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Estimation of Sugar Content, Lipid Peroxidase and Glutathione in Different Tumor Tissues

Pratiksha Singh[1], Alibha Rawat[2], N. Ganesh[3]

[1]Department of Research, Jawaharlal Nehru Cancer Hospital and ResearchCenter, Idgah Hills, Bhopal (M.P.), India

Abstract: ***Introduction:*** ***A mass or cluster of cells formed due to lack of contact inhibition property and cell losing its property of division, is termed as tumor (Benign tumor), another form of tumor is malignant tumor (cancer) due to the cause of metastasis, it spread widely throughout the body and leads to the cancer. Several studies have been done in order to know the effect of tumor on the biochemistry of cells such as sugar level, lipid peroxidase content and glutathione level in tumor tissue. The current review explores the studies done to analyze these three parameters, i.e.; sugar level estimation, lipid peroxidase analysis, and glutathione analysis in different tumor tissues to study how they are affected by the tumor condition.*** ***Method:*** ***Extensive electronic search was done to select relevant studies and analyzed and summarized here.*** ***Result:*** ***The studies done have successfully established the change in the levels of these parameters in tumor condition that throw light into the cellular damage caused by tumor.***

Keywords: Biochemical analysis, glutathione level, lipid peroxidase, oxidative stress, sugar level, tumor

1. Introduction

A tumor is an unusual mass or lump of tissue formed when cells divide more than they should or do not divide at needed time. The uncontrolled division of cell accumulates and a tumor is formed which grows bigger and eventually spread (metastasize) to the other different body parts, leading to the cancer. Tumor can be differentiated into benign and malignant tumor such that benign tumor is an abnormal growth of cells which does not spread to the other body parts, the way cancer can, the growth of benign tumor is initiated due to environmental toxins, diet, local trauma, inflammation and genetics. Whereas malignant tumor is made of cancerous cells which can invade nearby tissues, the cell lost the ability of contact inhibition due to which cell losses its ability to divide and mass of cells become a tumor, which may also represent mutation as changes in the DNA sequence.[1-2]

Tumor condition modifies its environment by several approaches and causes aberration from the normal levels of various biochemical parameters including sugar levels, lipid peroxidation level and glutathione level. Several methods and analysis have been put forwarded to identify these parameters separately. By evaluation these parameters together and comparing it with healthy human (devoid of tumor) to see whether these three parameters may cause deleterious impact to the person having tumor by raising or declining their levels can have very useful application like in determining prognosis and treatment plan.

These biochemical changes can have detrimental as well as beneficial effect on the tumor growth. For example, lipid peroxidase, an enzyme which damages cell by stealing electrons via free radical formation from lipids in the cell membrane leading to its damage, which can lead to cancer. Glutathione is a natural antioxidant found in blood that acts as free radical scavenger and helps in cellular protection but its role in tumor tissues is a little obscure or contradictory. While some studies suggests glutathione (GSH) deficiency leads to an increased susceptibility to oxidative stress implicated in the progression of cancer, elevated GSH levels increase the antioxidant capacity and the resistance to oxidative stress as observed in many cancer cells, some other studies suggest that once a tumor has been established, elevated levels of glutathione may act to protect cancerous cells by conferring resistance to chemotherapeutic drugs and hence, its increased level indicates further damage to cells (Balendiran *et al.*, 2004**).** Sugar act as fuel for the growth of tumor cells more than normal cells up to 200 times. The excess sugar in the body is the cause of rapid cancerous growth, which leads to the abnormal functioning of insulin, the hormone that controls the amount of sugar in blood. Tumor cells require glucose for aerobic glycolysis and this mechanism is responsible for cancer cells and step towards further growth of cancer. Aerobic glycolysis induces the acidic environment, which favor the development of invasive phenotypic tumor, the change in pH around tumor cells may lead to the tumor development. The malignant tumor develop and spread throughout the body, excessive sugar load can then lead to the pancreatic cancer.[17-18]

The current review attempts to explore these three parameters separately by summarizing the studies done on this field one by one.

Role of lipid per-oxidation in carcinogenesis: Lipid peroxidase is a free radical mediated chain of reactions that initiate oxidative damage of polyunsaturated lipids, the chain reaction which leads to the damage of fatty acids it can cause mutual cross linking and polymerization of membrane components. Free radicals are initiators and terminators of lipid per-oxidation process.

