CAPUTO-FABRIZIO FRACTIONAL DERIVATIVE CHOLERA MODEL

[1]

Abstract

We develop a cholera transmission model by incorporating Caputo-Fabrizio fractional derivatives to account for memory effects, enhancing realism in capturing vaccination dynamics and optimal re-vaccination time. Analysis of the model show that the Disease Free Equilibrium is asymptotically stable whenever $\tilde{R}_0 < \frac{1}{2-q}$ and if $\tilde{R}_0 > \frac{1}{2-q}$ the Endemic Equilibrium is asymptotically stable. Numerical simulations of the model indicates that when q is high the model mimics classical models, while when q is low the transmission intensity reduces and there is delays in outbreaks. Simulations of the waning effect of the vaccine reveals that it takes approximately 2.083 years for an individual to be re-vaccinated after full cholera vaccine dosage. Thus the study advocates for timely re-vaccination for targeted public health interventions to be realized.

Subject Classification: xxxxxx

Keywords: Fractional-order, Stability, Waning effect

1 Introduction

Cholera is an acute intestinal infection caused by bacterium *Vibrio cholerae*. Once the bacteria is ingested, it causes vomiting and watery diarrhoea leading to dehydration and eventually cause a drop in blood pressure and kidney failure. Watery loose bowels are the initial symptoms which appear in cholera patients. If not immediately treated, conceivable death may happen within few days since the incubation period of cholera is between 24 hours and 5 days, see [4].

[1]

Cholera is transmitted through ingestion of food or water contaminated with the bacterium *Vibrio cholerae*. The infection can spread rapidly in populations without safe drinking water, adequate sanitation and hygiene and those with limited medical resources, see in [4]. It is controlled through a combination of sanitation, provision of clean water and hygiene (WASH) practices. The World Health Organization (WHO)in [13] recommends the use of oral cholera vaccines, Dukoral and Shanchol for those at high risk, see in [5]. Though these vaccines are considered to reduce the spread of the disease, they are documented not to be 100% effective and also wane with time in the human body, see in [12].

Mathematical models play a key role in cholera transmission by allowing researchers to simulate and predict the spread of the disease within a population. The models have been widely used to assess the effectiveness of vaccination and estimate the effort required to eliminate an infection from the population. Thus, this study seeks to develop a mathematical model to investigate the optimal time to re-vaccinate individuals so as to provide continuous immunity against cholera.

This paper is divided into the following sections; In section two we develop the model, in section three we perform qualitative analysis of the model, in section four stability analysis of the model is done, and in section five and six, we perform numerical simulation and conclusion of the model.

2 Development of the Model

The original ODE model, as described in [8], is reformulated using non-singular Caputo-Fabrizo fractional derivatives to incorporate memory effects. This modification avoids dimensional mismatching and retains the kernel's exponential decay property. We develop a Caputo Fabrizio model using fractional derivatives of order q, that takes the form:-

$$\begin{aligned}
{}_0^{CF}\mathcal{D}_t^q S &= f_1(S) := \Lambda - \phi S - \beta_2 S\lambda(B) - \mu S + \eta R,\\
{}_0^{CF}\mathcal{D}_t^q V &= f_2(V) := \phi S - (1-\delta)\beta_1 V\lambda(B) - \mu V,\\
{}_0^{CF}\mathcal{D}_t^q I &= f_3(I) := \beta_2 S\lambda(B) + (1-\delta)\beta_1 V\lambda(B) - (\mu + d + \gamma + \alpha)I,\\
{}_0^{CF}\mathcal{D}_t^q R &= f_4(R) := \gamma I - (\mu + \eta)R,\\
{}_0^{CF}\mathcal{D}_t^q Z &= f_5(Z) := \alpha I - (\epsilon + \rho)Z,\\
{}_0^{CF}\mathcal{D}_t^q B &= f_6(B) := \psi + \epsilon Z - \rho B,
\end{aligned} \tag{1}$$

where: $\lambda(B) := \frac{B}{K+B}$ and $(0 < \delta < 1)$ is the waning rate of the vaccine, subject to non-negative initial conditions

$$S(0) \geq 0, V(0) \geq 0, I(0) \geq 0, R(0) \geq 0, Z(0) \geq 0, \text{ and } B(0) \geq 0.$$

We let the total human population at time t be denoted by $N(t)$ which is divided into four compartmental sub-classes, that is; susceptible $S(t)$ to denote the size of the population at a time t that are not infected to Cholera; $V(t)$ to be the vaccinated individuals at a time t ; $I(t)$ to represent the infected individuals at a time t, while $R(t)$ to be the number of individuals who have recovered from cholera at a time t. We classify the pathogen population into two compartments; environmental pathogen to be denoted by $B(t)$ and human pathogens to be described by $Z(t)$ at a time t. New recruitment (which is mainly by birth) is assumed to enter the population at a constant rate Λ, and ϕ is regarded as rate of vaccination. Assuming that the vaccine is imperfect (wanes with time), we denote δ waning rate of the vaccine. For instance if $\delta \equiv 0$, it means that the waning rate of the vaccine is high and individuals are at high risk of contracting the disease, while if $\delta \equiv 1$ it implies that the waning rate of the vaccine is at low level and hence vaccine is completely effective in preventing infection.

