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A fractional model for the dynamics of TB virus

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ABSTRACT

In this paper, we present a nonlinear fractional order model in the Caputo sense to explore and simulate the TB dynamics. Using the TB confirmed notified cases from the year 2002 to 2017 in Khyber Pakhtunkhwa, Pakistan, we estimate the model parameters and demonstrate that the proposed fractional model provides a good fit to the real data. Initially, we compute the basic reproduction number and the model equilibria. Then, the existence and uniqueness of the model are shown via generalized mean value theorem. Further, we explore the local and global stability of the disease free equilibria in fractional environment. Finally, numerical results are obtained in order to validate the importance of the arbitrary order derivative and theoretical results. We conclude that the fractional epidemic model is more generalized than the classical model, which give more information about the disease dynamics and give a good agreement to the real data of TB infection.

1. Introduction

Tuberculosis (TB) infection caused by bacillus *Mycobacteriumtuberculosis* is life threatening to public health throughout the world. The TB disease is usually transmitted through the air by TB infected people when they cough, spit, sneeze or speak. In the human body, preferentially lungs are affected with this infection, nevertheless it may also invade other parts including the brain, spine, kidneys, central nervous system etc. The classical symptoms of a TB infected person include chronic cough, with blood-containing sputum, night sweats, fever, and weight loss [1]. TB was ranked the top infectious killer in 2016, and more than 1.7 million people died from TB, among which nearly 400,000 people were also infected with HIV. According to WHO data reported in 2016, about 10.4 millIon new TB infective cases are estimated in the world out of which 10% people are co-infected with HIV. Mostly, the TB deaths occur in the middle income countries of the world, like India, Indonesia, China, Philippines, Pakistan, Nigeria, and South Africa carry more than 60% of the whole TB burden [2].

The dynamics of communicable diseases can be explored effectively with the help of mathematical models and provide useful information to the spread and control of the communicable diseases. In the last few decades, a number of mathematical models were developed to understand the TB infection dynamics. For example, Waaler et al. [3], initiated to study the dynamics of TB infection in 1962. Later on, a compartmental model for the TB disease was developed in [4]. The stability analysis is of key interest of the researchers in epidemiological models. The global stability analysis of the TB infection with incomplete treatment was carried out in [5]. A similar study of TB model was discussed by Liu and his coauthors and can be found in [6]. To explored the seasonal effects on TB infection, Liu et al. developed the TB model in [7] and applied the epidemiological data to estimate the model parameters. The dynamics of the TB disease in high endemic regions of Asia-Pacific was investigated by presenting a realistic TB model [8]. Zhang et al. [9] proposed the TB transmission model for possible control of TB infection in China. A compartmental model of the TB infection with relapse has been discussed in [10]. Recently, the optimal controlling strategies were explored by Kim et al. to minimize the TB disease in the Philippines population [11].

The above mentioned TB models are based on ordinary (or delay) integer-order derivative. However, such models have some limitations as they do not provide any information about the memory and learning mechanism. Moreover, in the real world explanation the models based on the integer-order derivative are unable to explore the dynamics between two distinct points. Mathematical models with fractional order are more realistic and helpful than the integer-order models, because they provide a powerful instrument to incorporate memory and hereditary properties into the systems and are helpful to minimize the errors arising from the neglected parameters in modeling, [12,13].

In order to overcome such limitations of integer-order derivative, various type of non-local or fractional orders derivatives were

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proposed in literature [13–15], and have been used extensively to solve a number of real world problems in engineering, viscoelasticity, Physics, epidemiology, and others [16–18]. Mathematical models with fractional order differential system got more attention in recent years. The purpose of fractional modeling of the biological systems is to get a deeper understanding of the complex behavioral patterns of various communicable diseases. Moreover, mathematical models with fractional order derivative provide a better fit to the real data instead of integer order models. In [19], the authors developed a fractional order model to explored the dynamics of the outbreaks of influenza A (H1N1), and concluded that the fractional order model provides a good agreement with real data. A similar analysis has been carried out by Diethelm [20] providing a fractional model for the dynamics of a dengue fever outbreak in Cape Verde islands and shown a good agreement for the real dengue data. Pinto and Machado [21], introduced a fractional model for the dynamics and controlling strategies of malaria. A non-integer order model for TB disease including three strains has been presented in [22]. Recently, a detail analysis has been presented to explore the effect of diabetes and resistant strains in the dynamics of TB infection using a fractional order model [23]. A non-integer order model for TB infection and its global stability using Lypanove theory is presented by Weronika et al. [24].

In Pakistan, TB is a leading public health problem and one of the major causes of morbidity and mortality. Pakistan is one of the highest countries with TB infection and ranked fifth among the twenty two countries having high burden of this infection. Annually more than 0.5 million new cases including 15,000 children are notified and more than seventy thousand Pakistanis die because of TB infection each year. Due to high global prevalence of multi drug resistant tuberculosis (MDR-TB), Pakistan ranked fourth in the world [2,25,26]. TB is also a major health problem and leading case of death in the province of Pakistan named Khyber Pakhtunkhwa. According to national TB control program (NTP) about 462920, TB infected cases are registered and treated from 2002 till 2017 in Khyber Pakhtunkhwa, [27]. In this paper, we consider the new TB infected cases from 2002 to 2017 obtained from the website of NTP [27], and use the data to fit and estimate the model parameters used in our proposed model.

