

Tüberküloz Hastalığının Matematiksel Modellemesine Caputo Kesirli Türevinin Etkisi

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ÖZ

Kesirli türev ve integral operatörlerinin en önemli avantajlarından biri olan hafıza etkisi, bir hastalığın belirgin bir özelliğidir. Mikobakteriyum tüberküloz, akciğerleri etkileyen hafızaya bağlı bu tür tehlikeli hastalıklardan biridir. Bu nedenle, bu ciddi halk sağlığı enfeksiyonu hafıza etkisine sahip Caputo operatörü aracılığıyla araştırılmıştır. İlk olarak, çözümlerin pozitifliği, hastalıksız denge ve endemik denge noktaları gibi önerilen modelin bazı temel özellikleri sunulmuştur. Daha sonra, söz konusu hastalık modelini karakterize etmek için temel üreme sayısı hesaplanmıştır. Ayrıca, bu temel hesaplamalar kullanılarak kararlılık analizi gerçekleştirilmiştir ve tüberküloz enfeksiyonunun seyri hakkında yorumlar yapılmıştır. Öte yandan, tam sayı olmayan mertebenin mikobakteriyum tüberküloz yayılımı üzerindeki etkisini göstermek için sayısal simülasyonlar gerçekleştirilmiştir. Son olarak, klasik ve kesirli matematiksel modeller arasındaki karşılaştırma analizi çeşitli grafiklerle desteklenmiştir. Sonuçlar, kesirli sıranın tüberküloz yayılımını seyrini büyük ölçüde etkileyebileceğini ve bu küresel sağlık sorunu hakkında daha spesifik tahminlere izin verdiğini göstermektedir.

The Impact of Caputo Fractional Derivative on Mathematical Modeling of Tuberculosis Disease

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ABSTRACT

Memory effect, one of the most important advantages of fractional derivative and integral operators, is a prominent characteristic of a disease. Mycobacterium tuberculosis is one of such memory-dependent precarious disease that affects the lungs. Therefore, we investigate this serious public health infection by means of the Caputo operator having memory. Firstly, some fundamental features of the proposed model such as the positiveness of solutions, the disease-free equilibrium, and endemic equilibrium points are presented. Then, the basic reproduction number to characterize the disease model under consideration is calculated. In addition, stability analysis is performed by using these basic calculations, and comments are made on the course of the tuberculosis infection. On the other hand, we numerical simulations in order to show the effect of non-integer order on the mycobacterium tuberculosis transmission are carried out. Lastly, comparison analysis between the classical and fractional mathematical models is supported by various graphs. The results show that fractional order can greatly affect the course of the tuberculosis transmission and allow for more specific predictions about this global health issue.

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1. Introduction

Mycobacterium tuberculosis (MTB) is a dangerous and life-threatening disease causing infection in the lungs and damage to other organs. It is also a long-term bacterial and contagious infectious disease caused by the Mycobacterium tuberculosis. Although it is one of the oldest known diseases, its cause is known with certainty, it can be treated, and it is a preventable disease, it still remains one of the most common and fatal infectious diseases in the world, and more than 3 million people die from tuberculosis every year. Moreover, one in three people in the world has contracted tuberculosis, and currently, more than 10 million new MTB patients are diagnosed each year according to WHO. The MTB disease is transmitted from human to human through air. The bacillus is spread into the air by droplets in the saliva of an active tuberculosis patient through coughing, sneezing, or other means, and the infection spreads by ingesting particles suspended in the air. The most common symptoms of the MTB are fever, chills, night sweats, loss of appetite, weight loss, and fatigue (Murphy et al., 2003; Khajanchi et al., 2018; Ojo et al., 2023). In order to control and prevent the infectious diseases, one must be well-versed in the disease mechanism and transmission dynamics. This helps predict disease progression and develop eradication strategies. Since diseases change over time, investigating epidemic dynamics is a crucial theoretical avenue for gaining insight into transmission dynamics and control. Mathematical modeling enables us to analyze and comprehend the transmission process of various infectious diseases. Moreover, mathematical models make a major contribution to analyze and comprehend the transmission dynamics of various diseases. Also, disease models provide better policy to control or prevent the spread of future infections. Analysis of disease via mathematical tools enables crucial predictions about infection and estimates of future outcomes that are impossible to calculate by alternative means. Numerous system models have been developed to understand the biological process of tuberculosis. They can also be used to assess the impact of public health intervention strategies and to suggest the best course of action to combat tuberculosis (Qureshi et al., 2021). Moreover, there are many tuberculosis models in the literature based on real-data to predict the future spread and control of the disease (Ullah et al., 2018; Khan et al. 2019).

Fractional-order models offer more reliable and accurate results about the process of diseases compared to traditional models. In addition, the definition of hereditary characteristics and memory gives it an advantage over traditional models. Fractional mathematical models have the feature of representing the dynamics between two non-local points (Qureshi et al., 2021). Especially in recent years, various theories and ideas related to fractional operators have been put forward and developed. Fractional calculus is frequently used in modeling of real-world problems in engineering, physics, psychology, medicine, economics and many other areas. Therefore, we prefer to analyze theoretically and numerically the transmission dynamics of tuberculosis disease by presenting the effect of non-integer order. Additionally, several studies in the literature have explored the joint analyses of tuberculosis and fractional derivatives (Sweilam et al., 2016; Zafar et al., 2022; Farman et al., 2023; Olaniyi et al., 2023). Due to the importance of the combination of non-local fractional derivatives with disease models in the

literature, we analyze the MTB model with the help of the Caputo derivative, which stands out with its advantages in application. This useful fractional operator with singular kernel is defined as follows:

$${}_c D^\omega \phi(t) = \frac{1}{\Gamma(n - \omega)} \int_a^t \frac{\phi^{(n)}(\xi)}{(t - \tau)^{\omega - n + 1}} d\xi, \quad (1.1)$$

where $Re \geq 0$ and $n = [Re(\omega)] + 1$ (Miller et al., 1993). Thanks to the Caputo definition, the MTB system, which is considered in the usual classical form in the study (Mustapha et al., 2022), is redefined and analyzed in fractional terms, and more precise results are obtained. It is investigated both theoretically and numerically, and the effect of the fractional order on the results in both cases is shown by comparing it with the integer-order derivative. We refer the reader to (Jarad et al., 2017; Acay et al., 2020; Acay et al., 2021a; Acay et al., 2021b; Inc et al., 2021; Uçkan et al., 2021; Yusuf et al., 2021) for more application of fractional operators and disease models.