Cholera transmission in this paper is considered to be only through environment-to-human pathways, in particular, suscpetible individuals are infected by ingesting environmental vibrio-cholerae and the infection rates are $\beta_1 \frac{B}{K+B}$ and $\beta_2 \frac{B}{K+B}$ where β_1 is the probability of vaccinated individuals getting infected and β_2 is the transmission probability of unvaccinated individuals. The parameter K stands for carrying capacity of the pathogen while μ and d represents natural death rate and disease induced death rate respectively. The recovered group join the susceptible class at the rate denoted by η and infected cohort joins recovery class at the rate γ. We denote α as the growth rate of human vibrios within the body, and ϵ to be the rate at which vibrios is excreted to the environment. Finally, ψ is the intrinsic growth rate of human vibrios and ρ is the death rate of vibrios.

3 Qualitative Analysis of the Model

3.1 Existence and Uniqueness

In this section we show existence and uniqueness of Equation (1) using fixed point theorem, as described in [3]. Equation (1) is in CF fractional integral form, which is equivalent to the voltera integral equation type of order $0 < q < 1$ given thus:

$$\begin{aligned} S(t) &= S(0) + \frac{(1-q)}{\mathcal{M}(q)} f_1(S(t)) + \frac{q}{\mathcal{M}(q)} \int_0^t f_1(S(\tau)) d\tau, \\ V(t) &= V(0) + \frac{(1-q)}{\mathcal{M}(q)} f_2(V(t)) + \frac{q}{\mathcal{M}(q)} \int_0^t f_2(V(\tau)) d\tau, \end{aligned}$$

$$
\begin{aligned}
I(t) &= I(0) + \frac{(1-q)}{\mathcal{M}(q)} f_3(I(t)) + \frac{q}{\mathcal{M}(q)} \int_0^t f_3(I(\tau)) d\tau, \\
R(t) &= R(0) + \frac{(1-q)}{\mathcal{M}(q)} f_4(R(t)) + \frac{q}{\mathcal{M}(q)} \int_0^t f_4(R(\tau)) d\tau, \\
Z(t) &= Z(0) + \frac{(1-q)}{\mathcal{M}(q)} f_5(Z(t)) + \frac{q}{\mathcal{M}(q)} \int_0^t f_5(Z(\tau)) d\tau, \\
B(t) &= B(0) + \frac{(1-q)}{\mathcal{M}(q)} f_6(B(t)) + \frac{q}{\mathcal{M}(q)} \int_0^t f_6(B(\tau)) d\tau.
\end{aligned} \tag{2}
$$

Next, the Kernels f_1, f_2, f_3, f_4, f_5, and f_6 are shown to be Lipschtizian. To do so, Lemma 1 is stated and proven.

Lemma 1. *The vector field in Equation (1) is autonomous and is Lipschitz continuous.*

Proof. For any (S, V, I, R, Z, B) and $(S^*, V^*, I^*, R^*, Z^*, B^*)$, Equation (1) shows that, $f_1(S, V, I, R, Z, B) = f_1(S)$ and $f_1(S^*, V^*, I^*, R^*, Z^*, B^*) = f_1(S^*)$. Then,

$$
\begin{aligned}
\|f_1(S) - f_1(S^*)\| &\leq \|\phi(S(t) - S^*(t)) + \beta_2(\lambda(B)S(t) - \lambda(B^*)S^*(t)) + \mu(S(t) - S^*(t))\| \\
&\leq \|(S(t) - S^*(t))\|(\phi + \mu + \beta_2\epsilon_1) \\
&= l_1\|(S(t) - S^*(t))\|,
\end{aligned} \tag{3}
$$

where $0 < l_1 = \phi + \mu + \beta_2\epsilon_1$ and $\epsilon_1 = max\{\|\lambda(B)\|, \|\lambda(B^*)\|\} < 1$. Where for any $\|x(t)\| = \sup|x(s)|$ with $|.|$ denoting the usual euclidean norm. Hence $f_1(S)$ is Lipschitzian.

Using the same procedure, $f_2(V)$, $f_3(I)$, $f_4(R)$, $f_5(Z)$, and $f_6(B)$ are also Lipschitzian. Hence the vector field in Equation (1) is Lipschitz continuous.

Hence, we state the following theorem

Theorem 1. *Let* $0 < q < 1, f \in C, \quad M = sup\{|f(t,x)|, x \in C\}$

$$\|f(t,x) - f(t,y)\| \leq K\|x - y\| \quad \textit{for any} \quad x, y \in C.$$

Then the IVP ${}^{CF}_{t_0}\mathcal{I}^q_t x(t) = f(t, x(t)) \;\; t \in J$ *and with* $f \in C$, $x(t_0) = x_0, \quad t_0 \in J$ *has a unique solution on* J *if* $\max\left\{K\left(\frac{1-q}{\mathcal{M}(q)} + \frac{qb}{\mathcal{M}(q)}\right)\right\} < 1$ *where* K *is a Lipschitz constant.*

□

3.2 Positivity and Boundedness of the solution

Positivity and boundedness of solutions are proven, confining trajectories to a biologically feasible region Ω, where human and pathogen populations remain non-negative and bounded.

