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### SELENIUM LEVELS AND ITS SIGNIFICANCE IN CANCER PREVENTION: A BRIEF REVIEW

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**Abstract:** Cancer is the second leading cause of death in developed and developing countries. In India, the prevalence of cancer is estimated to be around 2.5 million, with about 5, 50,000 deaths per annum and 8, 00,000 new cases. Nutrition plays an important role in cancer, because the nutrient deficiencies such as Folic acid, Vitamin B12, Vitamin C, Vitamin E, Selenium and anti-oxidants like carotenoids ( $\alpha$ - carotene,  $\beta$ - carotene, lycopene, lutein, cryptoxanthin) can be a significant contributing factor in modifying multistage process of carcinogenesis and it has been estimated that 30-40 percentage of all cancers can be prevented by lifestyle and dietary modifications. Selenium is an essential trace element, confers its antioxidant properties in incorporation with selenoproteins helps in some physiological conditions and in many disease processes including cancer but it also produces toxic effects when administered at higher concentrations. Several studies suggest that low levels of Selenium may be a risk factor of carcinogenesis. This review illustrates the role of Selenium in prevention of various cancers like colorectal cancer, prostate cancer, lung cancer and breast cancer.

**Keywords:** Cancer, Selenium, Anti-oxidant properties, Colorectal cancer, Prostate cancer, Lung cancer, Breast cancer



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## **INTRODUCTION**

Cancer is a condition which is characterised by abnormal cell growth in an uncontrolled way <sup>[1]</sup>. Among various diseases, cancer has become a major threat to human beings globally, incidence has been expected to 7.5 billion by 2020 and approximations predict that about 15 million new cancer cases will be diagnosed. In India, prevalence of cancer is estimated to be around 2.5 million, with about 5,50,000 deaths per annum and 8,00,000 new cases due to increase in size of population, and growth in proportion of elderly persons as a result of improved life expectancy following control of communicable diseases <sup>[2,3,4,5]</sup>. Most frequently affected organs are lungs, breast, colon, rectum and stomach <sup>[6]</sup>. It is widely estimated that 80-90% of human cancers may be attributable to environmental and various life style factors like tobacco chewing, alcohol consumption and dietary habits <sup>[7]</sup>.

It is becoming clear from the continuing researches that nutrition plays a major role in cancer process and it has been estimated by the American Institute for Cancer Research and World Cancer Research Fund that 30-40% of all cancers can be controlled by appropriate diets, physical activity and maintenance of appropriate body weight <sup>[8]</sup>. Selenium, a trace element, an essential nutrient of fundamental importance with anti-cancer properties, can prevent the transformation of normal cells in to malignant cells and activation of oncogenes in transformed cells <sup>[9, 10, 11,12]</sup>. The efficacy of Selenium can be related to "U" shaped curve in terms of health benefits, low levels associated with many conditions like increased risk of cancer, infections and male infertility, decreased immune system, thyroid function and several neurological conditions <sup>[13,14,15]</sup>. Whereas Selenosis can be linked to higher occurrence of Type 2 Diabetes Mellitus, worsens the gastric non-cardia cancer <sup>[16, 17]</sup>. Rayman MP suggested that a review paper reported that in prospective studies published in the 1980s and early 1990s involving 8000 to 11000 individuals, low Selenium status was associated with significantly increased risks of cancer incidence and mortality <sup>[14]</sup>. However, there are no guidelines regarding inclusion and exclusion criteria of selenium supplementation in radiotherapy consists of Selenium supplementation, applicable cancer types, dose of supplementation, chemical forms of Selenium, duration of supplementation and possible side effects. First, benefits and risks of Selenium use in radiotherapy should be clarified; such information is still insufficient <sup>[9]</sup>.

## **MECHANISM OF ACTION:**

Selenium is an essential nutrient for human beings which is necessary for the activation of glutathione peroxidises (GSH-Px) that protects DNA and other cellular molecules from oxidative damage <sup>[18]</sup>. The Selenium-dependent enzyme glutathione peroxidase, decomposes H<sub>2</sub>O<sub>2</sub> and various hydro and lipid peroxides. The important metabolic functions of Selenium is due to the production of membrane lipids and macromolecules from oxidative damage by combating

against reactive oxygen species, and the activation of antioxidant proteins such as glutathione peroxidase, thioredoxin reductase, leads to decreased levels of hydrogen peroxide. Selenium also plays a key role in regulating the G1-phase of the cell cycle, DNA damage, controls cell mediated immunity and B-cell function <sup>[19, 20, 21]</sup>. In most of the human cancers like prostate cancer, breast cancer, lung cancer and colorectal cancer the levels of Selenium-binding protein 1 was found to be decreased <sup>[22]</sup>.