The current article is structured as: In Section 2, we present the compartmental disease model for transmission dynamics of tuberculosis infection with hospitalization and reinfection through Caputo fractional operator. Model diagram of fractional system and all biological parameter descriptions and values are given in this section. Then, in Section 3, we address some basic analysis of the fractional MTB model, that is, positivity of the system solutions, stability analysis. Also, such dynamical features as the basic reproduction number, disease-free steady-state and endemic steady-state are shown for the fractional model under consideration. On the other hand, in Section 4, we give a numerical scheme to visualize the fractional MTB model with Caputo operator. Lastly, some crucial conclusions and future recommendations of our research study are introduced for better understanding the dynamics of mycobacterium tuberculosis disease.

2. Description of the Fractional Tuberculosis Transmission Model

In this section, we investigate the mathematical model of mycobacterium tuberculosis (MTB) transmission in humans with hospitalization and reinfection given in (Mustapha et al., 2022). Due to the known advantages of fractional derivatives in examining disease models, the mentioned model is defined and analyzed with the Caputo derivative. We define the tuberculosis transmission model under Caputo operator as follows:

$$\begin{aligned}
{}_c D^\omega S(t) &= \frac{1}{\Gamma(1-\omega)} \int_0^t \frac{S'(\xi)}{(t-\xi)^\omega} d\xi = \lambda^\omega - \beta^\omega S(t) + \gamma^\omega R(t) - \delta^\omega S(t), \\
{}_c D^\omega E(t) &= \frac{1}{\Gamma(1-\omega)} \int_0^t \frac{E'(\xi)}{(t-\xi)^\omega} d\xi = \beta^\omega S(t) - (\chi^\omega + \delta^\omega) E(t), \\
{}_c D^\omega A(t) &= \frac{1}{\Gamma(1-\omega)} \int_0^t \frac{A'(\xi)}{(t-\xi)^\omega} d\xi = \eta^\omega \chi^\omega E(t) - (\theta_1^\omega + \kappa_1^\omega + \alpha_1^\omega + \delta^\omega) A(t), \\
{}_c D^\omega I(t) &= \frac{1}{\Gamma(1-\omega)} \int_0^t \frac{I'(\xi)}{(t-\xi)^\omega} d\xi = (1 - \eta^\omega) \chi^\omega E(t) - (\theta_2^\omega + \kappa_2^\omega + \alpha_2^\omega + \delta^\omega) I(t), \\
{}_c D^\omega H(t) &= \frac{1}{\Gamma(1-\omega)} \int_0^t \frac{H'(\xi)}{(t-\xi)^\omega} d\xi = \theta_1^\omega A(t) + \theta_2^\omega I(t) - (\alpha_3^\omega + \kappa_3^\omega + \delta^\omega) H(t), \\
{}_c D^\omega R(t) &= \frac{1}{\Gamma(1-\omega)} \int_0^t \frac{R'(\xi)}{(t-\xi)^\omega} d\xi = \kappa_1^\omega A(t) + \kappa_2^\omega I(t) + \kappa_3^\omega H(t) - (\gamma^\omega + \delta^\omega) R(t),
\end{aligned} \tag{2.1}$$

where

$$\beta^\omega = \frac{\rho^\omega (\sigma_1 E(t) + \sigma_2 H(t) + \sigma_3 A(t) + I(t))}{N}$$

and $0 < \omega \leq 1$. Here, the population is divided into 6 groups: susceptible individuals ($S(t)$), exposed individuals ($E(t)$), asymptomatic MTB infected individuals with no clinical symptoms of MTB ($A(t)$), MTB infected individuals with clinical symptoms ($I(t)$), hospitalized individuals ($H(t)$), and recovered individuals ($R(t)$). The total number of population is represented by $N(t)$, so that $N(t) = S(t) + E(t) + A(t) + I(t) + H(t) + R(t)$.

In deriving the analysis of the model under investigation, we assume the following conditions:

- A closed population where the total number of individuals remains constant, considering recruitment and mortality rates.
- Homogeneous mixing of individuals, meaning that each susceptible individual has an equal probability of encountering an infectious individual.
- No external interventions (such as vaccination or treatment campaigns) affecting the transmission dynamics during the study period.
- The fractional-order model maintains the same biological assumptions as integer-order models while incorporating memory effects.
- The transmission rate remains time-invariant over the study period.

These assumptions are consistent with those in classical epidemiological models, allowing a direct comparison between integer-order and fractional-order models while investigating the impact of memory effects on disease dynamics.

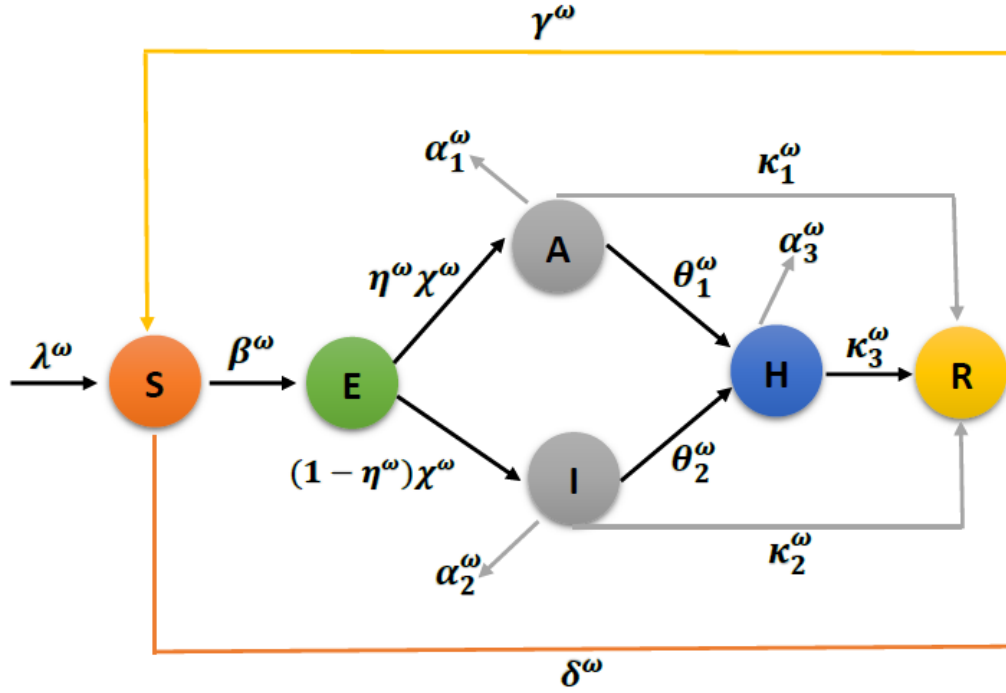


Figure 1: Diagram of the MTB model

Figure 1 shows the flow chart of the MTB mathematical model while Table 1 includes the description and values of the parameters. We use these all values in Section 4 to obtain the graphs of the system solutions. Fractional system (2.1) is constructed with care of dimensional analysis among the system parameters and derivatives. In other saying, the non-integer order ω does not invade dimensional analysis. Because, parameters of the MTB model includes the non-integer order ω except $\sigma_1, \sigma_2, \sigma_3$ (dimensionless parameters).