Theorem 2. *The solution of Equation (1) is bounded and positive for all time $t \geq 0$ in the region $\Omega \in \{\mathbb{R}^4_+ \times \mathbb{R}^2_+\}$,*

$$\Omega = \Big\{(S,V,I,R) \in \mathbb{R}^4_+; (Z,B) \in \mathbb{R}^2_+ : (S(t),V(t),I(t),R(t)) \leq \frac{\Lambda}{\mu}, (Z(t),B(t)) \leq \frac{\psi}{\rho}\Big\}$$

Proof. (i) (Boundedness) Consider the fractional derivative of the human population. Let $N(t) := S(t) + V(t) + I(t) + R(t)$. Adding the corresponding left and right terms in first four equations of Equation (1) gives:

$$\begin{aligned} {}^{CF}_{0}\mathcal{D}^q_t N(t) &= \Lambda - \mu N(t) + R(t) - (d+\alpha)I(t), \\ &\leq \Lambda - \mu N(t). \end{aligned} \tag{4}$$

Taking Laplace transform, Equation (4) becomes

$$\begin{aligned} \mathcal{L}\{{}^{CF}_{0}\mathcal{D}^q_t N(t)\} &\leq \mathcal{L}\{\Lambda - \mu N(t)\}, \\ \frac{\mathcal{M}(q)(sN(s) - N_0)}{q + s(1-q)} &\leq \frac{\Lambda}{s} - \mu N(s), \\ \Big[\frac{s\mathcal{M}(q)}{q+(1-q)s} + \mu\Big]N(s) &\leq \frac{\Lambda}{s} + \frac{\mathcal{M}(q)N_0}{q+s(1-q)}, \\ N(s) &\leq \Big(\frac{\Lambda}{s} + \frac{\mathcal{M}(q)N_0}{q+s(1-q)}\Big)\Big[\frac{s\mathcal{M}(q)}{q+(1-q)s} + \mu\Big]^{-1} \end{aligned} \tag{5}$$

where $N(s) := \mathcal{L}\{N(t)\}$. Taking the inverse Laplace transform of Equation(5),

$$\begin{aligned} N(t) &\leq \frac{\Lambda}{\mu} + \Big(\frac{\Lambda(1-q) + \mathcal{M}(q)N_0}{\mathcal{M}(q) + \mu(1-q)} - \frac{\Lambda}{\mu}\Big)\exp\Big(\frac{-\mu t}{\mathcal{M}(q) + \mu(1-q)}\Big) \\ \lim_{t\to\infty} N(t) &\leq \frac{\Lambda}{\mu} \end{aligned} \tag{6}$$

Hence, the solutions to the human population dynamics will be bounded for all time t.

Adding the corresponding left and right terms in last two equations of Equation (1), describing pathogen population, gives

$$\begin{aligned} {}^{CF}_{0}\mathcal{D}^q_t N_B(t) &= \psi - \rho N_B(t) + \alpha I \\ &\leq \psi - \rho N_B + \frac{\alpha\Lambda}{\mu} \end{aligned} \tag{7}$$

where $N_B(t) = Z(t) + B(t)$. Taking Laplace transform to both sides of Equation (7) becomes, in a manner analogous to the case of the human population,

$$N_B(t) \leq \frac{\psi}{\rho} + \frac{\alpha\Lambda}{\mu}.$$

Hence, the solution to the vibrios population dynamics will be bounded for all time t, and thus the solution of Equation (1) is bounded for all $t \geq 0$.

(ii) (Positivity) Using the first equation of Equation (1),

$$\begin{aligned} {}_0^{CF}\mathcal{D}_t^q S &= \Lambda - (\phi + \mu + \beta_2\lambda(B))S + \eta R, \\ &\geq \Lambda - (\phi + \mu + \beta_2\epsilon_1)S, \end{aligned} \tag{8}$$

where $\epsilon_1 = \|\lambda(B)\| < 1$. Using Laplace transform on Equation (8):

$$S(t) \geq \frac{\Lambda}{(\phi + \mu + \beta_2\epsilon_1)} =: \gamma_1 > 0$$

which is non-negative for all time t. Using the same procedure and utilizing the use of Laplace transform, all the state variables are positive for all time t.

□

Equation (1)is positive and bounded, hence the model decsribes human and vector population.

3.3 Equilibrium Points

In this paper, there are two types of equilibrium points, namely; Disease Free Equilibrium (DFE) point (in the absence of cholera) and Endemic Equilibrium (EE) point (in the presence of the cholera). To obtain the DFE, we set ${}_0^{CF}\mathcal{D}_t^q S = 0, {}_0^{CF}\mathcal{D}_t^q V = 0, {}_0^{CF}\mathcal{D}_t^q I = 0, {}_0^{CF}\mathcal{D}_t^q R = 0, {}_0^{CF}\mathcal{D}_t^q Z = 0, {}_0^{CF}\mathcal{D}_t^q B = 0$, with $I = R = Z = B = 0$, thus the model developed in Equation (1) has a DFE given by

$$E_{0C} = \left(\frac{\Lambda}{\mu + \phi}, \frac{\phi\Lambda}{\mu(\phi + \mu)}, 0, 0, 0, 0\right). \tag{9}$$

The Endemic Equilibrium (EE) states of the model is given by:

$$\begin{aligned} S^* &= \frac{\Lambda(\eta + \mu)(d + \alpha + \gamma + \mu)(\mu + (1 - \delta)\beta_2\lambda(B^*))}{\Theta}, \quad V^* = \frac{\Lambda(\eta + \mu)(d + \alpha + \gamma + \mu)\phi}{\Theta}, \\ I^* &= \frac{(\eta + \mu)}{\gamma}R^*, \quad R^* = \frac{\Lambda}{\eta}\Big(1 + \frac{\zeta}{\Theta}\Big), \quad Z^* = \frac{\alpha}{(\epsilon + \rho)}I^*, \quad B^* = \frac{\psi}{\rho} + \frac{\epsilon Z^*}{\rho}, \end{aligned} \tag{10}$$

where

$$\zeta = (\eta+\mu)(d+\alpha+\gamma+\mu)(\mu+(1-\delta)\lambda(B)\beta_2)(\mu+\phi+\lambda(B)\beta_1),$$

and

$$\Theta = \gamma\eta(1-\delta)\phi\beta_2\lambda(B)+\Big(\mu+(1-\delta)\beta_2\lambda(B)\Big)\Big(\gamma\eta\lambda(B)\beta_1+(d+\alpha+\mu+\gamma)(\eta+\mu)(\mu+\phi\beta_1\lambda(B))\Big).$$

