4. Model Analysis

4.1. **The Basic Reproduction Number, R_0.** We use the Next Generation Matrix. It is comprised of two parts: F and V^{-1},

$$R_0 = \rho(FV^{-1})$$

Where

$$F = \left|\frac{\partial f_i x_{(0)}}{\partial x_j}\right| , \qquad V = \left|\frac{\partial v_i x_{(0)}}{\partial x_j}\right|$$

ρ = spectral value (highest eigenvalue)
On the estimation,We used the following disease compartments:

$$D_t^{\alpha}E(t) = \beta_1 SI_1 + \beta_2 SI_2 - (\mu+\phi)E$$
$$D_t^{\alpha}I_1(t) = \phi E - I_1(\gamma+\mu+\sigma)$$
$$D_t^{\alpha}I_2(t) = \gamma I_1 - I_2(\mu+\delta_1+\rho\theta)$$
$$D_t^{\alpha}T(t) = \rho\theta I_2 - (\delta_2+\mu)T$$

Define

$$f_i = \begin{pmatrix} \beta_1 SI_1 + \beta_2 SI_2 \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

$$v_i = \begin{pmatrix} (\mu+\phi)\mathrm{E} \\ -\phi E + (\gamma+\sigma+\mu)I_1 \\ -\gamma I_1 + (\mu+\delta_1+\rho\theta)I_2 \\ -\rho\theta I_1 + (\mu+\delta_2)\mathrm{T} \end{pmatrix}$$

$$FV^{-1} = \begin{pmatrix} \frac{\Lambda}{(\mu+\nu)}\left(\frac{\beta_1\phi}{ab} + \frac{\beta_2\phi\gamma}{abc}\right) & \frac{\Lambda}{(\mu+\nu)}\left(\frac{\beta_1\phi}{b} + \frac{\beta_2\gamma}{bc}\right) & \frac{\Lambda}{(\mu+\nu)}\left(\frac{\beta_2}{c}\right) & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

where $a = (\mu+\phi), b = (\mu+\gamma+\sigma), c = (\mu+\delta_1+\rho\theta), d = (\mu+\delta_2)$
By characteristic equation, we have the dominant eigenvalue as follow:

$$R_0 = \frac{\Lambda\phi}{(\mu+\mu)(\mu+\phi)(\mu+\gamma+\sigma)}(\beta_1 + \frac{\beta_2\gamma}{(\mu+\delta_1+\rho\theta)}) \tag{12}$$

4.2. **Equilibrium Points and Stability.**

4.2.1. *Stability analysis of the disease free equilibrium point.* Interestingly, calculating the basic reproduction number using the next generation method approach automatically proves LAS (Locally Asymptotically Stable) of DFE[20]. Thus if R_0 is less than one, the DFE of the Hepatitis B model in systems (6) is Locally Asymptotically Stable but unstable if R_0 is greater than one. Epidemiological,$R_0 < 1$ implies that Hepatitis B will fizzle out with time and$R_0 > 1$ implies that an epidemic occurs.

4.2.2. *Stability analysis of the endemic equilibrium point.* The fractional model(6) is used in this case.The Jacobian matrix of the system is given as:

$$J = \begin{pmatrix} -(\mu+\beta_1 I_1+\beta_2 I_2+\nu) & 0 & -\beta_1 S & -\beta_2 S & 0 & 0 \\ \beta_1 I_1+\beta_2 I_2 & -(\mu+\phi) & \beta_1 S & \beta_2 S & 0 & 0 \\ 0 & \phi & -(\gamma+\sigma+\mu) & 0 & 0 & 0 \\ 0 & 0 & \gamma & -(\mu+\delta_1+\rho\theta) & 0 & 0 \\ 0 & 0 & 0 & \rho\theta & -(\mu+\delta_2) & 0 \\ \nu & 0 & \sigma & 0 & 0 & -\mu \end{pmatrix} \tag{13}$$

