Mathematical Models Of Cancer Cells In Tumor Immune Interaction And Control Growth Of Cancer Cells With Chemotherapy

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Abstract-
In this paper, we discussed some mathematical models of cancer growth and included of all affective parameter and observation for each mathematical models then we analyzed about each outcome. We designed more effective mathematical models of cancer growth and included effect of chemotherapy in two systems. All parameters have different role in each system because value of these parameters change in each system. Sensitive tumor cells, resistant cells and immune system are main important parameters in our mathematical models. We defined our mathematical models in two systems and ordinary differential equation. We analyzed overall mathematical model and provide important result in this paper. Draw graph for each mathematical models and two table of description before and after using chemotherapy.

Keywords: Sensitive tumor cells, resistant cells and immune system and chemotherapy etc.

Introduction: -
Continuous and discrete mathematical models which describe the formation of the capillary sprout by a solid tumor (1) and drug regimens for precision medicine (2) after discussed heterogeneity in renal cell carcinoma (3), effects of radiotherapy and immunotherapy on tumor-immune dynamics. Cancer continues to be a predominant cause of mortality globally (13-14), with millions of new diagnoses each year (4). linear-quadratic formula and progress in fractionated radiotherapy. A primary objective in cancer treatment is to diminish or eradicate tumor proliferation while preserving adjacent healthy tissues (5). Numerous therapeutic approaches have been developed throughout the years, including surgery, radiation therapy, chemotherapy, immunotherapy, and targeted medicines. Nonetheless, these therapies frequently entail constraints like toxicity, medication resistance, and variable patient responses and formulate linear-quadratic formula and progress in fractionated radiotherapy (6). Mathematical model for relating the drug sensitivity of growth of tumor cells to their spontaneous mutation rate (7).
A dynamical theory of growth of tumor cells, treatment response as chemotherapy, and post vascular dormancy (8). Model-based clinical drug development (combined therapy as chemotherapy) in the past, present and future and provide a dynamical mathematical model (9-10) and growth rate of tumor cells optimal controls for mathematical models with pharmaco-kinetic/pharmaco-dynamic effects of chemotherapy (11).
Nonlinear ordinary differential equation modeling of cancer: Bridging the gap between immune cells and tumors cells (12) and provide a mathematical model for with mixed chemotherapy on tumor cells in two different stages under depression effect (16-17) for tumor dynamics and treatment resistance evolution of solid tumors (22). Cancer cells more reactive whenever interaction tumor immune cells and used chemotherapy to control of growth of cancer cells so oncology drug development for treatment (21).

Some Mathematical models of cancer growth: -
We discussed in this paper different and various mathematical model for cancer growth in different situation. We represented growth rate of cancer cells in tumor immune interaction cells. Growth rate of cancer cells is affected from various parameters. If we control to various parameter then growth rate of cancer cells will be to controlled. First of all, we study in following mathematical models.

1. Exponential Mathematical Model: –

In this model, growth rate of cancer cells is directly affected. If various parameter be in cancer cells, then growth rate of cancer cells is very high and if against then we can control to increase of cancer cells. This completing process represented by mathematical equations. V^* represents cancer cells after growing rate of cancer cells, V affected cancer cell from various parameters. Then

$$V^* \propto V$$
$$V^* = \alpha V \quad (1)$$

In equation (1), α is proportionally constant in this mathematical models. It represents growths rate of cancer cells in equation (1).
In this case, growth rate of cancer cells is speedily developed interaction between immune and cancer cells for next stage.

