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Mathematical modeling with mixed chemotherapy on tumor cells in two different stages under depression effect

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Abstract

Doctors and experts have developed different many methods for treatment of tumor growth. Many treatment methods are used for tumor growth. Such as immunotherapy, radiotherapy, hormone therapy targeted therapy, chemotherapy, surgery etc. Mixed chemotherapy has been used in this paper to control tumor growth. We have mentioned tumor growth in two stages under depression effect and we have found that the effect of tumor growth varies in both stages. Different mathematical models have been presented for both stages and solved by governing equations. This type of complex and challenging problem has been given a unique solution using all effective parameters.

Keywords: Chemotherapy, tumor therapy, dynamical systems, laplace adomian decomposition method

1. Introduction

The word cancer was first introduced by Greek physician Hippocrates who is named “Father of Medicine”. Hippocrates used five main cancer groups, including Sarcomas, Lymphomas, Carcinomas, Leukemias and Brain tumors [1]. There are main types of cancer treatment methods which are immunotherapy, chemotherapy, surgery and radiotherapy. Radiation therapy used to kill malignant cells. Radiation therapy is an important and effective way to control of tumor growth [2]. The logic of controlling for tumor growth rather than elimination is based on evolutionary theory [3]. A small of quantity of residual tumors cells stopped by different treatment methods in primary stage. In the second stage, the rate of tumor growth increases very much, then it becomes very difficult to control it [4]. Cancers can be classified as liquid (hematopoietic and lymphoid cancers). Leukemia represents hematologic malignancy of blood cells [5]. Molecular data is used in classifying tumors. The molecular data is helpful in these studies about the whole tumor mass. They found genetic differences tumor growth between primary stage and secondary stage [6]. Groups of myeloid cells have created to tumor growth development by inhibition of immune responses. Tumor cells have two differential states in cancer progession. 1. An antitumorigenic role and 2. Promoting tumor progression [7]. Immunotherapy developed to control tumor growth. Cancer immunology have been translated into clinical of immune based approaches to tumor treatment. Clinical data have indicated to potential benefit. It is used of power of the immune with traditional chemotherapy [8]. Chemotherapy used for cancer treatment deals with drugs effecting tumor cells to ability reduce and divide. The drug creates the tumor cells weak and destroys by bloodstream [9].

2. Our model

Kuznestov’s model modified in included growth rate law and fractional cells kill term with chemotherapy as follows

$$\frac{dE}{dt} = s + \frac{\rho ET}{\alpha + T} - c_1 ET - d_1 E - \alpha_1 (1 - e^{-c}) E$$

$$\frac{dT}{dt} = rT(1 - bT) - c_2 ET - \alpha_2 (1 - e^{-c}) T \quad (1)$$

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$$\frac{dC}{dt} = -d_2C$$

Where

$s, \rho, \alpha_1, \alpha_2, c_1, c_2, r, b$ are positive parameters [1]. We included different mathematical model in primary stage and secondary stage under the depression because quantity of tumor cells is small in primary stage than secondary stage. The depression effect is nothing in primary stage so some parameter will change in primary stage and the depression effect is large in secondary stage in Kuznestov's model. This parameter will decide growth rate of tumor cells and effective in primary stage under the depression.

Effect of some parameters $s, \rho, \alpha_1, \alpha_2, r, b$ are powerful because effect of depression $d' \leq 0$ and $c_1 \leq 0, c_2 \leq 0$

$$\frac{dE}{dt} = s + \frac{\rho ET}{\alpha + T} - c_1 ET - d_1 E - \alpha_1(1 - e^{-c})E - d'E$$

$$\frac{dT}{dt} = rT(1 - bT) - c_2 ET - \alpha_2(1 - e^{-c})T + d'nT \tag{2}$$

$$\frac{dC}{dt} = nT - d_2C$$

Term $c_1 ET$ and $c_2 ET$ will be rejected. For stability tumor cells and immune cells $(1 - e^{-c})$ will have to replace $(e^c - 1)$ then new equations are:

$$\frac{dE}{dt} = s + \frac{\rho ET}{\alpha + T} - d_1 E - \alpha_1(e^c - 1)E - d'E$$

$$\frac{dT}{dt} = rT(1 - bT) - \alpha_2(e^c - 1)T + d'nT \tag{3}$$

$$\frac{dC}{dt} = nT - d_2C$$

Where d' will show depression duration in interaction between immune cells and tumor cells and nT will show number of tumor cells.