3.4 Reproduction Number

In this section we derive the reproduction number for fractional derivative. In the context of Caputo-Fractional derivatives, the number of secondary infections produced by a single infected individual can be expressed as the product of the expected duration of the infectious period and the rate at which secondary infections occur, see in [11]. The expected time the index case spends in each compartment is given by the integral

$$\int_0^\infty \varphi(t,x_0)dt \tag{11}$$

The function $\varphi(t,x_0)$ is interpreted as the probability that the index case (introduced at time $t=0$) is in disease state at time t. With $N := \mathcal{M}(q)I + (1-q)V$ being invertible,

$$\begin{aligned} \varphi(t,x_0) &= \mathcal{M}(q)e^{-qNVt}Nx_0 \\ \int_0^\infty \varphi(t,x_0)dt &= \mathcal{M}(q)\int_0^\infty e^{-qNVt}Nx_0dt = \frac{\mathcal{M}(q)}{q}V^{-1}x_0 \end{aligned} \tag{12}$$

The expected number of secondary infections produced by the index case is

$$\begin{aligned} \mathcal{M}(q)\int_0^\infty Fe^{-qNVt}Nx_0dx &= \mathcal{M}(q)F\int_0^\infty e^{-qNVt}Nx_0dt \\ &= \frac{\mathcal{M}(q)}{q}FV^{-1}x_0 \end{aligned} \tag{13}$$

where FV^{-1} are the eigenvalues in the Caputo-Fabrizo sense, and thus the next generation matrix for the Caputo-Fabrizo fractional differential equation is

$${}^{CF}R_0 = \frac{\mathcal{M}(q)}{q}\frac{qR_0}{\mathcal{M}(q)-(1-q)R_0} = \frac{\mathcal{M}(q)R_0}{\mathcal{M}(q)-(1-q)R_0} \tag{14}$$

Since $\mathcal{M}(q)=1$, the reproduction number for the Caputo-Fabrizio model is

$${}^{CF}R_0 = \tilde{R}_0 = \frac{R_0}{1-(1-q)R_0}. \tag{15}$$

where R_0 is the reproduction number for the integer model and is given by

$$R_0 = \frac{\alpha\epsilon}{\rho(\epsilon+\rho)Y}\Big[\frac{\beta_2\Lambda}{K(\phi+\mu)}+(1-\delta)\frac{\beta_1\phi\Lambda}{K\mu(\mu+\phi)}\Big]. \tag{16}$$

4 Stability Analysis

Local and global stability of Equation(4) is assessed via Jacobian matrices and use of Lyapunov functions respectively.

4.1 Disease Free Equilibrium

To investigate local stability of the DFE, we state Proposition 1.

Proposition 1. *If* $\tilde{R}_0 < \frac{1}{2-q}$, *then* E_{0C} *of Equation (1) is locally asymptotically stable.*

Proof. The Jacobi matrix of Equation of (1) at DFE (E_{0C}) is:

$$J(E_{0C}) = \begin{pmatrix} -\phi-\mu & 0 & 0 & \eta & 0 & -\frac{\beta_2\Lambda}{K(\phi+\mu)} \\ \phi & \mu & 0 & 0 & 0 & -(1-\delta)\frac{\beta_1\phi\Lambda}{K\mu(\phi+\mu)} \\ 0 & 0 & -Y & 0 & 0 & \frac{\beta_2\Lambda}{(\phi+\mu)} + (1-\delta)\frac{\beta_1\phi\Lambda}{K\mu(\phi+\mu)} \\ 0 & 0 & \gamma & -(\mu+\eta) & 0 & 0 \\ 0 & 0 & \alpha & 0 & -(\epsilon+\rho) & 0 \\ 0 & 0 & 0 & 0 & \epsilon & -\rho \end{pmatrix}. \tag{17}$$

On using Mathematica solver, three of the eigenvalues are $\lambda_1 := -(\phi+\mu), \lambda_2 := -\mu$ and $\lambda_3 := -(\mu+\eta)$. The other three eigenvalues are obtained from the following reduced matrix

$$J_1E_0) := \begin{pmatrix} -(\mu+d+\gamma+\alpha) & 0 & \frac{\beta_2\Lambda}{K(\phi+\mu)} + (1-\delta)\frac{\beta_1\phi\Lambda}{K\mu(\phi+\mu)} \\ \alpha & -(\epsilon+\rho) & 0 \\ 0 & \epsilon & -\rho \end{pmatrix} \tag{18}$$

Applying Hurwitz Criterion, see for instance [10], the trace of $J_1(E_{0C})$ is

$$-\rho - Y - (\epsilon+\rho) \tag{19}$$

and is negative while its determinant is positive if

$$\frac{-\beta_2\epsilon\alpha\Lambda}{K\rho(\phi+\mu)} - \epsilon\alpha(1-\delta)\frac{\beta_1\phi\Lambda}{K\mu\rho(\phi+\mu)} + (\mu+d+\gamma+\alpha)(\epsilon+\rho) > 0 \tag{20}$$

Using the expression of R_0, Equation (20) reduces to

$$Y(\epsilon+\rho)(1-R_0) > 0 \tag{21}$$

hence guarantees local asymptotic stability if $R_0 < 1$. Since $\tilde{R}_0 = \frac{R_0}{1-(1-q)R_0} < 1$, from the last equality, we have

$$\begin{aligned} R_0 &< 1-(1-q)R_0 \\ &< \frac{1}{2-q} \end{aligned} \tag{22}$$

Thus $\tilde{R}_0 \approx R_0 < \frac{1}{2-q}$, and hence guarantees local asymptotic stability if $\tilde{R}_0 < \frac{1}{2-q}$. □

To determine the global stability of the DFE, a Lyapunov functional is constructed to enable us determine the global stability of the DFE.

