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Optimal Control and General Fractional Description for a Complex Biological System

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Abstract: The main objective of this research is to investigate a new mathematical model involving the general form of Caputo fractional derivative to explore a real case of cholera outbreak. In this model, the effect of vaccination is included, and an optimal control strategy is carried out for the purpose of treatment through quarantine. We then solve the fractional optimal control problem by a forward-backward sweep iterative algorithm and present some comparative results in order to verify the model and show the efficacy of the vaccination and optimal control treatments. Simulation results show that the combination of quarantine and vaccination reduces the numbers of infected people and bacteria concentration effectively.

Keywords: Fractional calculus, general fractional derivative, cholera outbreak, vaccination, optimal control.

1 Introduction

Mathematical models have attracted a growing interest in biology mainly because of their utilities in different disciplines of medicine and health [1–3]. These models, for instance, are employed for a projection of how infectious diseases progress. [4]. Cholera is one of the most common infectious illnesses, and it affects all human races. Almost 3-5 million people worldwide have been affected by cholera, and 28800-130000 deaths occurred in a year by this disease. As a result, many researchers examined several mathematical models for the cholera disease spread. In [5], a mathematical model was proposed for cholera considering vaccination effect. The authors in [6] presented a novel model for the 1973 cholera outbreak in the European Mediterranean area. The detailed analysis of a cholera transmission dynamics in Yemen was conducted in [7]. The researchers in [8] developed a model featuring an effective intervention strategy for controlling the cholera disease. Some other relevant researches can also be found in [9, 10].

Mathematical models using ordinary differential equations have been proven to be helpful in apprehending the dynamics of biological systems. Nevertheless, the behavior of most biological processes has memory or aftereffects, while such effects are ignored in classical integer-order mathematical descriptions. On the other hand, fractional-order systems are more appropriate than integer-order ones in many fields since they can express phenomena linked to memory and affected by hereditary properties [11, 12]. As a result, developing biological mathematical models using fractional differential equations (FDEs) has attracted enormous interest recently [13–15].

Luchko and Yamamoto, in 2016, offered a new fractional differential operator with a general kernel function [16]. The flexibility of this operator's kernel selection allows a wide variety of practical applications [17–20]. Indeed, various asymptotic behaviors can be expressed by varying the kernel in the general derivative. This fact enables us with more precise predictions about the potential behavior of real-world phenomena compared to the standard fractional formulations. However, it is imperative to conduct further research on this operator's properties and establish more theorems for its analysis. In addition, convenient numerical and analytical methods must be studied to solve the fractional equations containing the aforementioned operator.

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Motivated by the upper discussion, this paper offers a new mathematical model for an outbreak of cholera disease. This new model also investigates the influence of vaccination on the spread of the disease. Furthermore, a suitable control scheme is suggested for the purpose of quarantine treatment, which reduces the number of infected people and bacteria concentration. We solve the fractional optimal control problem by a forward-backward sweep iterative algorithm. Finally, we conduct some comparative results to confirm the validation of the model and reveal the significance of quarantine-vaccination strategy.

This paper is organized as follows. Section 2 covers the elementary principles of FDEs. Section 3 concentrates on the new model. For the purpose of treatment, an effectual optimal control strategy is proffered in Section 4. Numerical results are analyzed in Section 5. Also, concluding remarks are given at the end of this paper.

2 Definitions and concepts

The definitions of general fractional derivatives and integrals, as well as their main properties, are covered in this section. The left-sided Riemann-Liouville (RL) and Caputo fractional derivatives in general sense are, respectively, defined as [16]

$$ {}^{RL}\mathscr{D}^{\alpha}_{0,t} f(t) = \frac{d}{dt}\int_0^t f(z)K_l(t-z)\,dz, \tag{1} $$

$$ {}^{C}\mathscr{D}^{\alpha}_{0,t} f(t) = \int_0^t \dot{f}(z)K_l(t-z)\,dz, \tag{2} $$

in which $\alpha \in (0,1)$, $f:[0,+\infty)\to\mathbb{R}$ is an absolutely continuous function such that $\dot{f}\in L_{1,loc}(\mathbb{R}^+)$, and K_l is a general kernel. Note that the above-mentioned operators are linear, which means

