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Effect of Age on Selenium and PSA Levels of Prostate Cancer Patients

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Abstract: ***This study determined levels of serum selenium and prostate specific antigen (PSA) in patients diagnosed with prostate cancer. The patients aged from 40 years and above were among those attending the Urology Clinic of Abia State University Teaching Hospital, Aba, from October, 2006 to March, 2008.Samples of sixty (60) patients were analyzed for serum PSA using the Enzyme Immunoassay method and selenium using the electrothermal atomic absorption spectrometry (AAS).Serum samples of forty (40) aged-matched controls selected randomly from a cross section of socioeconomic groups were also analyzed for serum PSA and selenium. The mean serum PSA and selenium concentrations of the 60 patients were 33.2±18.55µg/L and 17.47±9.47µg/L respectively. The controls had mean serum PSA and selenium concentrations of 2.88±1.65µg/L and 83±29.91µg/L respectively. The mean serum PSA of patients were significantly (p<0.05) higher than those of controls, while the mean selenium concentration of controls were significantly (p<0.05) higher than those of patients. The serum PSA values increased with increase in age, while serum selenium values showed a decline with increase in age. These finding showed that men with low serum selenium are at risk of developing prostate cancer. It also suggests the need to include serum selenium as a routine test for men from 40years of age and above.***

Keywords: Prostate specific antigen, cancer, selenium, malignant

1. Introduction

Prostate carcinoma is a neoplastic change in the cellular and acinar structure of the Prostate gland resulting in the gradual invasion by malignant growth, first of its own tissue and then of periprostatic and more distant structure (Mera, 1997).Prostate cancer is a health concern for men over the age of 45 years world – wide and the most common neoplasm and the second most common cause of cancer death in men(Magoha, 1997). Research has shown that prostate cancer is the most common non-skin cancer in America affecting 1 in 6 men (Carter *et al.*, 1992). The older you are the most likely you are to be diagnosed with prostate cancer, although only 1 in 10,000 under 40 years of age actually get diagnosed. The rate shoots up to 1 in 38 for ages 40 – 59 years and 1 in 4 for ages 60 – 69 years. In fact, more than 65% of all prostate cancers are diagnosed in men over the ages of 65 years (Carter *et al.*, 1992). Selenium is a trace mineral that is essential for good health but required only in small amounts (Thomson, 2004). It is a constituent of glutathione peroxidase and iodothyronine deiodinases. Selenium is incorporated into proteins to make selenoproteins, which are important antioxidant enzymes. The antioxidant properties of selenoproteins help prevent cellular damage from free radicals. Free radicals are natural by-products of oxygen metabolism that may contribute to the development of chronic disease such as cancer, and heart disease (Goldhaber, 2003).

The clinical laboratory plays vital role in the screening, diagnosis, management and monitoring of prostate cancer, through the determination of prostate specific antigen which is a useful biomarker for the assessment of prostate carcinoma (Stenman, 1997; Witherspoon, 1997; Oesterling *et al.*, 1993).

Observational studies indicate that death from cancer, including lung, colorectal, and prostate cancer is lower among people with higher blood levels or intakes of selenium (Fleet, 1997). Research also shows that a daily supplement containing 200µg of selenium lowered the incidence of prostate cancer (Combs *et al.*, 1997).

Prostate cancer or carcinoma is a significant public health problem (Eeles *et al.*, 1997). It has remained the most commonly diagnosed malignancy for men over 50 years (Parker *et al.*, 1997) hence resulting to death. It is primarily a disease of the older men (Mera, 1997., Eeles *et al.*, 1997) and occurs more frequently with increasing age (Newling, 1996). Over 90% of the prostate cancer deaths occur in men over 65 years (Parkes *et al.*, 1995) with half (50%) of them being under 75 years (Whelan, 1997).

The disease is even more prevalent among blacks, who have the highest rate among 24 countries having reasonably accurate mortality data (Masco *et al*., 2012). In Nigeria, prostate cancer has a greater aggressive tendency in persons in the 6th and 7th decades of life (Ojo and Rufai, 1993). Both moderate and heavy consumption of alcohol has been implicated as a contributor to prostate cancer risk and the risk increases with increase in age (Brown and Uzeofu, 2014). Globally seventy five percent (75%) of the men with moderately differentiated tumours of the prostate lose 4 – 5years of life and those with poorly differentiated tumours lose 6 – 8 years of life (Albertson *et al.*, 1995). Despite its frequency and growing impact on mortality and morbidity, prostate carcinoma has been a relatively neglected subject of investigation particularly with regard to the efficiency of potentially curative treatment (Chamberlain *et al.*, 1997; Eeles *et al.*, 1997).

This neglect is worse in developing countries like Nigeria where inadequate functional medical facilities and socio-economic factors have seriously militated against health care delivery system. Thus, this study was designed to determine the level of selenium in patients diagnosed with prostate cancer and apparently healthy individuals in Aba, South East

Nigeria. This work will strengthen the need to make studies into the antioxidant activities of selenium a research priority.

2. Materials and Methods

2.1 Design and characterization of subjects

The subjects comprised 60 men, aged 40 years and above suspected to have prostate carcinoma. They were attending the Urology Clinic of Abia State University Teaching Hospital, Aba. Forty (40) apparently healthy men also aged 40 years and above were included in the study as controls. The controls were selected randomly from a cross section of socioeconomic groups. An informed consent was acquired, according to the guidelines from the Abia State University Teaching Hospital Research Ethics Committee.

2.2 Specimen collection

The subjects were seated and about 5ml of the venous blood samples collected from subjects and control which was dispensed into plain sample containers properly labeled with sample identification code and age. The blood samples were left to coagulate spontaneously, centrifuged at 1000 rpm for 5 minutes and the serum separated immediately into plain sterile sample bottles with Pasteur pipette and stored frozen in the refrigerator at 10^{o}C (1-15) days prior to analysis.

