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QUANTIFYING THE IMPACT OF IMMUNOTHERAPY RESPONSE OF BREAST CANCER STAGES: A COMPUTATIONAL APPROACH FOR MATHEMATICAL MODEL AND NUMERICAL SIMULATION

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Abstract. Breast cancer is a complicated disease that can be treated with a variety of approaches such as Chemotherapy, Immunotherapy, Targeted Therapy, and Hormonal Therapy. A type of cancer treatment known as Immunotherapy can assist the immune system in identifying and attacking cancer cells to combat them. This study investigates a system of differential equations that considers the stages of breast cancer as well as the influence of immunotherapy on patients who are in a dormant condition. We analysed the temporal dynamics of the model by examining the stability and behavior of its equilibrium point. To determine the equilibrium point's stability, we applied the Routh-Hurwitz Criterion, which allowed us to conclude that the equilibrium point is asymptotically stable. Numerical simulations that demonstrated the persistence of the stable equilibrium regardless of the initial conditions, without any further prerequisites, were run to validate our findings. These results suggest that after the five patient sub-populations converge to the equilibrium point, they will eventually reach a state of stability.

Keywords: breast cancer; immunotherapy; system of differential equations; stages of breast cancer; dormancy; numerical simulation; mathematical modeling.

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1. INTRODUCTION

Breast cancer is a prevalent malignant disease that ranks among the primary reasons for cancer-related fatalities in women globally [1]. It exhibits the most elevated incidence rate in comparison to other cancers. This condition occurs when breast cells undergo uncontrolled proliferation, leading to an abnormal shape of the breast. Breast cancer ranks as the second most prevalent cancer globally, after lung cancer, and it has the potential to affect women of any age. Fortunately, breast cancer death rates have been decreasing continuously since 1989, resulting in a significant overall decrease of 43% by 2020. The World Health Organization (WHO) states that breast cancer killed 685,000 people globally and impacted 2.3 million women. At the end of 2020, around 7.8 million women had been diagnosed with breast cancer in the last five years, signifying the worldwide average. This statistic reveals that breast cancer holds the highest prevalence among all types of cancer globally [2].

Global health researchers continue to grapple with the exact causes of breast cancer. Medical specialists have the capacity to identify only a limited number of risk factors that affect a woman's chances of getting breast cancer. Age and race are two risk variables that cannot be changed; however, there are other modifiable risk factors, such as smoking, drinking, and dietary habits, especially those that can be influenced by individual behavior and environmental factors.

The severity of cancer is determined by its stages. To determine the stages of cancer, healthcare workers employ the TNM approach (Tumor, Node, Metastasis). This method examines three crucial elements: the tumor size, the involvement of lymph nodes, and the presence of distant organ metastases. This methodical technique helps doctors accurately describe the severity and course of the condition, enabling proper treatment planning and patient care. Breast cancer treatment might be simple if it is discovered early. However, as the cancer progresses to higher stages, the chances of recovery decrease. There are numerous methods for preventing and treating cancer, including surgery, targeted therapeutic medications, hormone therapy, immunotherapy, radiotherapy, and complementary and alternative therapies. As is true for the majority of cancers, the likelihood of a successful course of treatment increases with early discovery and diagnosis of breast cancer.

Breast cancer dormancy refers to a period during which breast cancer cells remain clinically undetectable in the body, either before or after treatment. It is believed that during dormancy, cancer cells are in a state of arrested growth, which can last for months, years, or even decades[3, 5, 4].

Immunotherapy represents an innovative cancer treatment approach, leveraging the immunological system of the body to effectively target and combat cancer cells. Checkpoint inhibitors, an example of an immunotherapy medicine, function by disabling immune system restrictions so that the body may more effectively combat cancer cells [6]. There is evidence to suggest that breast cancer dormancy may be related to the immunological response of the body to cancer cells. In particular, there is a belief that the immunological system might have a role in regulating the growth of dormant cancer cells [7]. During the last few years, immunotherapy is gaining popularity as a treatment option for breast cancer, including both early-stage and metastatic illness. However, while immunotherapy has shown promise in some types of cancer, such as melanoma and lung cancer, its effectiveness in breast cancer has been more limited.

