Research article

Transmission dynamics of breast cancer through Caputo Fabrizio fractional derivative operator with real data

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Abstract: In this paper, we studied the dynamical behavior of various phases of breast cancer using the Caputo Fabrizio (CF) fractional order derivative operator. The Picard-Lindelof (PL) method was used to investigate the existence and uniqueness of the proposed system. Moreover, we investigated the stability of the system in the sense of Ulam Hyers (UH) criteria. In addition, the two-step Adams-Bashforth (AB) technique was employed to simulate our methodology. The fractional model was then simulated using real data, which includes reported breast cancer incidences among females of Saudi Arabia from 2004 to 2016. The real data was used to determine the values of the parameters that were fitted using the least squares method. Also, residuals were computed for the integer as well as fractional-order models. Based on the results obtained, the CF model's efficacy rates were greater than those of the existing classical model. Graphical representations were used to illustrate numerical results by examining different choices of fractional order parameters, then the dynamical behavior of several phases of breast cancer was quantified to show how fractional order affects breast cancer behavior and how chemotherapy rate affects breast cancer behavior. We provided graphical results for a breast cancer model with effective parameters, resulting in fewer future incidences in the population of phases III and IV as well as the disease-free state. Chemotherapy often raises the risk of cardiotoxicity, and our proposed model output reflected this. The goal of this study was to reduce the incidence of cardiotoxicity in chemotherapy patients while also increasing the pace of patient recovery. This research has the potential to significantly improve outcomes of patients and provide information of treatment strategies for breast cancer patients.

Keywords: cardiotoxicity; epidemiology; PL technique; two-step AB scheme; UH stability

1. Introduction

As per medical experts, breast cancer is characterized by the abnormal development and division of cells inside the breast tissue. This condition poses a significant risk to health and is mostly seen in the female population. According to [1], compared to other types of cancer, the most people get breast cancer. It kills breast tissue and cells, causing the breasts to grow out of control and change shape. Several risk factors have been found that put women at a higher chance of getting breast cancer. Dietary habits, personal experience of malignancy, alcohol consumption, smoking, weight status, dense breast tissue, physical inactivity, reproductive history (including pregnancy and breastfeeding), menstrual history, genetic predisposition, racial background, life span history, specific breast changes, and getting older are all factors to consider. The main clinical presentations of breast cancer include lymphadenopathy, nipple discharge, nipple retraction, breast/nipple pain, presence of flaky skin on the breast/nipple, skin irritation, appearance of skin dimpling with erythema, changes in breast form or size, localized breast tissue thickening, and either complete or partial breast swelling. Tumor, node, and metastatic stages are used by medical professionals to evaluate a patient's cancer state and calculate their prospects of remission.

The odds of recovery are higher at earlier stages. Bisphosphonates, bone marrow transplants, gene therapy, hormone therapy, immunotherapy, surgery, stem cell therapy, targeted cancer medications, radiation, and

complementary and alternative treatments are only a few of the therapeutic methods that have been created to prevent cancer. Chemotherapy is the most popular kind of treatment for the aforementioned conditions, and it uses medications to destroy cancer cells. The medications used in chemotherapy are either administered intravenously to the patient or taken orally, with some efficacy but potential cardiac risks. Cardiotoxicity is a negative side effect that may affect both adults and children [2]. Mathematical models are employed to analyze the complicated dynamics of illnesses and offer precise outcomes for infection reduction and control.

One of the most rapidly expanding subfields of mathematical analysis is called fractional calculus, and it is concerned with the study of both derivatives and integrals of any arbitrary order [3, 4]. The nonlocality is a major advantage of the nonclassical derivatives that helps in the depiction of memory and hereditary characteristics of the system. As most of the biological processes involve the memory effect in the study of the epidemiological model fractional derivatives play a vital role.

Recent advancements suggest that fractional interpreters exhibit superior accuracy, utility, and reliability compared to the conventional derivative method. Contemporary fractional derivative operators are now being formulated in order to elucidate practical phenomena. Many mathematical models including integer and fractional order have been created in the literature for the detailed analysis of various diseases such as diabetes [5, 6], breast cancer [7], cancer treatment model [8, 9], HIV/AIDS [10, 11], lung cancer [12], Covid-19 [13–15], and in several other scientific and technological disciplines such as biology [16–18], chemistry [19], engineering [20–26], and most of the references cited therein.

The various techniques, such as the analytical methods [27–29], the semi-analytic methods [30–35], and the numerical methods [36–41] are found in the literature for solving fractional differential equations. Moreover, in [42], the solution of the fractional Sawada-Kotera-Ito equation using Caputo and Atangana-Baleanu (AB) derivatives have been derived. In [43], a robust computational analysis of residual power series involving general transform to solve fractional differential equations has been proposed. Abdeljawad et al. in [44] derived a

higher-order extension of AB fractional operators with respect to another function and a Gronwall-type inequality. In [45], the authors provide studies on the coupled snap system with integral boundary conditions in the G-Caputo sense. The authors in [46], studied the nonlocal multi-order implicit differential equation involving Hilfer fractional derivative on unbounded domains. In [47], an efficient variable step-size rational method for stiff, singular, and singularly perturbed problems has been given. The development of the reproducing kernel Hilbert space algorithm for the numerical pointwise solution of the time-fractional nonlocal reaction-diffusion equation is provided in [48].

In fractional calculus, a number of fractional operators are offered for the study of real issues. In contrast, these operators have a power law kernel and can merely partly simulate physical obstacles. Caputo and Fabrizio (CF) [49] introduced a unique fractional operator with a nonsingular kernel to address these issues and constraints. This revolutionary operator's results are more appropriate and have several applications. In [50], the authors studied the fractional mathematical modeling of the human liver. Ullah et al. in [51] analyzed a fractional model for the dynamics of tuberculosis infection. In [52], the authors proposed fractional cancer treatment. In [53], the authors studied the application of the CF derivative to a cancer model with unknown parameters. Ngungu et al. in [54] focused on mathematical epidemiological modeling and analysis of monkeypox dynamics with non-pharmaceutical intervation using real data from the UK. In [55], the authors developed the mathematical modeling of the immune-chemotherapeutic treatment of breast cancer under some control parameters, and the majority of the references listed therein have adequately represented the diseases transmission process with therapy and unidentified parameters.

The breast cancer classical mathematical model was categorized into five epidemiological groups by authors in [56]. However, it fails to optimally capture nonlocal behavior for the dynamics of the cancer, and the deviation between the real data and the data obtained through the simulation of the classical model is found to be large. Moreover, the freedom of having access to the real data is the

chief motivation behind detailed analysis of the breast cancer model under the CF fractional-order differential operator. These precise fractional calculus findings and consequences drive us to examine and analyze the dynamics of breast cancer using actual data, which are reported cases in Saudi Arabia from 2004 to 2016 [57]. It is noteworthy to mention that, unlike several previous studies, we have diligently ensured dimensional uniformity throughout the process of fractionalization.