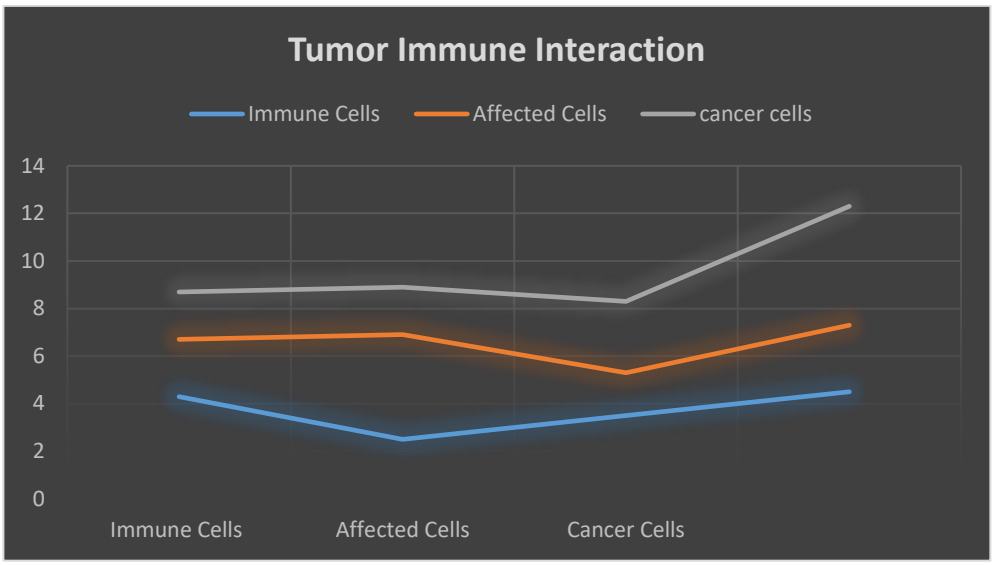

Fig.(1.1)

2. Mendelsohn Mathematical Model: -

In this mathematical model, exponential model modified and provide a new mathematical model. This model represents growth rate of cancer cells and include a second parameter b. b represents growth of population in this mathematical model.

$$V^* = \alpha V^b \qquad (2)$$

Equation (2) describe that cancer cells is affected growth rate of cancer cells and growth of population.

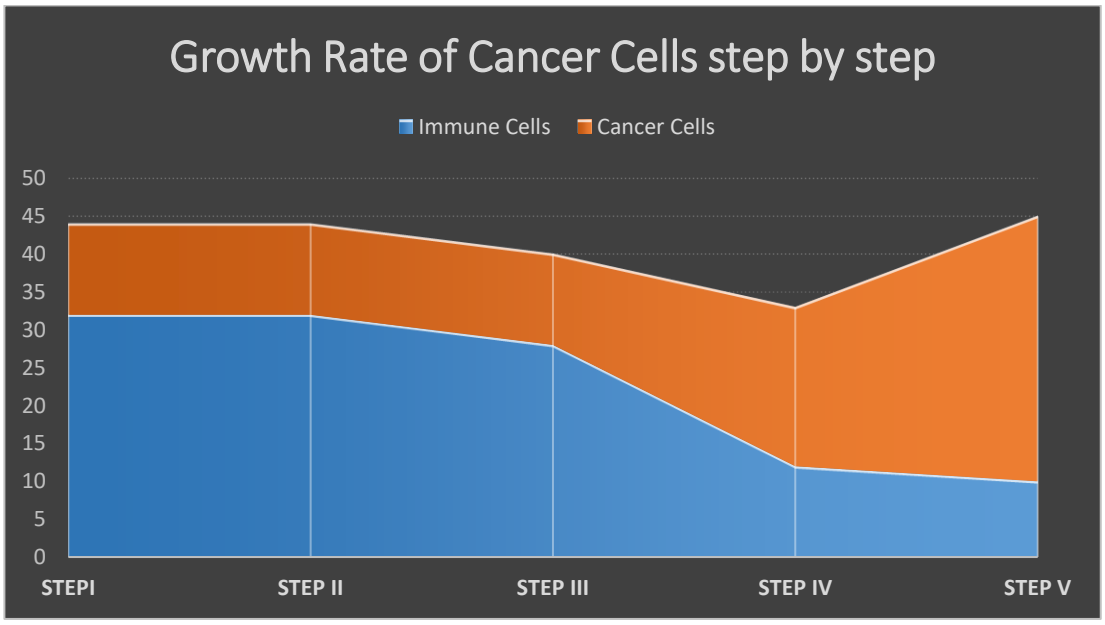

Fig (1.2)