3. Modified Kuznetsov model with effective parameters:

Some parameters will directly effect of number of tumor cells when tumor cells fight with immune cells then tumor cells will defeat immune cells if tumor cells is powerful than immune cells otherwise immune cells will defeat tumor cells in against condition. We will discuss here two effective parameter which will effect tumor cells and immune cells.

1. Birth rate

When cancer cells create in the body then the tumor cells will start to divide immune cells in the body. Tumor cells increase in a specific part of the body. The immune cells interaction with tumor cells then immune cells decrease and tumor cell increase.

$$B(T) = T \left(\frac{T^3}{3} - \frac{(a+b)T^2}{2} + abT \right), 0 < a < \frac{b}{3}$$

$$B(T) = rT \left(\frac{T^2 - T + 2}{2} \right), r > 0$$

Where

$\frac{-(a+b)T^2}{2}$ will represent for the intraspecific competition. Value of $a = 59.79759503909$ and $b = 2059.797697153575$ will satisfy in our model [1]. These values is putting in equation (3)

$$\frac{dE}{dt} = s + \frac{\rho ET}{\alpha + T} - d_1 E - \alpha_1(e^c - 1)E - d'E$$

$$\frac{dT}{dt} = \left[\frac{T^4}{3} - \frac{(a+b)T^3}{2} + abT^2 \right] - \alpha_2(e^c - 1)T + d'nT \tag{4}$$

$$\frac{dC}{dt} = nT - d_2C$$

And

$$\frac{dE}{dt} = s + \frac{\rho ET}{\alpha + T} - d_1 E - \alpha_1(e^c - 1)E - d'E$$

$$\frac{dT}{dt} = rT \left(\frac{T^2}{2} - T + 2 \right) - \alpha_2(e^c - 1)T + d'nT \tag{5}$$

$$\frac{dC}{dt} = nT - d_2C$$

These values come on the initial conditions are $E(0) = \mu_1$, $T(0) = \tau$, and $C(0) = \mu_2$

3. Depression

Depression will effect on immune cells then immune cells will interaction with tumor cells then immune cells will defiantly defeat from tumor cells.

2. Fractional cell kill term

The new cells create in the body after replacing previous immune cells and tumor cells.

Notations of our model Estimated value

- s = Normal rate of flow o immune cells into tumor site 1.3×10^4
- ρ = Maximum immune cells recruitment rate 1.245×10^{-1}
- α_1 = Fractional immune cells kill by chemotherapy 3.4×10^{-2}
- α_2 = Fractional tumor cells kill by chemotherapy 0.9
- c_1 = Immune cells death rate due to interaction with tumor cells 3.420×10^{-10}
- c_2 = Fractional tumor cells kill by immune cells 1.1×10^{-7}
- d_1 = Nature death rate of immune cells 4.120×10^{-2}
- d_2 = Rate of chemotherapy drug decay 3.466×10^{-1}
- α = Steepness coefficient of immune cells recruitment 2.020×10^7 [1].

3. The solution of the modified kuznestov model with effective parameters:

We will use to Adomian decomposition algorithm method for the solution of our model.

We have

$$\frac{1}{\alpha + T} = \frac{1}{\alpha} \left[\frac{1}{1 + \frac{T}{\alpha}} \right] = \frac{1}{\alpha} \left[1 - \frac{T}{\alpha} + \frac{T^2}{\alpha^2} - \frac{T^3}{\alpha^3} + \dots \right] (e^c - 1) = [C + \frac{C^2}{2!} + \frac{C^3}{3!} + \dots]$$