Table 1. Description of the parameters of MTB model

Parameter	Definition	Sample Value	Units	Source
λ	Recruitment rate	53	1/Day	Mustapha et al., 2022
δ	Naturel death rate	0.0047	1/Day	Mustapha et al., 2022
ρ	Transmission probability of MTB	0.000535	1/Day	Mustapha et al., 2022
χ	Progression of latent state of MTB	0.001	1/Day	Mustapha et al., 2022
η	Proportion of infected individuals	0.00071	1/Day	Mustapha et al., 2022
$\kappa_1, \kappa_2, \kappa_3$	Recovery rates	0.000453, 0.000543, 0.000234	1/Day	Mustapha et al., 2022
γ	Loss of immunity	0.00271	1/Day	Mustapha et al., 2022
$\alpha_1, \alpha_2, \alpha_3$	Death rate	0.0002, 0.0003, 0.0004	1/Day	Mustapha et al., 2022
θ_1, θ_2	Hospitalization rate	0.2849, 0.22806	1/Day	Mustapha et al., 2022
$\sigma_1, \sigma_2, \sigma_3$	Modification for the decrease/increase of MTB	[0, 1)	Dimensionless	Mustapha et al., 2022

The fractional system model given above is studied biologically and mathematically, and a comparative analysis is performed between the solutions obtained by classical derivative and those obtained by Caputo fractional derivative.

3. Mathematical Analysis of the Fractional MTB Infection Model

In this section, we show the fundamental properties of the fractional-type model under investigation. Firstly, positive invariant set for the fractional MTB model is given by Theorem 1 as below:

Theorem 1. The closed set $I = \{(S, E, A, I, H, R) \in R^6 : 0 \leq S + E + A + I + H + R \leq \frac{\lambda^\omega}{\delta^\omega}\}$ is a positive invariant set for the fractional model (2.1).

Proof. The following steps are utilized to prove the non-negativity of system (2.1) solution:

$$\begin{aligned}
{}_c D^\omega S(t)|_{S(t)=0} &= \lambda^\omega + \gamma^\omega \geq 0, \\
{}_c D^\omega E(t)|_{E(t)=0} &= \beta^\omega S(t) \geq 0, \\
{}_c D^\omega A(t)|_{A(t)=0} &= \eta^\omega \chi^\omega E(t) \geq 0, \\
{}_c D^\omega I(t)|_{I(t)=0} &= (1 - \eta^\omega) \chi^\omega E(t) \geq 0, \\
{}_c D^\omega H(t)|_{H(t)=0} &= \theta_1^\omega A(t) + \theta_2^\omega I(t) \geq 0, \\
{}_c D^\omega R(t)|_{R(t)=0} &= \kappa_1^\omega A(t) + \kappa_2^\omega I(t) + \kappa_3^\omega H(t) \geq 0,
\end{aligned} \tag{3.1}$$

This means that the solutions of the model handled are non-negative. On the other hand, by adding the equations of the fractional system (2.1), we have

$${}_c D^\omega N(t) \leq \lambda^\omega - \delta^\omega N(t) - (\alpha_1^\omega A(t) + \alpha_2^\omega I(t) + \alpha_3^\omega H(t)) \leq \lambda^\omega - \delta^\omega N(t). \quad (3.2)$$

If we use the property of Caputo operator, we get

$$N(t) \leq \left(N(0) - \frac{\lambda^\omega}{\delta^\omega} \right) \times E_\omega(-\delta^\omega t^\omega) + \frac{\lambda^\omega}{\delta^\omega}. \quad (3.3)$$

Under the property of Mittag-Leffler function $E_\omega(\cdot)$, we reach

$$(S(t) + E(t) + A(t) + I(t) + H(t) + R(t)) \leq \frac{\lambda^\omega}{\delta^\omega}, \quad (3.4)$$

and so the defined set I is positive invariant region for the fractional MTB infection model including Caputo operator.

The effective reproduction number is a critical threshold parameter for characterizing mathematical disease models. So let us calculate the reproduction number (R_0) for the proposed fractional model. But before that we show the existence of disease-free equilibrium point (DFE), E^0 . In the absence of the MTB infection ($E^* = 0, A^* = 0, I^* = 0, H^* = 0$), the system (2.1) reduces to $\lambda^\omega - \delta^\omega S = 0$. Solving, we obtain DFE as

$$E^0 = (S^*, E^*, A^*, I^*, H^*, R^*) = \left(\frac{\lambda^\omega}{\delta^\omega}, 0, 0, 0, 0 \right). \quad (3.5)$$

Now, benefiting from the DFE, we calculate R_0 with the help of next generation matrix method as follows. Also, the stability of DFE is investigated by using this efficient method (Van den Driessche et al., 2002). The matrix F_i (the rate of appearance of new infections in compartment i) and the matrix V_i (subtracting the transfer of individuals out of the compartment i from the rate of transfer of individuals into compartment i) are given by

$$F_i = \begin{bmatrix} \frac{\rho^\omega(\sigma_1 E + \sigma_2 H + \sigma_3 A + I)}{N} \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}, \quad V_i = \begin{bmatrix} (\chi^\omega - \delta^\omega)E \\ -\eta^\omega \chi^\omega E + (\theta_1^\omega + \kappa_1^\omega + \alpha_1^\omega + \delta^\omega)A \\ (\eta^\omega - 1)\chi^\omega E + (\theta_2^\omega + \kappa_2^\omega + \alpha_2^\omega + \delta^\omega)I \\ -\theta_1^\omega A - \theta_2^\omega I + (\alpha_3^\omega + \kappa_3^\omega + \delta^\omega)H \\ -\lambda^\omega + \beta^\omega S - \gamma^\omega R + \delta^\omega S \\ -\kappa_1^\omega A - \kappa_2^\omega I - \kappa_3^\omega H + (\gamma^\omega + \delta^\omega)R \end{bmatrix},$$