Proposition 2. *The disease free equilibrium E_{0C} is globally asymptotically stable if $\tilde{R}_0 < \frac{1}{2-q}$, otherwise it is unstable.*

Proof. We consider the following Lyapunov functional

$$L_0(t) = \{S(t) - S_0 - S_0 \ln \frac{S(t)}{S_0}\} + \{V(t) - V_0 - V_0 \ln \frac{V(t)}{V_0}\} \tag{23}$$

Taking the derivative of L_0 in Equation (23) along the trajectory of the solutions, we obtain

$$\begin{aligned} {}_0^{CF}\mathcal{D}_t^q L_0(t) &= \dot{S}(t) - \frac{S_0}{S(t)}(\Lambda - \phi S_0 - \mu S_0) + \dot{V}(t) - \frac{V_0}{V(t)}(\phi S_0 - \mu V_0) \\ &\leq \Lambda\Big(1 - \frac{S_0}{S(t)}\Big) - \mu S_0\Big(1 - \frac{S_0}{S(t)}\Big) - \phi S_0\Big(1 - \frac{S_0}{S(t)}\Big) - \mu V_0\Big(1 - \frac{S_0}{S(t)}\Big) \end{aligned} \tag{24}$$

It follows that ${}_0^{CF}\mathcal{D}_t^q L_0(t) \leq 0$. at the DFE. Therefore, by Lasalle's invariance principle, as described in [7], the system has a global asymptotic stability provided $\tilde{R}_0 < \frac{1}{2-q}$. □

4.2 Endemic Equilibrium

Cholera is endemic or persistent in the population if

$$E_C^* := (S^*(t), V^*(t), I^*(t), R^*(t), Z^*(t), B^*(t)) \in \mathbb{R}_+^6$$

for all $t > 0$. To investigate the local stability of the EE for the fractional derivative cholera model, we state the following Proposition 3.

Proposition 3. *If $\tilde{R}_0 > \frac{1}{2-q}$, then E_C^* is an equilibrium state in Ω and is locally asymptotically stable.*

Proof. To investigate the stability of E_C^* of Equation (1), we linearize the system at E_C^* to obtain:-

$$J(E_C^*) := \begin{pmatrix} -\phi - \frac{\beta_2 B^*}{K+B^*} - \mu & 0 & 0 & \eta & 0 & -\frac{\beta_2 S^* K}{(K+B^*)^2} \\ -\phi & -(1-\delta)\frac{\beta_1 B^*}{K+B^*} - \mu & 0 & 0 & 0 & -(1-\delta)\frac{\beta_1 V^* K}{(K+B^*)^2)} \\ \frac{\beta_2 B^*}{K+B^*} & (1-\delta)\frac{\beta_1 B^*}{K+B^*} & -Y & 0 & 0 & M \\ 0 & 0 & \gamma & -(\mu+\eta) & 0 & 0 \\ 0 & 0 & \alpha & 0 & -(\epsilon+\rho) & 0 \\ 0 & 0 & 0 & 0 & \epsilon & -\rho \end{pmatrix} \tag{25}$$

where $M = \frac{\beta_2 S^* K}{(K+B^*)^2} + (1-\delta)\frac{\beta_1 V^* K}{(K+B^*)^2}$. We use a Mathematica solver to determine the eigenvalues of the matrix in Equation (25), and the results were,

$$\lambda_1 = -\phi - \beta_2\lambda(B^*) - \mu,\ \lambda_2 = -(1-\delta)\beta_1\lambda(B^*) - \mu,\ \lambda_3 = -(\mu + d + \gamma + \alpha),$$

and

$$\lambda_4 = -(\mu+\eta),\ \lambda_5 = -(\epsilon+\rho),\ \lambda_6 = -\rho.$$

Hence the eigenvalues $z_i, i = 1, ..., 6$ of Equation (**??**) are given by $z_i = \frac{q\lambda_i}{\mathcal{M}(q)-(1-q)\lambda_i}$ Since $q \in (0,1)$, $\mathcal{M}(q) > 0$, and $z_i < 0$. For asymptotic stability, all the eigenvalues should be negative. On replacing B^*,

$$B^* = \frac{\psi}{\rho} - \frac{\alpha\epsilon\Lambda(-\eta-\mu)}{\eta\gamma(\epsilon+\rho)}\Big[-1 + \frac{(-\eta-\mu)(d+\alpha+\gamma+\mu)(-\mu+(-1+\delta)\lambda(B)\beta_2)(-\mu-\phi-\lambda(B)\beta_1)}{\Theta}\Big], \tag{26}$$

the first two eigenvalues will remain positive whenever $\tilde{R}_0 > \frac{1}{2-q}$.