Lipid per-oxidation proceeds by three distinct mechanisms:

- Free radical mediated oxidation
- Free radical independent non-enzymatic oxidation
- Enzymatic oxidation [3]

Some studies have been done to evaluate the association between lipid per-oxidation in normal and tumor tissues. Studies have established that compared with their normal counterparts, many types of cancer cells have increased levels of reactive oxygen species (ROS). An increase in

ROS level is associated with abnormal cancer cell growth and reflects abnormality in the normal redox reactions and homeostasis, which could be due to failure in ROS scavenging activity **(Toyokuni *et al.*, 1995).**

Irani *et al.*, (1997) explored the mechanism of increased ROS production in cancer cells and suggested that the increase of ROS production may depend on various diverse mechanisms including oncogenes activation, aberrant metabolism, mitochondrial dysfunction, and loss of functional p53. Growth factors and cytokines too stimulate the production of ROS to exert their diverse biological effects in cancer **(Bae *et al.*, 2000).**

While link between increased ROS and cancer is well established, there is debate over level of lipid peroxidation products and cancer growth with contradictory results in different animal studies. **Hammer *et al.*, (1997)** demonstrated that levels of lipid peroxidation products in the hepatoma cells were lower than in normal liver cells. To the contrary, lipid peroxidation products like malondialdehyde and HNE were found to be increased in colorectal cancer tissues in other experimental results **(Skrzydlewska *et al.*, 2002).** These diverse results in different types of tumor tissues could be due to diverse causes like tissue environment, level of inflammation etc.

Role of Glutathione during carcinogenesis: Several studies have been done to evaluate the role of glutathione during cancer development and progression. As per the study of **Traverso *et al.*, (2013),** glutathione is a tripeptide of glutamate, cysteine and glycine found at high concentration and its functionality originates from sulfhydryl group. The detoxification capability of glutathione has inspired the clinical studies of its tissue levels in relation to cancer therapy. It is a useful prognostic marker in hematological cancer.[9]

Gamcsik *et al.*, (2012), studied glutathione levels in various types of cancer and demonstrated that it tends to be elevated in breast, ovarian, head and neck, and lung cancer and lower in brain and liver tumors compared to healthy tissue. On the other hand, cervical, colorectal, gastric, and esophageal cancers show both higher and lower levels of tumor glutathione. Hence, it can be concluded that the level of this natural antioxidant can have different effect on different types of tissues.

Role of blood sugar level in carcinogenesis

The blood sugar level can be estimated by several tests which includes glucose tolerance test, thyroid stimulating hormone(TSH) and adrenocorticotropic hormone (ACTH) in which glucose tolerance test involve the metabolic process such as glycogenesis, glycogenolysis, neo-glycogenesis, glycolysis and hexose monophosphate shunt.

Blood sugar levels have been linked to cancer growth and progression as it provides the fuel for cancer growth. How sugar is metabolized in cancer cells is an area of study that has interested many researchers worldwide. According to a study done by **Annibaldi *et al.*, (2010),** cancer cells alter their metabolism in order to support their rapid proliferation and expansion across the body. In particular, tumor cells use glucose for aerobic glycolysis instead of oxidative phosphorylation. The acquisition of this pathway by the transformed cancerous cells confers a selective growth advantage to these cells.

Epidemiological studies have shown that hyperglycemia raises the prevalence and mortality of certain malignancies, like breast, liver, bladder, pancreatic, colorectal, endometrial cancers. Hyperglycemia can promote the proliferation, invasion and migration, induce the apoptotic resistance and enhance the chemo-resistance of tumor cells **(Li *et al.*, 2019).**

Warburg (1956) first proposed that elevated blood glucose was associated with tumorigenesis. Since then, many researchers have found that hyperglycemia can promote tumor development **(Pandey *et al.*, 2011).**

Rawat A, Ganesh N. (**2017)** studied the link between diabetes mellitus and breast cancer and found a significant association between these two diseases by chromosomal aberration assay and found out an increased load of chromosomal aberrations in both diabetic females and breast cancer females when compared to normal healthy females.

