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A Fractional Approach To Chronic Pulmonary Aspergillosis Control In ICU Settings

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Abstract
In this article, a fractional-order model of chronic pulmonary aspergillosis in intensive care unit patients is developed. The solution's singularity is derived using fixed point theory. To determine the best control techniques, we introduce three control techniques using Pontryagin's maximum principle. Laplace transform allows simulating the fractional-order derivatives analytically. Analytical simulation of fractional-order derivatives is carried out by using Laplace transform. A deeper comprehension of the chronic pulmonary aspergillosis transmission patterns resulted from an analysis of the graphical results.

Keywords: Mathematical modeling, Fractional derivative, Chronic pulmonary aspergillosis, ICU patients.

1.Introduction:

Chronic pulmonary aspergillosis (CPA) is a fatal condition caused by the fungus Aspergillus fumigatus, which is known to cause lung infections. For an extended period, CPA goes untreated, which can have detrimental effects on one's health [1]. Research on A. fumigatus's transmission mechanisms is underway to enhance diagnostic and treatment outcomes considering that physicians still know the cause and mode of A. fumigatus domination. CPA is a lung condition that develops over time and has a bad prognosis, with a mortality rate of approximately 40–50 percent after five years [2]. Lung cancer, non-tuberculous mycobacterial infections (NTM), chronic obstructive pulmonary disease (COPD), pulmonary tuberculosis (PTB), and mildly immuno-compromised persons are the main groups affected [3].

Early on in the illness's course, the majority of CPA patients have clinically minimal symptoms; some, however, suffer symptoms much later in life. The asymptomatic phase can last up to ten years in certain cases [4]. Even with treatment, weight loss may still become more noticeable and occur more gradually over time. Possible symptoms include weariness, breathlessness and chest discomfort. In these patients, fever and sweating are rare medical signs. When they do become apparent, they are typically an indication of a CPA reaction that could result in intrusive fungal diseases or secondary infections, such as tuberculosis or bacterial pneumonia [5].

Mathematical modeling is an essential tool in the study of dynamics involved in the spread and transmission of a disease among humans because it allows one to analyze the various possible routes of transmission, identify the consequential ones, and investigate the impact of different control strategies on mitigating the spread and mortality associated with a disease [6]. Numerous studies have been conducted recently on the mathematical modeling of nosocomial infections [7], which are brought on by various bacterial and fungal pathogens that are resistant to multiple drugs [8], [9]. Still, further research is required in this field.
Furthermore, individuals suffering from serious fungal infections frequently need to receive necessary treatment for an underlying infection. Creating a fractional mathematical model for Aspergillus-related fungal infections in critical care units is the aim of this research project. For the most effective analysis of biological and technical systems, fractional-order differential equations are utilized. Physical and biological systems numerical models are made up of several fractional-order derivatives [10], [11]. While fractional order is useful in many contexts, here its main application is to memory dynamics, which is a feature shared by many biological systems. By applying differential equations that are built using the fractional derivative, one can examine the mechanisms behind the spread of infectious diseases, including pneumonia, HIV and AIDS, and other illnesses [12]. Chronic Pulmonary Aspergillosis infections evolve gradually with long-term immune response and tissue damage. ICU pathogen dynamics often exhibit temporal dependence which fractional derivatives represent effectively. Fractional models provide better accuracy for biological systems with non-local behaviour, unlike classical integer-order models.
The arrangement of the paper is as follows: the model is proposed for the transmission dynamics of the Chronic pulmonary aspergillosis in section 1 and Caputo-Fabrizio fractional derivative is introduced in section 2. The model singularity solution is derived

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using fixed point theory in section 3. The numerical simulation is investigated for the fractional-order model using the Laplace transforms in section 4. In section 5, we incorporate control variables and analyse the best control using Pontryagin's maximum principle. Graphical results are illustrated in section 6.

2. Mathematical Model:

Depending on the infection's stage of chronic pulmonary aspergillosis, patients in intensive care units are divided into four groups: susceptible (S), colonized (C_p), infected (I_p), fungal load in the environment (F).

$$\begin{aligned} S(t) &= A - \beta_F SF - \beta_A SI_p - \left(d_p + \epsilon_p + \mu'_p\right)S \\ C_p(t) &= \beta_F SF + \beta_A SI_p + \epsilon_p S - (\sigma_p + \Lambda_p + \kappa_p \\ &\quad + \mu'_p)C_p \\ I_p(t) &= \Lambda_p C_p - \left(\mu_p + \gamma_p + \mu'_p\right) I_p \\ F(t) &= \phi_p I_p + \left(\eta_p + \rho_p - \delta_p\right)F \end{aligned} \tag{2.1}$$

with $S(0) = S_0, C_p(0) = C_{p_0}, I_p(0) = I_{p_0}, F(0) = F_0$, where A - Admission rate of intensive care unit patients, d_p - discharge rate of intensive care unit patients, β_A - transmission rate of infection from infected to susceptible individuals, β_F - transmission rate of Aspergillus fungal infection from environment, μ_p - disease induced death rate, μ'_p - natural death rate, γ_p - rate of people getting cured through anti-fungal treatment, Λ_p - rate of people who have infected by the species, σ_p - rate of people who can develop innate of adaptive immunity through first line actors, ϵ_p - rate of people who have chronic lung disease, κ_p - probability of lack of surveillance and under diagnosis of the disease, ϕ_p - rate of use of contaminated medical equipment by infected patients, η_p - rate of contamination in hospital environment, ρ_p – exposure rate to Aspergillus spores from the environment due to water damage or poor ventilation in hospital, δ_p - disinfection of hospital environment.