By using matrices F_i and V_i , we can get the matrices F (the rate of new infection cases) and V (the matrix including rest of the terms):

$$F = \begin{bmatrix} \rho^\omega \sigma_1 & \rho^\omega \sigma_3 & \rho^\omega & \rho^\omega \sigma_2 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix},$$

$$V = \begin{bmatrix} \chi^\omega - \delta^\omega & 0 & 0 & 0 \\ -\eta^\omega \chi^\omega & \theta_1^\omega + \kappa_1^\omega - \alpha_1^\omega + \delta^\omega & 0 & 0 \\ -\chi^\omega(1 - \eta^\omega) & 0 & 0 & 0 \\ 0 & -\theta_1^\omega & -\theta_2^\omega & \alpha_3^\omega + \kappa_3^\omega + \delta^\omega \end{bmatrix}.$$

So the matrix V^{-1} can be written as

$$V^{-1} = \begin{bmatrix} \frac{1}{B_1} & 0 & 0 & 0 \\ \frac{\eta^\omega \chi^\omega}{B_1 B_2} & \frac{1}{B_2} & 0 & 0 \\ \frac{\chi^\omega B_5}{B_1 B_3} & 0 & \frac{1}{B_3} & 0 \\ \frac{\chi^\omega (\eta^\omega B_3 \theta_1^\omega + B_2 B_5 \theta_2^\omega)}{B_1 B_2 B_3 B_4} & \frac{\theta_1^\omega}{B_2 B_4} & \frac{\theta_2^\omega}{B_3 B_4} & \frac{1}{B_4} \end{bmatrix}.$$

Here, $B_1 = \chi^\omega \delta^\omega$, $B_2 = \theta_1^\omega + \kappa_1^\omega + \alpha_1^\omega + \delta^\omega$, $B_3 = \theta_2^\omega + \kappa_2^\omega + \alpha_1^\omega + \delta^\omega$, $B_4 = \alpha_3^\omega + \kappa_3^\omega + \delta^\omega$, $B_5 = 1 - \eta^\omega$. On the other hand, the matrix FV^{-1} is

$$FV^{-1} = \begin{bmatrix} B_7 & \frac{\rho^\omega \sigma_3}{B_2} + \frac{\rho^\omega \sigma_2 \theta_1^\omega}{B_2 B_4} & \frac{\rho^\omega}{B_3} + \frac{\rho^\omega \sigma_2 \theta_2^\omega}{B_3 B_4} & \frac{\rho^\omega \sigma_2}{B_4} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix},$$

and $B_6 = \gamma^\omega \delta^\omega$, $B_7 = \frac{\rho^\omega \sigma_1}{B_1} + \frac{\rho^\omega \sigma_3 \eta^\omega \chi^\omega}{B_1 B_2} + \frac{\rho^\omega \chi^\omega B_5}{B_1 B_3} + \frac{\rho^\omega \sigma_2 \chi^\omega (\eta^\omega B_3 \theta_1^\omega + B_2 B_5 \theta_2^\omega)}{B_1 B_2 B_3 B_4}$. As a result of all calculations performed the reproduction number is given by

$$R_0 = \frac{\rho^\omega (\eta^\omega \chi^\omega B_3 B_4 \sigma_3 + \eta^\omega \chi^\omega B_3 \sigma_2 \theta_1^\omega + \chi^\omega B_2 B_5 \sigma_2 \theta_2^\omega + \chi^\omega B_2 B_4 B_5 + B_2 B_3 B_4 \sigma_1)}{B_1 B_2 B_3 B_4}.$$

So the following theorem can be given:

Theorem 2. The DFE of the proposed fractional model (2.1) is locally asymptotically stable if $R_0 < 1$ and unstable when $R_0 > 1$.

Now we present the analysis of the endemic equilibrium of the fractional MTB model. It is well-known that if $E \neq 0, A \neq 0, I \neq 0, H \neq 0$, the infection persists and the disease model has an endemic equilibrium (EE) point indicated by $EE = (S^*, E^*, A^*, I^*, H^*, R^*)$. Also, it can be noted that when $R_0 < 1$, the infection may disappear and for $R_0 > 1$, the infection persists. In order to obtain EE, we solve the fractional model (2.1) in terms of the β^ω and obtain

$$\begin{aligned}
S^* &= \frac{B_1 B_2 B_3 B_4 B_5 B_6 \lambda^\omega}{B_2 B_3 B_4 B_6 (\beta^\omega + \delta^\omega) - \chi^\omega \gamma^\omega \beta^\omega B_2 B_5 (B_4 \kappa_2^\omega + \theta_2^\omega \kappa_3^\omega) - \eta^\omega \chi^\omega \gamma^\omega \beta^\omega B_3 (B_4 \kappa_1^\omega + \theta_1^\omega \kappa_3^\omega)}, \\
E^* &= \frac{B_2 B_3 B_4 B_6 \beta^\omega \lambda^\omega}{B_1 B_2 B_3 B_4 B_6 - \chi^\omega \gamma^\omega B_2 B_5 (B_4 \kappa_2^\omega + \theta_2^\omega \kappa_3^\omega) - \eta^\omega \chi^\omega \gamma^\omega B_3 (B_4 \beta^\omega \kappa_1^\omega + \beta^\omega \theta_1^\omega \kappa_3^\omega) + B_1 B_2 B_3 B_4 B_6 \delta^\omega}, \\
A^* &= \frac{B_3 B_4 B_6 \eta^\omega \chi^\omega \beta^\omega \lambda^\omega}{B_1 B_2 B_3 B_6 - \chi^\omega \gamma^\omega B_2 B_5 (B_4 \kappa_2^\omega + \theta_2^\omega \kappa_3^\omega) - \eta^\omega \chi^\omega \gamma^\omega \beta^\omega B_3 (B_4 \kappa_1^\omega + \theta_1^\omega \kappa_3^\omega) + B_1 B_2 B_3 B_4 B_6 \delta^\omega}, \\
I^* &= \frac{B_2 B_4 B_5 B_6 \chi^\omega \beta^\omega \lambda^\omega}{B_1 B_2 B_3 B_4 B_6 - \chi^\omega \gamma^\omega B_2 B_5 (B_4 \kappa_2^\omega + \theta_2^\omega \kappa_3^\omega) - \eta^\omega \chi^\omega \gamma^\omega \beta^\omega (B_4 \kappa_1^\omega + \theta_1^\omega \kappa_3^\omega) + B_1 B_2 B_3 B_4 B_6 \delta^\omega}, \\
H^* &= \frac{\chi^\omega \beta^\omega \lambda^\omega B_6 (B_2 B_5 \theta_2^\omega + B_3 \theta_1^\omega \eta^\omega)}{B_1 B_2 B_3 B_4 B_6 - \chi^\omega \gamma^\omega B_2 B_5 (B_4 \kappa_2^\omega + \theta_2^\omega \kappa_3^\omega) - \eta^\omega \chi^\omega \gamma^\omega \beta^\omega B_3 (B_4 \kappa_1^\omega + \theta_1^\omega \kappa_3^\omega) + B_1 B_2 B_3 B_4 B_6 \delta^\omega}, \\
R^* &= \frac{\chi^\omega \beta^\omega \lambda^\omega (B_2 B_5 (B_4 \kappa_2^\omega + \theta_2^\omega \kappa_3^\omega) + \eta^\omega \chi^\omega \beta^\omega B_3 (B_4 \kappa_1^\omega + \theta_1^\omega \kappa_3^\omega))}{B_1 B_3 B_4 B_6 (\beta^\omega + \delta^\omega) - \chi^\omega \gamma^\omega \beta^\omega B_2 B_5 (B_4 \kappa_2^\omega + \theta_2^\omega \kappa_3^\omega) - \eta^\omega \chi^\omega \gamma^\omega \beta^\omega B_3 (B_4 \kappa_1^\omega + \theta_1^\omega \kappa_3^\omega)}.
\end{aligned}$$