3. Pearl- Verhulst Mathematical Model: -

This model represents logistic growth rate of tumor cells b is carrying capacity of population. This model is modified by Pearl – Verhulst from mathematical model. If we reduce carrying capacity of population in this mathematical model, then growth rate of cancer cells is directly decreasing.

$$V^* = \alpha V(1 - \frac{V}{b}) \qquad (3)$$

In equation (3), growth rate of cancer cells depends on carrying capacity of population b.

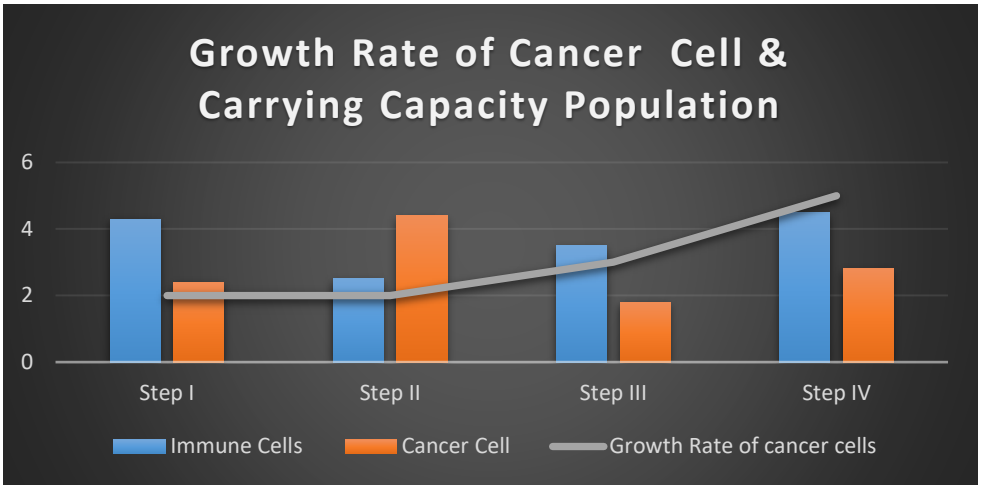

Fig. (1.3)

4. Linear Mathematical Model: -

This model modified from equation (1) and (2).

$$V^* = \frac{\alpha V}{V+b} \quad (4)$$

This model represents a linear equation growth rate of cancer, carrying capacity of population and affected cancer cells.

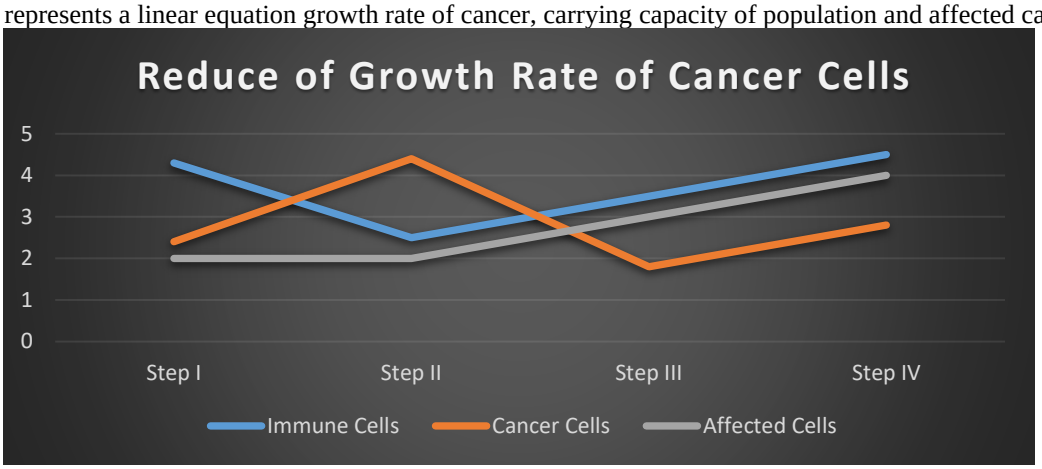

Fig. (1.4)