3. Model Analysis:

Even though mathematical models based on integer derivatives occasionally fail to accurately represent real-world issues, this is typically due to the fact that reality is not always accurately converted to a mathematical formula or there is not enough data available to enable an accurate conversion. The Caputo fractional derivative of order α of a sufficiently smooth function $f(t)$, for $0 < \alpha < 1$, is defined as

$${}^{C}D_t^{\alpha} f(t) = \frac{1}{\Gamma(1-\alpha)} \int_0^t (t-\tau)^{-\alpha} f'(\tau)\, d\tau$$

In this definition the kernel captures memory and hereditary effects. Having said that, these models have been used with considerable effectiveness in recent decades, necessitating the use of human prediction. We have constructed a mathematical model based on the Caputo-Fabrizio fractional derivative [13], [14], [15], [16] in this part to forecast the chronic pulmonary aspergillosis infection in healthcare institutions. For the reasons outlined above, the Caputo-Fabrizio fractional derivative is employed in the standard mathematical model (3.1). The fractional-order system is

$$\begin{aligned} {}^{CF}D_t^{\alpha} S &= A - \beta_F SF - \beta_A SI_p - \left(d_p + \epsilon_p + \mu'_p\right)S \\ {}^{CF}D_t^{\alpha} C_p &= \beta_F SF + \beta_A SI_p + \epsilon_p S - (\sigma_p + \Lambda_p + \kappa_p \\ &\quad + \mu'_p)C_p \\ {}^{CF}D_t^{\alpha} I_p &= \Lambda_p C_p - \left(\mu_p + \gamma_p + \mu'_p\right) I_p \\ {}^{CF}D_t^{\alpha} F &= \phi_p I_p + \left(\eta_p + \rho_p - \delta_p\right)F \end{aligned} \tag{3.1}$$

4. Fractional Approach:

As the distinct solution of the fractional system (3.1) is examined and it turns out to be

$$\begin{aligned} \frac{1}{\lambda^{\alpha-1}} {}^{CF}D_t^{\alpha} S &= G_1(t, S) \\ \frac{1}{\lambda^{\alpha-1}} {}^{CF}D_t^{\alpha} C_p &= G_1(t, C_p) \\ \frac{1}{\lambda^{\alpha-1}} {}^{CF}D_t^{\alpha} I_p &= G_1\left(t, I_p\right) \\ \frac{1}{\lambda^{\alpha-1}} {}^{CF}D_t^{\alpha} F &= G_1(t, F) \end{aligned} \tag{4.1}$$

The fractional derivative theorem allows us to obtain

$$\begin{aligned} S - S(0) &= \frac{1}{\lambda^{\alpha-1}\,\Gamma(\alpha)} \int_0^t G_1(\tau, S)(t-\tau)^{\alpha-1}\, d\tau \\ C_p - C_p(0) &= \frac{1}{\lambda^{\alpha-1}\,\Gamma(\alpha)} \int_0^t G_1\left(\tau, C_p\right)(t-\tau)^{\alpha-1}\, d\tau \\ I_p - I_p(0) &= \frac{1}{\lambda^{\alpha-1}\,\Gamma(\alpha)} \int_0^t G_1\left(\tau, I_p\right)(t-\tau)^{\alpha-1}\, d\tau \\ F - F(0) &= \frac{1}{\lambda^{\alpha-1}\,\Gamma(\alpha)} \int_0^t G_1(\tau, F)(t-\tau)^{\alpha-1}\, d\tau \end{aligned} \tag{4.2}$$

Theorem 4.1:

The kernel G_1 satisfy the Lipschitz condition and contraction if the

$0 \le \beta_F k_1 + \beta_A k_2 + d_p + \epsilon_p + \mu'_p < 1$ *hold.*

Proof:

Let us consider for S and S_1,

$$\begin{aligned} &\left|\left|G_1(t, S) - G_1(t, S_1)\right|\right| \\ &\quad = \left|\left|-\beta_F\, F(S - S_1) - \beta_A I_p (S - S_1)\right.\right. \\ &\quad\quad \left.\left. - \left(d_p + \epsilon_p + \mu'_p\right)(S - S_1)\right|\right| \\ &\le \beta_F \left|\left|F\right|\right| \left|\left|S - S_1\right|\right| + \beta_A \left|\left|I_p\right|\right| \left|\left|S - S_1\right|\right| \\ &\quad\quad + \left(d_p + \epsilon_p + \mu'_p\right)\left|\left|S - S_1\right|\right| \\ &\le \left[\beta_F k_1 + \beta_A k_2 + d_p + \epsilon_p + \mu'_p\right]\left|\left|S - S_1\right|\right| \end{aligned}$$

Hence, $v_1 = \beta_F k_1 + \beta_A k_2 + d_p + \epsilon_p + \mu'_p$, where $\left|\left|F\right|\right| = k_1, \left|\left|I_p\right|\right| = k_2$, is bounded function. Therefore,

$$\left|\left|G_1(t, S) - G_1(t, S_1)\right|\right| \le v_1 \left|\left|S - S_1\right|\right| \tag{4.3}$$

Thus, the G_1 is contraction and the Lipschitz condition is obtained if $0 \le \beta_F k_1 + \beta_A k_2 + d_p + \epsilon_p + \mu'_p < 1$. For each relation, we also derive the lipschitz condition.

