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DESIGN MATHEMATICAL MODEL FOR PREVENTION AND CONTROL OF BREAST CANCER THROUGH CANCEROUS-IMMUNE INTERACTIONS

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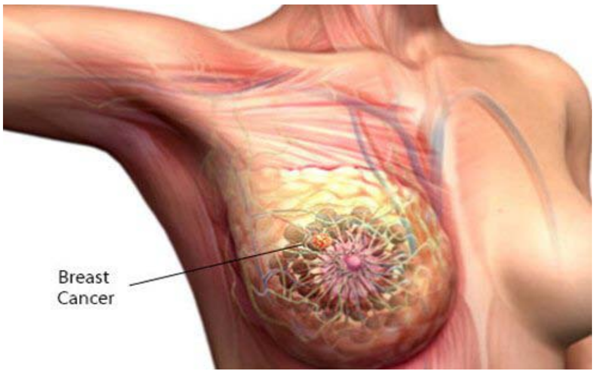
ABSTRACT

This paper focus on mathematical modelling in field of breast cancer therapy. In current work we developed biomedical applicable mathematical model of immunotherapy for cytotoxic activity as prevention and control of breast cancer. Here we designed the mathematical model using prey- predator system that applied as cancerous-immune cell interaction. The cancerous cell and immune cell are represent prey and predator respectively. The current model and their parameter definitely helpful tool for prevention, control and treatment of not only on breast cancer but also implementable on other lethal cancer. The proposed mathematical model might be developed better medical understanding of retention of tumor cell growth in breast cancer through immunological response in initial stage.

Keywords: *Mathematical Modeling, Cancerous cell, Immune cell, Immunotherapy, Breast cancer therapy.*

1. INTRODUCTION

Cancer is a lethal disease that occurs as uncontrolled growth of abnormal cell. These abnormal proliferated cells are also known as cancer cells. This increased cell division becomes a tumor. Some types of cancer cell rapidly proliferated and can be outspread to other parts of the body. The particular body part where the abnormal cancerous cell has start to uncontrolled grow, the name of cancer on the basis of that respective body organ like breast cancer, lung cancer, oral cancer, bone cancer, ovarian cancer etc. Cancer is the second leading cause of death globally (National cancer institute 2016). Breast cancer is the most lethal cancer in world and it is a one of the leading fatal disease in woman with higher death rates. Million of woman suffering from breast cancer in developed and less developed countries. The chance of breast cancer increased specially in those countries where there is no proper patients diagnosis in initial stage and lack of health awareness (American society of cancer research).



The ducts and lobes are most common site on breast where the cancerous cell proliferated and become a tumor as ductal carcinoma and lobular carcinoma. Proper understanding the oncology of breast cancer will helpful tool for prevention, control and cure. If breast cancer diagnoses in early stage the survival rate enhance.

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Immunology is the branch of the medical science that enlighten the knowledge of the immune system. The immune is self protective system of body from cancer, infection and other illness. Immune system able to prevent, control and treat cancer. Immunotherapy is able to change the face of modern medicine science. Immunological researches are helpful tool in understanding of how to control, prevent and treat breast cancer. Immunotherapy might be good tool for prevent and eliminate cancer through enhance natural power of body. Immune system has played the lead role in breakthrough treatment of a number of cancers. Immunotherapy is one of the effective approach in prevention and control of breast cancer and also give boosting effect on treatment therapy. When number of cancerous cell increased in breast tissue, the response of immune cell automatically enhance. As effective body functioning, the immune system detects and destroys abnormal cancerous cells and prevents breast cancers.

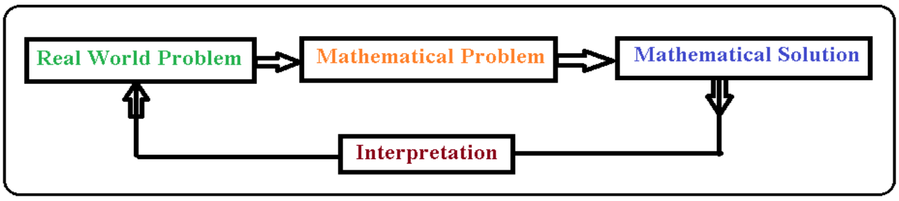
In this paper design the mathematical model of breast cancer for prevention, control and treatment through cancerous-Immune cell interactions. Some researchers has designed mathematical models on tumour–immune interactions and developed the understanding of immune system on tumour as immunotherapy including [1-5]. Developed the mathematical model for treatment of breast cancer is a not easier task is the calculation of biological parameters from existential data. The previous developed mathematical modeling becomes a more complex as deal with number of cell population in same platform and finding out the solution in term of treatment. The model designed by many researches on cancerous-immune cell interaction are intricate.