Studying the progression of breast cancer over time has proven to be challenging, but the use of mathematical models and computer simulations can aid in monitoring tumor growth, observing cellular distribution, and identifying genetic mutations that contribute to aggressive growth and metastasis. Mufudza[8] conducted research on the effects of elevated estrogen levels on breast cancer dynamics, integrating an immune cell population to simulate the body's innate response to tumor growth. In [9], a mathematical model was developed to describe the gradual changes a breast stem cell goes through to become a cancer cell, using four differential equations to represent the process. The authors of [10] explored the role of excess estrogen in breast cancer development and its effect on the body's natural immune response. Boushaba et al.[11] proposed a mathematical model to delve into the role of enzyme kinetics in regulating tumor dormancy. They assumed that the balance between the activities of proteases and protease inhibitors could determine whether tumor cells remained dormant or resumed growth. The model predicted that changes in the expression levels of proteases and inhibitors could cause the tumor to transition from a dormant state to a proliferative state. The authors suggested that their model could provide insight into the mechanisms underlying breast cancer dormancy and

help to identify potential targets for therapy. Mehdizadeh et al.[12], introduced a mathematical model depicting immunological dormancy in triple-negative breast cancer, a subtype of breast cancer lacking receptors for estrogen, progesterone, or HER2/neu. The model is based on the idea that dormant tumor cells can remain in a state of dormancy for years, and that the immune system plays a critical role in preventing these cells from growing and spreading. Hence, the studies mentioned earlier do not seem to have concentrated on the specific development of a population-level mathematical model for breast cancer [16, 15, 13, 14]. To address this gap, this work investigates a mathematical model that analyses breast cancer patients' stages and dormancy impacted by immunotherapy responses.

As a result, the structure of this study is as follows: The first section focuses on developing a mathematical model to represent the different stages of breast cancer in patients and their response to immunotherapy. This model incorporates a system of differential equations to describe the five compartments. Subsequently, we investigate the temporal dynamics of this model, including the equilibrium point and its stability. To assess the stability of the equilibrium point, we use the Routh-Hurwitz Criterion, which allows us to identify an asymptotically stable equilibrium point. To validate our results, we conduct numerical simulations. The findings from these simulations indicate that the equilibrium point remains stable for all initial conditions, even in the absence of any additional constraints. Consequently, these findings demonstrate that the five patient sub-populations will stabilize once they reach the equilibrium point.

2. FORMULATING THE MODEL

In formulating of the model, we considered the population of breast cancer patients in a hospital, categorizing them into Stage 1, Stage 2, Stage 3, Stage 4, Dormancy and Disease-free sub-populations based on the first medical report. All patients are presumed to receive immunotherapy at the hospital, and while some patients experience recovery during treatment, others may experience a worsening of their condition when receiving immunotherapy.

Different sub-populations of breast cancer patients are represented by the model's five compartments, each of which is symbolised by the variables A, B, C, D, and E. Cancer patients in stages 1 and 2 are included in sub-population A, while sub-population B represents patients with breast cancer in stages 3 of the disease. Cancer patients in the Dormancy phase, which can

endure for years while cancer cells alter their genetic composition and get ready for the next stage of development, are included in sub-population D, while those with stage 4 cancer make up sub-population C. In Figure (1), we can see a diagram of the compartments.