Theorem 3. The EE points of the fractional system (2.1) is globally asymptotically stable when $R_0 > 1$ and unstable for $R_0 < 1$.

After performing some basic mathematical calculations for the fractional MTB infection model above, numerical analysis is carried out and how the fractional-order affects the disease dynamics is clearly observed in the graphs as follows:

4. Visual Results and Discussions

In the current section, we carry out numerical analysis of the fractional MTB disease model with the help of the Caputo operator. For this objective, fractional predictor-corrector method (Diethelm et al., 2002, Diethelm et al., 2004, Qureshi et al., 2019) is employed and we show the effect of non-integer order ω on the solutions with various graphs. The predictor-corrector method is given as follows.

Firstly, we write the fractional MTB infection model in the following form:

$$\begin{aligned}
{}_c D^\omega S(t) &= G_1(t, S, E, A, I, H, R), \\
{}_c D^\omega E(t) &= G_2(t, S, E, A, I, H, R), \\
{}_c D^\omega A(t) &= G_3(t, S, E, A, I, H, R), \\
{}_c D^\omega I(t) &= G_4(t, S, E, A, I, H, R), \\
{}_c D^\omega H(t) &= G_5(t, S, E, A, I, H, R), \\
{}_c D^\omega R(t) &= G_6(t, S, E, A, I, H, R).
\end{aligned} \tag{4.1}$$

For the time step interval Δt such that $t_i = i\Delta t, i = 0, 1, \dots, N$ and T is the upper limit of the integration interval, let $\Delta t = \frac{T}{N}$. Accordingly, the algorithm of the predictor part required for the numerical method to be used is

$$\begin{aligned} S_{n+1}^r &= S(0) + \sum_{i=1}^n a_{\omega, i, n+1} G_1(t_i, S_i, E_i, A_i, I_i, H_i, R_i), \\ E_{n+1}^r &= E(0) + \sum_{i=1}^n a_{\omega, i, n+1} G_2(t_i, S_i, E_i, A_i, I_i, H_i, R_i), \\ A_{n+1}^r &= A(0) + \sum_{i=1}^n a_{\omega, i, n+1} G_3(t_i, S_i, E_i, A_i, I_i, H_i, R_i), \\ I_{n+1}^r &= I(0) + \sum_{i=1}^n a_{\omega, i, n+1} G_4(t_i, S_i, E_i, A_i, I_i, H_i, R_i), \\ H_{n+1}^r &= H(0) + \sum_{i=1}^n a_{\omega, i, n+1} G_5(t_i, S_i, E_i, A_i, I_i, H_i, R_i), \\ R_{n+1}^r &= R(0) + \sum_{i=1}^n a_{\omega, i, n+1} G_6(t_i, S_i, E_i, A_i, I_i, H_i, R_i), \end{aligned}$$

and in a similar way, the algorithm of the corrector part for the numerical technique is given by

$$\begin{aligned} S_{n+1}^r &= S(0) + b_{\omega, n+1, n+1} G_1(t_i, S_i^r, E_i^r, A_i^r, I_i^r, H_i^r, R_i^r) + \sum_{i=1}^n b_{\omega, i, n+1} G_1(t_i, S_i, E_i, A_i, I_i, H_i, R_i), \\ E_{n+1}^r &= E(0) + b_{\omega, n+1, n+1} G_2(t_i, S_i^r, E_i^r, A_i^r, I_i^r, H_i^r, R_i^r) + \sum_{i=1}^n b_{\omega, i, n+1} G_2(t_i, S_i, E_i, A_i, I_i, H_i, R_i), \\ A_{n+1}^r &= A(0) + b_{\omega, n+1, n+1} G_3(t_i, S_i^r, E_i^r, A_i^r, I_i^r, H_i^r, R_i^r) + \sum_{i=1}^n b_{\omega, i, n+1} G_3(t_i, S_i, E_i, A_i, I_i, H_i, R_i), \\ I_{n+1}^r &= I(0) + b_{\omega, n+1, n+1} G_4(t_i, S_i^r, E_i^r, A_i^r, I_i^r, H_i^r, R_i^r) + \sum_{i=1}^n b_{\omega, i, n+1} G_4(t_i, S_i, E_i, A_i, I_i, H_i, R_i), \\ H_{n+1}^r &= H(0) + b_{\omega, n+1, n+1} G_5(t_i, S_i^r, E_i^r, A_i^r, I_i^r, H_i^r, R_i^r) + \sum_{i=1}^n b_{\omega, i, n+1} G_5(t_i, S_i, E_i, A_i, I_i, H_i, R_i), \\ R_{n+1}^r &= R(0) + b_{\omega, n+1, n+1} G_6(t_i, S_i^r, E_i^r, A_i^r, I_i^r, H_i^r, R_i^r) + \sum_{i=1}^n b_{\omega, i, n+1} G_6(t_i, S_i, E_i, A_i, I_i, H_i, R_i). \end{aligned}$$

On the other hand, the following equations are valid:

$$\begin{aligned} a_{\omega, i, n+1} &= \frac{1}{\Gamma(\omega + 1)} [(n - i + 1)^\omega - (n - i)^\omega], \\ b_{\omega, i, n+1} &= \frac{(\Delta t)^\omega}{\Gamma(\omega + 2)}, \end{aligned}$$

and

$$\begin{cases} n^{\omega+1} - (n - \omega)(n + 1)^{\omega}, & i = 0 \\ (n - i + 2)^{\omega+1} - 2(n - i + 1)^{\omega+1} + (n - i)^{\omega+1}, & 1 \leq i \leq n \\ 1, & i = n + 1 \end{cases}$$

Also, $r = \min(1 + \omega, 2)$ is the accuracy order of the fractional predictor-corrector method.