$$\begin{aligned} \left|\left|G_2\left(t, C_p\right) - G_2\left(t, C_{p_1}\right)\right|\right| &\le v_2 \left|\left|C_p - C_{p_1}\right|\right| \\ \left|\left|G_3\left(t, I_p\right) - G_3\left(t, I_{p_1}\right)\right|\right| &\le v_3 \left|\left|I_p - I_{p_1}\right|\right| \\ \left|\left|G_2(t, F) - G_2(t, F_1)\right|\right| &\le v_4 \left|\left|F - F_1\right|\right| \end{aligned}$$

where, $v_2 = \sigma_p + \Lambda_p + \kappa_p + \mu'_p, v_3 = \mu_p + \gamma_p + \mu'_p, v_4 = \eta_p + \rho_p - \delta_p$ are bounded functions if $0 \leq v_i < 1$, then $G_i, i = 1,2,3,4$ are contraction. Considering the recursive equations that follow, the system (4.2)

$$H_{1_r} = S_r - S_{r-1} = \frac{1}{\lambda^{1-\alpha}\,\Gamma(\alpha)}\int_0^t \big(G_1(\tau, S_{r-1}) - G_1(\tau, S_{r-2})\big)(t-\tau)^{\alpha-1}\,d\tau$$

$$H_{2_r} = C_{p_r} - C_{p_{r-1}} = \frac{1}{\lambda^{1-\alpha}\,\Gamma(\alpha)}\int_0^t \Big(G_2\big(\tau, C_{p_{r-1}}\big) - G_2\big(\tau, C_{p_{r-2}}\big)\Big)(t-\tau)^{\alpha-1}\,d\tau$$

$$H_{1_r} = I_{p_r} - I_{p_{r-1}} = \frac{1}{\lambda^{1-\alpha}\,\Gamma(\alpha)}\int_0^t \Big(G_3\big(\tau, I_{p_{r-1}}\big) - G_3\big(\tau, C_{p_{r-2}}\big)\Big)(t-\tau)^{\alpha-1}\,d\tau$$

$$H_{1_r} = F_r - F_{r-1} = \frac{1}{\lambda^{1-\alpha}\,\Gamma(\alpha)}\int_0^t \big(G_4(\tau, F_{r-1}) - G_4(\tau, F_{r-2})\big)(t-\tau)^{\alpha-1}\,d\tau$$

with the initial conditions. Consider the equation,

$$\big\|H_{1_r}\big\| = \big\||S_r - S_{r-1}\big\| = \left\|\tfrac{1}{\lambda^{1-\alpha}\,\Gamma(\alpha)}\textstyle\int_0^t \big(G_1(\tau, S_{r-1}) - G_1(\tau, S_{r-2})\big)\,(t-\tau)^{\alpha-1}\,d\tau\right\|$$

$$\leq \frac{1}{\lambda^{1-\alpha}\,\Gamma(\alpha)}\int_0^t \big\|\big(G_1(\tau, S_{r-1}) - G_1(\tau, S_{r-2})\big)(t-\tau)^{\alpha-1}\big\|\,d\tau$$

with the condition (4.3).

$$\big\|H_{1_r}\big\| \leq \frac{1}{\lambda^{1-\alpha}\,\Gamma(\alpha)} v_1 \int_0^t \big\|H_{1_{(r-1)}}(\tau)\big\|\,d\tau \quad (4.4)$$

Similarly we get,

$$\big\|H_{2_r}\big\| \leq \frac{1}{\lambda^{1-\alpha}\,\Gamma(\alpha)} v_2 \int_0^t \big\|H_{2_{(r-1)}}(\tau)\big\|\,d\tau$$

$$\big\|H_{3_r}\big\| \leq \frac{1}{\lambda^{1-\alpha}\,\Gamma(\alpha)} v_3 \int_0^t \big\|H_{3_{(r-1)}}(\tau)\big\|\,d\tau \quad (4.5)$$

$$\big\|H_{4_r}\big\| \leq \frac{1}{\lambda^{1-\alpha}\,\Gamma(\alpha)} v_4 \int_0^t \big\|H_{4_{(r-1)}}(\tau)\big\|\,d\tau$$

This can be written as

$$S_r = \sum_{j=1}^{n} H_{1_j}, C_{p_r} = \sum_{j=1}^{n} H_{2_j}, I_{p_r} = \sum_{j=1}^{n} H_{3_j},$$

$$F_r = \sum_{j=1}^{n} H_{4_j}$$

Theorem 4.2:

The fractional model (3.1) gives the system of solutions if there exist t_1 such that $\frac{1}{\lambda^{1-\alpha}\,\Gamma(\alpha)} t_1 b_i < 1 i$.

Proof:

By utilizing recursive approach (4.4) and (4.5) can be expressed as

$$\big\|H_{1_r}\big\| \leq \big\||S_r(0)\big\|\left[\tfrac{1}{\lambda^{1-\alpha}\,\Gamma(\alpha)} b_1 t\right]^r,$$

$$\big\|H_{2_r}\big\| \leq \big\|C_{p_r}(0)\big\|\left[\tfrac{1}{\lambda^{1-\alpha}\,\Gamma(\alpha)} b_2 t\right]^r$$

$$\big\|H_{3_r}\big\| \leq \big\|I_{p_r}(0)\big\|\left[\tfrac{1}{\lambda^{1-\alpha}\,\Gamma(\alpha)} b_3 t\right]^r,$$

$$\big\|H_{4_r}\big\| \leq \big\||F_r(0)\big\|\left[\tfrac{1}{\lambda^{1-\alpha}\,\Gamma(\alpha)} b_4 t\right]^r$$