At EEP, the Jacobian matrix becomes:

$$J^* = \begin{pmatrix} -(\mu+\beta_1 I_1^*+\beta_2 I_2^*+\nu) & 0 & -\beta_1 S^* & -\beta_2 S^* & 0 & 0 \\ \beta_1 I_1+\beta_2 I_2^* & -(\mu+\phi) & \beta_1 S^* & \beta_2 S^* & 0 & 0 \\ 0 & \phi & -(\gamma+\sigma+\mu) & 0 & 0 & 0 \\ 0 & 0 & \gamma & -(\mu+\delta_1+\rho\theta) & 0 & 0 \\ 0 & 0 & 0 & \rho\theta & -(\mu+\delta_2) & 0 \\ \nu & 0 & \sigma & 0 & 0 & -\mu \end{pmatrix} \tag{14}$$

where

$S^* = \frac{(\mu+\phi)(\mu+\gamma+\sigma)(\mu+\delta_1+\rho\theta)}{\phi(\beta_2\gamma+\beta_1(\mu+delta_1+\rho\theta))}$

$I_1^* = \frac{\phi\Lambda}{(\mu+\phi)(\mu+\gamma+\sigma)} - \frac{(\mu+\delta_1+\rho\theta)(\mu+\nu)}{(\beta_2\gamma+\beta_1(\mu+\delta_1+\rho\theta))}$

$I_2^* = \frac{\phi\Lambda\gamma[(\beta_2\gamma+\beta_1(\mu+\delta_1+\rho\theta))-(\mu+\delta_1+\rho\theta)(\mu+\nu)(\mu+\gamma+\sigma)(\mu+\phi)]}{(\mu+\delta_1+\rho\theta)(\mu+\gamma+\sigma)((\beta_2\gamma+\beta_1(\mu+\delta_1+\rho\theta))}$

Next, we find the Characteristic equation which is given by $|J^* - \lambda I| = 0$, where λ is the eigenvalue.

For simplicity, let

$a = \mu+\nu, b = \beta_1 I_1^* + \beta_2 I_2^*, h = a+b, c = \phi+\mu, d = \gamma+\sigma+\mu, e = \mu+\delta_1+\rho\theta, f = \beta_1 S^*, g = \beta_2 S^*, k = \mu+\delta_2$

$$\implies |J^0 - I\lambda| = \begin{bmatrix} -h-\lambda & 0 & -f & -g & 0 & 0 \\ b & -c-\lambda & f & g & 0 & 0 \\ 0 & \phi & -d-\lambda & 0 & 0 & 0 \\ 0 & 0 & \gamma & -e-\lambda & 0 & 0 \\ 0 & 0 & 0 & \rho\theta & -k-\lambda & 0 \\ \nu & 0 & \sigma & 0 & 0 & -\mu-\lambda \end{bmatrix} = 0 \tag{15}$$

$$\implies (\mu+\lambda)(k+\lambda)\begin{bmatrix} -h-\lambda & 0 & -f & -g \\ b & -c-\lambda & f & g \\ 0 & \phi & -d-\lambda & 0 \\ 0 & 0 & \gamma & -e-\lambda \end{bmatrix} = 0 \tag{16}$$

it can be observed that $\lambda_1 = -\mu, \lambda_2 = -k < 0$

$$\implies \begin{bmatrix} -h-\lambda & 0 & -f & -g \\ b & -c-\lambda & f & g \\ 0 & \phi & -d-\lambda & 0 \\ 0 & 0 & \gamma & -e-\lambda \end{bmatrix} = 0 \tag{17}$$

$\implies -(h+\lambda)[-(c+\lambda)(d+\lambda)(e+\lambda) + \phi f(e+\lambda) + \phi g\gamma] + \phi f(e+\lambda)b + \phi g\lambda b = 0.$
Further work yields:
$\lambda^4 + (c+d+e+h)\lambda^3 + (cd+ce+de+hc+hd+he-f\phi)\lambda^2 + (hce+hde+cde+hcd+f\phi b - f\phi e - g\phi\gamma - f\phi h)\lambda + hcde + fbe\phi + gb\gamma\phi - feh\phi - hg\gamma\phi = 0$
Let the coefficients of$\lambda^4, \lambda^3, \lambda^2, \lambda$ and the constant be represented as$a_0, a_1, a_2, a_3, a_4, a_5$ so that
$a_0 = 1$
$a_1 = (c+d+e+h)$
$a_3 = (cd+ce+de+hc+hd+he-f\phi)$
$a_4 = (hce+hde+cde+hcd+f\phi b - f\phi e - g\phi\gamma - f\phi h)$
$a_5 = hcde + fbe\phi + gb\gamma\phi - feh\phi - hg\gamma\phi.$

According to Routh-Hurwitz's criterion, all the roots of the equation will be less than zero if the following conditions are met:

(1) if all the coefficients and constant terms are greater than zero;
(2) If $a_1a_2 > a_3$ and $a_3 > \frac{a_1^2 a_4}{a_1a_2 - a_3}$.