The graphs obtained for different values of ω and the biological parameter values in Table 1 are shown in Figure 2 and 3 by means of fractional-type predictor-corrector method. On these graphs, the MTB disease model containing the classical derivative and the model containing the Caputo derivative are compared. The time-dependent change of the state variables $S(t), E(t), A(t), I(t), H(t), R(t)$ belonging to the system (2.1) is first plotted in the classical case in Figure 2. Then, the comparison of the classical model (when $\omega = 1$) with the fractional model for $\omega = 0.9, 0.8, 0.7$ is given in Figure 3. The point to note here is how the fractional order ω changes the behavior of the solution curves. Moreover, the increase and decrease in number of susceptible individuals, exposed individuals, asymptomatic MTB infected individuals with no clinical symptoms of MTB, MTB infected individuals with clinical symptoms, hospitalized individuals, and recovered individuals can be easily observed on the graphs. For instance, in Figure 2, while the susceptible class increase more rapidly for the integer-order version ($\omega = 1$), in Figure 3, it increases more slowly for non-integer order values smaller than 1. Similarly, by looking at the increase and decrease rates of the other classes, we can see the effect of the non-integer order ω on the state variables.

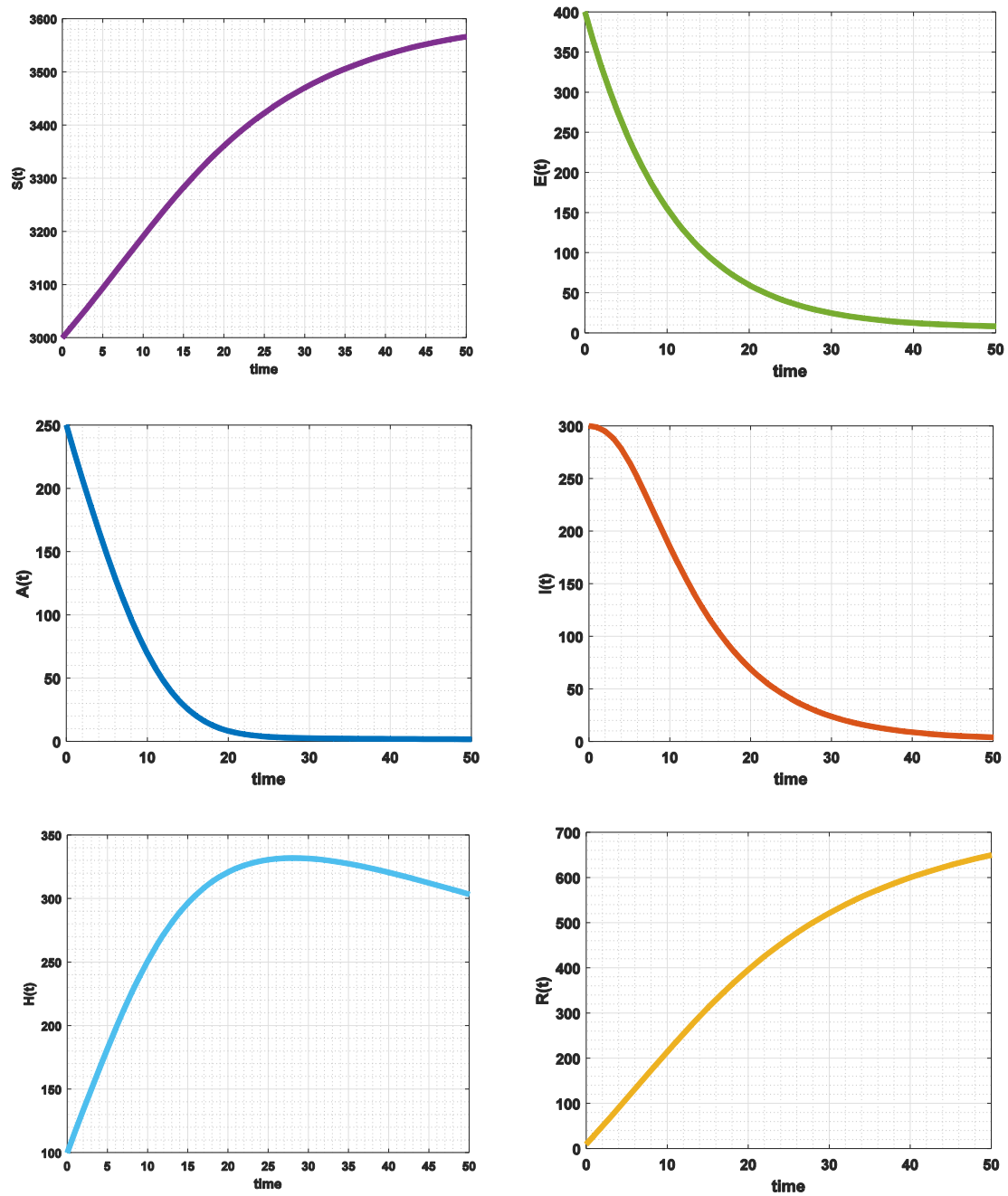
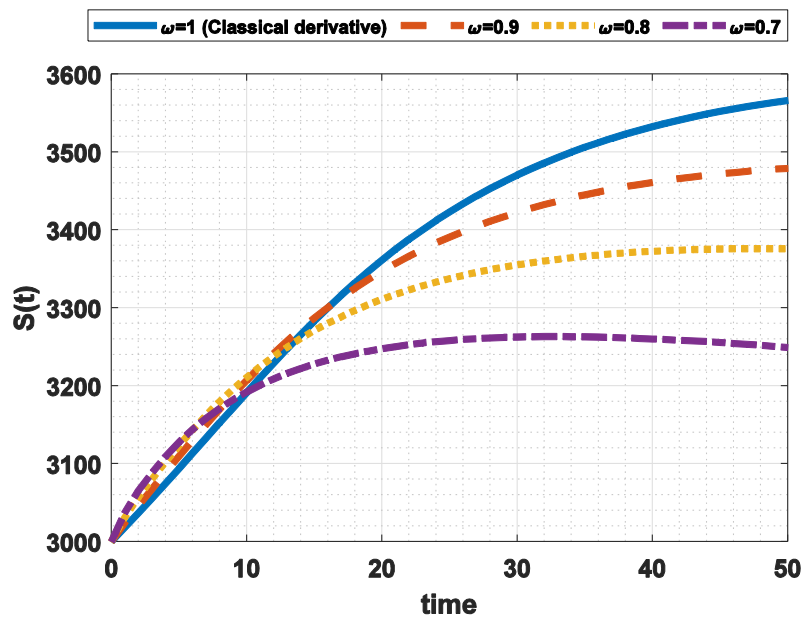
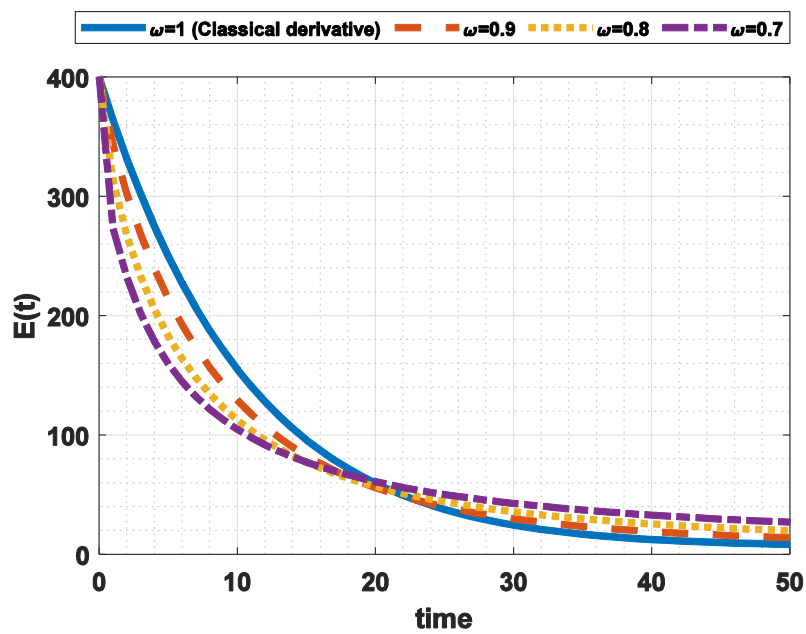