We assume,

$$S - S(0) = S_r - B_{1_r}, C_p - C_p(0) = C_{p_r} - B_{2_r}, I_p - I_p(0) = I_{p_r} - B_{3_r}, F - F(0) = F_r - B_{4_r}$$

where,

$$\big\|B_{1_r}\big\| = \left\|\frac{1}{\lambda^{1-\alpha}\,\Gamma(\alpha)}\int_0^t \big(G_1(\tau, S) - G_1(\tau, S_{r-1})\big)d\tau\right\| \leq \frac{1}{\lambda^{1-\alpha}\,\Gamma(\alpha)} b_1 \big\|S - S_{r-1}\big\| t \quad (4.6)$$

we obtain $\big\|B_{1_r}(t)\big\| \to 0$ as $r \to \infty$. This can be retrieved for all functions. The proof is now complete. Assume (3.1) has another solution $S_1, C_{p_1}, I_{p_1}, F_1$. We have

$$S - S_1 = \frac{1}{\lambda^{1-\alpha}\,\Gamma(\alpha)}\int_0^t \big(G_1(\tau, S) - G_1(\tau, S_{r-1})\big)d\tau$$

$$\big\|S - S_1\big\| = \frac{1}{\lambda^{1-\alpha}\,\Gamma(\alpha)}\int_0^t \big\|\big(G_1(\tau, S) - G_1(\tau, S_{r-1})\big)\big\|\,d\tau$$

$$\big\|S - S_1\big\| \leq \frac{1}{\lambda^{1-\alpha}\,\Gamma(\alpha)} b_1(t)\big\|(S(t) - S_1(t))\big\|$$

$$\big\|S - S_1\big\|\left(1 - \frac{1}{\lambda^{1-\alpha}\,\Gamma(\alpha) b_1 t}\right) \leq 0 \quad (4.7)$$

Hence, $\big\|S - S_1\big\| = 0$. Therefore, $S = S_1$. In a similar manner, we may derive this outcome for each of the model's equations.

5. Numerical Simulation:

Consider the model,

$$\begin{aligned} {}^{CF}D_t^{\alpha} S &= G_1(t, S) \\ {}^{CF}D_t^{\alpha} C_p &= G_2(t, C_p) \\ {}^{CF}D_t^{\alpha} I_p &= G_3\big(t, I_p\big) \\ {}^{CF}D_t^{\alpha} F &= G_4(t, F) \end{aligned} \quad (5.1)$$

By taking Laplace transform on both sides of (3.1), we have

$$\frac{F(\alpha)s^{\alpha}L\{S\} - s^{\alpha-1}S(0)}{(1-\alpha)\left(s^{\alpha} + \frac{\alpha}{1-\alpha}\right)} = L\big\{A - \beta_F SF - \beta_A SI_p - \big(d_p + \epsilon_p + \mu'_p\big)S\big\}$$

$$\frac{F(\alpha)s^{\alpha}L\{C_p\} - s^{\alpha-1}C_p(0)}{(1-\alpha)\left(s^{\alpha}+\frac{\alpha}{1-\alpha}\right)} = L\{\beta_F SF + \beta_A SI_p + \epsilon_p S - (\sigma_p + \Lambda_p + \kappa_p + \mu'_p)C_p\}$$

$$\frac{F(\alpha)s^{\alpha}L\{I_p\} - s^{\alpha-1}I_p(0)}{(1-\alpha)\left(s^{\alpha}+\frac{\alpha}{1-\alpha}\right)} = L\left\{\Lambda_p C_p - \left(\mu_p + \gamma_p + \mu'_p\right)I_p\right\}$$

$$\frac{F(\alpha)s^{\alpha}L\{F\} - s^{\alpha-1}F(0)}{(1-\alpha)\left(s^{\alpha}+\frac{\alpha}{1-\alpha}\right)} = L\{\phi_p I_p + (\eta_p + \rho_p - \delta_p)F\}$$

By rearranging the equations, we get

$$L\{S\} = \frac{S(0)}{s} + \frac{s^{\alpha}(1-\alpha)+\alpha}{s^{\alpha}(F(\alpha))}L\{A - \beta_F SF - \beta_A SI_p - (d_p + \epsilon_p + \mu'_p)S\}$$

$$L\{C_p\} = \frac{C_p(0)}{s} + \frac{s^{\alpha}(1-\alpha)+\alpha}{s^{\alpha}(F(\alpha))}L\{\beta_F SF + \beta_A SI_p + \epsilon_p S - (\sigma_p + \Lambda_p + \kappa_p + \mu'_p)C_p\}$$

$$L\{I_p\} = \frac{I_p(0)}{s} + \frac{s^{\alpha}(1-\alpha)+\alpha}{s^{\alpha}(F(\alpha))}L\left\{\Lambda_p C_p - \left(\mu_p + \gamma_p + \mu'_p\right)I_p\right\} \quad (5.2)$$

$$L\{F\} = \frac{F(0)}{s} + \frac{s^{\alpha}(1-\alpha)+\alpha}{s^{\alpha}(F(\alpha))}L\{\phi_p I_p + (\eta_p + \rho_p - \delta_p)F\}$$

Taking inverse Laplace transform on (5.2) , gives

$$S = S(0) + L^{-1}\left[\left(\frac{s^{\alpha}(1-\alpha)+\alpha}{s^{\alpha}(F(\alpha))}\right)L\{A - \beta_F SF - \beta_A SI_p - \left(d_p + \epsilon_p + \mu'_p\right)S\}\right]$$

$$C_p = C_p(0) + L^{-1}\left[\left(\frac{s^{\alpha}(1-\alpha)+\alpha}{s^{\alpha}(F(\alpha))}\right)L\{\beta_F SF + \beta_A SI_p + \epsilon_p S - (\sigma_p + \Lambda_p + \kappa_p + \mu'_p)C_p\}\right]$$

$$I_p = I_p(0) + L^{-1}\left[\left(\frac{s^{\alpha}(1-\alpha)+\alpha}{s^{\alpha}(F(\alpha))}\right)L\left\{\Lambda_p C_p - \left(\mu_p + \gamma_p + \mu'_p\right)I_p\right\}\right]$$

$$F = F(0) + L^{-1}\left[\left(\frac{s^{\alpha}(1-\alpha)+\alpha}{s^{\alpha}(F(\alpha))}\right)L\{\phi_p I_p + (\eta_p + \rho_p - \delta_p)F\}\right]$$