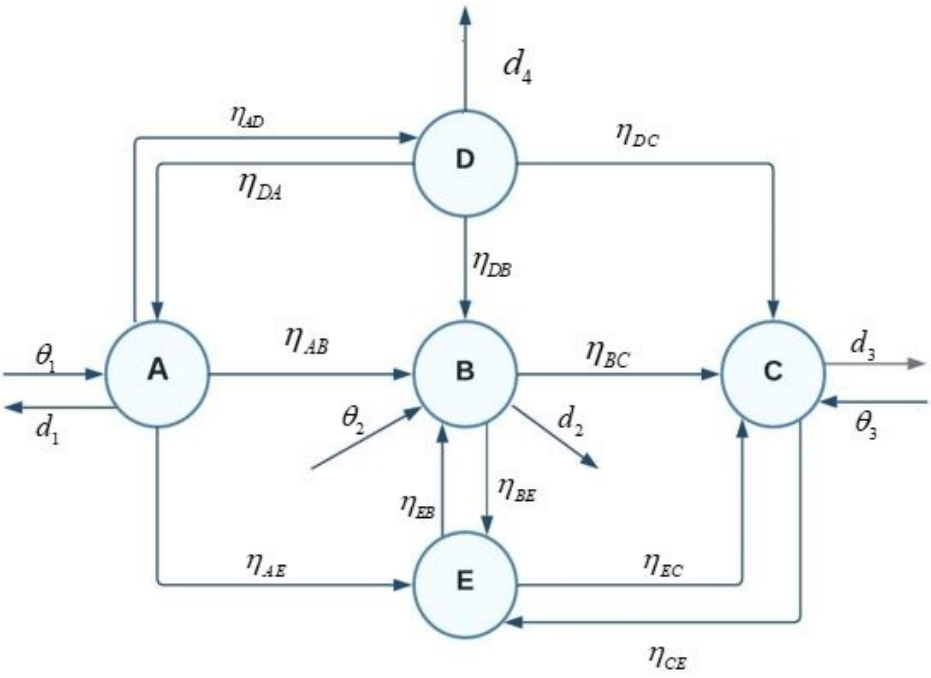

FIGURE 1. Compartment Diagram

Breast cancer patients in stages 1 and 2 are represented by sub-population A, whereas those in stages 3 are represented by sub-population B. Patients in the Dormancy phase, which can endure for years while cancer cells alter their genetic composition and get ready for the next stage of development, are included in sub-population D, while those with stage 4 cancer make up sub-population C.

Newly diagnosed patients with stage 1 and 2 cancers are categorised into sub-population A at a rate denoted by θ_1. Once patients are in sub-population A and receive immunotherapy, they have two potential outcomes: either they recover and become disease-free at a rate η_{AE} or experience worsening of their condition at a rate η_{AB}. Additionally, patients in stage 1 and 2 have the possibility of transitioning to a Dormancy state. In the unfortunate event of death, patients in stage 1 and 2 may experience a natural death at a rate of d_1.

Patients who were first treated in hospital had mainly stage 3 cancer, so they were grouped into sub-population B with a rate θ_2. Sub-population B may increase with changes from stage 1 and 2 with a rate η_{AB} and from Dormancy by η_{DB}. This sub-population is more intensive immunotherapy than sub-population A where the patient dies from cancer with a rate d_2, move to the recover sub-population with a rate η_{BE}, become more worse with a rate η_{BC}.

Patients who came for treatment for the first time can also diagnosed with stage 4 or metastasis, so they were grouped in sub-population C with a rate θ_3. This sub-population is unlikely that immunotherapy can cure cancer, so the rate towards a disease-free η_{CE} is assumed to be the least compared to η_{AE} and η_{BE}. Sub-population C has the ability to increase in two ways: by transitioning from stage 3 cancer at a rate of η_{EC} and by waking up from a time of dormancy at a rate of η_{BC}. Furthermore, the sub-population C is vulnerable to cancer-related mortality, which occur at a rate of d_3.

As mentioned earlier, Dormancy is the period of inactive cancer cells that can last for years. Patients in sub-population D come from sub-population A with a rate η_{AD}. Patients who are in this sub-population if they die are assumed to experience natural death with a rate d_4.

In sub-population E, disease-free individuals originate from sub-populations A, B, and C.

Given the assumptions mentioned earlier, we can express the interaction between breast cancer and immunotherapy treatment using the subsequent set of ordinary differential equations $(ODEs)$:

$$
\begin{cases}
\dfrac{dA}{dt} = \theta_1 + \eta_{DA}D - \eta_{AD}A - \eta_{AE}A - \eta_{AB}A - d_1A, \\
\dfrac{dB}{dt} = \theta_2 + \eta_{AB}A + \eta_{DB}D + \eta_{EB}E - \eta_{BE}B - \eta_{BC}B - d_2B, \\
\dfrac{dC}{dt} = \theta_3 + \eta_{BC}B + \eta_{DC}D + \eta_{EC}E - \eta_{CE}C - d_3C, \\
\dfrac{dD}{dt} = \eta_{AD}A - \eta_{DA}D - \eta_{DB}D - \eta_{DC}D - d_4D, \\
\dfrac{dE}{dt} = \eta_{BE}B + \eta_{CE}C + \eta_{AE}A - \eta_{EB}E - \eta_{EC}E,
\end{cases} \tag{1}
$$

with a vector's initial condition being appropriate

$$A(0) > 0;\ B(0) > 0;\ C(0) > 0;\ D(0) > 0.$$

3. Model Analysis

This section is dedicated to the examination of the existence and stability of the equilibrium point, which also functions as the critical point of the system (1).