The following is the outline of article: Section 2 explains the fractional calculus requirements for system analysis. Section 3 uses a CF framework to develop a fractional order model for breast cancer. Section 4 gives the Picard-Lindelof (PL) technique and the fixed-point theorem to investigate the existence and uniqueness of a proposed system. In Section 5, we numerically investigate the dynamics of the proposed model with variation in input parameters. Finally, final observations are offered in the concluding portion.

2. Preliminaries

Definition 2.1. *Let* $f \in \mathbb{H}^1(\iota_1, \iota_2)$ *and* $0 < r < 1$, *then the CF fractional derivative* [49] *is defined as follows:*

$$({}^{cf}_0 D^r_t N)(t) = \frac{P(r)}{1-r} \int_{\iota_1}^t N'(\delta) \exp\left[-\frac{r(t-\delta)}{1-r}\right] d\delta, \quad (2.1)$$

where $P(r)$ *is a normalizing function with the property that* $P(0) = P(1) = 1$.

Definition 2.2. [58] *If* $0 < r < 1$, *then the CF fractional integral of order* r *of a function* N *is:*

$$({}^{cf}_0 I^r_t N)(t) = \frac{2(1-r)}{(2-r)P(r)} N(t) + \frac{2r}{(2-r)P(r)} \int_0^t N(\delta) d\delta. \quad (2.2)$$

3. Formulation of fractional mathematical model

Authors in [56] classified the breast cancer model into five epidemiological categories. During the initial medical report, the overall population of breast cancer patients was divided into phases 1 and 2 ($\mathbb{S}_{12}$), phase 3 ($\mathbb{S}_3$), phase 4 ($\mathbb{S}_4$), disease-free state ($\mathbb{S}_R$), and cardiotoxic ($\mathbb{S}_E$) subpopulations.

The traditional system is described as:

$$\begin{cases} \frac{d\mathbb{S}_{12}}{dt} = \Delta - (\rho + \nu)\mathbb{S}_{12}, \\ \frac{d\mathbb{S}_3}{dt} = \Gamma + \nu\mathbb{S}_{12} + \psi\mathbb{S}_R - (\sigma + \mu + \kappa + \chi)\mathbb{S}_3, \\ \frac{d\mathbb{S}_4}{dt} = \Omega + \mu\mathbb{S}_3 + \phi\mathbb{S}_R - (\tau + \omega + \delta)\mathbb{S}_4, \\ \frac{d\mathbb{S}_R}{dt} = \rho\mathbb{S}_{12} + \sigma\mathbb{S}_3 + \tau\mathbb{S}_4 - (\psi + \phi + \zeta)\mathbb{S}_R, \\ \frac{d\mathbb{S}_E}{dt} = \zeta\mathbb{S}_R + \omega\mathbb{S}_4 + \kappa\mathbb{S}_3 - \eta\mathbb{S}_E, \end{cases} \quad (3.1)$$

where the following are the parameters of the system (3.1): Δ: people who have been diagnosed with cancer at stages 1 and 2; Γ: people suffering with stage 3 cancer; Ω: cancer patients in the fourth stage; ρ: chemotherapy recovery in phases 1 and 2; σ: chemotherapy recovery at stage 3; τ: chemotherapy recovery at stage 4; μ: people in worse health enter the stage 4 population; ν: people in worse health enroll in class $\mathbb{S}_3$; κ: patients undergoing severe treatment that induces cardiotoxicity; ω: people undergoing treatment for stage 4 cancer who suffer cardiotoxicity; ζ: at the disease-free stage, patients who have had extensive chemotherapy, which leads to cardiotoxicity; χ: cancer-related death at stage 3; δ: cancer-related death at stage 4; η: cardiotoxic patients' mortality rate; ψ: people who regress to stage 3; ϕ: people who regress to stage 4.

Now, to better approximate the spread of breast cancer with varying treatment rates into various compartments and to quantitatively demonstrate the influence of the above-mentioned parameters, the integer order model must be replaced by a fractional order model. The goal of this research is to extend the traditional system (3.1) by adding a fractional time derivative operator that allows for the analysis of memory effects in an arbitrary-order system. During the process of fractionalization, the dimensional consistency for each of the equations in the model has been maintained. We place the fractional order power r on each time-dimensional parameter to make the equal time dimension ($time^{-r}$) on both sides of the model. The proposed breast cancer transmission model, which includes the CF derivative, is offered as:

$$\begin{cases} {}^{cf}_0 D^r_t \mathbb{S}_{12} = \Delta^r - (\rho^r + \nu^r)\mathbb{S}_{12}, \\ {}^{cf}_0 D^r_t \mathbb{S}_3 = \Gamma^r + \nu^r\mathbb{S}_{12} + \psi^r\mathbb{S}_R - (\sigma^r + \mu^r + \kappa^r + \chi^r)\mathbb{S}_3, \\ {}^{cf}_0 D^r_t \mathbb{S}_4 = \Omega^r + \mu^r\mathbb{S}_3 + \phi^r\mathbb{S}_R - (\tau^r + \omega^r + \delta^r)\mathbb{S}_4, \\ {}^{cf}_0 D^r_t \mathbb{S}_R = \rho^r\mathbb{S}_{12} + \sigma^r\mathbb{S}_3 + \tau^r\mathbb{S}_4 - (\psi^r + \phi^r + \zeta^r)\mathbb{S}_R, \\ {}^{cf}_0 D^r_t \mathbb{S}_E = \zeta^r\mathbb{S}_R + \omega^r\mathbb{S}_4 + \kappa^r\mathbb{S}_3 - \eta^r\mathbb{S}_E, \end{cases} \quad (3.2)$$

with initial conditions: $\mathbb{S}_{12}(0) = \mathbb{S}_{12_0}, \mathbb{S}_3(0) = \mathbb{S}_{3_0}, \mathbb{S}_4(0) = \mathbb{S}_{4_0}, \mathbb{S}_R(0) = \mathbb{S}_{R_0}, \mathbb{S}_E(0) = \mathbb{S}_{E_0}$.