2. Conclusion

These biochemical parameters, i.e; sugar level, lipid peroxidation level and glutathione levels are very good indicators of cancer development and progression and can be used as prognostic markers during cancer treatment. All the studies have demonstrated interesting facts regarding their specific roles in the process of carcinogenesis. There are some contradictory results regarding the level of lipid peroxidation products as well as glutathione level in different types of tumour tissues but this variation could be due to various factors whose mechanisms are unknown.

References

[1] **A Birbrair, T Zhang, ZM Wang, ML Messi, JD Olson, A Mintz, O Delbono,** Type-2 pericytes participate in normal and tumoral angiogenesis. *American Journal of physiology. Cell physiology.* 2014; **307**(1); C25-38.
[2] **Mach, Jean-Pierre,** Changing of the guard at the editorial level! *Tumor biology*. 1999;
[3] **20**(6); 293.
[4] **O. Warburg, Franz Wind, Negelein,** The metabolism of tumors in the body. *The Journal of general physiology.* 1927; **8**(6): 519-30.
[5] **Alessandro Annibaldi,** Glucose metabolism in cancer cells. *Curr Opin Clin Nutr Metab Care.* 2010; **13**(4): 466-70.
[6] **Kevin H. Cheeseman,** Studied on lipid peroxidation in normal and tumor tissues. *Biochem. J*. 1998; **250**; 247-252.
[7] **Devi GS,** Free radicals antioxidant enzymes and lipid peroxidation in different types of leukemias. *Clin Chim Acta*. 2000; **293**(1-2):53-62.
[8] **Elzbieta Skrydlewska,** Lipid peroxidation and antioxidant status in colorectal cancer. *World J Gastroenterol*;2005; **11**; 403-406.
[9] **Michael P. Gamcsik,** Glutathione levels in human tumors. *Biomarkers*. 2012; **17**(8): 671- 691.

[10] **Nicola Traverso,** Role of glutathione in cancer progression and chemoresistance. *Oxid Med Cell Longev*. 2013.
[11] **Kshipra Chandrakant Deshpande, Mina Milind Kulkarni, Dinesh V. Rajput,** Evaluation of glutathione peroxidase in the blood and tumor tissue of oral squamous cell carcinoma patients. *J Oral Maxillofac Pathol*. 2018; 22; 447.
[12] **Balendiran GK, Dabur R, Fraser D.** The role of glutathione in cancer. *Cell biochemistry and function.* 2004; 22(6): 343-52.
[13] **S. Toyokuni,** "Persistent oxidative stress in cancer," *FEBS Letters*, vol. 358, no. 1, pp. 1–3, 1995.
[14] **K. Irani, Y. Xia, J. L. Zweier et al.,** "Mitogenic signaling mediated by oxidants in Ras-transformed fibroblasts," *Science*, vol. 275, no. 5306, pp. 1649–1652, 1997.
[15] **Y. S. Bae, J. Y. Sung, O. S. Kim *et al.*,** "Platelet-derived growth factor-induced H_2O_2 production requires the activation of phosphatidylinositol 3-kinase," *Journal of Biological Chemistry*, Vol. 275, no. 14, pp. 10527–10531, 2000.
[16] **Hammer, M. Ferro, H. M. Tillian *et al.*,** "Effect of oxidative stress by iron on 4-hydroxynonenal formation and proliferative activity in hepatomas of different degrees of differentiation," *Free Radical Biology and Medicine*, Vol. 23, no. 1, pp. 26–33, 1997.
[17] **E. Skrzydlewska, A. Stankiewicz, M. Sulkowska, S. Sulkowski, and I. Kasacka,** "Antioxidant status and lipid peroxidation in colorectal cancer," *Journal of Toxicology and Environmental Health A*, vol. 64, No. 3, pp. 213–222, 2001.
[18] **Li, W., Zhang, X., Sang, H. *et al.*** Effects of hyperglycemia on the progression of tumor diseases. *J Exp Clin Cancer Res* **38,** 327 (2019).
[19] **Warburg O, (1956).** On the origin of cancer cells. *Science*; 123:309–14.
[20] **A, Forte V, Abdallah M, *et al.*** Diabetes mellitus and the risk of cancer. Minerva Endocrinol. 2011;36:187–209.
[21] **Rawat A, Ganesh N.** Cytogenetic analysis of breast cancer females along with females with diabetes and thyroid issues to find a possible link. *Indian J. Sci. Res.* 20(2): 329-334, 2018.