3.1. Equilibrium Point. By setting all of the fractional derivatives of the system (1) to zero, we can determine its equilibrium point, which is indicated by the equation $P^* = (\mathscr{A}^*, \mathscr{B}^*, \mathscr{C}^*, \mathscr{D}^*, \mathscr{E}^*)$. An equilibrium point exists, and it is

$$\mathscr{A}^* = \frac{\theta_1 k_4}{\alpha}, \qquad \mathscr{B}^* = \frac{\beta}{k_2 \alpha \nu}, \qquad \mathscr{C}^* = \frac{\gamma}{k_2 k_3 \alpha \nu}, \qquad \mathscr{D}^* = \frac{\theta_1 \eta_{AD}}{\alpha}, \qquad \mathscr{E}^* = \frac{\sigma}{\alpha \nu}$$

where,

$$k_1 = \eta_{AD} + \eta_{AE} + \eta_{AB} + d_1; \qquad k_2 = \eta_{BE} + \eta_{BC} + d_2$$

$$k_3 = \eta_{CE} + d_3; \qquad k_4 = \eta_{DA} + \eta_{DB} + \eta_{DC} + d_4; \qquad k_5 = \eta_{EB} + \eta_{EC}$$

$$\alpha = \eta_{AD}(\eta_{DB} + \eta_{DC} + d_4) + k_4(\eta_{AE} + \eta_{AB} + d_1)$$

$$\begin{aligned}\beta = {} & (\theta_2(\eta_{AD}(\eta_{DB} + \eta_{DC} + d_4) + k_4(\eta_{AE} + \eta_{AB} + d_1)) + \eta_{AB} k_4 \theta_1 + \eta_{DB}\eta_{AD}\theta_1)(\eta_{CE} d_2 \eta_{EB} \\ & + d_3(\eta_{BC} + d_2)\eta_{EB} + k_2 d_3 \eta_{EC}) + \eta_{EB}(k_3 \eta_{BE}(\theta_2(\eta_{AD}(\eta_{DB} + \eta_{DC} + d_4) + k_4(\eta_{AE} + \eta_{AB} + d_1)) \\ & + \eta_{AB} k_4 \theta_1 + \eta_{DB}\eta_{AD}\theta_1) + \eta_{CE}(k_2(\eta_{AD}(\eta_{DB} + \eta_{DC} + d_4) + k_4(\eta_{AE} + \eta_{AB} + d_1))\theta_3 \\ & + \eta_{BC}(\theta_2(\eta_{AD}(\eta_{DB} + \eta_{DC} + d_4) + k_4(\eta_{AE} + \eta_{AB} + d_1)) + \eta_{AB} k_4 \theta_1 + \eta_{DB}\eta_{AD}\theta_1) \\ & + k_2 \eta_{DC}\eta_{AD}\theta_1) + k_2 k_3 k_4 \eta_{AE}\theta_1)\end{aligned}$$