4. Qualitative analysis of fractional system

The present study aims to thoroughly examine the fractional system. The PL technique was used to investigate the presence and singularity of the offered solutions for the system (3.2). To begin the process, the system (3.2) is transformed into an integral equation with arbitrary order by applying (2.2) to both sides, resulting in

$$\begin{cases} \mathbb{S}_{12}(t) - \mathbb{S}_{12}(0) = {}^{cf}I_t^r\{N_1(t, \mathbb{S}_{12})\}, \\ \mathbb{S}_3(t) - \mathbb{S}_3(0) = {}^{cf}I_t^r\{N_2(t, \mathbb{S}_3)\}, \\ \mathbb{S}_4(t) - \mathbb{S}_4(0) = {}^{cf}I_t^r\{N_3(t, \mathbb{S}_4)\}, \\ \mathbb{S}_R(t) - \mathbb{S}_R(0) = {}^{cf}I_t^r\{N_4(t, \mathbb{S}_R)\}, \\ \mathbb{S}_E(t) - \mathbb{S}_E(0) = {}^{cf}I_t^r\{N_5(t, \mathbb{S}_E)\}, \end{cases} \quad (4.1)$$

where

$$N_1(t, \mathbb{S}_{12}) = \Delta^r - (\rho^r + \nu^r)\mathbb{S}_{12},$$

$$N_2(t, \mathbb{S}_3) = \Gamma^r + \nu^r \mathbb{S}_{12} + \psi^r \mathbb{S}_R - (\sigma^r + \mu^r + \kappa^r + \chi^r)\mathbb{S}_3,$$

$$N_3(t, \mathbb{S}_4) = \Omega^r + \mu^r \mathbb{S}_3 + \phi^r \mathbb{S}_R - (\tau^r + \omega^r + \delta^r)\mathbb{S}_4,$$

$$N_4(t, \mathbb{S}_R) = \rho^r \mathbb{S}_{12} + \sigma^r \mathbb{S}_3 + \tau^r \mathbb{S}_4 - (\psi^r + \phi^r + \zeta^r)\mathbb{S}_R,$$

$$N_5(t, \mathbb{S}_E) = \zeta^r \mathbb{S}_R + \omega^r \mathbb{S}_4 + \kappa^r \mathbb{S}_3 - \eta^r \mathbb{S}_E,$$

are contractions with respect to the functions $\mathbb{S}_{12}, \mathbb{S}_3, \mathbb{S}_4, \mathbb{S}_R$, and $\mathbb{S}_E$, respectively. Applying (2.2) on (4.1), we obtain

$$\begin{cases} \mathbb{S}_{12}(t) - \mathbb{S}_{12}(0) = \Omega(r)N_1(t, \mathbb{S}_{12}) + \omega(r)\int_0^t N_1(y, \mathbb{S}_{12})dy, \\ \mathbb{S}_3(t) - \mathbb{S}_3(0) = \Omega(r)N_2(t, \mathbb{S}_3) + \omega(r)\int_0^t N_2(y, \mathbb{S}_3)dy, \\ \mathbb{S}_4(t) - \mathbb{S}_4(0) = \Omega(r)N_3(t, \mathbb{S}_4) + \omega(r)\int_0^t N_3(y, \mathbb{S}_4)dy, \\ \mathbb{S}_R(t) - \mathbb{S}_R(0) = \Omega(r)N_4(t, \mathbb{S}_R) + \omega(r)\int_0^t N_4(y, \mathbb{S}_R)dy, \\ \mathbb{S}_E(t) - \mathbb{S}_E(0) = \Omega(r)N_5(t, \mathbb{S}_E) + \omega(r)\int_0^t N_5(y, \mathbb{S}_E)dy, \end{cases} \quad (4.2)$$

where

$$\Omega(r) = \frac{2(1 - r)}{(2 - r)P(r)}, \quad \omega(r) = \frac{2r}{(2 - r)P(r)}.$$

By Picard's iterative algorithm,

$$\begin{cases} \mathbb{S}_{12_{n+1}}(t) = \Omega(r)N_1(t, \mathbb{S}_{12_n}) + \omega(r)\int_0^t N_1(y, \mathbb{S}_{12_n})dy, \\ \mathbb{S}_{3_{n+1}}(t) = \Omega(r)N_2(t, \mathbb{S}_{3_n}) + \omega(r)\int_0^t N_2(y, \mathbb{S}_{3_n})dy, \\ \mathbb{S}_{4_{n+1}}(t) = \Omega(r)N_3(t, \mathbb{S}_{4_n}) + \omega(r)\int_0^t N_3(y, \mathbb{S}_{4_n})dy, \\ \mathbb{S}_{R_{n+1}}(t) = \Omega(r)N_4(t, \mathbb{S}_{R_n}) + \omega(r)\int_0^t N_4(y, \mathbb{S}_{R_n})dy, \\ \mathbb{S}_{E_{n+1}}(t) = \Omega(r)N_5(t, \mathbb{S}_{E_n}) + \omega(r)\int_0^t N_5(y, \mathbb{S}_{E_n})dy. \end{cases} \quad (4.3)$$

The solutions are achieved as follows:

$$\lim_{n\to\infty} \mathbb{S}_{12_n}(t) = \mathbb{S}_{12}(t), \lim_{n\to\infty} \mathbb{S}_{3_n}(t) = \mathbb{S}_3(t), \lim_{n\to\infty} \mathbb{S}_{4_n}(t) = \mathbb{S}_4(t),$$

$$\lim_{n\to\infty} \mathbb{S}_{R_n}(t) = \mathbb{S}_R(t), \quad \lim_{n\to\infty} \mathbb{S}_{E_n}(t) = \mathbb{S}_E(t).$$

To demonstrate the existence of the solution, we use the PL approach and the Banach fixed point theorem.

Let

$$N_1^* = \sup_{\mathbb{C}[a,b_1]} \|N_1(t, \mathbb{S}_{12})\|, \quad N_2^* = \sup_{\mathbb{C}[a,b_2]} \|N_2(t, \mathbb{S}_3)\|,$$

$$N_3^* = \sup_{\mathbb{C}[a,b_3]} \|N_1(t, \mathbb{S}_4)\|, \quad N_4^* = \sup_{\mathbb{C}[a,b_4]} \|N_1(t, \mathbb{S}_R)\|,$$

$$N_5^* = \sup_{\mathbb{C}[a,b_5]} \|N_1(t, \mathbb{S}_E)\|,$$

where

$$\mathbb{C}[a, b_1] = [t - a, t + a] \times [\mathbb{S}_{12} - b_1, \mathbb{S}_{12} + b_1] = \mathbb{A} \times \mathbb{B}_1,$$

$$\mathbb{C}[a, b_2] = [t - a, t + a] \times [\mathbb{S}_3 - b_2, \mathbb{S}_3 + b_2] = \mathbb{A} \times \mathbb{B}_2,$$

$$\mathbb{C}[a, b_3] = [t - a, t + a] \times [\mathbb{S}_4 - b_3, \mathbb{S}_4 + b_3] = \mathbb{A} \times \mathbb{B}_3,$$

$$\mathbb{C}[a, b_4] = [t - a, t + a] \times [\mathbb{S}_R - b_4, \mathbb{S}_R + b_4] = \mathbb{A} \times \mathbb{B}_4,$$

$$\mathbb{C}[a, b_5] = [t - a, t + a] \times [\mathbb{S}_E - b_5, \mathbb{S}_E + b_5] = \mathbb{A} \times \mathbb{B}_5.$$