If all these conditions are met, then it follows that all the eigenvalues satisfy the condition $|arg(\lambda)| > \frac{\alpha\pi}{2}$.

5. Numerical Simulation

We used MATLAB to get the numerical solution of our model by applying Adams-type predictor-corrector method. This method is well known for numerical solutions of first-order problems[20].

Table 1. Estimated initial conditions and the parameters with values and their sources

Parameter	**Value**	**Source**
Λ	0.0260	Assumed
μ	0.0121	[21]
ν	0.0211	Assumed
ϕ	0.0012	[21]
δ_1	0.0026	Assumed
γ	0.03	Assumed
β_2	0.5310	Assumed
β_1	0.3810	Assumed
σ	0.9842	[22]
ρ	0.0026	Assumed
θ	0.2300	Assumed

Variable at initial condition	**Value**	**Source**
$S(0)$	1000	Estimated
$E(0)$	20	Estimated
$I_1(0)$	5	Estimated
$I_2(0)$	10	Estimated
$T(0)$	3	Estimated
$R(0)$	15	Estimated

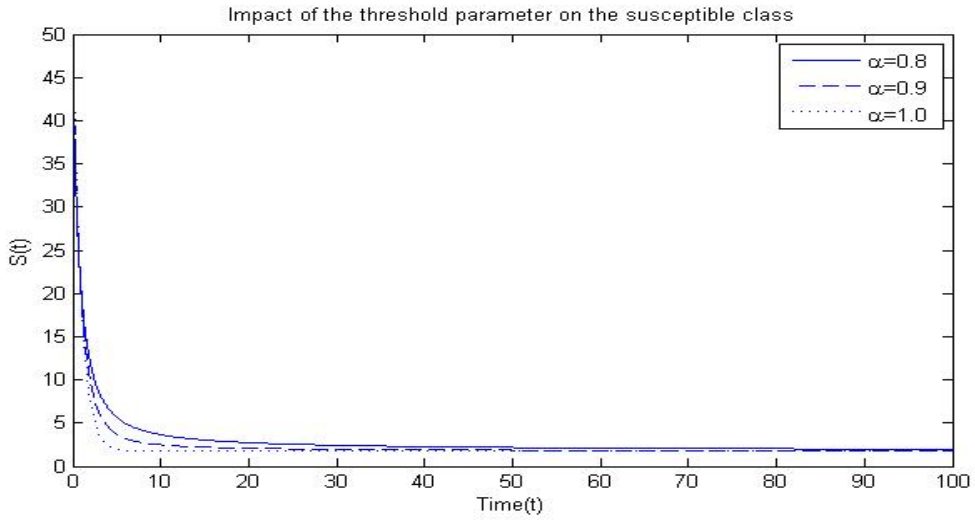


FIGURE 2. Dynamics of the Susceptible Population.

This graph shows the variation of the susceptible population with time when $R_0 < 1$.This shows that the model would be asymptotically stable when $R_0 < 1$ which means that the virus will not invade the population rather it will die off with time as the decreasing curve does not intercept the horizontal axis. This also shows that the fractional order (like $\alpha = 0.8$) gave a better result than the integer order ($\alpha = 1.0$).