$$ {}^{C}\mathscr{D}^{\alpha}_{0,t}(c_1f_1(t)+c_2f_2(t)) = c_1\,{}^{C}\mathscr{D}^{\alpha}_{0,t}f_1(t) + c_2\,{}^{C}\mathscr{D}^{\alpha}_{0,t}f_2(t), \tag{3} $$

$$ {}^{RL}\mathscr{D}^{\alpha}_{0,t}(c_1f_1(t)+c_2f_2(t)) = c_1\,{}^{RL}\mathscr{D}^{\alpha}_{0,t}f_1(t) + c_2\,{}^{RL}\mathscr{D}^{\alpha}_{0,t}f_2(t). \tag{4} $$

In addition, under some appropriate conditions for the kernel function $K_l(t)$ [16], a completely monotone function $M_l(t)$ exists for $t>0$ such that

$$ K_l(t) * M_l(t) = \int_0^{\infty} K_l(z)M_l(t-z)\,dz = 1. \tag{5} $$

Then for any $f\in L_{1,loc}(\mathbb{R}^+)$, we can write

$$ {}^{RL}\mathscr{I}^{\alpha}_{0,t}\left[{}^{C}\mathscr{D}^{\alpha}_{0,t}f(t)\right] = f(t)-f(0), \tag{6} $$

in which ${}^{RL}\mathscr{I}^{\alpha}_{0,t}$ is the general form of the left-sided RL fractional integral described by

$$ {}^{RL}\mathscr{I}^{\alpha}_{0,t} f(t) = \int_0^t f(z)M_l(t-z)\,dz. \tag{7} $$

Similarly, the right-sided Caputo and RL fractional derivatives can, respectively, be defined by

$$ {}^{C}\mathscr{D}^{\alpha}_{t,T} f(t) = \int_t^T \dot{f}(z)K_r(z-t)\,dz, \tag{8} $$

$$ {}^{RL}\mathscr{D}^{\alpha}_{t,T} f(t) = \frac{d}{dt}\int_t^T f(z)K_r(z-t)\,dz, \tag{9} $$

and the right-sided RL fractional integral can be expressed as

$$ {}^{RL}\mathscr{D}^{-\alpha}_{t,T} f(t) = \int_t^T f(z)M_r(z-t)\,dz. \tag{10} $$

In [21], there is another generalization that coincides with the above generalized definitions. Therefore, from [21] we have

$$ \int_0^T f_1(z)\,{}^{C}\mathscr{D}^{\alpha}_{0,t}f_2(z)\,dz = \int_0^T f_2(z)\,{}^{RL}\mathscr{D}^{\alpha}_{t,T}f_1(z)\,dz, \tag{11} $$

$$\int_0^T f_1(z)\,{}^{RL}\mathscr{D}_{0,t}^{\alpha} f_2(z)\,dz = \int_0^T f_2(z)\,{}^{C}\mathscr{D}_{t,T}^{\alpha} f_1(z)\,dz. \tag{12}$$

Here, we take into account some special cases according to the above general definitions. First, we select the kernel $K_l(t) = \frac{t^{-\alpha}}{\Gamma(1-\alpha)}$, $0 < \alpha < 1$, which results $M_l(t) = \frac{t^{\alpha-1}}{\Gamma(\alpha)}$. Therefore, the conventional RL and Caputo fractional derivatives together with the RL fractional integral are recovered from the equations (1), (2), and (7), respectively [22]. Besides, we can consider $K_l(t) = \int_0^1 \frac{t^{-\alpha}}{\Gamma(1-\alpha)} dp(\alpha)$, where p is a Borel measure on $[0,1]$, or $K_l(t) = \sum_{n=1}^{k} a_n \frac{t^{-\alpha_n}}{\Gamma(1-\alpha_n)}$, $0 < \alpha_1 < \ldots < \alpha_k < 1$, in which the derivative of distributed order and the multi-term derivatives are obtained, respectively [16].