□

Theorem 3. *The endemic equilibrium E_C^* of the model in Equation (1) is globally asymptotically stable in Ω whenever $\tilde{R}_0 > \frac{1}{2-q}$.*

Proof. Consider the following Lyapunov functional

$$\begin{aligned} L_1(t) &= S(t) - S^* - S^* \ln\frac{S(t)}{S^*} + V(t) - V^* - V^*\ln\frac{V(t)}{V^*} + I(t) - I^* - I^*\ln\frac{I(t)}{I^*} \\ &+ R(t) - R^* - R^*\ln\frac{R(t)}{R^*} + Z(t) - Z^* - Z^*\ln\frac{Z(t)}{Z^*} + B(t) - B^* - B^*\ln\frac{B(t)}{B^*} \end{aligned} \tag{27}$$

Differentiating $L_1(t)$ and using Equation (1) we obtain,

$$\begin{aligned} {}_0^{CF}\mathcal{D}_t^q L_1(t) &\leq -\mu(S-S^*) + \Lambda\Big(1 - \frac{S^*}{S(t)}\Big) + \beta_2\lambda(B)\Big(S^* - S\frac{I^*}{I(t)}\Big) + \mu(V-V^*) \\ &+ (1-\delta)\beta_1 B\lambda(B)\Big(V^* - V\frac{I^*}{I(t)}\Big) - (\mu+d)(I-I^*) + \gamma(I^* - I\frac{R^*}{R(t)}) \\ &- \mu(R-R^*) + \eta\Big(R^* - R\frac{S^*}{S(t)}\Big) + \alpha\Big(I^* - I\frac{Z^*}{Z(t)}\Big) + \phi\Big(S^* - S\frac{V^*}{V(t)}\Big) \\ &+ \rho(Z^*-Z) + \epsilon\Big(Z^* - Z\frac{B^*}{B(t)}\Big) + \psi\Big(1 - \frac{B^*}{B(t)}\Big) - \rho(B-B^*). \end{aligned} \tag{28}$$

Since the geometric mean is less than arithmetic mean, see in [6], then the following inequalities hold

$$\begin{aligned} 1 - \frac{S^*}{S(t)} &\leq 0,\ S^* - S\frac{I^*}{I(t)} \leq 0\ \ V^* - V\frac{I^*}{I(t)} \leq 0,\ \ I^* - I\frac{R^*}{R(t)} \leq 0 \\ R^* - R\frac{S^*}{S(t)} &\leq 0\ \ , I^* - I\frac{Z^*}{Z(t)} \leq 0,\ \ Z^* - Z\frac{B^*}{B(t)} \leq 0\ \ 1 - \frac{B^*}{B(t)} \leq 0. \end{aligned}$$

Hence, it follows that ${}_0^{CFR}\mathcal{D}_t^q L_1(t) \leq 0$, and hence guarantees Global Asymptotic Stability. □

5 Numerical Simulation of the Model

We use Matlab software to illustrate the numerical simulations of Equation (1). The numerical values depend on the particular units chosen.

Table 1: **Parameter Estimates for the Model**

Description	**Parameters**	**Values**	**Source**
Recruitment rate	Λ	10,000 per year	Estimate
Probability of vaccinated individuals getting infected	β_1	[0.011-0.95] per year	[1],[12]
Transmission probability of un-vaccinated individuals	β_2	0.553 per year	[1]
Rate of vaccination of the Susceptibles	ϕ	1.7% per year	[4]
Mortality rate	μ	0.01562 per year	[12]
Waning rate of the vaccine	δ	after 3 years	[2]
Death rate due to the disease	d	6-8 hours	[13]
Rate of recovery from infection	γ	0 - 7 days	[12]
Disease induced death rate	d	0.0013 per year	[12]
Rate of conversion of recovered individuals to susceptible	η	0.00042 per year	[13]
Intrinsic growth rate of human vibrios	ψ	0.45758	[12]
Death rate of vibrios	ρ	1.5- 4 hours	[13]
Growth rate of human vibrios within the body of infected individual	α	6 - 8 hours	[5]
Excretion of vibrios to the environment	ϵ	1.1-4.1 phage of particles per ml of watery stools	[20]

Due to fractional order q, the model shows a slower decrease in the number of susceptible individuals. From Figure 1, the susceptible individuals increases rapidly when q is high(memory is low) and increases very slowly when q is low(memory is high). This happens because the Caputo-Fabrizio model remembers previous states and reacts more gradually to the infection. Similarly, the number of vaccinated individuals increases sharply with increase in fractional order (q=0.9) and increases slowly to its optimum when (q=0.3). The slow dynamics of the vaccinated individuals is due to the low uptake of the cholera vaccines. Lower fractional orders introduces stronger memory effects, which models longer-lasting immunity or delayed waning immunity to cholera.