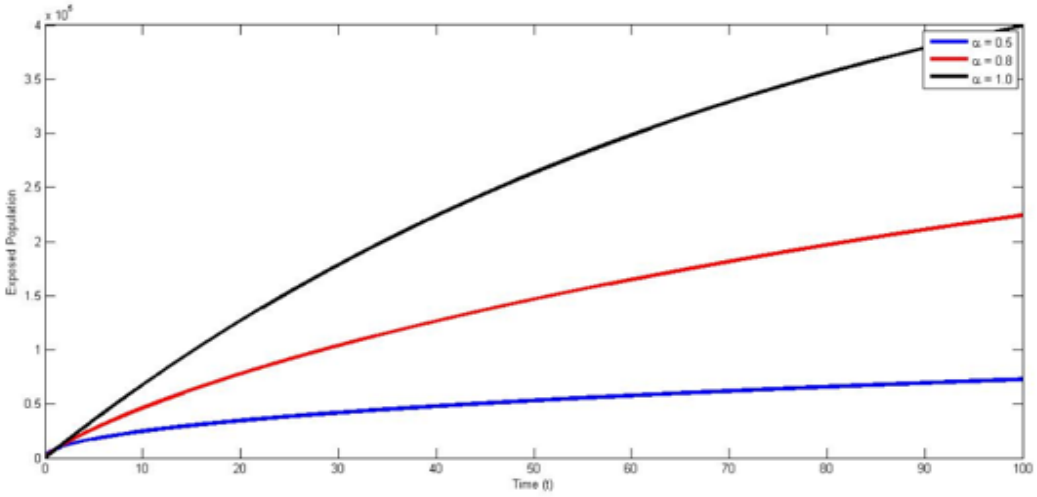


FIGURE 3. Dynamics of the Exposed population with $R_0 < 1$, $\beta_1 = 0.3810$ and $\beta_2 = 0.5310$.

The density of the Exposed nodes with varying values of α.

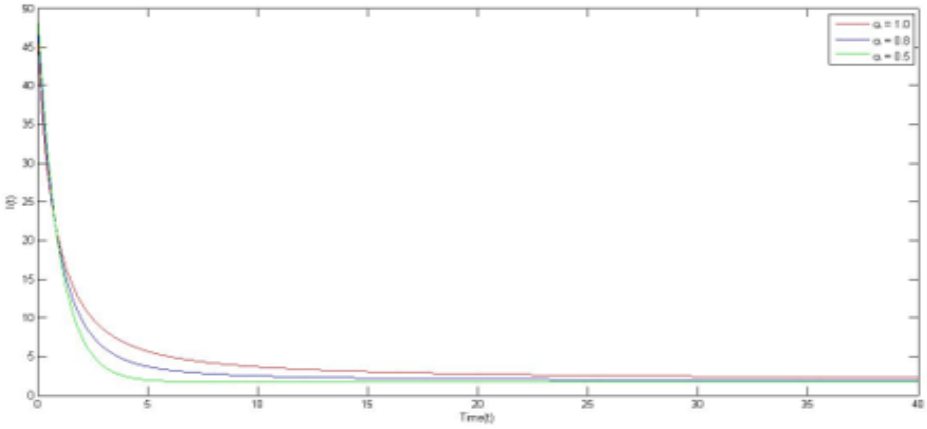


FIGURE 4. Dynamics of the Infectious Class with time when $\gamma = 0.03$

This shows that Infectious class decreases over time when $R_0 < 1$.

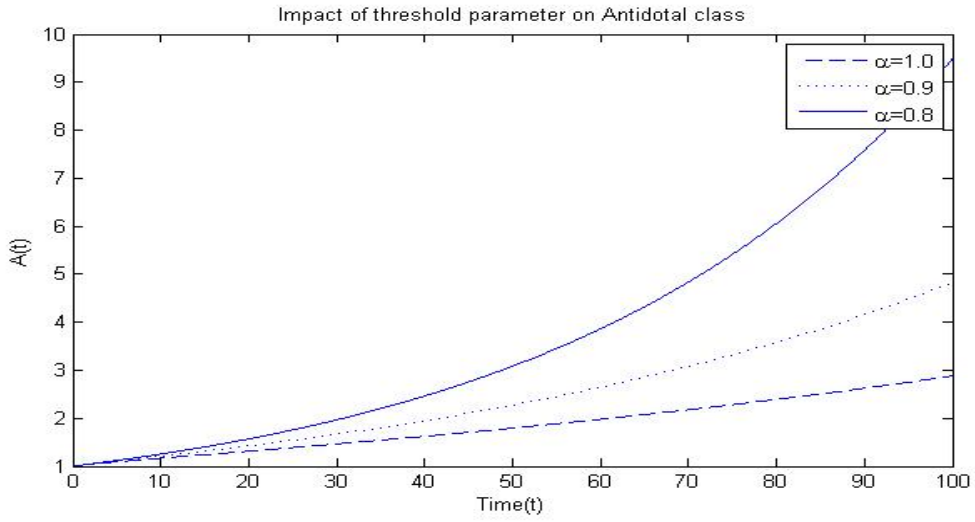


FIGURE 5. Dynamics of the Recovered Class

This shows that the Recovered class increases over time when $R_0 < 1$. Clearly, it can also be seen that as the value of α increases, the model becomes unstable telling us that the fractional case gives a better result than the classical case.