3 New fractional model

In the recent study [5], a conceptual model was suggested for a cholera outbreak including six components as follows

$$\begin{cases} S'(t) = \Upsilon + \varpi_1 R(t) + \varpi_2 V(t) - (\psi+\mu)S(t) - \dfrac{\beta S(t)}{C(t)+\rho} C(t), \\ I'(t) = \dfrac{\beta}{C(t)+\rho} C(t)S(t) - (\alpha_1+\gamma+\mu)I(t), \\ Q'(t) = \gamma I(t) - (\varepsilon+\alpha_2+\mu)Q(t), \\ R'(t) = \varepsilon Q(t) - (\varpi_1+\mu)R(t), \\ V'(t) = \psi S(t) - (\mu+\varpi_2)V(t), \\ C'(t) = \theta I(t) - \rho C(t), \end{cases} \tag{13}$$

with positive initial conditions. In this model, the human population $N(t)$ is classified into five distinct categories, which are explained as follows:

S: Susceptible population.

I: Infected population with symptoms.

Q: Individuals undergoing treatment in quarantine.

R: Recovered population.

V: Vaccinated population.

Moreover, the variable $C(t)$ denotes the bacterial concentration at a given time t, and the model parameters were explained in [5]. However, the classical model (13) does not include memory effects due to the existence of integer-order derivatives in the dynamics. To overcome this issue, here we modify the model (13) by replacing the ordinary time-derivative with the general fractional differentiation defined in Section 2. To avoid dimensional mismatching, we update the fractional operator (2) via an auxiliary parameter $\varsigma > 0$ [**?**]. Following these considerations, the new fractional model for the cholera outbreak is as the following system

$$\begin{cases} \frac{1}{\varsigma^{1-\alpha}}\,{}^{C}\mathscr{D}_{0,t}^{\alpha} S(t) = \Upsilon + \varpi_1 R(t) + \varpi_2 V(t) - \dfrac{\beta S(t)}{C(t)+\rho} C(t) - (\psi+\mu)S(t), \\ \frac{1}{\varsigma^{1-\alpha}}\,{}^{C}\mathscr{D}_{0,t}^{\alpha} I(t) = \dfrac{\beta}{C(t)+\rho} S(t)C(t) - (\alpha_1+\mu+\gamma)I(t), \\ \frac{1}{\varsigma^{1-\alpha}}\,{}^{C}\mathscr{D}_{0,t}^{\alpha} Q(t) = \gamma I(t) - (\alpha_2+\mu+\varepsilon)Q(t), \\ \frac{1}{\varsigma^{1-\alpha}}\,{}^{C}\mathscr{D}_{0,t}^{\alpha} R(t) = \varepsilon Q(t) - (\mu+\varpi_1)R(t), \\ \frac{1}{\varsigma^{1-\alpha}}\,{}^{C}\mathscr{D}_{0,t}^{\alpha} V(t) = \psi S(t) - (\varpi_2+\mu)V(t), \\ \frac{1}{\varsigma^{1-\alpha}}\,{}^{C}\mathscr{D}_{0,t}^{\alpha} C(t) = \theta I(t) - \rho C(t), \end{cases} \tag{14}$$

with the initial conditions $S(0) = S_0$, $Q(0) = Q_0$, $R(0) = R_0$, $I(0) = I_0$, $V(0) = V_0$, and $C(0) = C_0$, where $S_0, I_0, Q_0, R_0, V_0, C_0 \geqslant 0$.

4 Optimal control

This section discusses an optimal control treatment strategy for the cholera model (14). To do so, we add the control function $u(t)$ to the model, which describes the fraction of infectious people who are under treatment in quarantine till complete recovery. Here, only the interval $0 \leq u(t) \leq 1$ makes sense for the control, where $u(t) = 0$ corresponds to no control, and $u(t) = 1$ means all infectious individuals are in quarantine. To formulate the optimal control problem mentioned above, we define the quadratic cost functional as follows

$$J(u) = \frac{1}{2}\int_{t_0}^{t_f} \left(q_1 I^2(t) + q_2 C^2(t) + r u^2(t)\right) dt, \tag{15}$$

where the coefficients $q_1, q_2 \geq 0$ denote the relative costs of the state variables $I(t), C(t)$, respectively, and $r > 0$ is the cost of treatment. The dynamical model with control is also described as