5. Surface Mathematical Model:

This model represents that a cellular growth is possible only a thin layer of cancer cells. Growth rate of cancer cells depends on surface.

$$V^* = \frac{\alpha V}{(V+b)^{1/3}} \quad (5)$$

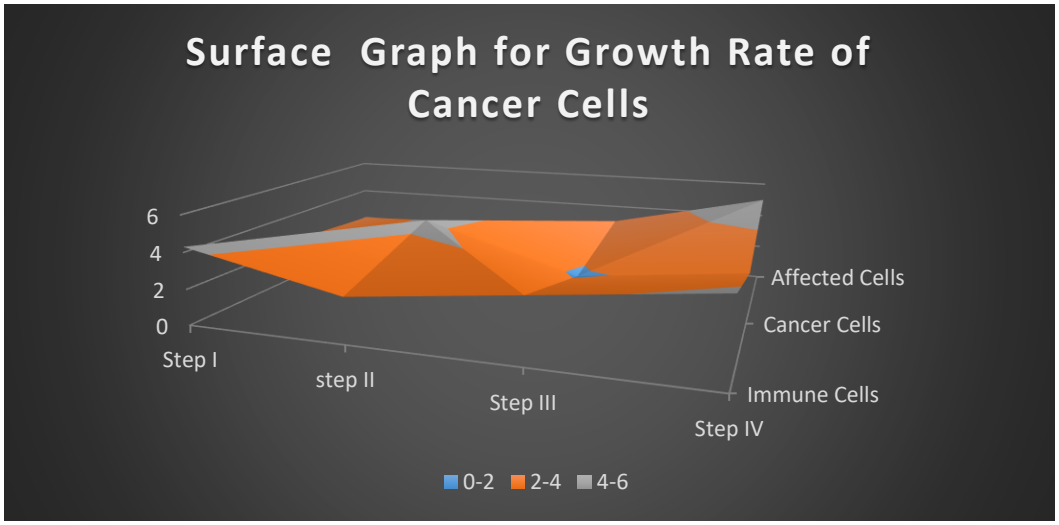

Fig. (1.5)

6. Gompertz Mathematical Model: -

This model describes growth rate of tumor cells only for Breast and Lungs Cancer cells.

$$V^* = \alpha V . \frac{b}{V+c} \quad (6)$$

This model is a Logistic model. It is sigmoidal curve which is asymmetrical to the inflection point.

7. Bertalanffy Mathematical Model: -

Cancer cell growth is indeed a phenomenon of restricted cellular growth at the tumor surface that the loss of cancer cell also occurs due to cell death.

$$V^* = \alpha V^{2/3} - bV \quad (7)$$

Now, we get a result from equation (1) & (7).

$$V^* = \frac{bV^{4/3}}{(1-V^{1/3})} \quad (8)$$

This mathematical model represents reduce to growth rate of cancer growth.