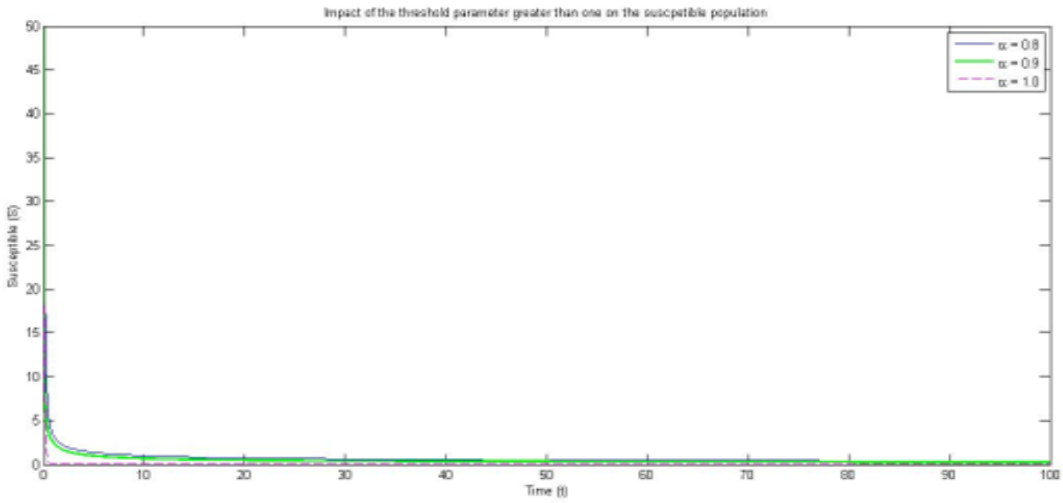


FIGURE 6. Dynamics of the Susceptible Class

The density of the Susceptible nodes with $R_0 > 1$ with different values of α.

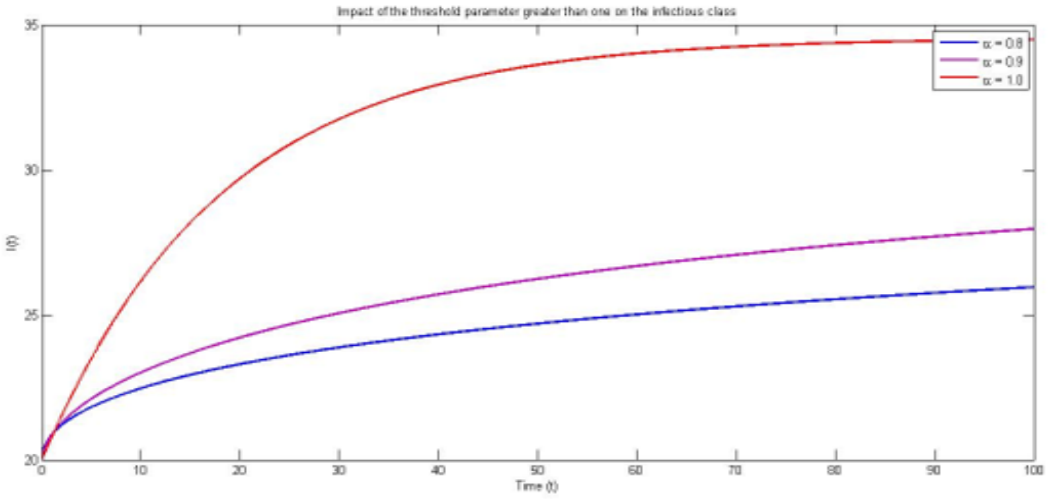


FIGURE 7. Dynamics of the Infectious Class

The density of the Infectious nodes with $R_0 > 1$ with different values of α.

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