$$\begin{cases} \frac{1}{\varsigma^{1-\alpha}} {}^{C}\mathscr{D}_{0,t}^{\alpha} S(t) = \Upsilon - \dfrac{\beta S(t)}{C(t)+\rho} C(t) - (\mu+\psi) S(t) + \varpi_1 R(t) + \varpi_2 V(t), \\ \frac{1}{\varsigma^{1-\alpha}} {}^{C}\mathscr{D}_{0,t}^{\alpha} I(t) = \dfrac{\beta}{C(t)+\rho} C(t) S(t) - (\alpha_1 + \mu + \gamma u(t)) I(t), \\ \frac{1}{\varsigma^{1-\alpha}} {}^{C}\mathscr{D}_{0,t}^{\alpha} Q(t) = \gamma u(t) I(t) - (\alpha_2 + \mu + \varepsilon) Q(t), \\ \frac{1}{\varsigma^{1-\alpha}} {}^{C}\mathscr{D}_{0,t}^{\alpha} R(t) = \varepsilon Q(t) - (\mu + \varpi_1) R(t), \\ \frac{1}{\varsigma^{1-\alpha}} {}^{C}\mathscr{D}_{0,t}^{\alpha} V(t) = \psi S(t) - (\varpi_2 + \mu) V(t), \\ \frac{1}{\varsigma^{1-\alpha}} {}^{C}\mathscr{D}_{0,t}^{\alpha} C(t) = \theta I(t) - \rho C(t), \\ S(0) = S_0, I(0) = I_0, Q(0) = Q_0, R(0) = R_0, V(0) = V_0, C(0) = C_0, \\ S_0, I_0, Q_0, R_0, V_0, C_0 \geqslant 0. \end{cases} \tag{16}$$

Thus, we consider the control problem (16) to minimize the cost functional (15). To solve this optimal control problem, we apply the Hamiltonian approach by defining the scalar function $\mathscr{H}(t) = \mathscr{L}_0(t) + \sum_{j=1}^{6} \mathscr{L}_j(t) f_j(t)$ where $\mathscr{L}_0(t)$ is the integrand of the cost functional (15), f_i is the i-th equation in the right-hand side of (16), and $\mathscr{L}_i(t) \in \mathbb{R}$ is the co-state variable, also known as the Lagrange multiplier. The optimal control is then obtained from

$$u^*(t) = \min\left\{1, \max\left\{\frac{\gamma I^*(t)}{r}(\mathscr{L}_2^*(t) - \mathscr{L}_3^*(t))\right\}\right\}, \tag{17}$$

where the optimal state and co-state variables satisfy the control system (16) as well as the costate equations

$$\begin{cases} {}^{RL}\mathscr{D}_{t,T}^{\alpha} \mathscr{L}_1(t) = \frac{\partial \mathscr{H}}{\partial S}(t), \\ {}^{RL}\mathscr{D}_{t,T}^{\alpha} \mathscr{L}_2(t) = \frac{\partial \mathscr{H}}{\partial I}(t), \\ {}^{RL}\mathscr{D}_{t,T}^{\alpha} \mathscr{L}_3(t) = \frac{\partial \mathscr{H}}{\partial Q}(t), \\ {}^{RL}\mathscr{D}_{t,T}^{\alpha} \mathscr{L}_4(t) = \frac{\partial \mathscr{H}}{\partial R}(t), \\ {}^{RL}\mathscr{D}_{t,T}^{\alpha} \mathscr{L}_5(t) = \frac{\partial \mathscr{H}}{\partial V}(t), \\ {}^{RL}\mathscr{D}_{t,T}^{\alpha} \mathscr{L}_6(t) = \frac{\partial \mathscr{H}}{\partial C}(t), \end{cases} \tag{18}$$

with the transversality conditions $\mathscr{L}_j(T) = 0$, $j = 1, 2, \ldots, 6$.

In the following, we present a sweep iterative algorithm to solve the control and adjoint systems (16) and (18) forward and backward in time, respectively. The stability and convergence of this method have also been proved in [24].