### COLORECTAL CANCER

Colon cancer is the most common among gastrointestinal cancer. It is usually develop either as a inherited or somatic genetic alterations over a lifetime. It begins in the cells of the glandular structures in the inner layers of the colon and gradually spreads into the wall of colon followed by lymphatic system and other organs <sup>[23]</sup>. The incidence and mortality rates varies markedly around the world and globally it is the third most commonly diagnosed cancer in males and the second in females around 1.2 million new cases and 608,700 deaths with a higher rate in males than in females estimated to have occurred till 2008 <sup>[24, 25]</sup>. Selenium is one of the dietary factor that accounts for colon cancer risk <sup>[26]</sup>. Low level of Selenium in body increases the risk of CRC and extreme low intake (<10 µg/day) results in severe symptoms as in Keshan disease <sup>[27, 28]</sup>. However, many studies do not support a protective role for Selenium against the risk of colorectal cancer <sup>[13]</sup>. But, mechanistic data suggest a role of Selenium and Selenoproteins in colorectal function and cancer prevention in humans and animal cell models <sup>[29]</sup>.

### PROSTATE CANCER

Prostate cancer is a malignant tumour that originates in the prostate gland and if it remains untreated in early stages, eventually it spreads through the blood and lymph fluid to other organs <sup>[30]</sup>. Prostate cancer ranks the second common cause for mortality for men in USA and the incidence increasing even in Asian countries which ranks 5th in incidence rate and 4th in cancer mortality for men. High consumption of dietary fats such as fatty acids, alpha lenoic acid in red meat/butter), deficiency of trace elements like selenium and low levels of Vitamin D3 and Vitamin E increases the risk of prostate cancer <sup>[31]</sup>. Many studies shows the relation between the oxidative stress to growth and progression of prostate cancer and the role of antioxidants like Selenium and Vitamin E have shown to decrease risks for prostate cancer <sup>[32]</sup>. The result of a randomized controlled trial, shows that Selenium supplementation reduces the recurrence of skin cancer as well as the supplementation of 200 µg/day of Selenium significantly reduces the prostate cancer incidence at the rate of 63% <sup>[33]</sup>.

### LUNG CANCER

Lung cancer is the most common cancer death and it is estimated 1.04 million new cases across the world in each year <sup>[34]</sup>. Several observational studies, case-control and cohort studies shows the association between Selenium status and lung cancer, in which low selenium status may considered as a risk factor for lung cancer. Although a few other case-control studies shows no association between serum Selenium levels and lung cancer risks <sup>[35, 36, 37]</sup>. A large-scale intervention studies shows that Selenium can be used against lung cancer either alone or in combination with beta-carotene and alpha-tocopherol <sup>[38, 39]</sup>.

#### **BREAST CANCER:**

Breast cancer is a malignant growth that begins with in the tissues of breast, 100 times more common among women world-wide and accounts for 18% of all female cancers <sup>[18, 40]</sup>. It is third most common cancerous type in humans and second leading cause of cancer death in women <sup>[41]</sup>. Much knowledge has been accumulated regarding aetiology and pathogenesis of breast cancer implicating genetic, hormonal and environmental factors <sup>[42]</sup>. Selenium is an essential but an intriguing trace element, plays an important role in the prevention of breast cancer via anti-oxidant effect <sup>[41]</sup>. Numerous studies shows that women with breast cancer are susceptible to have lower blood selenium levels than those of healthy controls, where as some studies failed to conform this observation <sup>[43, 44, 45]</sup>.

#### **CONCLUSION:**

The review of our literature suggests that Selenium is one of the important trace element which plays a key role in building our immune system and cancer prevention. It has also been proved that appropriate Selenium supplementation improved the general condition of the patients, their quality of life and reduces the side effects of radiotherapy. However, an inverse relationship has also been observed with high serum selenium levels in development of cancer. Hence, more evidence based information and additional research are recommended to ensure the therapeutic benefits of Selenium supplementation in cancer patients.