$$\begin{aligned}\gamma = {} & (k_2(\eta_{AD}(\eta_{DB} + \eta_{DC} + d_4) + k_4(\eta_{AE} + \eta_{AB} + d_1))\theta_3 + \eta_{BC}(\theta_2(\eta_{AD}(\eta_{DB} + \eta_{DC} + d_4) \\ & + k_4(\eta_{AE} + \eta_{AB} + d_1)) + \eta_{AB} k_4 \theta_1 + \eta_{DB}\eta_{AD}\theta_1) + k_2 \eta_{DC}\eta_{AD}\theta_1)(\eta_{CE} d_2 \eta_{EB} + d_3(\eta_{BC} + d_2)\eta_{EB} \\ & + k_2 d_3 \eta_{EC}) + (\eta_{BC}\eta_{EB} + k_2 \eta_{EC})(k_3 \eta_{BE}(\theta_2(\eta_{AD}(\eta_{DB} + \eta_{DC} + d_4) + k_4(\eta_{AE} + \eta_{AB} + d_1)) \\ & + \eta_{AB} k_4 \theta_1 + \eta_{DB}\eta_{AD}\theta_1) + \eta_{CE}(k_2(\eta_{AD}(\eta_{DB} + \eta_{DC} + d_4) + k_4(\eta_{AE} + \eta_{AB} + d_1))\theta_3 \\ & + \eta_{BC}(\theta_2(\eta_{AD}(\eta_{DB} + \eta_{DC} + d_4) + k_4(\eta_{AE} + \eta_{AB} + d_1)) + \eta_{AB} k_4 \theta_1 + \eta_{DB}\eta_{AD}\theta_1) \\ & + k_2 \eta_{DC}\eta_{AD}\theta_1) + k_2 k_3 k_4 \eta_{AE}\theta_1)\end{aligned}$$

$$\sigma = k_3\eta_{BE}(\theta_2(\eta_{AD}(\eta_{DB}+\eta_{DC}+d_4)+k_4(\eta_{AE}+\eta_{AB}+d_1))+\eta_{AB}k_4\theta_1+\eta_{DB}\eta_{AD}\theta_1)$$
$$+\eta_{CE}(k_2(\eta_{AD}(\eta_{DB}+\eta_{DC}+d_4)+k_4(\eta_{AE}+\eta_{AB}+d_1))\theta_3+\eta_{BC}(\theta_2(\eta_{AD}(\eta_{DB}+\eta_{DC}+d_4)$$
$$+k_4(\eta_{AE}+\eta_{AB}+d_1))+\eta_{AB}k_4\theta_1+\eta_{DB}\eta_{AD}\theta_1)+k_2\eta_{DC}\eta_{AD}\theta_1)+k_2k_3k_4\eta_{AE}\theta_1$$

$$\nu = \eta_{CE}d_2\eta_{EB}+d_3(\eta_{BC}+d_2)\eta_{EB}+k_2d_3\eta_{EC}$$

The significance of these equilibrium points lies in their crucial role in analysing this breast cancer model, as they provide insights into the conditions required for the virus to propagate. The investigation's findings are as follows:

Theorem 3.1. *The system (1) of breast cancer exhibits the presence of an equilibrium point without the need for any additional conditions.*

3.2. Analysing the Stability of Equilibrium Points. To assess the stability of the equilibrium point, we initially represent the equation in matrix form.

$$\mathscr{K} = \mathscr{G}\mathscr{H}+\Theta$$

With:

$$\mathscr{K}=\begin{bmatrix}\dot{A}\\ \dot{B}\\ \dot{C}\\ \dot{D}\\ \dot{E}\end{bmatrix};\mathscr{G}=\begin{bmatrix}-k_1 & 0 & 0 & \eta_{DA} & 0\\ \eta_{AB} & -k_2 & 0 & \eta_{DB} & \eta_{EB}\\ 0 & \eta_{BC} & -k_3 & \eta_{DC} & \eta_{EC}\\ \eta_{AD} & 0 & 0 & -k_4 & 0\\ \eta_{AE} & \eta_{BE} & \eta_{CE} & 0 & -k_5\end{bmatrix};\mathscr{H}=\begin{bmatrix}A\\ B\\ C\\ D\\ E\end{bmatrix} \text{ and } \Theta=\begin{bmatrix}\theta_1\\ \theta_2\\ \theta_3\\ 0\\ 0\end{bmatrix}$$

We will employ the Routh-Hurwitz Criterion [17] to ascertain the stability of the system.

To calculate the characteristic equation, we use $P(\lambda)=\det(\mathscr{G}-\lambda I)$. We obtain:

$$P(\lambda)=\begin{vmatrix}-k_1-\lambda & 0 & 0 & \eta_{DA} & 0\\ \eta_{AB} & -k_2-\lambda & 0 & \eta_{DB} & \eta_{EB}\\ 0 & \eta_{BC} & -k_3-\lambda & \eta_{DC} & \eta_{EC}\\ \eta_{AD} & 0 & 0 & -k_4-\lambda & 0\\ \eta_{AE} & \eta_{BE} & \eta_{CE} & 0 & -k_5-\lambda\end{vmatrix}$$