Consider a uniform norm on $\mathbb{C}[a, b_\iota], (\iota = 1, 2, 3, 4, 5)$ as given by

$$\|U(t)\|_\infty = \sup_{t\in[t-a,t+a]} |U(t)|.$$

We define the Picard operator as:

$$\triangle : \mathbb{C}(\mathbb{A}, \mathbb{B}_1, \mathbb{B}_2, \mathbb{B}_3, \mathbb{B}_4, \mathbb{B}_5) \to \mathbb{C}(\mathbb{A}, \mathbb{B}_1, \mathbb{B}_2, \mathbb{B}_3, \mathbb{B}_4, \mathbb{B}_5)$$

described by

$$\triangle(U(t)) = U_0(t) + \Omega(r)N(t, U(t)) + \omega(r)\int_0^t N(y, U(y))dy,$$

where

$$U(t) = \{\mathbb{S}_{12}(t), \mathbb{S}_3(t), \mathbb{S}_4(t), \mathbb{S}_R(t), \mathbb{S}_E(t)\},$$

$$U_0(t) = \{\mathbb{S}_{12}(0), \mathbb{S}_3(0), \mathbb{S}_4(0), \mathbb{S}_R(0), \mathbb{S}_E(0)\},$$

$$N(t, U(t)) = \{N_1(t, \mathbb{S}_{12}), N_2(t, \mathbb{S}_3), N_3(t, \mathbb{S}_4), N_4(t, \mathbb{S}_R), N_5(t, \mathbb{S}_E)\}.$$

We consider the solutions to the problem under examination are bounded within a time interval, that is,

$$\|U(t)\|_\infty \leqslant max\{b_1, b_2, b_3, b_4, b_5\} = b.$$

Let

$$N^* = max\left\{N_1^*, N_2^*, N_3^*, N_4^*, N_5^*\right\},$$

and $\exists\, t_0$, so $t \leqslant t_0$, then

$$\|\triangle U(t) - U_0(t)\|$$

$$= \left\| \Omega(r) N(t, U(t)) + \omega(r) \int_0^t N(y, U(y)) dy \right\|$$

$$\leqslant \Omega(r) \|N(t, U(t))\| + \omega(r) \int_0^t \|N(y, U(y))\| \, dy$$

$$\leqslant (\Omega(r) + \omega(r)t) \, N^*$$

$$\leqslant (\Omega(r) + \omega(r)t_0) \, N^*$$

$$\leqslant \mu^* N^*$$

$$\leqslant b,$$

where

$$\mu^* = (\Omega(r) + \omega(r)t_0) \leqslant \frac{b}{N^*}.$$

Further, we prove the following equality:

$$\|\triangle U_1 - \triangle U_2\| = \sup_{t \in \mathbb{A}} |U_1(t) - U_2(t)|.$$

Using the Picard operator, we get

$$\|\triangle U_1 - \triangle U_2\|$$

$$= \| \Omega(r) \{N(t, U_1(t)) - N(t, U_2(t))\}$$

$$\left. + \omega(r) \int_0^t \{N(y, U_1(y)) - N(y, U_2(y))\} \, dy \right\|$$

$$\leqslant \Omega(r) \|N(t, U_1(t)) - N(t, U_2(t))\|$$

$$+ \omega(r) \int_0^t \|N(y, U_1(y)) - N(y, U_2(y))\| \, dy$$

$$\leqslant \Omega(r)\gamma^* \|U_1(t) - U_2(t)\| + \omega(r)\gamma^* \int_0^t \|U_1(y) - U_2(y)\| \, dy$$

$$\leqslant (\Omega(r) + \omega(r)t_0) \, \gamma^* \|U_1(y) - U_2(y)\|$$

$$\leqslant \mu^* \gamma^* \|U_1(y) - U_2(y)\|$$

with $\gamma^* < 1$.

Since N is a contraction, then $\mu^*\gamma^* < 1$, so the discussed operator $\triangle$ is a contraction. Hence, system (3.2) has a unique solution.

5. Stability analysis of the proposed fractional model

In this section, we discuss the Ulam-Hyres (UH) stabiity (such as [59, 60]) of the proposed fractional model (3.2) using the notion of nonlinear functional analysis. For the sake of simplicity we consider the proposed model (3.2) as:

$$\begin{cases} {}^{cf}_0 D_t^r \mathbb{B}(t) = \Theta(t, \mathbb{B}(t)), \\ \mathbb{B}(0) = \mathbb{B}_0 \geq 0, \end{cases} \tag{5.1}$$

where

$$\mathbb{B}(t) = (\mathbb{S}_{12}(t), \mathbb{S}_3(t), \mathbb{S}_4(t), \mathbb{S}_R(t), \mathbb{S}_E(t))^T,$$

$$\mathbb{B}_0 = (\mathbb{S}_{12_0}, \mathbb{S}_{3_0}, \mathbb{S}_{4_0}, \mathbb{S}_{R_0}, \mathbb{S}_{E_0})^T,$$

$$\Theta(t, \mathbb{B}(t)) = (N_1, N_2, N_3, N_4, N_5)^T.$$

Applying fractional integral (2.2) on (5.1), we get

$$\mathbb{B}(t) = \mathbb{B}_0 + \Omega(r)\Theta(t, \mathbb{B}(t)) + \omega(r) \int_0^t \Theta(\delta, \mathbb{B}(\delta)) d\delta. \tag{5.2}$$

Definition 5.1. *The proposed system* (3.2) *is UH stable if* $\exists$ $\overline{\mu} > 0$ *with the following property. For any* $\epsilon > 0$ *and* $\overline{\mathbb{B}} \in \mathsf{B}$ *(Banach space), if*

$$\left| {}^{cf}_0 D_t^r \overline{\mathbb{B}}(t) - \Theta\left(t, \overline{\mathbb{B}}(t)\right) \right| \leq \epsilon, \tag{5.3}$$

then $\exists\, \mathbb{B} \in \mathsf{B}$ *satisfies system* (3.2) *with initial condition*

$$\mathbb{B}(0) = \overline{\mathbb{B}}(0) = \overline{\mathbb{B}}_0,$$

such that

$$\left\| \overline{\mathbb{B}} - \mathbb{B} \right\| \leq \overline{\mu}\epsilon.$$

where

$$\begin{cases} \overline{\mathbb{B}}(t) = \left(\overline{\mathbb{S}}_{12}(t), \overline{\mathbb{S}}_3(t), \overline{\mathbb{S}}_4(t), \overline{\mathbb{S}}_R(t), \overline{\mathbb{S}}_E(t)\right)^T, \\ \mathbb{B}_0 = \left(\overline{\mathbb{S}}_{12_0}, \overline{\mathbb{S}}_{3_0}, \overline{\mathbb{S}}_{4_0}, \overline{\mathbb{S}}_{R_0}, \overline{\mathbb{S}}_{E_0}\right)^T, \\ \Theta(t, \overline{\mathbb{B}}(t)) = \left(\overline{N}_1, \overline{N}_2, \overline{N}_3, \overline{N}_4, \overline{N}_5\right)^T, \\ \epsilon = max(\epsilon_j)^T; \quad j = 1, 2, 3, 4, 5, \\ \overline{\mu} = max(\overline{\mu}_j)^T; \quad j = 1, 2, 3, 4, 5. \end{cases}$$