Algorithm:
Step 1. Take an initial value for the control function $u(t)$.
Step 2. Use the current value of $u(t)$ and obtain the state trajectories by solving the control system (16) forward in time.
Step 3. Use the current values of the state and control functions and obtain the co-state variables by solving the adjoint system (18) along with the transversality conditions $\mathscr{L}_j(T) = 0$, $j = 1, 2, \ldots, 6$, backward in time.
Step 4. Update the control function from (17) by using the current values of the state and co-state variables.
Step 5. If the updated versions of the state, co-state, and control functions are close enough to their previous values, stop the algorithm, else go to Step 2.

Table 1: The values of parameters.

Parameter	Υ	μ	ϖ_1	ϖ_2	β	ρ
Value	$\frac{28.4N(0)}{365000}$	1.6×10^{-5}	$\frac{0.4}{365}$	$\frac{1}{1460}$	0.01694	10^7
Parameter	ψ	γ	α_1	α_2	θ	ρ
Value	0.005	1.15	6×10^{-6}	3×10^{6}	10	0.33

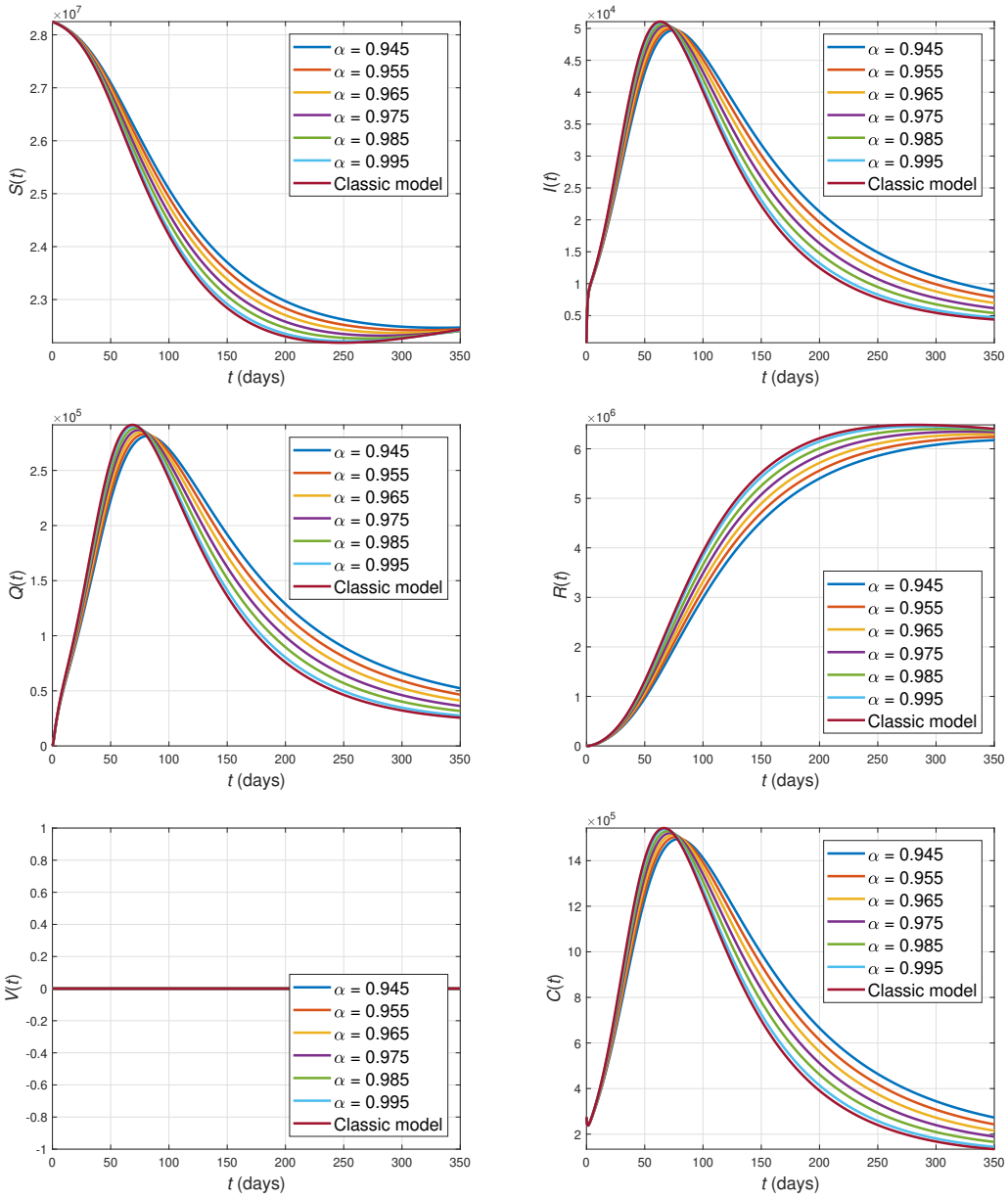

Fig. 1: Simulation of classic and fractional-order models (13) and (14) without vaccination.