The series solution obtained by the method are $S = \sum_{k=0}^{\infty} S_k$, $C_p = \sum_{k=0}^{\infty} C_{p_k}$, $I_p = \sum_{k=0}^{\infty} I_{p_k}$, $F = \sum_{k=0}^{\infty} F_k$. The recursive formula using the initial conditions is given by,

$$S_{k+1} = S_k(0) + L^{-1}\left[\left(\frac{s^{\alpha}(1-\alpha)+\alpha}{s^{\alpha}(F(\alpha))}\right)L\{A - \beta_F SF - \beta_A SI_p - \left(d_p + \epsilon_p + \mu'_p\right)S\}\right]$$

$$C_{p_{k+1}} = C_{p_k}(0) + L^{-1}\left[\left(\frac{s^{\alpha}(1-\alpha)+\alpha}{s^{\alpha}(F(\alpha))}\right)L\{\beta_F SF + \beta_A SI_p + \epsilon_p S - (\sigma_p + \Lambda_p + \kappa_p + \mu'_p)C_p\}\right]$$

$$I_{p_{k+1}} = I_{p_k}(0) + L^{-1}\left[\left(\frac{s^{\alpha}(1-\alpha)+\alpha}{s^{\alpha}(F(\alpha))}\right)L\left\{\Lambda_p C_p - \left(\mu_p + \gamma_p + \mu'_p\right)I_p\right\}\right]$$

$$F_{k+1} = F_k(0) + L^{-1}\left[\left(\frac{s^{\alpha}(1-\alpha)+\alpha}{s^{\alpha}(F(\alpha))}\right)L\{\phi_p I_p + (\eta_p + \rho_p - \delta_p)F\}\right]$$

Where $S_0 = S(0), C_{p_0} = C_p(0), I_{p_0} = I_p(0), \quad F_0 = F(0)$.

Therefore $S = \lim_{k\to\infty} S_k$, $C_p = \lim_{k\to\infty} C_{p_k}$, $I_p = \lim_{k\to\infty} I_{p_k}$, $F = \lim_{k\to\infty} F_k$.

The graphs are depicted [17] using the parameter values in table 1.

Table 1: Parameters and its values

Parameter	Values	Source
A	0.403	[18]
d_p	0.24	[19]
β_A	0.85	[20]
β_F	0.3	Assumed
μ_p	0.35	[21]
μ'_p	0.004	Assumed
γ_p	0.474	[22]
σ_p	0.31	Assumed
ϵ_p	0.00042	[23]
ϕ_p	0.15	[24]
η_p	0.2	[25]
δ_p	0.7	[25]
Λ_p	0.54	[26]
κ_p	0.9	[27]
ρ_p	0.7	[28]

6. Optimal Control:

The transmission model (3.1) is reconsidered by introducing three control inter-positions to minimize the infection of chronic pulmonary aspergillosis. The control variable w_1 denotes standard precautions implemented in ICU's, w_2 denotes the rate of infected individuals getting proper treatment like long-term oral antifungal therapy, w_3 denotes the rate of minimization of exposure to soil and dust in hospital.

$$\begin{aligned} S &= A - (1-w_1)\beta_F SF - (1-w_1)\beta_A SI_p - \left(d_p + \epsilon_p + \mu'_p\right)S \\ C_p &= (1-w_1)\beta_F SF + (1-w_1)\beta_A SI_p + \epsilon_p S - (\sigma_p + \Lambda_p + \kappa_p + \mu'_p)C_p \\ I_p &= \Lambda_p C_p - \left(\mu_p + \gamma_p + \mu'_p + w_2\right)I_p \\ F &= \phi_p I_p + \left(\eta_p + \rho_p - \delta_p - w_3\right)F \end{aligned} \quad (6.1)$$

The control set V is defined as $W = \{(w_1, w_2, w_3): 0 \leq w_1 \leq 1, 0 \leq w_2 \leq 1, 0 \leq w_3 \leq 1\}$. The main purpose of the system (6.1) is to infected population in ICU. Consider the objective function,

$$J = \int_0^T \left[C_p + I_p + F + \frac{r_1 w_1^2}{2} + \frac{r_2 w_2^2}{2} + \frac{r_3 w_3^2}{2} \right] dt \quad (6.2)$$

subject to the model (3.1), where $r_1, r_2, r_3 \geq 0$ and it represents the weight constraints. Pontryagin's Maximum principle [29], [30] enables us to prove the necessary condition of the problem. The $w^* = (w_1^*, w_2^*, w_3^*)$ is derived from the optimality problem by adjusting the control functions and is used to minimize the objective function.

$$J(w_1^*, w_2^*, w_3^*) = \min J(w_1(t), w_2(t), w_3(t)) \quad (6.3)$$

The existence of the optimal control is proved by using the integrand (6.2) and the model (6.1) are continuously differentiable in (S, C_p, I_p, F) and $w = (w_1, w_2, w_3)$.