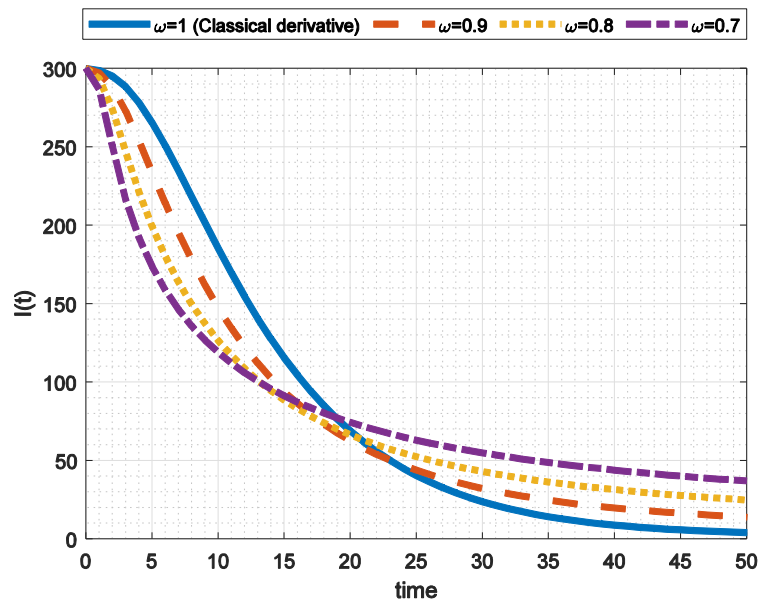
Figure 2: Profiles of solution functions of the classical-type MTB disease model (for $\omega = 1$ in the system (2.1)).



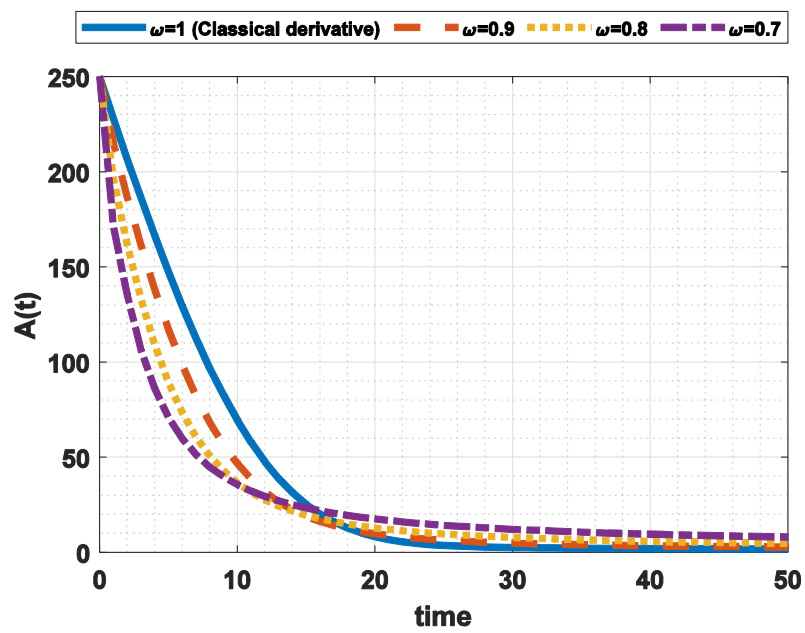
(A)



(B)



(C)



(D)