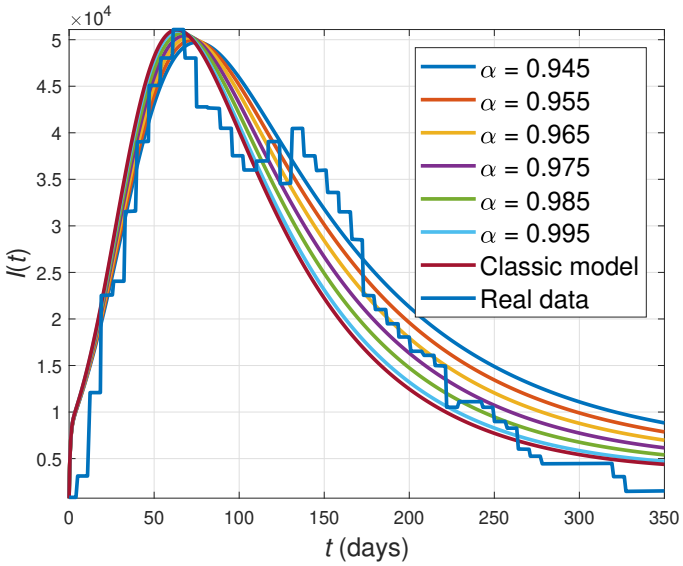

Fig. 2: Simulation of infectious people for different α.

Table 2: Absolute Error (AE) and Relative Error (RE) for the classic and fractional-order models (13) and (14).

Fractional order	AE	RE
0.945	4.7694×10^4	0.1793
0.955	4.3604×10^4	0.1639
0.965	4.2359×10^4	0.1593
0.975	4.4176×10^4	0.1661
0.985	4.8665×10^4	0.1830
0.995	5.5108×10^4	0.2072
Classic model	5.8846×10^4	0.2212

5 Simulation results

In order to explore the real cholera outbreak in Yemen from April 27, 2017, to April 15, 2018 [5], we consider the classic and fractional-order models (13) and (14). The initial conditions are considered as $(S_0, I_0, Q_0, R_0, C_0) = (28249670, 750, 0, 0, 0, 275000)$, and the model parameters can be seen in Table 1. The dynamical behaviors of the model when $\varpi_2 = \psi = 0$ for a power law kernel and various fractional orders are illustrated in figure 1. This figure shows that when the fractional order α decreases, the susceptible population grows uniformly. It is also observed that with the decrease of the fractional order in the early days, a sharp jump in the population of infected people occurs. Further, by decreasing α in the fractional model (14), the recovered population $R(t)$ decreases. In figure 2 and Table 2, some comparisons are performed between the fractional model (14) with a power law kernel, the classic integer-order model (13), and the real experimental observations of the cholera outbreak in Yemen; comparative results indicate that the fractional-order model (14) with $\alpha = 0.965$ is the best candidate to describe the cholera outbreak under investigation. Thus, for the purpose of treatment, we select this most realistic model and simulate the optimal control and vaccination strategies, as in Section 4, with the parameter values given in Table 1. The results obtained are shown in figure 3, which confirms that the optimal control treatment together with vaccination has a positive impact on the number of infected individuals, and reduces the concentration of bacteria monotonically.