#### **REFERENCES:**

1. Basma Talib Jasim. Determination of erythrocyte glutathione peroxidase activity and serum selenium level in patients with breast cancer. *Tikrit Journal of Pure Science*. 2011; 16: 4-8.
2. Imran Ali, Waseem A. Wani and Kishwar Saleem. Cancer scenario in India with future perspectives. *Cancer Therapy*. 2011; 8: 56-70.
3. Brayand F and Moller B. predicting the future burden of cancer. *Nature Reviews Cancer*. 2006; 6: 63-74.

4. Nandakumar A. Consolidated report of the population based cancer registries. National Cancer registry programme. Indian Council of Medical Research. 1990-1996; New Dehi, India.
5. Parkin D. M, Bray F, Ferlay J and Pisani P. Estimating the world cancer burden: Globocon 2000. International Journal of Cancer. 2001; 94: 153-156.
6. Murthy N.S and Aleyamma Mathew. Cancer epidemiology, prevention and control. Current Science. 2004; 86: 518-527.
7. WHO, The World Health Report, Geneva, 1997.
8. Michael S Donaldson. Nutrition and cancer: A review of the evidence for anti-cancer diet. Nutrition Journal. 2004; 3: 1-27.
9. Imra M Puspitasari, Rizky Abdulah, Chiho Yamazaki, Satomi Kameo, Takashi Nakano and Hiroshi Koyama. Updates on clinical studies of Selenium supplementation in radiotherapy. Radiation oncology. 2014; 9: 1-9.
10. Mary E. Reid et al.,The nutritional prevention of cancer: 400mcg per day Selenium treatment. Nutrition and cancer. 2007; 60: 155-163.
11. Sehrauzer GN. Anticarcinogenic effects of Selenium. Cellular and Molecular Life Sciences. 2000; 57: 18642-1873.
12. Sehrauzer GN. Nutritional Selenium supplements: Product types, quality and safety. The Journal of American College of Nutrition. 2001; 20: 1-4.
13. Marcin R Lener et al.,Can Selenium levels act as a marker of colorectal cancer risk? BioMed Central Cancer. 2013; 13: 1-6.
14. Rayman MP: The importance of Selenium to human health. Lancet. 2000; 356: 233-241.
15. Papp LV, Lu J, Holmgren A, Khanna KK. From Selenium to selenoproteins: synthesis, identity, and their role in human health. Antioxidant & Redox Signaling. 2007; 9: 775-806.
16. Zahra Hosseini Nezhad et al.,Serum Selenium level in patients with gastric non-cardia cancer and functional dyspepsia. Indian Journal of Medical Sciences. 2015; 40:214-218.
17. Rayman MP:Selenium and human health. Lancet. 2012; 379: 1256-1268.
18. Lokman Rejali, Mohd Hasni Jaafar and Noor Hassin Ismail. Serum Selenium level and other risk factors for breast cancer among patients in a Malaysian hospital. Environmental Health and Preventive Medicine. 2007; 12; 105-110.

19. Rayman MP. Selenium in cancer prevention; A review of the evidence and mechanism of action. *Proceedings of the Nutrition Society*. 2005; 64; 527-542.
20. Lee SR, Bar-Noy S, Kwon J, Levine RL, Stadtman TC and Rhee SG. Mammalian thioredoxin reductase: oxidation of the C-Terminal cysteine-selenocysteine active site forms a thio-selenide, and replacement of selenium with sulphur markedly reduces catalytic activity. *Proceedings of the National Academy of Sciences of the United States of America*. 2000; 97; 2521-2526.
21. Franca C.A.S, Nogueira C.R, Ramalho A, Carvalho C.P, Vieira S.L and Penna A.B.R.C. Serum levels of Selenium in patients with breast cancer before and after treatment of external beam radiotherapy. *Annals of Oncology*. 2010; 22: 1109-1112.
22. Qi Ying, Emmanuel Ansong, Alan M. Diamond, Zhaoxin Lu, Wancai Yang and Xiaomei Bie. Quantitative proteomic analysis reveals that anti-cancer effects of Selenium-binding Protein 1 in-vivo are associated with metabolic pathways. *Plos One*. 2015: 1-15.
23. Risio M. The natural history of adenomas. *Best Practice & Research Clinical Gastroenterology*. 2010; 24: 271-280.
24. Jemal A et al., Global cancer statistics. *CA A Cancer Journal for Clinicians*. 2011; 61: 69.
25. Siegel R, Naishadham D, Jemal A. Cancer statistics. *CA A Cancer Journal for Clinicians*. 2013; 63: 11.
26. Alexander Connelly-Frost, Charles Poole, Jessie A. Satia, Lawrence L. Kupper, Robert C. Millikan and Robert S. Sandler. Selenium, Folate and Colon cancer. *Nutrition Cancer*. 2009; 61: 165-178.
27. Rayman M.P. The argument for increasing Selenium intake. *Proceedings of the Nutrition society*. 2002; 61: 203-215.
28. Johnson, Fordyce C.C and Rayman M.P. Symposium on geographical and geological influences on nutrition: factors controlling the distribution of Selenium in the environment and their impact on health and nutrition. *Proceedings of the Nutrition society*. 2010; 69: 119-132.
29. Catherine Meplan and John Hesketh. The influence of Selenium and selenoprotein gene variants on colorectal cancer. *Mutagenesis*. 2012; 27: 177-186.
30. Glenn Doolan, Geza Benke and Graham Giles. An update on occupation and prostate cancer. *Asian Pacific Journal of Cancer Prevention*. 2014; 15: 501-516.
31. Clark LC et al., Decreased incidence of Prostate cancer with Selenium supplementation: Results of a cancer prevention trial. *British journal of urology*. 1998; 81: 730.