Remark 5.1. *Consider a small perturbation* $k \in \mathsf{C}[0, \mathsf{T}]$, *such that* $k(0) = 0$ *along with the following property :* $|k(t)| \leq \overline{\epsilon}$, *for* $t \in [0, \mathsf{T}]$ *and* $\overline{\epsilon} > 0$,

Lemma 5.1. *[10] The solution* $\overline{\mathbb{B}}_k(t)$ *of the perturbed system*

$$^{cf}_0 D_t^r \overline{\mathbb{B}}(t) = \Theta\left(t, \overline{\mathbb{B}}(t)\right) + k(t), \quad \overline{\mathbb{B}}(0) = \overline{\mathbb{B}}_0, \tag{5.4}$$

saisfies the relation:

$$\left\| \overline{\mathbb{B}}_k(t) - \overline{\mathbb{B}}(t) \right\| \leq \Phi\overline{\epsilon},$$

where

$$\Phi = \Omega(r) + \omega(r)T,$$

$$k(t) = (k_1(t), k_2(t), k_3(t), k_4(t), k_5(t))^T.$$

Proof. Applying fractional integral (2.2) on (5.4), we get

$$\overline{\mathbb{B}}_k(t) = \overline{\mathbb{B}}_0 + \Omega(r)\Theta\left(t, \overline{\mathbb{B}}(t)\right) + \omega(r)\int_0^t \Theta\left(\delta, \overline{\mathbb{B}}(\delta)\right) d\delta$$
$$+ \Omega(r)k(t) + \omega(r)\int_0^t k(\delta)d\delta. \quad (5.5)$$

Also,

$$\overline{\mathbb{B}}(t) = \overline{\mathbb{B}}_0 + \Omega(r)\Theta\left(t, \overline{\mathbb{B}}(t)\right) + \omega(r)\int_0^t \Theta\left(\delta, \overline{\mathbb{B}}(\delta)\right) d\delta. \quad (5.6)$$

Using Remark 5.1,

$$\left\|\overline{\mathbb{B}}_k(t) - \overline{\mathbb{B}}(t)\right\| \le \Omega(r)\,|k(t)| + \omega(r)\int_0^t |k(\delta)|\,d\delta$$
$$\le (\Omega(r) + \omega(r)T)\,\overline{\epsilon}$$
$$= \Phi\overline{\epsilon}.$$

This completes the proof. □

Theorem 5.1. *[10] The proposed fractional system (3.2) is UM stable if*

$$\left\|\overline{\mathbb{B}}(t) - \mathbb{B}(t)\right\| \le \overline{\mu\epsilon}.$$

Proof. Let $\overline{\mathbb{B}}$ be the solution of (5.3) and, due to uniqueness, $\mathbb{B}$ be a unique solution of the system (5.1), then

$$\left\|\overline{\mathbb{B}}(t) - \mathbb{B}(t)\right\| \le \left\|\overline{\mathbb{B}}_h(t) - \overline{\mathbb{B}}(t)\right\| + \left\|\overline{\mathbb{B}}_h(t) - \mathbb{B}(t)\right\|$$
$$\le \Phi\overline{\epsilon} + \Omega(r)\left\|\Theta(t, \overline{\mathbb{B}}(t)) - \Theta(t, \mathbb{B}(t))\right\|$$
$$+ \omega(r)\int_0^t \left\|\Theta(\delta, \overline{\mathbb{B}}(\delta)) - \Theta(\delta, \mathbb{B}(\delta))\right\| d\delta + \Phi\overline{\epsilon}$$
$$\le 2\Phi\overline{\epsilon} + \Phi\overline{\delta}\left\|\overline{\mathbb{B}}(t)) - \mathbb{B}(t))\right\|,$$

which implies that

$$\left\|\overline{\mathbb{B}}(t) - \mathbb{B}(t)\right\| \le \frac{2\Phi\overline{\epsilon}}{1 - \Phi\overline{\delta}} = \overline{\mu\epsilon},$$

where

$$\overline{\mu} = \frac{2\Phi}{1 - \Phi\overline{\delta}}.$$

Hence, the considered fractional system (3.2) is UM stable. □

6. Numerical algorithm on CF frame for dynamics of breast cancer model

The present part of the paper provides an approximate solution for the fractional order model (3.2) using two-step fractional Adams-Bashforth technique [37]. We discretized model (3.2) as follows:

$$\mathbb{S}_{12\iota+1} = \mathbb{S}_{12\iota} + M_1(r)N_1(t_\iota, \mathbb{S}_{12\iota}, \mathbb{S}_{3\iota}, \mathbb{S}_{4\iota}, \mathbb{S}_{R\iota}, \mathbb{S}_{E\iota}) - M_2(r)$$
$$N_1(t_{\iota-1}, \mathbb{S}_{12\iota-1}, \mathbb{S}_{3\iota-1}, \mathbb{S}_{4\iota-1}, \mathbb{S}_{R\iota-1}, \mathbb{S}_{E\iota-1}),$$
$$\mathbb{S}_{3\iota+1} = \mathbb{S}_{3\iota} + M_1(r)N_2(t_\iota, \mathbb{S}_{12\iota}, \mathbb{S}_{3\iota}, \mathbb{S}_{4\iota}, \mathbb{S}_{R\iota}, \mathbb{S}_{E\iota}) - M_2(r)$$
$$N_2(t_{\iota-1}, \mathbb{S}_{12\iota-1}, \mathbb{S}_{3\iota-1}, \mathbb{S}_{4\iota-1}, \mathbb{S}_{R\iota-1}, \mathbb{S}_{E\iota-1}),$$
$$\mathbb{S}_{4\iota+1} = \mathbb{S}_{4\iota} + M_1(r)N_3(t_\iota, \mathbb{S}_{12\iota}, \mathbb{S}_{3\iota}, \mathbb{S}_{4\iota}, \mathbb{S}_{R\iota}, \mathbb{S}_{E\iota}) - M_2(r)$$
$$N_3(t_{\iota-1}, \mathbb{S}_{12\iota-1}, \mathbb{S}_{3\iota-1}, \mathbb{S}_{4\iota-1}, \mathbb{S}_{R\iota-1}, \mathbb{S}_{E\iota-1}),$$
$$\mathbb{S}_{R\iota+1} = \mathbb{S}_{R\iota} + M_1(r)N_4(t_\iota, \mathbb{S}_{12\iota}, \mathbb{S}_{3\iota}, \mathbb{S}_{4\iota}, \mathbb{S}_{R\iota}, \mathbb{S}_{E\iota}) - M_2(r)$$
$$N_4(t_{\iota-1}, \mathbb{S}_{12\iota-1}, \mathbb{S}_{3\iota-1}, \mathbb{S}_{4\iota-1}, \mathbb{S}_{R\iota-1}, \mathbb{S}_{E\iota-1}),$$
$$\mathbb{S}_{E\iota+1} = \mathbb{S}_{E\iota} + M_1(r)N_5(t_\iota, \mathbb{S}_{12\iota}, \mathbb{S}_{3\iota}, \mathbb{S}_{4\iota}, \mathbb{S}_{R\iota}, \mathbb{S}_{E\iota}) - M_2(r)$$
$$N_5(t_{\iota-1}, \mathbb{S}_{12\iota-1}, \mathbb{S}_{3\iota-1}, \mathbb{S}_{4\iota-1}, \mathbb{S}_{R\iota-1}, \mathbb{S}_{E\iota-1}),$$
$$(6.1)$$