Motivated by the aforementioned work, in the present study, we derive a fractional order model for TB infection in Caputo sense. For the model parameters estimation we will use the real data of Khyber Pakhtunkhwa, Pakistan from 2002 till 2017 [27]. The remaining sections are organized as: Preliminaries of the fractional derivative is presented in the next section. In Section 3, we formulate the model, compute the basic reproduction number, model equilibria and prove the existence and uniqueness of the model solution. In Section 4, we present the stability analysis of disease free equilibria. In Section 5, we despite the model fitting curves to the real data and also present the long term behavior of TB infection. Numerical results are given in Section 6. Finally, the present work is concluded in Section 7.

2. Preliminaries

First we give the basic definitions regarding the Caputo fractional derivative and state related theorems [12,13].

Definition 1. The fractional integral of order $\alpha > 0$ for a function $g : R^+ \to R$ is defined by

$$I_t^{\alpha}(g(t)) = \frac{1}{\Gamma(\alpha)} \int_0^t (t-\chi)^{\alpha-1} g(\chi) d\chi.$$

Here and elsewhere Γ denotes the Gamma function.

Definition 2. The Caputo fractional order derivative for function $g \in C^n$ of order α is given below:

$$^{C}D_t^{\alpha}(g(t)) = I^{n-\alpha} D^n g(t) = \frac{1}{\Gamma(n-\alpha)} \int_0^t \frac{g^n(\chi)}{(t-\chi)^{\alpha+n-1}} d\chi,$$

which is well defined for absolutely continuous functions and $n-1 < \alpha < n \in N$. Note that the value of the Caputo fractional derivative of the function g at point t involves all the values of $g^n(\chi)$, for $\chi \in [0, t]$. Clearly $^{C}D_t^{\alpha}(g(t))$ tends to $g'(t)$ as $\alpha \to 1$.

Definition 3. [28] The constant z^* is an equilibrium point of the Caputo fractional dynamical system given below

$$^{C}D_t^{\alpha} z(t) = f(t, z(t)), \quad \alpha \in (0, 1), \tag{1}$$

if and only if, $f(t, z^*) = 0$.

Next to give an extension of the Lyapunov method for nonlinear system in Caputo sense we recall the following result [28,29].

Theorem 2.1. *If z^* be an equilibrium point for the non autonomous fractional order system given in (1) and $\Upsilon \in R^n$ be a domain containing z^* and let G: $[0, \infty) \times \Upsilon \to R$, be a continuously differentiable function such that*

$$V_1(z) \le G(t, z(t)) \le V_2(z), \tag{2}$$

and

$$^{C}D_t^{\alpha} G(t, z(t)) \le -V_3(z), \tag{3}$$

for all $\alpha \in (0, 1)$ and all $z \in \Upsilon$. Where $V_1(z)$, $V_2(z)$ and $V_3(z)$ are continuous positive definite functions on Υ, then the equilibrium point of system (1) is uniformly asymptotically stable.

3. Model formulation and basic properties

In this section, we present the proposed fractional model to describe the dynamics of TB infection. To develop the model, total human population is divided into five epidemiological subcompartments denoted by susceptible $S(t)$, Exposed $L(t)$, TB active $I(t)$, under treatment $T(t)$, and recovered individuals after treatment $R(t)$.

The transmission model for TB dynamics is given by the following system of non-linear fractional differential equations:

$$\begin{aligned}
^{C}D_t^{\alpha} S &= \Lambda - \frac{\beta SI}{N} - \mu S,\\
^{C}D_t^{\alpha} L &= \frac{\beta SI}{N} - (\mu + \epsilon)L + (1-\eta)\delta T,\\
^{C}D_t^{\alpha} I &= \epsilon L + \eta \delta T - (\mu + \gamma + \sigma_1) I,\\
^{C}D_t^{\alpha} T &= \gamma I - (\mu + \delta + \sigma_2 + \xi) T,\\
^{C}D_t^{\alpha} R &= \xi T - \mu R.
\end{aligned} \tag{4}$$

The initial conditions are

$$S(0) = S_0, L(0) = L_0, I(0) = I_0, T(0) = T_0, \text{ and } R(0) = R_0.$$

The fractional derivatives involved in the above model (4) is taken in Caputo sense and the parameter $\alpha \in (0, 1]$. We assume that all the functions S, L, I, T, R and their Caputo fractional derivatives are continuous for all $t \ge 0$. To start the analysis of the model (4), we show the existence, uniqueness, and non-negativity of the model solution.

The detail description of model parameters and their fitted or estimated numerical values are given in Table 1.

3.1. Existence of non-negative unique solution

To show the positivity of the model solution let us consider

$$R_+^5 = \{x \in R^5 | x \ge 0\} \text{ and } x(t) = (S(t), L(t), I(t), T(t), R(t))^T.$$