we get,

$$P(\lambda) = -\left(\lambda^2 + a_1\lambda + a_2\right)\left(\lambda^3 + b_1\lambda^2 + b_2\lambda + b_3\right) \tag{2}$$

where,

$$a_1 = k_1 + k_4;$$

$$a_2 = k_1k_4 - \eta_{AD}\eta_{DA} = \eta_{AD}(\eta_{DB} + \eta_{DC} + d_4) + k_4(\eta_{AE} + \eta_{AB} + d_1);$$

$$b_1 = k_2 + k_3 + k_5;$$

$$b_2 = k_2k_3 + k_2k_5 + k_3k_5 - \eta_{BE}\eta_{EB} - \eta_{CE}\eta_{EC};$$

$$b_3 = k_2k_3k_5 - k_2\eta_{CE}\eta_{EC} - \eta_{CE}\eta_{EB}\eta_{BC} - k_3\eta_{BE}\eta_{EB} = \eta_{CE}d_2\eta_{EB} + d_3(\eta_{BC} + d_2)\eta_{EB} + k_2d_3\eta_{EC}.$$

We can clearly see that this equation (2) has five eigenvalues.

Indeed, we consider the follow equations

$$\lambda^2 + a_1\lambda + a_2 = 0 \tag{3}$$

$$\lambda^3 + b_1\lambda^2 + b_2\lambda + b_3 = 0 \tag{4}$$

The equation (3) possesses two eigenvalues: λ_1 and λ_2. To examine their characteristics, we construct a Routh table for this equation, as follows:

$$\begin{array}{c|cc} \lambda^2 & 1 & a_2 \\ \lambda^1 & a_1 & 0 \\ \lambda^0 & a_2 & \end{array}$$

Hence, based on the Routh Array, all entries in the first column have positive signs, indicating that all real eigenvalues are negative [17].

Additionally, it is simple to demonstrate that

$$a_1 > 0, \qquad a_2 > 0.$$

We repeat the same process for (4), we get three eigenvalues: λ_3, λ_4 and λ_5.

The Routh table for this equation is have

$$\begin{array}{c|ccc} \lambda^3 & 1 & b_2 & 0 \\ \lambda^2 & b_1 & b_3 & 0 \\ \lambda^1 & c_1 & 0 & \\ \lambda^0 & b_3 & & \end{array}$$

where

$$c_1 = \frac{\begin{vmatrix} b_1 & 1 \\ b_3 & b_2 \end{vmatrix}}{a_1}$$

Further, it is easy to show that

$$b_1 > 0, \qquad c_1 = b_1 b_2 - b_3 > 0 \qquad \text{and} \qquad b_3 > 0$$

Furthermore, it is simple to demonstrate that the system (1) is locally asymptotically stable.

4. NUMERICAL SIMULATION AND DISCUSSION

In this section, we present multiple simulations conducted to analyse the outcomes of our proposed breast cancer model under immunotherapy treatment, employing the parameter values listed in Table 1. The simulations were performed using the following initial values: $(A_0, B_0, C_0, D_0, E_0) = (15, 30, 25, 30, 10)$. Considering the given parameter values, we achieved the following equilibrium point: $P^* = (\mathscr{A}^*, \mathscr{B}^*, \mathscr{C}^*, \mathscr{D}^*, \mathscr{E}^*) = (2.44, 17.18, 48.59, 1.23, 83.88)$.

FIGURE 2 displays the results of the numerical simulation.

Table 1. Parameters values.

Parameter	Values
θ_1	5
θ_2	20
θ_3	11
d_1	0.5
d_2	0.8
d_3	0.4
d_4	0.5
η_{AB}	0.5
η_{AD}	0.8
η_{AE}	0.4
η_{BC}	0.62
η_{BE}	0.30
η_{CE}	0.4
η_{DA}	0.3
η_{DB}	0.36
η_{DC}	0.42
η_{EB}	0.1
η_{EC}	0.2