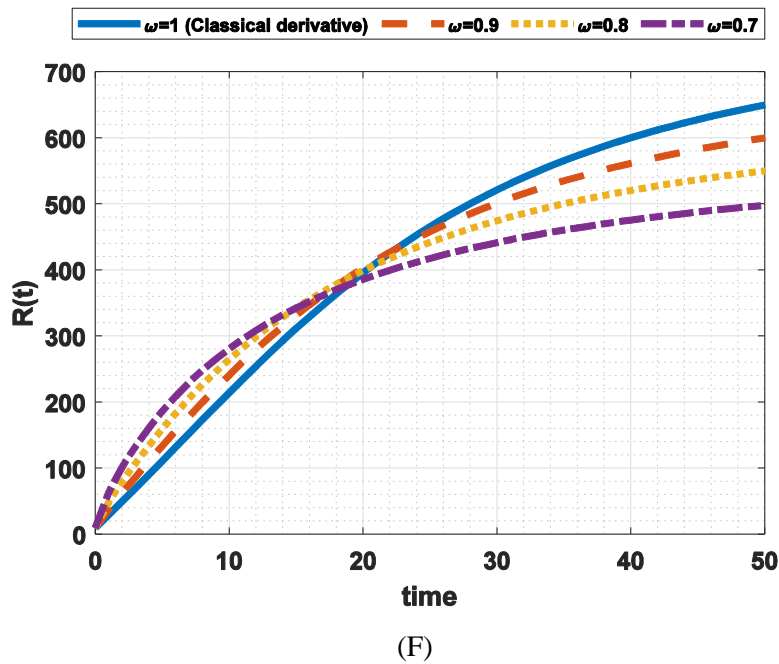
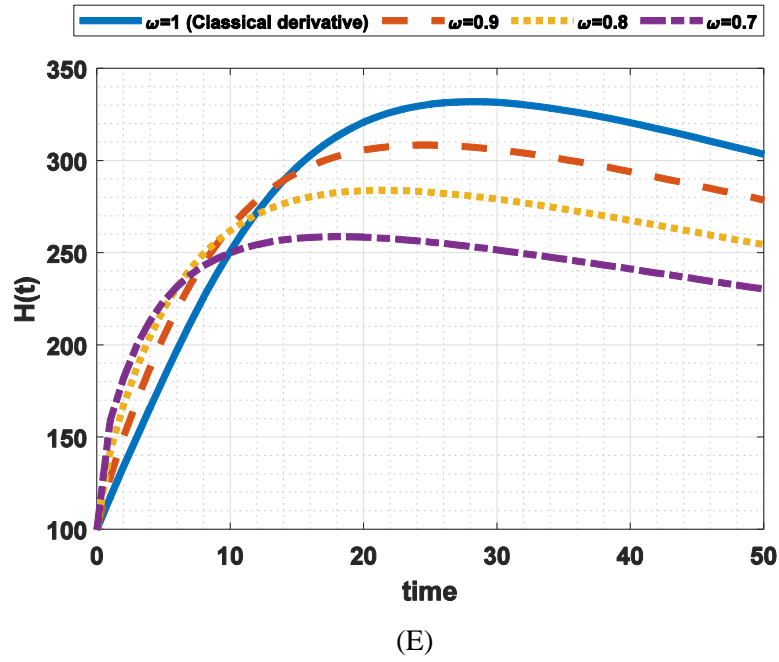


Figure 3: Comparison of solution functions between classical derivative ($\omega = 1$) and Caputo derivative (when $\omega = 0.9, 0.8, 0.7$) for the MTB disease model in (A), (B), (C), (D), (E), (F).

5. Concluding Remarks

Some crucial points and future directions of this study can be listed as follows:

1. It is well-known that non-integer order models have outperformed by their integer-order versions in many research area including biology, engineering, physics, epidemiology. For this reason, we preferred to employ an effective fractional derivative operator called Caputo for

investigating the mycobacterium tuberculosis disease model with reinfection and hospitalization. In this way, it is possible to reach more precise results regarding the course of the transmission dynamics of tuberculosis.

2. We perform an effective mathematical analysis belonging to the MTB model. Both theoretical and numerical results obtained with the fractional Caputo operator aim to contribute to disease eradication studies by shedding light on understanding the disease process.
3. In the numerical simulations, we considered fractional orders $\omega=0.7,0.8,0.9$ alongside the classical case ($\omega = 1$). The choice of these specific values is motivated by both mathematical feasibility and biological relevance. Fractional-order derivatives inherently capture memory effects in disease progression, meaning that past states influence the current infection dynamics.
4. From an epidemiological perspective, the fractional-order parameter ω can be interpreted as a measure of disease persistence and immune memory. Lower ω values ($\omega < 1$) represent scenarios where the disease exhibits stronger memory effects, potentially due to reinfection, prolonged latent periods, or variability in immune response. Higher ω values closer to 1 suggest that the disease follows dynamics similar to classical integer-order models, where recovery and transmission rates are more instantaneous.
5. The selected values ($\omega=0.7,0.8,0.9$) align with existing studies in fractional epidemiological modeling and allow us to observe the progressive impact of memory effects on tuberculosis dynamics. This approach provides a systematic way to compare the fractional and classical models and offers insights into how different memory effects influence disease transmission and control strategies. Future studies can further explore the impact of ω by fitting fractional models to real epidemiological data, optimizing ω based on empirical observations.
6. The theoretical results of this study include positive invariant set of fractional MTB model, stability analysis, reproduction number, disease-free and endemic steady-states. In accordance with the results of our current study, the DFE of the fractional model addressed is locally asymptotically stable if $R_0 < 1$ and stable if $R_0 > 1$. Also, the EE point of the proposed system is globally asymptotically stable for $R_0 > 1$ and unstable for $R_0 < 1$. It is worth noting that the reproduction number can be controlled much better via non-integer order as done in many studies in the literature.
7. Numerical results have been introduced to provide a better understanding of the transmission dynamics of tuberculosis infection. We have shown the effect of the non-integer order ω on the system solutions of the fractional MTB model on graphs. We have mentioned that non-integer order systems can express the complex dynamics of tuberculosis disease more accurately rather than traditional models.
8. Future studies would contain real-data on the tuberculosis disease to determine the better derivative definition more precisely. On the other hand, optimal control can be carried out in

the MTB model via the Caputo derivative. Moreover, other types of fractional operator definitions can be tried for better results.

9. In this study, the tuberculosis transmission model is analyzed for the first time using the Caputo fractional derivative, providing a novel perspective on the impact of memory effects in epidemiological modeling. Future studies can extend this work by validating the proposed model with real-world epidemiological data, further enhancing its applicability and reliability in predicting tuberculosis dynamics.

Declaration of Competing Interest

The author of the article declares that there is no conflict of interest.

Summary of Researchers' Contribution Declaration

The author declares that 100% contribution has been made to the article.

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