where

$$M_1(r) = \left(\frac{1-r}{P(r)} + \frac{3rh}{2P(r)}\right)$$

and

$$M_2(r) = \left(\frac{1-r}{P(r)} + \frac{rh}{2P(r)}\right).$$

7. Numerical simulation and discussion

The dynamical behavior of the proposed fractional system (3.2) is investigated numerically using (6.1) for the approximate solution of the state variables $\mathbb{S}_{12}(t), \mathbb{S}_3(t), \mathbb{S}_4(t), \mathbb{S}_R(t)$, and $\mathbb{S}_E(t)$ in (3.2). We take the initial values as $\mathbb{S}_{12}(0) = 30000, \mathbb{S}_3(0) = 12300, \mathbb{S}_4(0) = 783, \mathbb{S}_R(0) = 334, \mathbb{S}_E(0) = 10$ and parameters values: $\Delta = 14000, \Gamma = 80, \Omega = 90, \mu = 0.01, \nu = 0.034, \psi = 0.03, \phi = 0.3, \omega = 0.1, \zeta = 0.2, \chi = \delta = \eta = 0.0256$ [56], $\rho = 0.149(fitted), \kappa = 0.09(fitted), \sigma = 0.47(fitted),$ and $\tau = 0.01(fitted)$, as fitted with real data. In Figure 1, we used real data [57] from Kingdom of Saudi Arabia from 2004 to 2016 to fit the classical model (3.1) and the suggested fractional order model (3.2). This demonstrates that the fractional model better matches the actual data and may be used to forecast future instances than the classical model. Figure 2 shows a long-term estimate of the cases based on a fractional model. Here, we can see from Figure 2 that the data fits the model curve well, and we can also see that the number of long-term behavior cases grows in an exponential way over time. This case could be scary

because the number of cases could go up even more in the next few years if the health department does not use the right treatment methods to get rid of breast cancer.
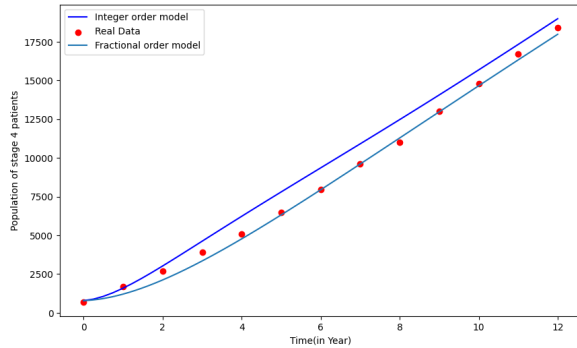

Figure 1. Fitting real data of breast cancer with integer and fractional order($r = 1$) models.
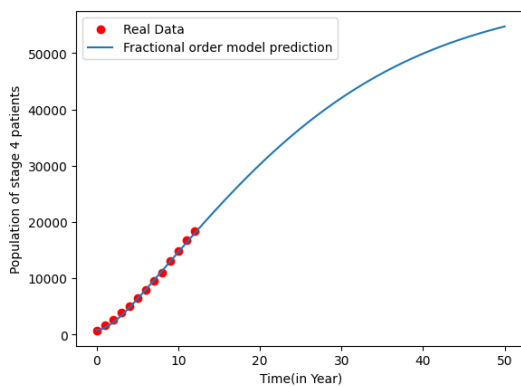

Figure 2. Fractional order ($r = 1$) model prediction with real data.

Figures 3–7 show how the model compartments change over time ($t = 50$ years) as the fractional-order r varies for each compartment. We discovered that the memory index r has a significant impact on the breast cancer model's solution route, and that controlling r gives us a lot of control over the way breast cancer behaves in all subgroups. Figures 8–11 show the solution of the proposed CF model while adjusting the input parameter κ. We found that raising this quantity makes fewer people get cancer in stage 3, stage 4, and disease-free states, implying that the cancer mortality rate would be reduced. However, increasing κ increases the number of people who are cardiotoxic, increasing the risk of cardiac mortality.
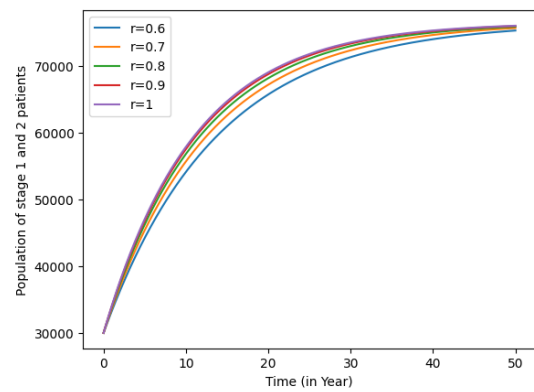
Figure 3. Simulation of stage 1 and 2 patients with variation of fractional order.
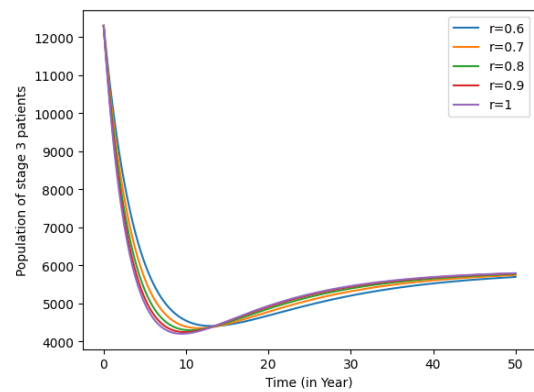
Figure 4. Simulation of stage 3 patients with variation of fractional order.
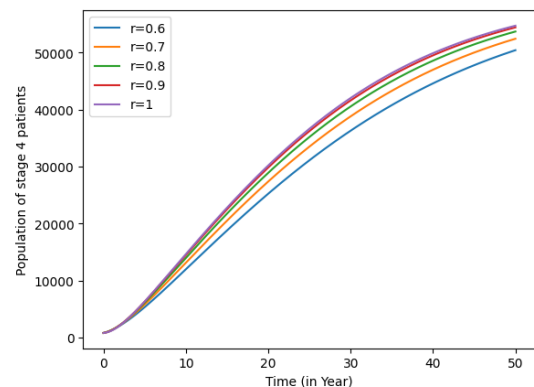
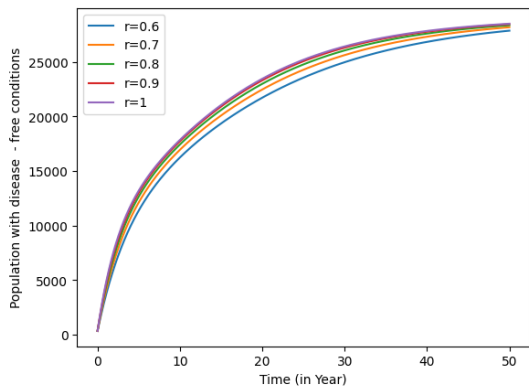**Figure 5.** Simulation of stage 4 patients with variation of fractional order.