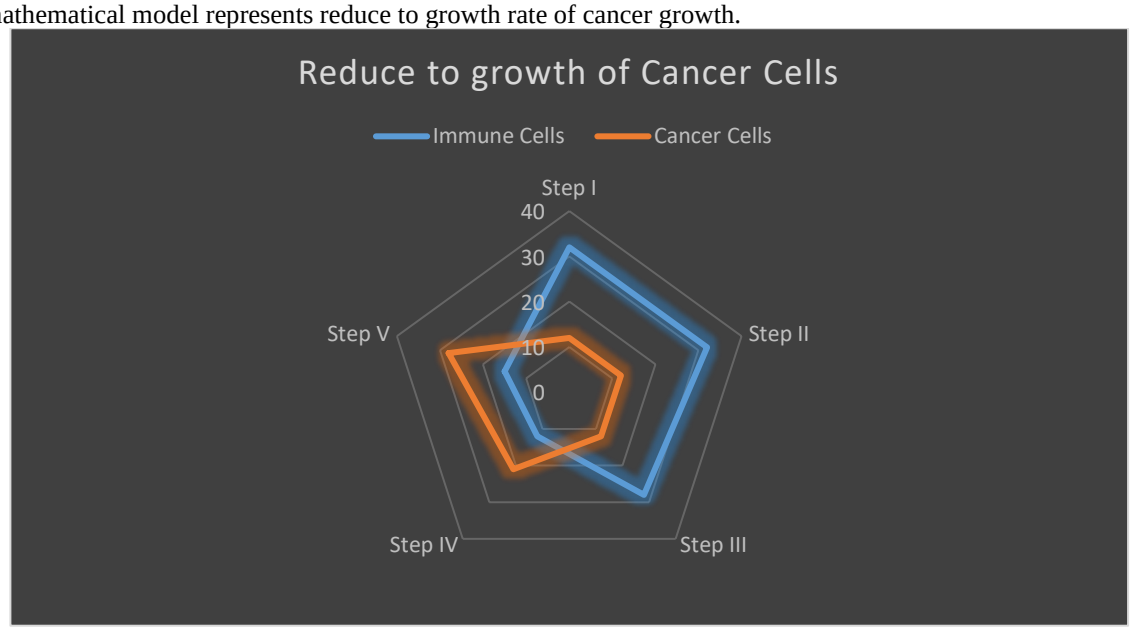

Fig. (1.6)

8. More affective Mathematical Model: -

Mostly affective all parameters are included in this mathematical model. We discussed of this mathematical model in two very affective and beneficial systems for patient.

$\frac{dN(t)}{dt} = aN(t)(1 - \frac{N(t)+R(t)}{T}) - \mu N(t) - pI(t)N(t)$
$\frac{dR(t)}{dt} = aR(t)\left(1 - \frac{N(t)+R(t)}{T}\right) + \mu N(t) - qI(t)R(t), \quad take \quad t \leq t^*$
$\frac{dI(t)}{dt} = r_1 I(t)N(t) + R(t) - dI(t)$

System -1

$\frac{dN(t)}{dt} = aN(t)\left(1 - \frac{N(t)+R(t)}{T}\right) - \mu N(t) - pI(t)N(t) - \frac{h.D(t)}{K+d(t)} N(t)$
$\frac{dR(t)}{dt} = aR(t)\left(1 - \frac{N(t)+R(t)}{T}\right) + \mu N(t) - qI(t)R(t), \quad take \quad t > t^*$
$\frac{dI(t)}{dt} = s + r_2 I(t)N(t) + R(t) - dI(t)$
$\frac{dD(t)}{dt} = \delta - \varphi D(t)$

System-2

Discussion about system -1

In system-1, this mathematical model represents sensitive tumor cells, resistant tumor cells and immune system before chemotherapy.

Parameters	Description
N(t)	sensitive tumor cells
R(t)	resistant tumor cells
I(t)	immune system
D(t)	drug concentration
a	intrinsic growth rate
p	recruitment potential
q	sensitive cancer cells and resistant cancer cells is measured by the parameter *q*.
r_1	difference between p and q
T	maximum carrying capacity of the tumor cells
μ	mutation rate
s	Source of immune cells
δ	rate of drug
φ	rate constant of drug

Table-1

1.1. Sensitive tumor cells: -

$$\frac{dN(t)}{dt} = aN(t)\left(1 - \frac{N(t)+R(t)}{T}\right) - \mu N(t) - pI(t)N(t) - \frac{h.D(t)}{K+d(t)}N(t)$$