Now, let s = p and use in equation (4)

$$\frac{dE}{dt} = p + \frac{\rho ET}{\alpha} \left[1 - \frac{T}{\alpha} + \frac{T^2}{\alpha^2} \right] - d_1 E - \alpha_1 \left[C + \frac{C^2}{2!} \right] E - d' E$$

$$\frac{dT}{dt} = \left[\frac{T^4}{3} - \frac{(a+b)}{2} T^3 + abT^2 \right] - \alpha_2 \left[c + \frac{C^2}{2!} \right] T + d' n T$$

$$\frac{dC}{dt} = nT - d_2 C$$

Then

$$\frac{dE}{dt} = p - d_1 E + \left(\frac{\rho}{\alpha} \right) ET - \alpha_1 EC - \frac{\alpha_1}{2} EC^2 - \frac{\rho}{\alpha^2} ET^2 + \frac{\rho}{\alpha^3} ET^3 - d' E$$

$$\frac{dT}{dt} = \left[\frac{T^4}{3} - \frac{(a+b)}{2} T^3 + abT^2 \right] - \alpha_2 TC - \frac{\alpha_2}{2} TC^2 + d' n T \tag{6}$$

$$\frac{dC}{dt} = nT - d_2 C$$

Applying Laplace transform to both sides of equation (6)

$$L \left[\frac{dE}{dt} \right] = L[p] - L[d_1 E] + L \left[\left(\frac{\rho}{\alpha} \right) ET \right] - L[\alpha_1 EC] - \frac{1}{2} L[\alpha_1 EC^2] - L \left[\frac{\rho}{\alpha^2} ET^2 \right] + L \left[\frac{\rho}{\alpha^3} ET^3 \right] - L[d' E]$$

$$L \left[\frac{dT}{dt} \right] = \frac{1}{3} L[T^4] - \frac{1}{2} L[(a+b)T^3] + L[abT^2] - L[\alpha_2 TC] - \frac{1}{2} L[\alpha_2 TC^2] + L[d' n T]$$

$$L \left[\frac{dC}{dt} \right] = L[nT] - L[d_2 C] \tag{7}$$

Applying the initial conditions on (7), we obtain

$$L[E] = \frac{\mu_1}{s} + \frac{p}{s^2} - \frac{d_1}{s} L[E] + \frac{1}{s} \left(\frac{\rho}{\alpha} \right) L[ET] - \frac{\alpha_1}{s} L[EC] - \frac{\alpha_1}{2s} L[EC^2] - \frac{\rho}{\alpha^2 s} L[ET^2] + \frac{\rho}{\alpha^3 s} L[ET^3] - \frac{d'}{s} L[E]$$

$$L[T] = \frac{\tau}{s} + \frac{1}{3s} L[T^4] - \frac{1}{2s} (a+b) L[T^3] + \frac{ab}{s} L[T^2] - \frac{c_2}{s} L[ET] - \frac{\alpha_2}{s} L[TC] - \frac{\alpha_2}{2s} L[TC^2] + \frac{d' n}{s} L[T]$$

$$L[C] = \frac{\mu_2}{s} L[T] + \frac{\mu_2}{s} - \frac{d_2}{s} L[C] \tag{8}$$

Applying Laplace Adomian decomposition method, we obtain

$$E = \sum_{n=0}^{\infty} E_n, T = \sum_{n=0}^{\infty} T_n \text{ and } C = \sum_{n=0}^{\infty} C_n \tag{9}$$

This equation will represent an infinite series (E_n = number of infinite immune cells, T_n = number of infinite Tumor cells and C_n = number of infinite element of drugs)

$$A = ET, B = EC, D = EC^2, F = ET^2, G = ET^3, H = T^4, I = T^3, P = T^2, Q = TC, R = TC^2$$

The non- linear operations A, B, D, F, G, H, I, P, Q and R

$$A = \sum_{n=0}^{\infty} A_n, B = \sum_{n=0}^{\infty} B_n, D = \sum_{n=0}^{\infty} D_n, F = \sum_{n=0}^{\infty} F_n, G = \sum_{n=0}^{\infty} G_n$$

$$H = \sum_{n=0}^{\infty} H_n, I = \sum_{n=0}^{\infty} I_n, P = \sum_{n=0}^{\infty} P_n, Q = \sum_{n=0}^{\infty} Q_n, R = \sum_{n=0}^{\infty} R_n \tag{10}$$