32. Venkataraghavan Ramamoorthy, Muni Rubens, Anshul Saxena and Nancy Shehadesh. Selenium and Vitamin E for prostate cancer – justifications for the select study. *Asian Pacific Journal of Cancer Prevention*. 2015; 16: 2619-2627.
33. Naomi et al., Plasma Selenium concentration and prostate cancer risk: results from the European prospective investigation in to cancer and nutrition (EPIC). *American Journal of Clinical Nutrition*. 2008; 88: 1567-1575.
34. Hanjing Zhuo, Allan H. Smith and Craig Steinmaus. Selenium and lung cancer: A quantitative analysis of heterogeneity in the current epidemiological literature. *Cancer Epidemiology, Biomarkers & Prevention*. 2004; 13: 771-778.
35. Paul Knekt, Jukka Marniemi, Lyly Teppo, Markku Heliövaara and Arpo Aromaa. Is low Selenium status a risk factor for lung cancer? *American Journal of Epidemiology*. 1998; 148: 975-981.
36. Goodman GE, Schaffer S, Bankson DD, Hughes MP and Omenn GS. Predictors of serum Selenium in cigarette smokers and the lack of association with lung and prostate cancer risk. *Cancer Epidemiology Biomarkers & Prevention*. 2001; 10: 1069-1076.
37. Mary E. Reid, Anna J. Duffield-Lillico, Linda Garland, Bruce W. Turnbull, Larry C. Clark and James R. Marshall. Selenium supplementation and lung cancer incidence: an update of the nutritional prevention of cancer trial. *Cancer Epidemiology Biomarkers & Prevention*. 2002; 11: 1285-1291.
38. Clark LC et al., Effects of Selenium supplementation for cancer prevention in patients with carcinoma of the skin. *Journal of American Medical Association*. 1996; 176: 1957-1963.
39. Blot WJ et al., Lung cancer and vitamin supplementation. *New England Journal of Medicine*. 1994; 331:614.
40. Ambrosone C.B. Oxidants and antioxidants in breast cancer. *Antioxidants Redox Signaling*. 2000; 2: 903-917.
41. Jyoti Yadav and Shubhriga. Selenium in breast cancer. *Indian Journal of Clinical Practice*. 2012; 23: 72-77.
42. Bock A, Forchhammer K, Heider J and Baron C. Selenoprotein synthesis: an expansion of the genetic code. *Trends in Biochemical Sciences*. 1991; 16: 463-467.
43. Lopez-Saez JB, Senra-Varela A, Pousa-Estevez L. Selenium in breast cancer. *Oncology*. 2003; 64: 227-231.

44. Hardell L et al., Levels of Selenium in plasma and glutathione peroxidase in erythrocytes and the risk of breast cancer. A case-control study. *Biological Trace Element Research*. 1993; 36: 99-108.

45. Maannsito S, Alfthan G, Virtanen M, Kataja V, Uusitupa M and Pietinen P. Toenail Selenium and breast cancer. A case- control study in finland. *European Journal of Clinical Nutrition*. 2000; 54: 98-103.