Sensitive Tumor Cells *N(t)* rapidly reactive with Immune Cells *I(t)* and the growth rate of production of tumor cells increases rapidly before chemotherapy in system (1). Sensitive Tumor Cells *N(t),* resistant tumor cells *R(t)* and maximum carrying capacity of the tumor cells T affect from each other. Sensitive Tumor Cells *N(t)* and resistant tumor cells *R(t)* represent direct relation because the nature of *N(t)* and *R(t)* is in favour of each other while the carrying capacity of tumor cells *T* increases and decreases, affecting *N(t)* and *R(t)* and thereby affecting sensitive cells as well (18). The mutation rate affects sensitive tumor cells *N(t).* If the mutation rate μ increases, the rate of sensitive tumor cells will decrease. Recruitment potential *p* and intrinsic growth rate *a* reduces tumor growth rate.

1.2 Resistant tumor cells: -

$$\frac{dR(t)}{dt} = aR(t)\left(1 - \frac{N(t)+R(t)}{T}\right) + \mu N(t) - qI(t)R(t)$$

Growth rate of tumor cells expressed in this mathematical model. Its depends on Sensitive Tumor Cells *N(t),* resistant tumor cells *R(t)* and carrying capacity of tumor cells *T* are main parameters. These parameters are directly related from each other so growth rate of tumor cells is also affected if values of these parameters change in any situation then growth rate of tumor cells will be affected.

Intrinsic growth rate, mutation rate and sensitive cancer cells and resistant cancer cells *q* included in this mathematical model. These parameters have changed to growth rate of cancer cells.

1.3 Immune system: -

$$\frac{dI(t)}{dt} = r_1 I(t)N(t) + R(t) - dI(t)$$

Immune system has very important role for defeating of cancer cells. Immune cells directly fight from cancer cells if immune system is very strong then cancer cells will never activate in even condition when immune system defeated from cancer cell then growth rate of cancer cells increase.

Immune system depends on various parameters as sensitive tumor cells *N(t),* resistant tumor cells *R(t),* and difference between *p* and *q.* These parameters made to a strong immune system when these parameters interaction with immune cells and it's have opposite nature then immune system be too loose.

Discussion about system -2

In system-2, this mathematical model represents sensitive tumor cells, resistant tumor cells and immune system after chemotherapy.

Parameters	Description
N(t)	sensitive tumor cells (after Chemotherapy)
R(t)	resistant tumor cells (after Chemotherapy)
I(t)	immune system (after Chemotherapy)
D(t)	drug concentration
a	intrinsic growth rate(after chemotherapy)
p	recruitment potential (after chemotherapy)

q	sensitive cancer cells and resistant cancer cells is measured by the parameter q (after chemotherapy)
r_1	difference between p and q (after chemotherapy)
T	maximum carrying capacity of the tumor cells (after chemotherapy)
μ	mutation rate (after chemotherapy)
s	Source of immune cells
δ	rate of drug
φ	rate constant of drug

Table-2

2.1. Sensitive tumor cells (after chemotherapy): -

$$\frac{dN(t)}{dt} = aN(t)\left(1 - \frac{N(t)+R(t)}{T}\right) - \mu N(t) - pI(t)N(t) - \frac{h.D(t)}{K+d(t)}N(t)$$

We observe that after chemotherapy sensitive Tumor Cells *N(t)* slowly reactive with Immune Cells *I(t)* and the growth rate of production of tumor cells decrease rapidly in system (2). Sensitive Tumor Cells *N(t)*, resistant tumor cells *R(t)* and maximum carrying capacity of the tumor cells *T* affect from each other will react slowly (19). *N(t)* and *R(t)* represent direct relation because the nature of *N(t)* and *R(t)* is in favour of each other while *T* only decreases, affecting *N(t)* and *R(t)* and thereby affecting sensitive cells as well. The mutation rate affects sensitive tumor cells *N(t)*. If the mutation rate μ increases, the rate of sensitive tumor cells will decrease. *p* and *a* is also affected and reduces tumor growth rate.