Where $A_n, B_n, F_n, H_n, I_n, P_n, Q_n, R_n$ are called the Adomian polynomials. Now we will expand as follows:

$$A_0 = E_0 T_0, B_0 = E_0 C_0$$

$$A_1 = E_0 T_1 + E_1 T_0, B_1 = E_0 C_1 + E_1 C_0$$

∴

$$D_0 = E_0 C_0^2, F_0 = E_0 T_0^2$$

$$D_1 = E_0 C_0^2 + 2E_0 C_0 C_1, F_1 = E_1 T_0^2 + 2E_0 T_0 T_1$$

$$D_2 = E_2 C_0^2 + 2E_0 C_0 C_2 + E_0 C_1^2 + 2E_1 C_0 C_1$$

$$F_2 = E_2 T_0^2 + 2E_0 T_0 T_2 + E_0 T_1^2 + 2E_1 T_0 T_1$$

∴

$$G_0 = E_0 T_0^3, H_0 = T_0^4$$

$$G_1 = E_1 T_0^3 + 3E_0 T_0^2 T_1, H_1 = 4T_1 T_0^3$$

$$G_2 = E_2 T_0^3 + 3E_0 T_0^2 T_2 + 3E_0 T_1^2 T_0 + 3E_1 T_0^2 T_1$$

$$I_0 = T_0^3, H_2 = 4T_2 T_0^3 + 6T_0^2 T_1^2$$

$$I = 3T_1 T_0^2$$

$$I_2 = 3T_2 T_0^2 + 3T_0 T_1^2$$

Applying this procedure with P_n, Q_n and R_n , now substituting (9) and (10) into (8) results.

$$L[\sum_{n=0}^{\infty} E_n] = \frac{\mu_1}{s} + \frac{p}{s^2} - \frac{(d_1+d')}{s} L[\sum_{n=0}^{\infty} E_n] + \frac{1}{s} \left(\frac{\rho}{\alpha}\right) L[\sum_{n=0}^{\infty} A_n] - \frac{\alpha_1}{s} L[\sum_{n=0}^{\infty} B_n] - \frac{\alpha_1}{2s} L[\sum_{n=0}^{\infty} D_n] - \frac{\rho}{\alpha^2 s} L[\sum_{n=0}^{\infty} F_n] + \frac{\rho}{\alpha^3 s} L[\sum_{n=0}^{\infty} G_n]$$

$$L[\sum_{n=0}^{\infty} T_n] = \frac{\tau}{s} + \frac{1}{3s} L[\sum_{n=0}^{\infty} H_n] - \frac{1}{2s}(a+b) L[\sum_{n=0}^{\infty} I_n] + \frac{ab}{s} L[\sum_{n=0}^{\infty} P_n] - \frac{\alpha_2}{s} L[\sum_{n=0}^{\infty} Q_n] - \frac{\alpha_2}{2s} L[\sum_{n=0}^{\infty} R_n] + \frac{d'n}{s} L[\sum_{n=0}^{\infty} T_n]$$

$$L[\sum_{n=0}^{\infty} C_n] = \frac{n}{s} L[\sum_{n=0}^{\infty} T_n] + \frac{\mu_2}{s} - \frac{d_2}{s} L[\sum_{n=0}^{\infty} C_n] \tag{11}$$

When $n = 0$ (this condition will represent primary stage of cancer), then

$$L[E_0] = \frac{\mu_1}{s} + \frac{p}{s^2}$$

$$L[T_0] = \frac{\tau}{s} \tag{12}$$

$$L[C_0] = \frac{\mu_2}{(s+d_2)}$$

Applying the inverse Laplace transform on (12), we get

$$E_0 = \mu_1 + pt$$

$$T_0 = \tau \quad (13)$$

$$C_0 = \mu_2 e^{-d_2 t}$$

Immune cells, tumor cells and effective of chemotherapy from depression (for primary stage), then $d' \leq 0$, then we get result

The number of immune cells at time $t = 0$ is represented by $E_0 = \mu_1 = 566666$ cells.

The number of tumor cells at time $t = 0$ is represented by $T_0 = \tau = 3181775$ cells.

Effective cells by chemotherapy at time $t = 0$ is represented by $C_0 = \mu_2 = 1.400$ mg/L.

This result is very good as long as both time and depression is 0 After some time, the number of tumor cells will increase, then $t = 1$, we get result

The number of immune cells at time $t = 1$ is represented by $E_0 = \mu_1 + p = 566666 + 13000 = 579666$ cells.

The number of tumor cells at time $t = 1$ is represented by $T_0 = \tau = 3181775$ cells.