Figure 6. Simulation of patients at disease-free state with variation of fractional order.
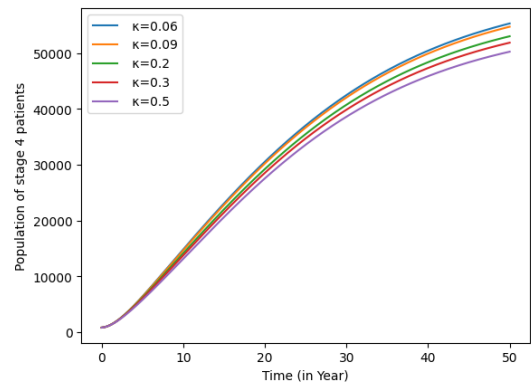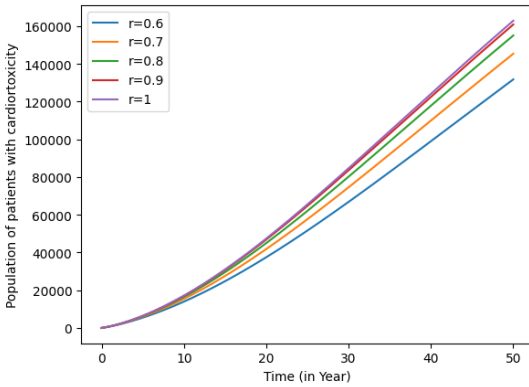

Figure 7. Simulation of cardiortoxicity patients with variation of fractional order.
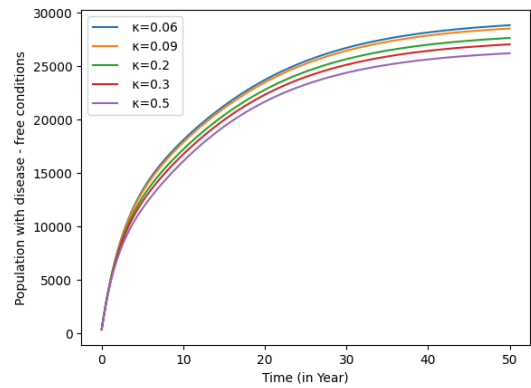
Figure 8. Effect of κ on stage 3 patients.

Figure 9. Effect of κ on stage 4 patients.

Figure 10. Effect of κ on patients at disease-free state.
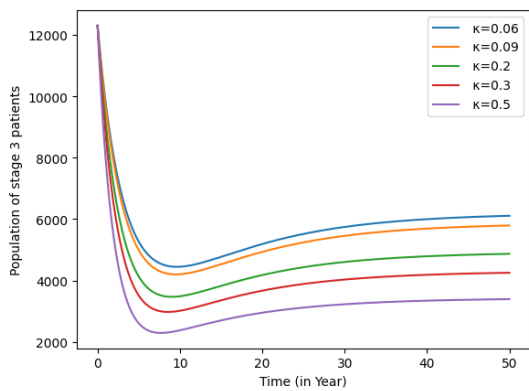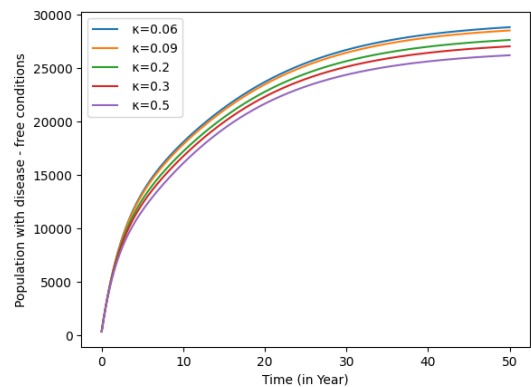
Figure 11. Effect of κ on cardiortoxicity patients.

The diagram shown in Figures 12–14 illustrates the effects of rigorous chemotherapy on patients diagnosed

with stage 4. This treatment approach has been found to potentially contribute to higher rates of morbidity and death within the population, particularly among those who experience cardiotoxicity. By intensifying the administration of chemotherapy to individuals in phase 4, populations with disease-free status, and those experiencing cardiotoxicity, it becomes evident that stage 4 and disease-free individuals exhibit significant improvements in disease reduction. However, the same level of improvement is not observed in individuals with cardiotoxicity. The adverse effects of chemotherapy have been shown to significantly increase the risk of developing cardiovascular complications in individuals. The simulations provide a visual representation of the parameters' functions, facilitating comprehension of strategies to reduce cancer and cardiac mortality rates in cancer patient healthcare facilities.
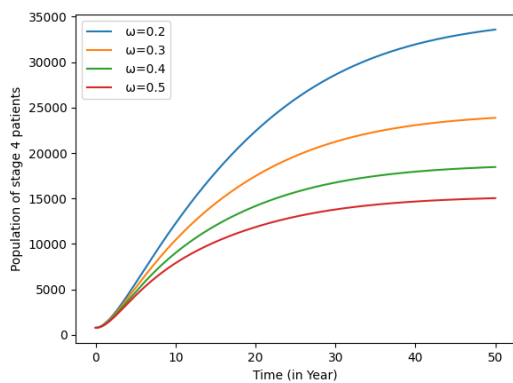

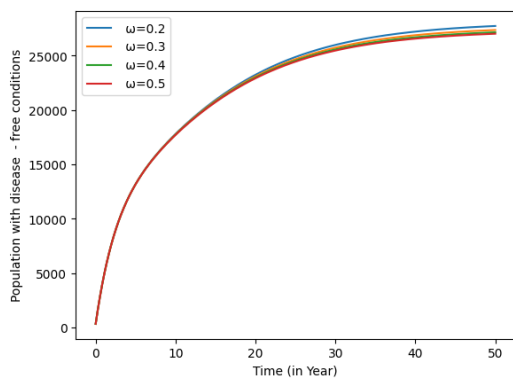**Figure 12.** Effect of ω on stage 4 patients.