The mathematical model created by L D Pillis *et al* [6] for treatment of cancer through chemo-immunotherapy as combine effect of immunotherapy and chemotherapy as a mix therapy. Evaluated the interaction of tumour cancurous cells and selective immune cell as natural killer (NK) cells, CD8+T cells and other lymphocytes and finally employs chemotherapy in their treatment modalities using ordinary differential equations (ODEs). R Kim *et al* [7] demonstrated the mathematical model of tumor immune interactions in cancer immunotherapy using monoclonal antibodies as alone or with another treatment. This model enlighten the application of monoclonal antibodies in cancer treatment. For enhance the result of treatment apply DC therapy and monoclonal antibody gave in combination. The mathematical model of M. H. F. Wilkinson et al [8] discussed prey- predator models of ecosystem with its dynamics and evolution. Model of prey- predator systems gave the better understanding the behaviour of two opposite species. The change in population of prey with respect to predator. S Khajanchi *et al*. [9] presented a mathematical model of tumor immune cells interaction as a stability and bifurcation analysis. The model discuss fundamental process of tumor cell proliferation and effect of immunity on its inhibition as control. The model closely describe the time related bifurcation, stability and steady state parameter. H Gonzalez *et al.* [10] has described roles of the immune system in cancer therapy as detection of tumor in initial stage. The mathematical model created by L G Pillis *et al* [11] for describes tumor-immune interactions using a system of differential equations and validated it. The model enlighten the role of natural killer (NK) and CD8+ T cells in cancer treatment. In this paper M Agarwal *et al* [12] deals with nonlinear ordinary differential equations for describing the interaction between cancer and immune cells during immunotherapy and notified the cancer cell population decrease considerably due to proliferation of lymphocytes. Yanan Liu *et al* [13] presented the model of directly and indirectly cancer interact with human immune system, such interactions developed the understanding and functioning of immunotherapy against cancer.

The mathematical model developed by F. B. Charles *et al* [14] for treatment of cancer through immunotherapy by applied predator-prey model. The model gave the clinical application of mathematics using four parameters in the form of tumor cell and immune cell. The model and its parameter made the good understanding of inhibition of cancerous cell by immune response and explain the tumor immunity interaction. This model also describe the tumor and immune cell equilibrium and dynamical phenomena. Kalyan Das *et al.* [15] presented a mathematical model using prey–predator system. The proposed system studied the analysis of infection control and its stability study as steady state. In order to describe cancerous and immune cells interaction, Senol Kartal *et al* [16] created the mathematical model for tumor-immune cell interaction through Lotka-Volterra predator-prey system. The model denoted the stability, equilibrium and oscillation in tumor and immune system.

2. MATHEMATICAL MODELING

Mathematical modeling is a systematic approach that identifies real world problems and solves in mathematical conceptual way as equation, formula, theorem and finally interpreted these result in the language of the real world. The Mathematical modeling is an important approach that translating real world problems into mathematical problems, solving the mathematical problems by apply appropriate mathematical tool and terms then finally interpreting these resulting solutions in the language of the real world. Mathematical model are describe in terms of differential equations when the situation involves some continuous variables varying with respect to some other continuous variables. Implementation of mathematical modeling in biomedical science definitely gives the effective and easier approach for breast cancer treatment in initial stage. Designed new mathematical model facilitated the discovery of new diagnostics, prevention and treatments of breast cancer. Breast cancer in broad spectrum disease that always encouraged researchers to find out the appropriate solution.



3. MATHEMATICAL CALCULATION

When the patient suffering from breast cancer, the breast cell show extra proliferation and become a tumor. It will spread in surrounded tissue and show malignancy. The generated cancerous cells are foreign substance for body and the protected system of human body activated as immune response.

Let T(t) and I(t) be the population of cancerous cell and immune cell respectively at time t. We represent the relation between cancerous cell and immune cell by the pair of first order non-liner ordinary differential equation.

$$\frac{dT}{dt} = mT - nTI$$

$$\frac{dT}{dt} = T\left(m - nI\right) \quad (1)$$

Where $m, n > 0$

$$\frac{dI}{dt} = sTI - rI$$

$$\frac{dI}{dt} = I\left(sT - r\right) \quad (2)$$

Where $r, s > 0$

T is the number of cancerous cell in body at time t.