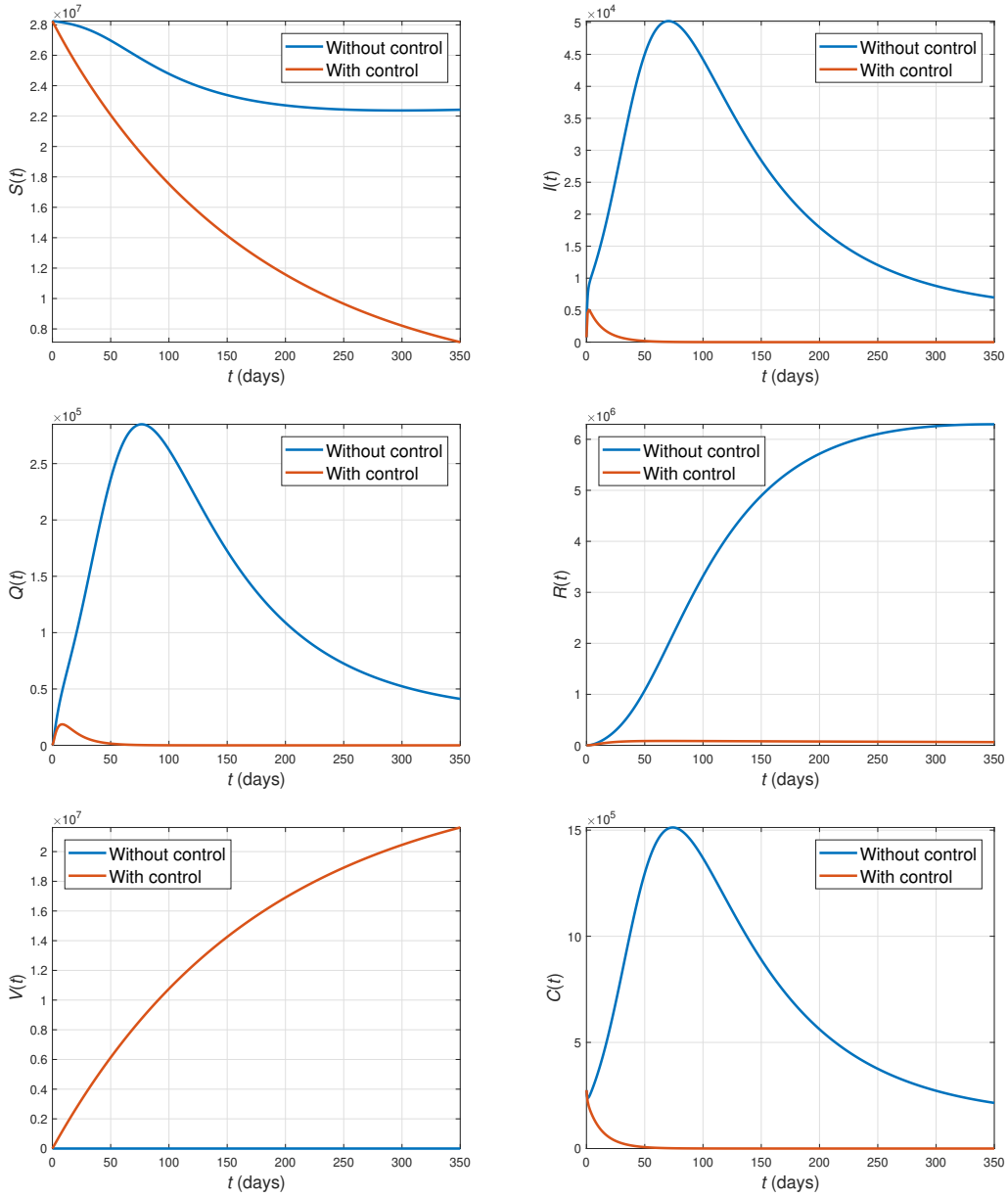

Fig. 3: Optimal control treatment together with vaccination for the cholera outbreak in Yemen.

6 Conclusion

This paper investigated a new mathematical model for a real case of cholera outbreak by employing fractional derivatives in general sense. The effect of vaccination was also included to the model, and the treatment through quarantine was examined by an optimal control strategy in order to reduce the numbers of infected people and bacteria concentration. The fractional optimal control problem was then solved by a forward-backward sweep iterative algorithm. According to the reported simulation results, a better approximation was attained when the problem was modeled in fractional sense compared to the classical model, and the quarantine-vaccination treatment had positive impacts on the number of people who were infected and reduced the concentration of bacteria monotonically.

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