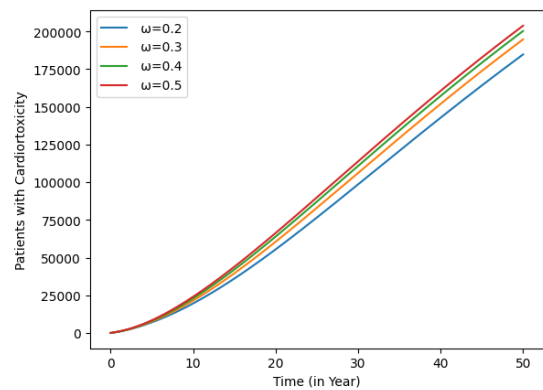**Figure 13.** Effect of ω on patients at disease-free state.

Figure 14. Effect of ω on cardiortoxicity patients.

Figures 15–18 depict the simulation of the model compartment in the disease-free condition with intense treatment. The findings show a little rise in the cardiotoxicity population, whereas there are minor reductions in the population of phases 3, 4, and the disease-free state. Figure 15 shows that there is minimal improvement in the decline of instances in phase 3 sufferers. Figure 16 shows a significant decrease in cases among phase 4 patients. Figure 17 shows a significant drop in the number of patients in the disease-free state, but Figure 18 shows a modest rise in the number of instances of cardiotoxicity. The CF operator demonstrates a 66.64% improvement in the accuracy of estimating actual data compared to the classical order model as determined by

$$\frac{\text{classical model norm - fractional model norm}}{\text{classical model norm}} = \frac{11045.11902 - 3685}{11045.11902}$$
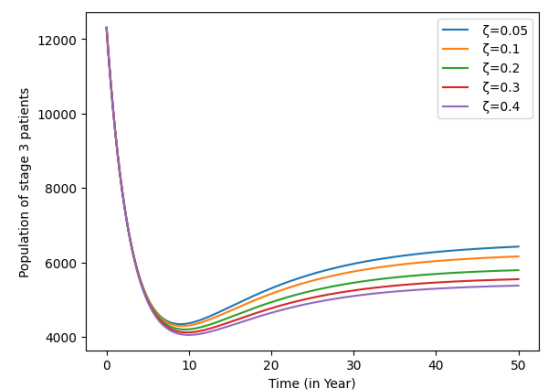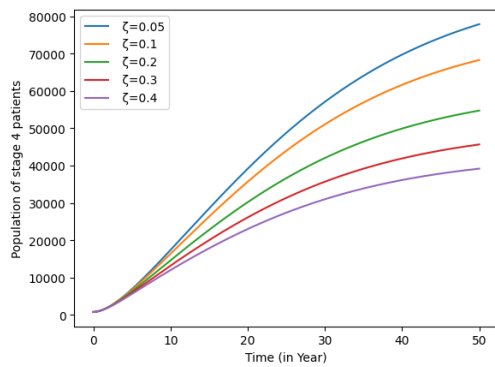$$= 0.6664.$$

Figure 15. Effect of ζ on stage 3 patients.

Figure 16. Effect of ζ on stage 4 patients.
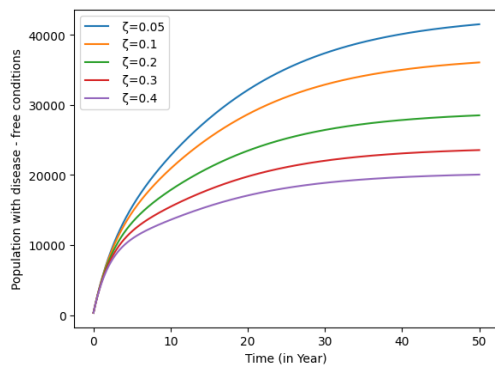

Figure 17. Effect of ζ on disease-free state patients.
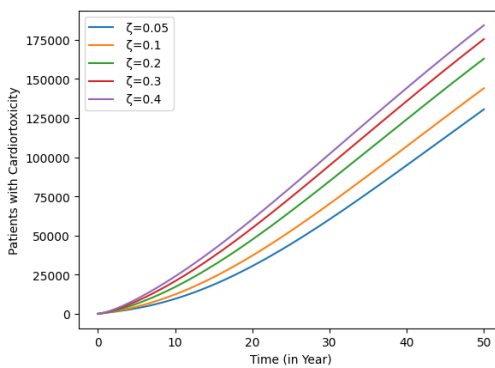

Figure 18. Effect of ζ on cardiortoxicity patients.

8. Conclusions

We developed a mathematical model in a fractional framework for breast cancer in this research to study the impact of treatment at various phases, incorporating the CF derivative and various chemotherapy rates. The PL technique is established for the system's existence and uniqueness. We have constructed some results for UH stability and have shown that our proposed model is UH stable. The numerical simulations supported our approach using the two-step AB algorithm. Through graphical representations, we illustrated the impact of fractional order and the effect of chemotherapy rates on breast cancer dynamics. Using real incidence data, the CF operator demonstrates a 66.64% improvement in the accuracy of estimating actual data compared to the classical order model. Notably, we identified effective parameters (κ, ω, and ζ) associated with reduced occurrences of stages 3 and 4 as well as disease-free states in breast cancer modeling. Our results emphasized the increased risk of cardiotoxicity linked with chemotherapy, indicating that pretreatment may be beneficial in mitigating such risks. Our research seeks to reduce cardiotoxicity prevalence among chemotherapy patients and improve their recovery rates, with implications for public health decision-making. Furthermore, by elucidating breast cancer mechanisms through the CF operator, our study paves the way for targeted therapies to minimize cardiotoxicity, thereby improving patient outcomes and guiding future breast cancer treatment strategies. In future work, we want to leverage our actual data-oriented estimated parameter values to anticipate breast cancer patients utilizing various models and fractional derivative operators. Using the provided data, certain optimal controls may also be added in the same model.

Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

Conflict of interest

All authors confirm that they have no competing interests related to this article.

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