2.2. Resistant tumor cells (after chemotherapy): -

$$\frac{dR(t)}{dt} = aR(t)\left(1 - \frac{N(t)+R(t)}{T}\right) + \mu N(t) - qI(t)R(t)$$

We observe that after chemotherapy, growth rate of tumor cells reduces for some time in this mathematical model. Its depends on *N(t)*, *R(t)* and *T* are main parameters but after chemotherapy reaction of all affected parameters slow. Now these parameters are not directly related from each other so growth rate of tumor cells is also affected if values of these parameters change after chemotherapy then growth rate of tumor cells will be reduced.

a, *p* and *q* included in this mathematical model. These parameters have changed to growth rate of cancer cells. $\frac{h.D(t)}{K+d(t)}$ which is assumed to follow the Michaelis–Menten kinetics.

2.3. Immune system (after chemotherapy): -

$$\frac{dI(t)}{dt} = s + r_2 I(t)N(t) + R(t) - dI(t)$$

Immune system will be affected after chemotherapy by the way immune cells will be balance after some time but immune cell will be energetic and immune cells defeated to cancer cells in tumor immune interaction. Immune cells directly fight from cancer cells if immune system will be very strong then cancer cells will never activate for some time and growth rate of tumor cells will be decreased.

After chemotherapy, immune system depends on various parameters as *N(t)*, *R(t)*, and difference between *p* and *q*. These parameters will release to making a strong immune system after chemotherapy. Natural source *s* will be affected by chemotherapy but *s* will be balanced itself after some time and generate healthy immune cells.

Drug Concertation: -

$$\frac{dD(t)}{dt} = \delta - \varphi D(t)$$

The development of drug resistance is one of the most significant obstacles in the field of chemotherapy. The mechanisms of resistance and their implications for treatment have been extensively investigated using mathematical models (20). Drug concertation control to growth of tumor cells. Mostly we use chemotherapy for reduce to number of cancer cells. Almost cancer finish after chemotherapy but after some time cancer cell generate and symptoms of cancer seemed in patient body.

Drug concertation depends on rate of drug δ and rate constant of drug φ .The natural death of immune cells is given by the term $-dI(t)$. The pharmacokinetics of the drug is described in system 2, where φ is the constant rate of drug delivery and δ is the elimination rate of the drug. Cancer cells can develop resistance to drugs over time, which may necessitate increasing concentrations or combining therapies. As Pharmacokinetics, Pharmacodynamics…etc.

Combination Therapies: Combining different drugs can sometimes allow for lower concentrations of each drug while maintaining effectiveness, which can reduce side effects.

Discussion and result: - we discuss about some mathematical models growth of cancer cells regarding in this paper and observe that cancer cells are rapidly reactive in patient body if patient body is not fit for making a strong immune system. Growth of cancer cells uncontrolled if we have no best immune system and proper treatment. We observe in this paper

chemotherapy and best immune system are best choice for control of cancer cells. System (1) represents interaction of cancer cells and immune cells. Growth rate of immune cells reduce in system but growth rate of cancer cells is positively increasing.

Conclusion: -

Cancer cells uncontrolled in system (1) but we observe of system (2) and founded that growth of cancer cell can be to controlled by chemotherapy and healthy food. Table (1) and table (2) represent to including parameters in this mathematical models before and after using to chemotherapy. Sensitive tumor cells N(t) and resistant tumor cells R(t) are main components in affective mathematical models. When sensitive tumor cells N(t) growth in system (1), then resistant tumor cells R(t) fail or weak than sensitive tumor cell but we study system (2), after using chemotherapy found that sensitive tumor cells N(t) weak than resistant tumor cells R(t). Drug (Chemotherapy) used to control growth of cancer cells in this paper. Effects of chemotherapy D(t) are beneficial for cancer patient.

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