I is the number of immune cell in body at time t.

$\frac{dT}{dt}$ and $\frac{dI}{dt}$ represent the growth rate of cell population.

m, n, r, s are positive real parameters describing the interaction of cancerous cell and immune cell.

Cancerous cell equation (1) becomes

$$\frac{dT}{dt} = mT - nTI$$

Here the above equation describe the cancerous cell have an unlimited proliferation capacity by using nutrition from body and exponentially convert into breast tumor. Cancerous cell freely uncontrolled grow when body immune system are week and unable to recognized foreign cancerous cell.

The rate of immune cell upon the cancerous cells is assumed to be proportional to the rate at which the cancerous cell and immune cell interact, this is represent above by nTI, the n is a parameter that indicates how efficiently immunes cell control the population of carcinogenic cancerous cell.

If either T or I is zero, then there are no immunes response that means if no proliferation of cancerous cell in breast tissue, the immunes system are also an inactive mode.

Immunes cell equation (2) becomes

$$\frac{dI}{dt} = sTI - rI$$

In this equation sTI represent the active mode of immunes cell population with proper functioning. If the foreign carcinogenic substance as cancerous cell reflect in body then enhance the response of immune cell spontaneous. rI represent there is no need to functioning of immune cell in absence of foreign cancerous cell as it leads to an exponential decay of cancerous cell. When no cancerous cell present at breast tissue, the response of immune cell are automatically decrease.

Solving of cancerous and immunes cell equation:

$$\frac{dT}{dt} = mT - nTI$$

$$\frac{dT}{dt} = sTI - rI$$

The first equation is homogenous in T and the second equation is homogenous in I.

From equation (1) and (2)

$$\frac{dI}{dT} = \frac{I(sT-r)}{T(m-nI)}$$

$$\frac{(m-nI)dI}{I} = \frac{(r-sT)dT}{T}$$

$$\frac{(m-nI)dI}{I} + \frac{(r-sT)dT}{T} = 0$$

After integrating we have

$$r\log T - sT + m\log I - nI = C \tag{3}$$

Where C is constant depending on the initial condition.

Above system of equation (1) and (2) yields two solutions

$$\{T = 0, I = 0\} \text{ and } \left\{I = \frac{m}{n}, T = \frac{r}{s}\right\}$$

Hence there are two cell population (cancerous cell and immunes cell) in equilibrium positions. These are points at which cancerous cell and immunes cell in steady states. At this point there is no cancerous cell detected as tumor growth and immunes system also in inactive as sleeping mode.

Steady state of fixed point

The stability of an equilibrium point determines using Jacobian Matrix of the model

The Jacobian Matrix of the model is

$$J(T,I) = \begin{bmatrix} \frac{d}{dT}(mT - nTI) & \frac{d}{dT}(mT - nTI) \\ \frac{d}{dT}(sTI - rI) & \frac{d}{dT}(sTI - rI) \end{bmatrix} \tag{4}$$

$$J(T,I) = \begin{bmatrix} (m - nI) & (-nT) \\ sI & (sT - r) \end{bmatrix} \tag{5}$$

This is linearization of the model at an equilibrium point.

The eigenvalue of the matrix determine the stability of the equilibrium point.

First fixed point (Disappearance)

Evaluated Jacobian matrix (equation-5) at point (0, 0) it becomes

$$J(0,0) = \begin{bmatrix} m & 0 \\ 0 & -r \end{bmatrix}$$

The eigenvalue of this matrix are

$$\lambda_1 = m,\ \lambda_2 = -r$$

The eigenvalues denoted that how the model act around the stationary point. In the model m and r are always higher than zero. The sign of the eigenvalues is always opposite as counting of immunes cell in active mode the population of cancerous cell get inactive and when the lack of immunity as the immunes cell are not performing properly the cancerous cell proliferated rapidly. In stability of fixed point is an important for achieving steady state. For stable model the cell population of both cancerous cell and immunes cell work opposite functioning and still get zero. If cancerous cell present in body, the immunes cell recognized it and immune system fight against to cancer cell as self protective system of body to produce cytotoxic effect on cancerous cell. As immunes are actively responding it decreases the population of cancerous cell and prevent and control the proliferation of cancerous cell. At stable point there is no cancerous cell detected as tumor growth and immunes system also in sleeping mode. The populations of cancerous cell and immunes cell when get infinitesimally close to zero then effective control and recover breast cancer.