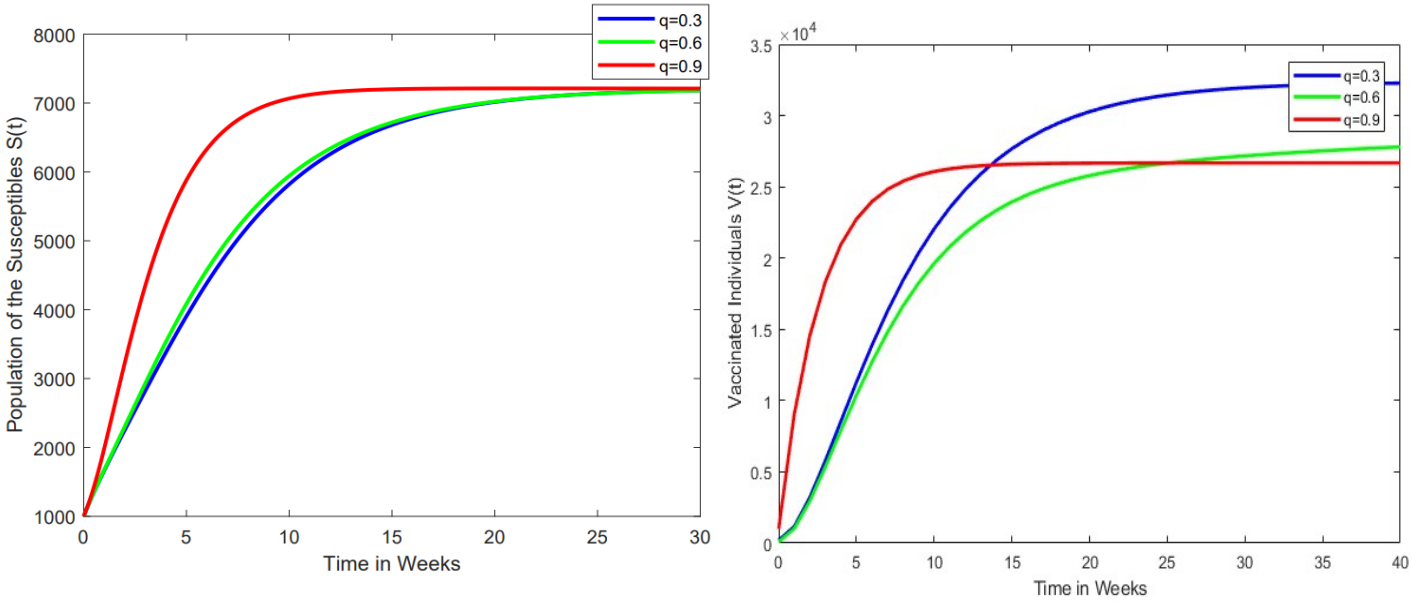

Figure 1: Simulation of the Susceptible and Vaccinated individuals in the Caputo-Fabrizio model with different order

Simulations in Figure 2 and Figure 3 reveals that higher q (near 1, weaker memory) accelerates convergence to equilibrium resembling ODE behaviour. Lower q (strong memory, near zero) exhibits slower dynamics, emphasizing historical influences on transmission.

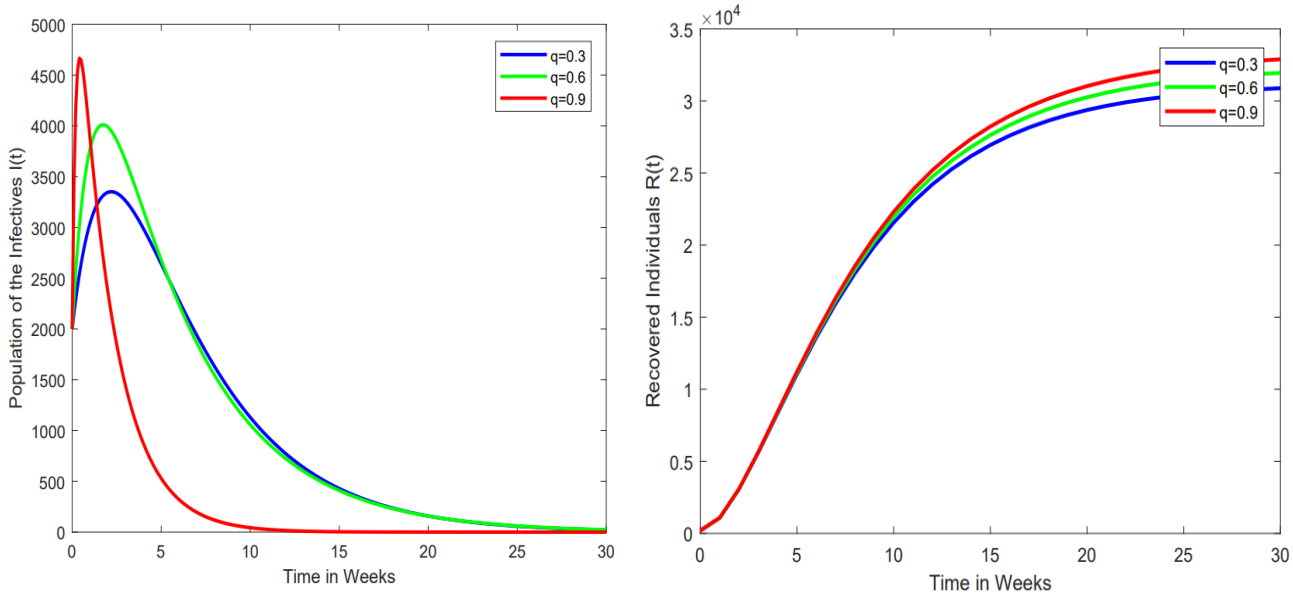

Figure 2: Simulation of the Infected and Recovered individuals in the Caputo-Fabrizio model with different order