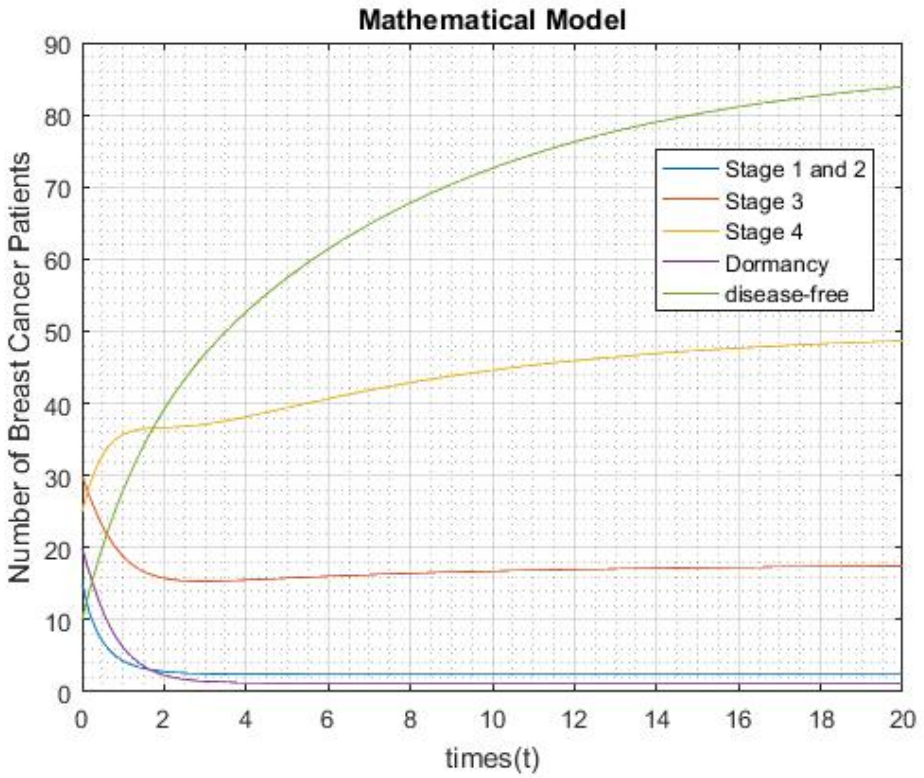

FIGURE 2. The simulation result of the model with initial condition $(A_0, B_0, C_0, D_0, E_0) = (15, 30, 25, 30, 10)$

In Figure 2, the equilibrium conditions are depicted starting from the 7th period, revealing the changes in various sub-populations. Initially, the Stage 1 and 2 sub-populations, which began with 15 patients, decreased to 2 patients under equilibrium conditions. Similar results were observed for the Stage 3 sub-population, which at equilibrium dropped from 30 patients to 17.

Conversely, the sub-population with Stage 4 cancer experienced a notable increase from 25 patients initially to 48 patients at equilibrium. Meanwhile, the disease-free sub-population grew from 10 patients to 83 patients at equilibrium. Moreover, the sub-population in the dormancy phase escalated from 20 patients initially to 1 patient at equilibrium.

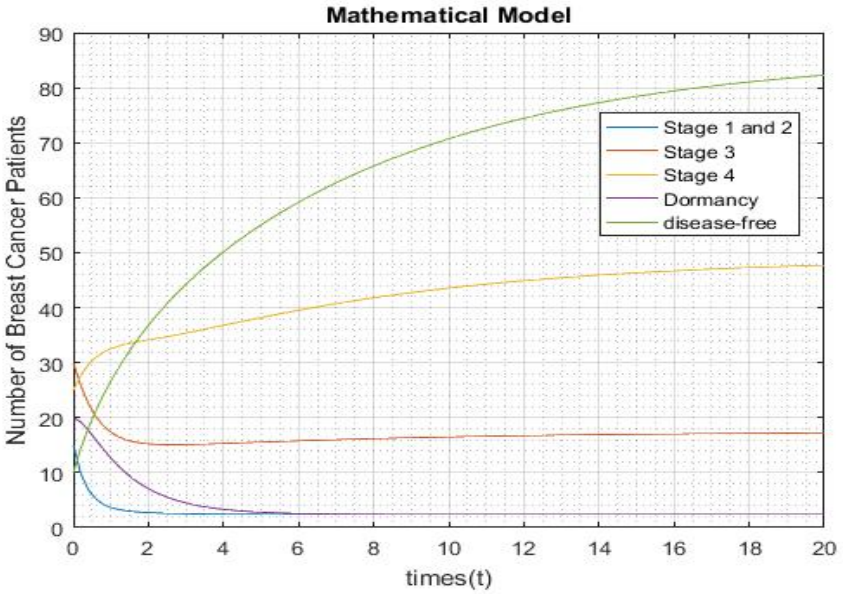

FIGURE 3. The simulation result with $\eta_{DA} = 0.1$, $\eta_{DB} = 0.1$ and $\delta_{DC} = 0.1$