Effective cells by chemotherapy at time $t = 1$ is represented by

$$C_0 = \mu_2 e^{-d_2} = 1.400 \times e^{-0.3466} = 1.400 \times 0.707 = 0.9899 \text{ mg/L.}$$

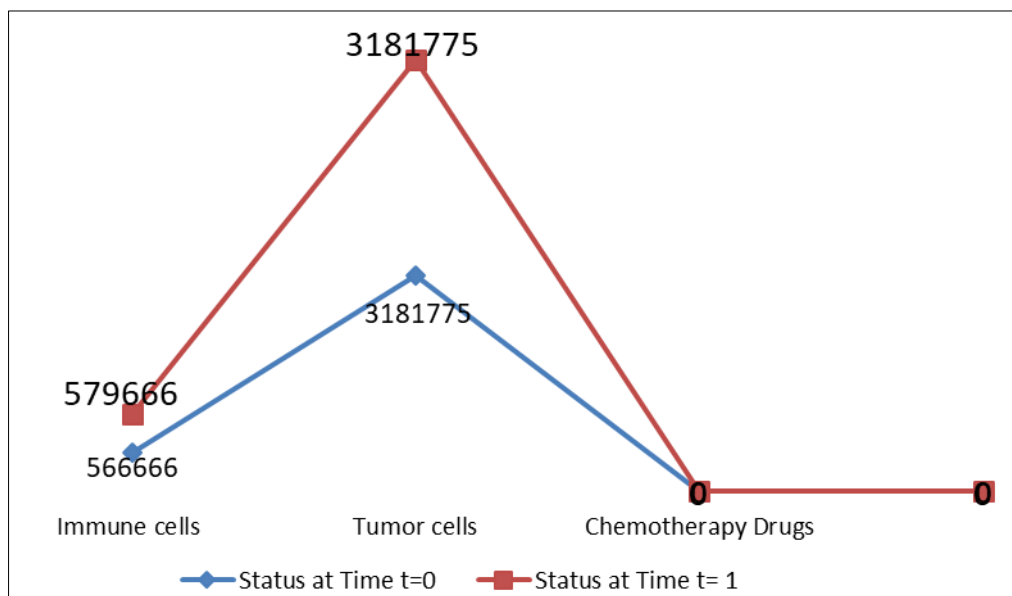


Fig 1: Status of Immune cells, Tumor Cells and Chemotherapy with Depression at Time $t = 0$ & 1

And when $n = 1$ (this condition will represent last of primary stage and start of second stage), then

$$L [E_1] = -\frac{(d_1+d')}{s} L[E_0] + \frac{1}{s} \left(\frac{\rho}{\alpha}\right) L [A_0] - \frac{\alpha_1}{s} L [B_0] - \frac{\alpha_1}{2s} L [D_0] - \frac{\rho}{\alpha^2 s} L [F_0] + \frac{\rho}{\alpha^3 s} L [G_0]$$

$$L [T_1] = \frac{1}{3s} L [H_0] - \frac{1}{2s}(a+b) L [J_0] + \frac{ab}{s} L [P_0] - \frac{\alpha_2}{s} L [Q_0] - \frac{\alpha_2}{2s} L [R_0] + \frac{d'n}{s} L [T_0]$$

$$L [C_1] = \frac{n}{s} L [T_0] - \frac{d_2}{s} L [C_0] \quad (14)$$

Substituting (13) into (14), we obtain

$$L [E_1] = -\frac{(d_1+d')}{s} L [\mu_1 + pt] + \frac{1}{s} \left(\frac{\rho}{\alpha}\right) L [(\mu_1 + pt)\tau] - \frac{\alpha_1}{s} L [(\mu_1 + pt) \mu_2 e^{-d_2 t}] - \frac{\alpha_1}{2s} L [(\mu_1 + pt)(\mu_2 e^{-d_2 t})^2] - \frac{\rho}{\alpha^2 s} L [(\mu_1 + pt) \tau^2] + \frac{\rho}{\alpha^3 s} L [(\mu_1 + pt) \tau^3]$$

$$L [T_1] = \frac{1}{3s} L [\tau^4] - \frac{1}{2s}(a+b) L [\tau^3] + \frac{ab}{s} L [\tau^2] - \frac{\alpha_2}{s} L [\tau \mu_2] - \frac{\alpha_2}{2s} L [\tau \mu_2^2] + \frac{d'n}{s} L [\tau]$$

$$L [C_1] = \frac{n}{s} L [\tau] - \frac{d_2}{s} L [\mu_2 e^{-d_2 t}] \quad (15)$$