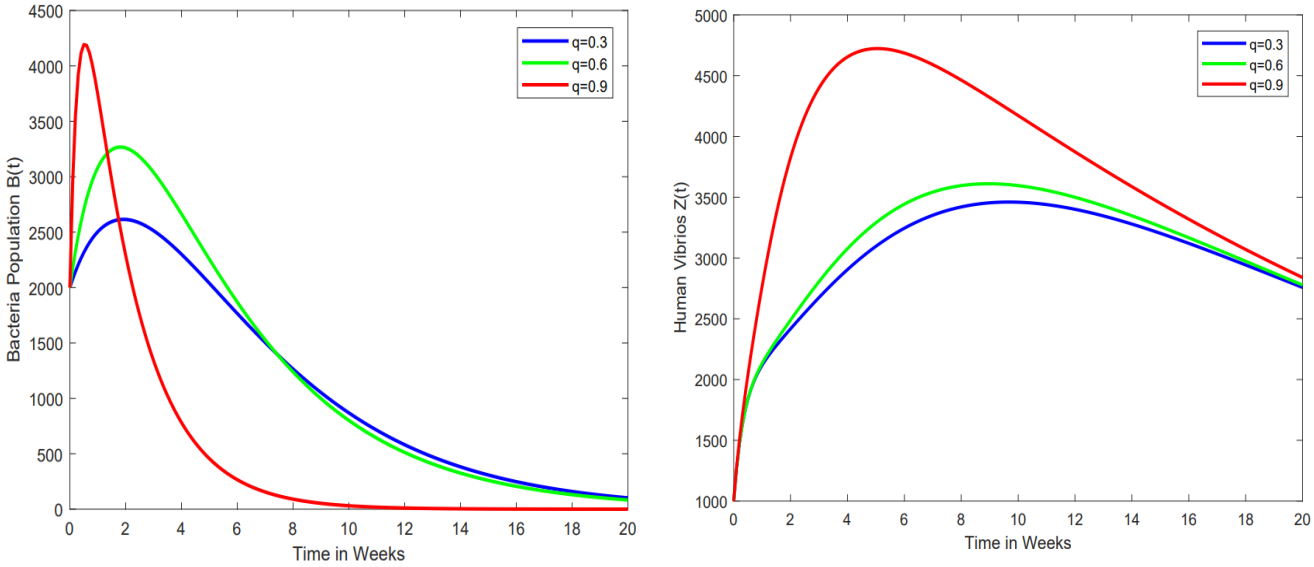

Figure 3: Simulation of the Human Vibrio and Bacteria populationin the Caputo-Fabrizio model with different order

The efficacy of the vaccine is observed to be dependent on the waning effect. The efficacy of the vaccine is ranked between 0 and 100%. Simulation of the data from when an individual was last administered with the vaccine is plotted versus the efficacy of the vaccine.

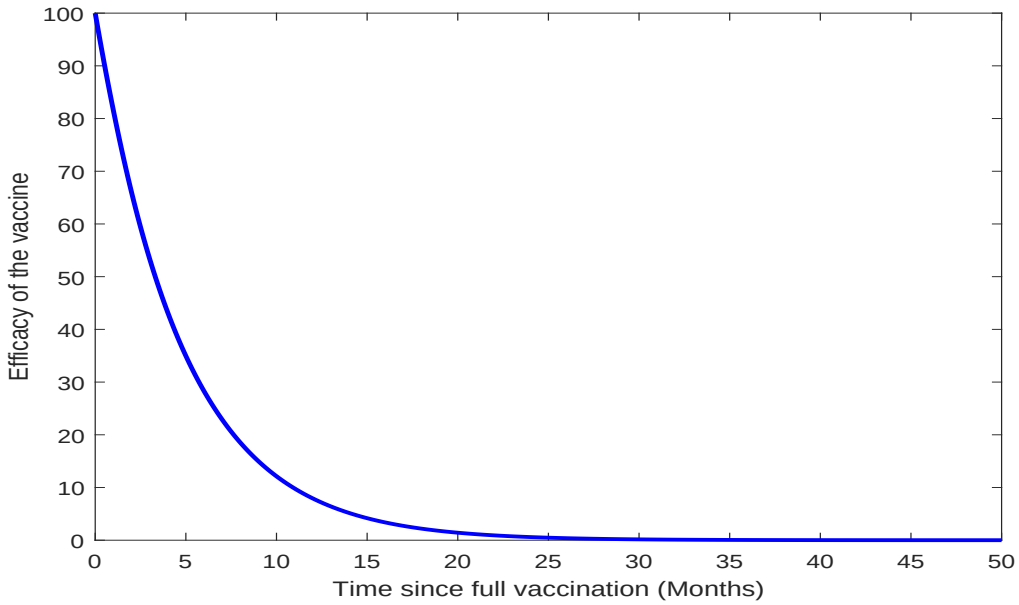

Figure 4: Simulation of Efficacy and waning effect of the vaccine

With the assumption that the vaccine is 100% efficacious, a simulation of the decline (waning) of the efficacy of the vaccine in the body showed that it takes

approximately 25 months (2.083 years) for the cholera vaccine to be depleted in body. This shows that it takes 2.083 years for an individual to be re-vaccinated after full cholera vaccination. This results is closer to studies done by WHO [13], that is, a single dose of cholera vaccine (Shanchol and Euvichol)povides a significant protection against cholera for at most three years.

6 Conclusion

The Caputo-Fabrizio framework provides a more nuanced understanding of cholera dynamics by integrating memory effects which traditional ODEs cannot capture. Fractional order q critically influences model predictions, lower q reduces transmission intensity and delays outbreaks, while higher q mimics classical models. On performing stability analysis, if the reproduction number $\tilde{R}_0 < \frac{1}{2-q}$, the DFE is locally and globally asymptotically stable, while if $\tilde{R}_0 > \frac{1}{2-q}$, the endemic equilibrium is locally and globally asymptotically stable. Additionally, graphical simulations show that it takes approximately 2.083 years for an individual to be re-vaccinated after full cholera vaccination.

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