Theorem 6.1:

Let the control function $w = (w_1, w_2, w_3) \in \Omega$ be measurable on $0 \leq t \leq T$. Then there exists w^* minimizing the objective functional $J(w_1, w_2, w_3)$ of (6.1) with

$$w_1^* = max\left\{min\left\{\frac{1}{r_1}[\lambda_2 - \lambda_1][\beta_F SF + \beta_A SI_p], 1\right\}, 0\right\}$$

$$w_2^* = max\left\{min\left\{\frac{1}{r_2}[\lambda_3 I_p], 1\right\}, 0\right\}$$

$$w_3^* = max\left\{min\left\{\frac{1}{r_3}[\lambda_4 F], 1\right\}, 0\right\}$$

Proof:

The necessary conditions of the optimal problem is proved by generating the Hamiltonian and is defined as

$$\tilde{H} = C_p + I_p + F + \frac{r_1 w_1^2}{2} + \frac{r_2 w_2^2}{2} + \frac{r_3 w_3^2}{2} + \lambda_1 S + \lambda_2 C_p + \lambda_3 I_p + \lambda_4 F \quad (6.4)$$

where $\lambda_1, \lambda_2, \lambda_3, \lambda_4$ are the adjoint variables for S, C_p, I_p, F state variables.

$$\frac{d\lambda_1}{dt} = (\lambda_1 - \lambda_2)(1 - w_1)\beta_F F + (\lambda_1 - \lambda_2)(1 - w_1)\beta_A I_p + \lambda_1(d_p + \epsilon_p + \mu'_p) - \lambda_2 \epsilon_p$$

$$\frac{d\lambda_2}{dt} = -1 + \lambda_2(\sigma_p + \Lambda_p + \kappa_p + \mu'_p) + \lambda_3 \Lambda_p$$

$$\frac{d\lambda_3}{dt} = -1 + \lambda_1(1 - w_1)\beta_A S - \lambda_2(1 - w_1)\beta_A S + \lambda_3(\mu_p + \gamma_p + \mu'_p + w_2) - \lambda_4 \phi_p$$

$$\frac{d\lambda_4}{dt} = -1 + \lambda_1(1 - w_1)\beta_F S - \lambda_2(1 - w_1)\beta_A S - \lambda_4(\eta_p + \rho_p - \delta_p - w_3)$$

with $\lambda_i(t) = 0, i = 1, 2, 3, 4$.

By Pontryagin's maximum principle, the optimality condition is

$$\frac{\partial \tilde{H}}{\partial w_1} = r_1 w_1 + (\lambda_1 - \lambda_2)\beta_F SF + (\lambda_1 - \lambda_2)\beta_A SI_p$$

$$\frac{\partial \tilde{H}}{\partial w_2} = r_2 w_2 - \lambda_3 I_p$$

$$\frac{\partial \tilde{H}}{\partial w_3} = r_3 w_3 - \lambda_4 F$$

After some manipulations, the optimal control can be written as

$$w_1^* = \max\left\{\min\left\{\frac{1}{r_1}[\lambda_2 - \lambda_1][\beta_F SF + \beta_A SI_p], 1\right\}, 0\right\}$$

$$w_2^* = \max\left\{\min\left\{\frac{1}{r_2}[\lambda_3 I_p], 1\right\}, 0\right\}$$

$$w_3^* = \max\left\{\min\left\{\frac{1}{r_3}[\lambda_4 F], 1\right\}, 0\right\}$$

7. Graphical Discussion:

Figure 1 depicts how the susceptible population behaves when single control techniques 1 through 3 are applied. The first technique involves activating the w_1 control, the second involves activating the w_2 control, and the third involves activating the w_3 control. It is evident from control interventions that the susceptible population is decreased with the activation of environmental disinfection control. Figure 2 illustrates how a single control affects a colonized colony. As we can see, prevention and control work well to reduce the number of colonized persons. Figure 3 shows that when the treatment control is turned on, the influence of a single control on the infected population rapidly declines. Strategy 2 reduces the number of affected people to a satisfactory level. When the environmental control is turned on, the fungal load significantly decreases, as seen in Figure 4. Since the overall minimizing of infection makes the single control strategies undesirable, the following analysis will look at two and three control combinations.

Figures 5 through 8 show how the two and three control treatments affected the fungal load and susceptible, colonized, infected population in the hospital setting. In this case, strategies 4 through 6 show how two controls are combined, and strategy 7 shows how all of the controls are intervened. The activation of treatment and environmental controls is represented by strategy 5, the activation of prevention and treatment controls is represented by strategy 6, and so on. Figure 5 illustrates that, in comparison to other combinations, strategies 4, 6, and 7 exert effort to raise the sensitive population at the same level, whereas strategy 5 exerts less effort. It's evident from figure 6 that strategies 4, 6, and 7 work harder to reduce the colonized population at the same rate. To keep the number of infected people at the same level, strategies 4 and 7 in Figure 7 exert more effort. Strategy 7 invests more effort to lower the amount of fungi present in the environment, as seen in Figure 8. According to the graphs, strategy 7 significantly lowers the number of colonized, sick patients as well as the amount of fungi present in the environment.