Applying inverse Laplace transform on equation (15), we get

$$E_1 = \mu_1 [-(d_1 + d') + \tau \left(\frac{\rho}{\alpha}\right) - \alpha_1 \mu_2 e^{-d_2 t} - \frac{\alpha_1 \mu_2^2}{2} e^{-2d_2 t} - \frac{\rho \tau^2}{\alpha^2} + \frac{\rho \tau^3}{\alpha^3}] t + p [-(d_1 + d') + \tau \left(\frac{\rho}{\alpha}\right) - \alpha_1 \mu_2 e^{-d_2 t} - \frac{\alpha_1 \mu_2^2}{2} e^{-2d_2 t} - \frac{\rho \tau^2}{\alpha^2} + \frac{\rho \tau^3}{\alpha^3}] \frac{t^2}{2} T_1 = \left[\frac{\tau^4}{3} - \frac{(a+b) \tau^3}{2} + ab \tau^2 - \alpha_2 \tau \mu_2 - \frac{\alpha_2 \tau \mu_2^2}{2} + d'n \tau\right] t C_1 = n \tau - [d_2 \mu_2 e^{-d_2 t}] t \quad (16)$$

Immune cells, tumor cells and effective of chemotherapy from depression (for last of primary stage and start of second stage), then $0 < d' \leq 1$, then we get result. The number of immune cells at time $t = 1$ is represented by

$$E_1 = \mu_1[-(d_1 + d') + \tau \left(\frac{\rho}{\alpha}\right) - \alpha_1 \mu_2 e^{-d_2} - \frac{\alpha_1 \mu_2^2}{2} e^{-2d_2} - \frac{\rho \tau^2}{\alpha^2} + \frac{\rho \tau^3}{\alpha^3}] + p[-(d_1 + d') + \tau \left(\frac{\rho}{\alpha}\right) - \alpha_1 \mu_2 e^{-d_2} - \frac{\alpha_1 \mu_2^2}{2} e^{-2d_2} - \frac{\rho \tau^2}{\alpha^2} + \frac{\rho \tau^3}{\alpha^3}] \frac{1}{2}$$

$$E_1 = 566666[-(0.04120 + 1) + 3181775(1.245 \times \frac{10^{-8}}{2.020}) - 0.034 \times 1.4 \times 0.707 - 0.017 \times 1.96 \times 0.4999 - 199.1207 + 2.485] + 0.00013[-1.04120 + 3181775 \times 0.616336633 \times 10^{-8} - 0.03365 - 0.16656 - 199.1207 + 2.485] \frac{1}{2} E_1 = 1.13378510 \times 10^8 \text{ cells}$$

The number of tumor cells at time $t = 1$ is represented by $T_1 = [\frac{\tau^4}{3} - \frac{(a+b)\tau^3}{2} + ab\tau^2 - \alpha_2\tau\mu_2 - \frac{\alpha_2\tau\mu_2^2}{2} + d'n\tau]$

$$T_1 = [3.416304759 \times 10^{25} - 1059.797697 \times 3.221131059 \times 10^{19} + 123170.9486 \times 1.012369215 \times 10^{13} - 4009036.5 - 2806325.55 + 3181775] T_1 = 3.412910969 \times 10^{10} \text{ cells}$$

Effective cells by chemotherapy at time $t = 1$ is represented by $C_1 = n\tau - [d_2\mu_2 e^{-d_2}] = 3181775 - 0.3466 \times 1.4 \times 0.707 = 3181774.657 \text{ mg/L}$ Then $1 < d' \leq \infty$, then we get result.