For the second simulation, we will try to low the relapse rates η_{DA}, η_{DB}, and η_{DC} to 0.1. As shown in Figure 3, the results of the simulation are largely similar to those of the initial simulation, with the exception of a small increase in the sub-population in dormancy phase, which now consists of 2 patients.

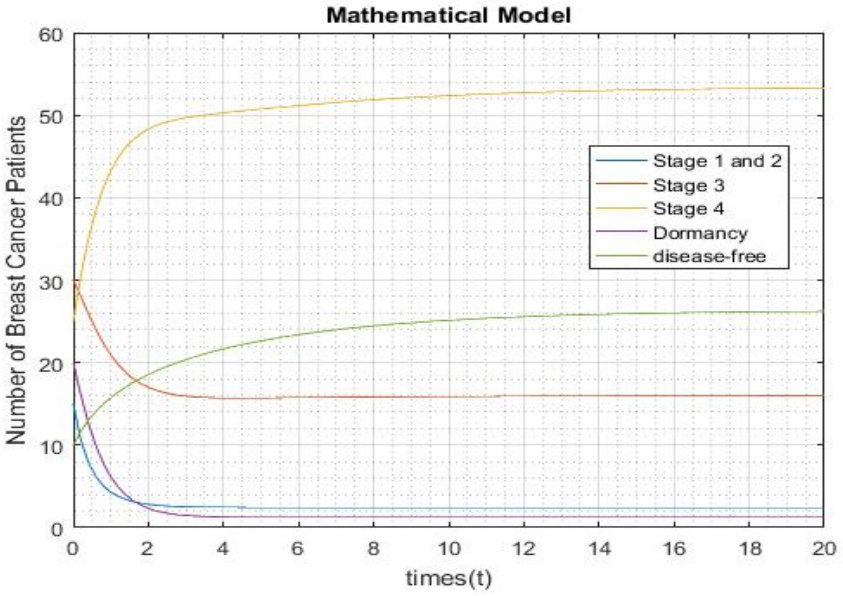

FIGURE 4. The simulation result with $\eta_{BE} = 0.1$ and $\eta_{CE} = 0.1$

FIGURE 4 presents the simulation results obtained by setting the relapse rates η_{BE} and η_{CE} to 0.1 for both sub-populations. Under these conditions, we observed a notable rise in the Stage 4 sub-population to 54 patients and an increase in the disease-free sub-population to 26 patients at equilibrium. However, for the other sub-populations, the results remained consistent with those obtained in the initial simulation.

These simulation results are consistent with the dynamic analysis, which shows that the endemic equilibrium point exists and is stable without any conditions.

5. CONCLUSION

Mathematical modeling can be used to help predict the response of breast cancer to immunotherapy and optimize treatment plans. The various cancer responses that occur after immunotherapy, such as complete response, partial response, stable disease, and progressive disease, can be mathematically modeled using a system of differential equations that take into account the changes in cancer stage. This mathematical model allows for the prediction and evaluation of the cancer response to immunotherapy and may assist in treatment decision-making. Nonetheless, it is important to acknowledge that constructing a mathematical model of cancer responses is a complex task that requires a thorough understanding of the underlying biological mechanisms and actions of immunotherapy. One potential application of this study is to make an early prognosis of the progression of breast cancer in a population receiving immunotherapy as treatment.

To determine the evolution of patient sub-populations over time, a dynamic analysis is performed, which leads to the identification of a stable equilibrium point. To further investigate the solutions, numerical simulations are conducted. The simulation results reveal that the sub-population status remains constant at a specific time, irrespective of the initial conditions, as long as all parameters remain unchanged. This significant finding suggests that the system's equilibrium point is stable and not influenced by any particular conditions.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests.

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