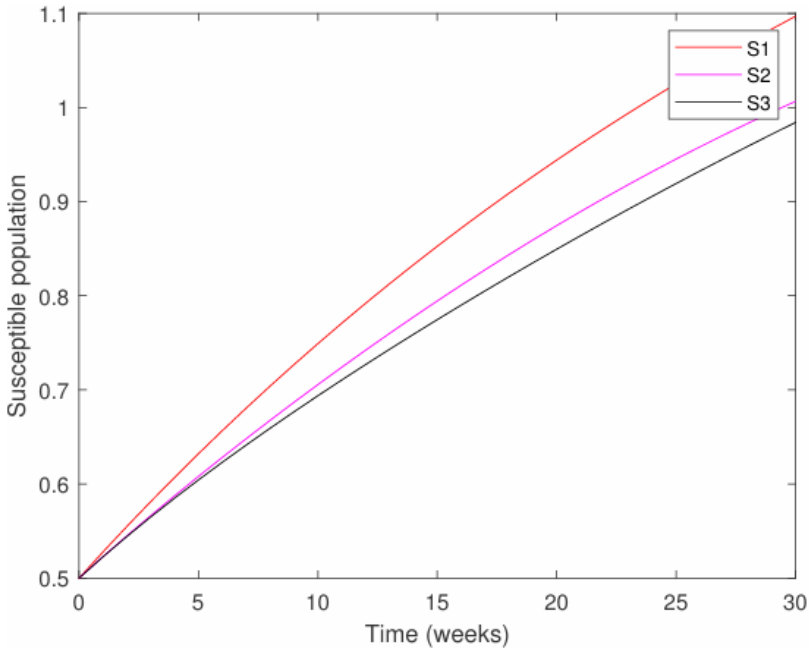

Figure 1. Influence of single control in susceptible population

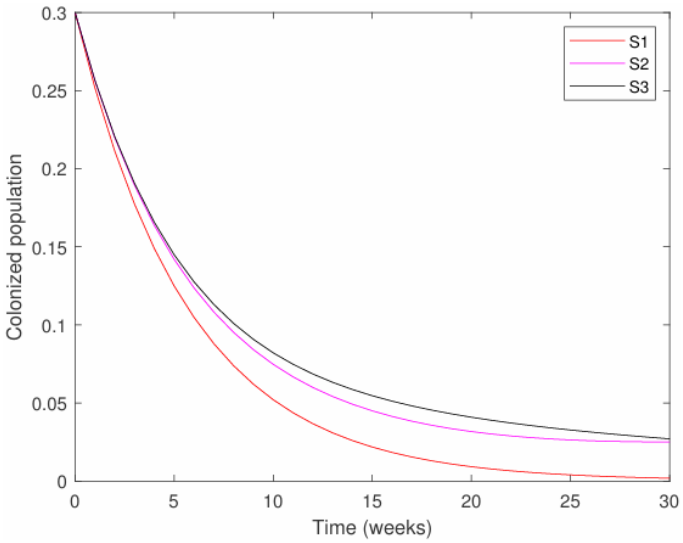

Figure 2. Influence of single control in colonized population

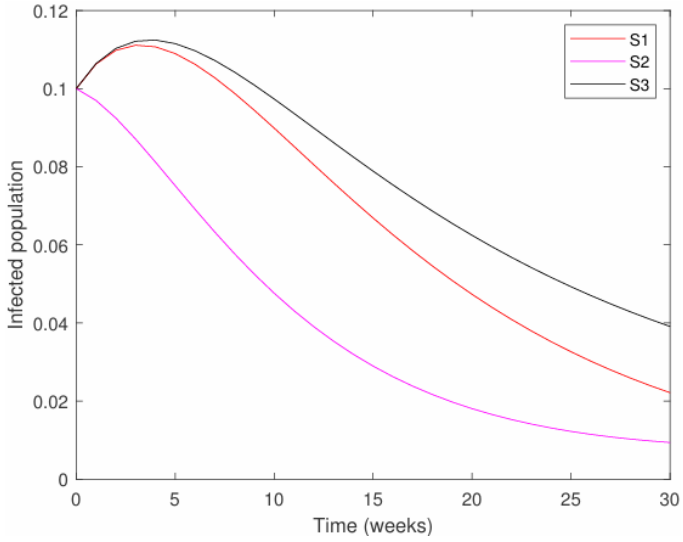

Figure 3. Influence of single control in infected population

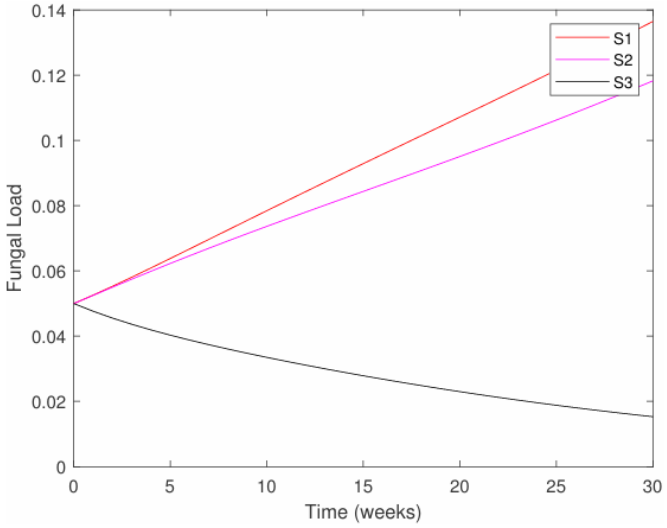

Figure 4. Influence of single control in fungal load

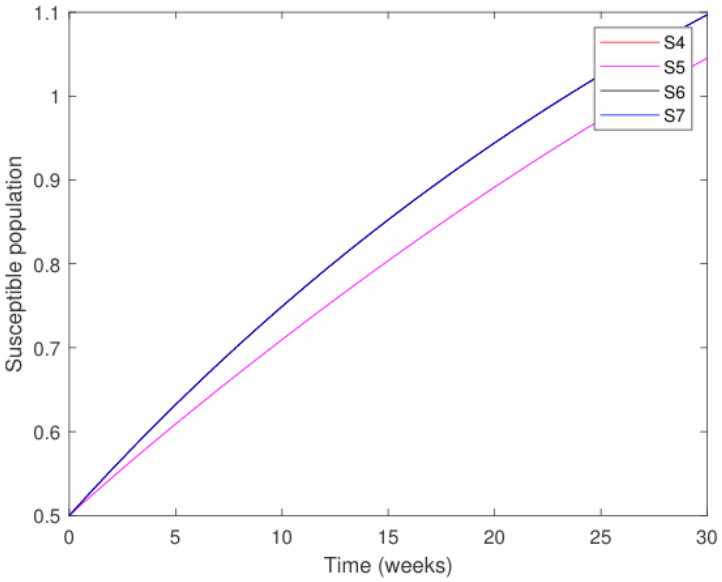

Figure 5. Influence of double and all the controls in susceptible population

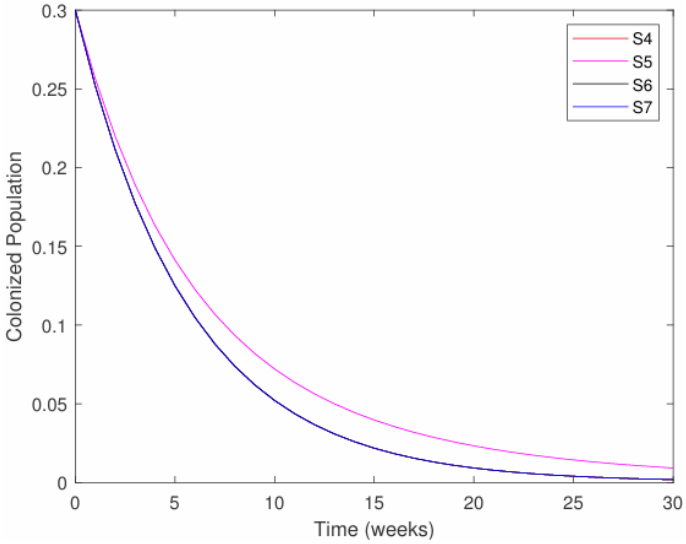

Figure 6. Influence of double and all the controls in colonized population

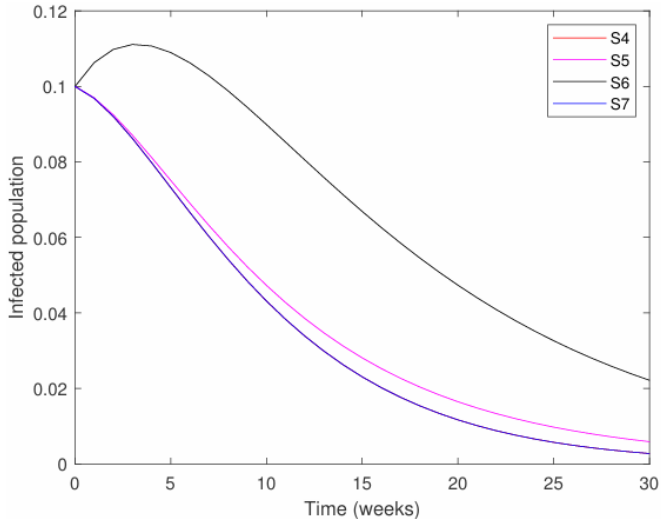

Figure 7. Influence of double and all the controls in infected population

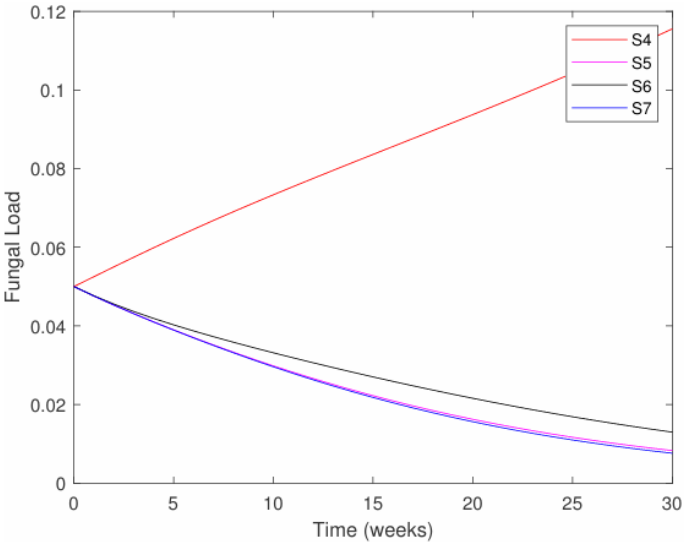

Figure 8. Influence of double and all the controls in Fungal load

Conclusion:

This work presents a model of chronic pulmonary aspergillosis using a fractional-order derivative of Caputo-Fabrizio. Fractional-order derivatives are unique and exist, as shown by fixed point theory. With three control variables-environmental control, treatment control, and preventative control-Pontryagin's maximum principle enables the identification of the most effective control measures. To obtain analytical results, we use the Laplace transform to simulate fractional-order derivatives. The control variables work together to influence the decrease in the colonized, infected population and the increase in susceptible instances, which ultimately results in the total reduction of infection in patients receiving intensive care units. In order to study the co-infection of the fungal illness, this model might be altered in subsequent research by adding the secondary disease.

Declaration:

The authors declare that they have no known competing financial interest or personal relationships that could have appeared to influence the work reported in this paper.

Conflict of Interests:

The authors have not disclosed any competing interests.

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