The number of immune cells at time $t = 2$ is represented by

$$E_1' = \mu_1[-(d_1 + d') + \tau \left(\frac{\rho}{\alpha}\right) - \alpha_1 \mu_2 e^{-2d_2} - \frac{\alpha_1 \mu_2^2}{2} e^{-4d_2} - \frac{\rho \tau^2}{\alpha^2} + \frac{\rho \tau^3}{\alpha^3}] \times 2 + p[-(d_1 + d') + \tau \left(\frac{\rho}{\alpha}\right) - \alpha_1 \mu_2 e^{-2d_2} - \frac{\alpha_1 \mu_2^2}{2} e^{-4d_2} - \frac{\rho \tau^2}{\alpha^2} + \frac{\rho \tau^3}{\alpha^3}] \times 2 E_1' = 566666[-(0.04120 + 1) + 3181775(1.245 \times \frac{10^{-8}}{2.020}) - 0.034 \times 1.4 \times 0.499973591 - 0.017 \times 1.96 \times 0.2499735917 - 199.1207 + 2.485] \times 2 + 0.00013[-1.04120 + 3181775 \times 0.616336633 \times 10^{-8} - 0.034 \times 1.4 \times 0.499973591 - 0.017 \times 1.96 \times 0.2499735917 - 199.1207 + 2.485] \times 2 E_1' = 227291979.5 \text{ cells}$$

The number of tumor cells at time $t = 2$ is represented by $T_1' = [\frac{\tau^4}{3} - \frac{(a+b)\tau^3}{2} + ab\tau^2 - \alpha_2\tau\mu_2 - \frac{\alpha_2\tau\mu_2^2}{2} + d'n\tau] \times 2 - \frac{c_2\tau p}{2} t^2$

$$T_1' = [3.416304759 \times 10^{25} - 1059.797697 \times 3.221131059 \times 10^{19} + 123170.9486 \times 1.012369215 \times 10^{13} - 198330.4083 - 4009036.5 - 2806325.55 + 3181775] \times 2 T_1' = 6.82578222 \times 10^{25} \text{ cells}$$

Effective cells by chemotherapy at time $t = 2$ is represented by $C_1' = n\tau - [d_2\mu_2 e^{-d_2t}] t = 3181775 - 0.3466 \times 1.4 \times 0.499973591 = 3181774.757 \text{ mg/L}$

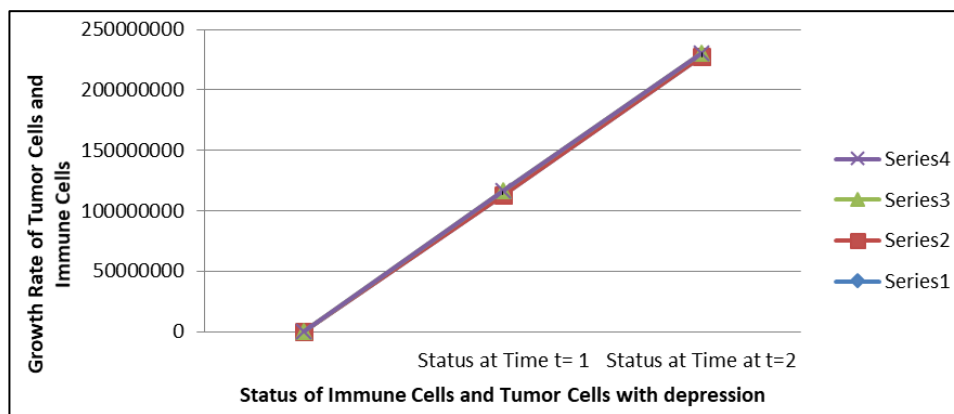


Fig 2: Status of Immune Cells and Tumor Cells with Depression at Time t=1 & 2

4. Results and Discussions

We found that the rate of tumor growth is lower effective in primary stage than secondary stage. Effect of some positive parameters $s, \rho, \alpha_1, \alpha_2, r, b$ are weakness because effect of depression $d' \geq 0$ and $c_1 \geq 0, c_2 \geq 0$ for secondary stage. We have found to result that the rate of tumor growth is very large and number of immune cells will decrease in secondary stage. Finally patient will die from cancer.

6. Conclusions

We have analyzed that tumor growth depends on decreasing of immune cells. In this paper, we have obtained the result of the mathematical model that depression reduces the number of immune cells and increases the number of tumor cells. Depression in the primary stage does not effect both immune cells and tumor cells in any way because in the primary stage the patient does not know that he has cancer. As soon as he comes to know, the effect of depression effects the patient. As the effect of depression increases, the patient loses immunity capacity, leading to increased tumor cells. When the effect of depression increases, the

tumor cells increase greatly, due to which the effect of chemotherapy is very low, almost inactive and the patient can die from depression.

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