Second fixed point (Variation)

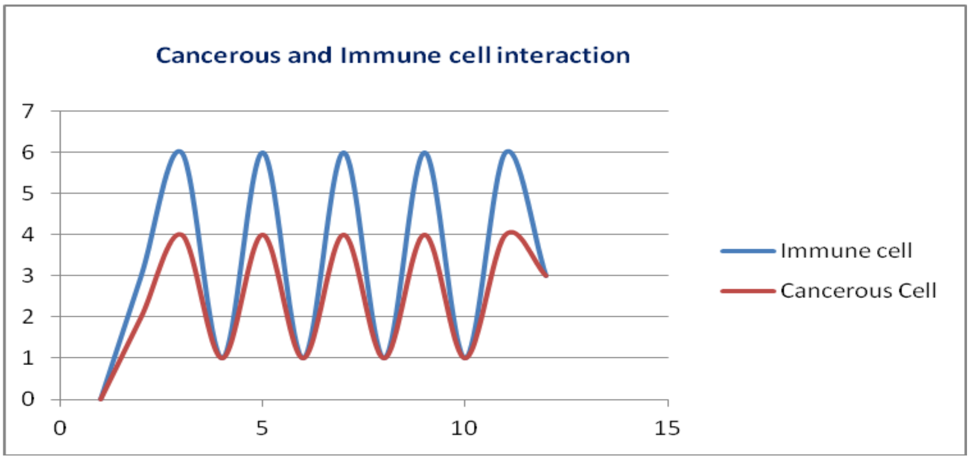
Evaluated Jacobian matrix(equation-5) at point $\left(\frac{r}{s},\frac{m}{n}\right)$ it becomes

$$J\left(\frac{r}{s},\frac{m}{n}\right) = \begin{bmatrix} 0 & \dfrac{-nr}{s} \\ \dfrac{sm}{r} & 0 \end{bmatrix}$$

The eigenvalue of this matrix are

$$\lambda_1 = i\sqrt{mn}, \qquad \lambda_2 = -i\sqrt{mn},$$

The eigenvalues denoted that how the model act around the stationary point. Here both eigenvalue imaginary and associate to each other, these eigenvalue indicate that the population of cancerous cell and immunes cell get vary. It give the good predictive approach that change in the population of cancerous cell in breast tissue, the response of immunes system automatically altered and alert. If the counting of cancerous cell variated correspondingly the immunes cell also performing for the same. When the proliferation of cancerous cell increase the performance of immunes cell enhance and when the no cancerous cell detect in body the immunes cell get switch off as inactive mode.



4. CONCLUSION

In this paper design the mathematical model that can serve as a effective tool for prevention and control of breast cancer treatment. Immunity work as protective system of body against foreign cancerous cell. The developed mathematical model of cancerous-immune cell interaction worked as prey- predator system. The current model demonstrated that the immunotherapy is one of the effective approaches for prevention and treatment of breast cancer and also give boosting effect on the cancer therapy. When appearance of abnormal cancerous cell count enhance at breast tissue, the response of immune cell automatically increase and immune system produce cytotoxic effect on cancerous cell. As immunes are actively responding it decreases the population of cancerous cell and prevent and control the proliferation of cancerous cell. The current model and their parameter might be effective tool for prevention, control and treatment of breast cancer in initial stage. The proposed mathematical model might be helpful approach in the field of bio-medical science for better understanding of antitumor effect in breast cancer through immunological response. The immune system to fight against diseases such as cancer. It give boosting effect on natural defenses system so it works harder and smarter to identify and destroys breast cancer cells. When appearance of foreign abnormal cancerous cell in breast tissue body consider it as a antigen and against the foreign cancerous cell the immune system get activated as antibody, resulting the cancerous immune cell interaction worked as antigen-antibody reaction that extinction of cancerous cell. It also shows the primary sign, symptoms as alarm in the patient to get alert and go for diagnosis and treatment in initial stage. By improving the body immune system using different immune booster approach like healthy balanced lifestyle, healthy food habits, bio immunological preparations, naturopathy, yoga and meditation.

5. FUTURE SCOPE OF THE RESEARCH

In current study we developed mathematical model of cancerous immune cell interaction for prevention and control of breast cancer in initial stage. This model useful for effective treatment of breast cancer. The design mathematical model worked as an intelligent system that can be use for effective treatment of breast cancer patients. In future this model might be helpful tool for prevention and treatment of other lethal disease and disorder.

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