2.3 Assay of Prostate – Specific Antigen (PSA) aand Selenium.

Serum prostate-specific antigen (PSA) was analyzed by Enzyme Immunoassay using prostate – specific antigen kit from Syntron Bioresearch Incorporated, California, United States America.Serum selenium was determined by Electrothermal Atomic Absorption Spectrometry and interferences were removed using Deuterium background correction to ensure precision.

3. Results

Table 1 shows the comparison of the means of serum prostate specific antigen (PSA) concentrations in patients and controls. The results show that in all the age groups the difference in serum prostate specific antigen (PSA) concentrations between patients and controls were statistically significant ($p<0.05$) using the students t-test.Significant increase ($p<0.05$) in PSA levels was also observed in the population as the age of both the test and control subjects increases.

Table 1: Comparison of the mean ± SD of prostate specific antigen (PSA) in both patients and controls

Age Class	PSA (µg/L)		P- Value
	Subjects (µg/L)	Control (µg/L)	
40 – 49	13.0 ± 0.70 (n=2)	0.99 ± 0.27 (n=8)	p<0.05
50 – 59	28.17 ± 8.80 (n=9)	1.82 ± 0.48 (n= 10)	p<0.05
60 – 69	31.15 ± 7.08 (n=20)	2.99 ± 0.82 (n=11)	p<0.05
70 – 79	35.00 ± 0.50 (n=22)	4.05 ± 0.95 (n=8)	p<0.05
80 - 89	45.20 ± 2.30 (n=7)	5.90 ± 0.12 (n=3)	p<0.05

Table 2 shows the comparison of the means of serum selenium concentrations in both patients and control subjects. The result shows that in all the age groups the difference in serum selenium concentration between patients and control subjects were statistically significant ($p<0.05$) using the students t-test. Similarly, significant decrease ($p<0.05$) in selenium levels as observed in both the patients and test subjects as their ages increases

Table 2: Comparison of the mean ± SD of selenium in both patients and controls

Age Class	Selenium (µg/L)		P- Value
	Subjects (µg/L)	Control (µg/L)	
40 – 49	26.00 ± 0.00 (n=2)	109.0±18.70 (n=8)	p<0.05
50 – 59	18.20 ± 9.42 (n=9)	108.0±20.30 (n=10)	p<0.05
60 – 69	16.85 ± 9.05 (n=20)	74.6± 16.90 (n=11)	p<0.05
70 – 79	19.14 ±10.55 (n=22)	53.40 ± 8.30 (n=8)	p<0.05
80 – 89	10.57 ± 4.43 (n=7)	40.30 ±9.40 (n=3)	p<0.05

4. Discussion

Serum prostate specific antigen (PSA) and selenium levels in patients diagnosed with prostate carcinoma and compared with those without prostate cancer as controls came into focus in this study. The effect of age on the risk of prostate cancer was also investigated. The study shows that the mean values of prostate specific antigen (PSA) for patients were above the normal range, while the mean values of serum selenium was below or lower than the normal range. This observation is in agreement with the studies of Robinson *et al.* (1997), Salonen *et al.*(1993) and Li *et al.*(2004). The mean values for serum prostate specific antigen (PSA) and selenium concentrations for apparently healthy individuals or controls were within the normal/reference ranges which also agree with the study of Fleet (1997) and Duffield *et al. (*2002).

World Health Organisation (WHO) recommended that the normal/reference range for serum prostate specific antigen (PSA) concentration should be 0-4µg/L (Howanitz, 1996), while serum selenium concentration in the plasma or serum is expected to be 46-143µg/L (Iyengar *et al.*, 1978). Results from this study showed that the distribution of prostate specific antigen (PSA) and selenium concentrations agree with the studies of Fleet (1997) and Duffield *et al.* (2002).The study also showed an inverse relationship between serum prostate specific antigen (PSA) and selenium in subjects diagnosed with prostate cancer, which is similar to the findings of Robinson *et al.*(1997), Salonen *et al.*(1993) and Li *et al.* (2004).The study further agrees with the result of chemo-preventive effect of selenium against a variety of malignancies including prostate cancer in a number of case controlled epidemiologic studies by Brooks *et al.* (2001), Helzlsouer *et al*. (2000) and Yashizawa *et al*.(1998). The observation of low selenium level in patients diagnosed with prostate cancer in this study agrees with earlier reports that subjects with low serum selenium level are at risk of developing prostate cancer (Fleet, 1997; Brinkman *et al.*, 2006).The decrease in mean serum selenium concentrations in subjects diagnosed with prostate cancer which declines with increase in age of the subjects that was observed in this study has also been reported by Brooks *etal.* (2001).

The highest incidence of prostate cancer observed in this study was between 70-79 years age group (n=22) which also agrees with the reports of Mera (1997) and Eeles *etal.* (1997). It has been reported that prostate cancer is primarily a disease of older men and occurs more frequently with increase in age (Newling, 1996). It is necessary that prostate specific antigen (PSA) threshold that is more specific for an age groups be specified as this would help to determine when to conduct a biopsy (Nixon and Brawer, 1997). The age range (70-79) years has the widest recommended reference range of 0-6.5µg/L (Oesterling *et al.*, 1993). Studies conducted in western Nigeria also reported increase in prostate cancer with age(Ojo and Rufai, 1993).The present study was conducted in South East Nigeria and the result obtained was is in agreement with the findings of the studies made in western Nigeria.

Prostate cancer has greater aggressiveness in persons in the 6^{th} and 7^{th} decades of life. The finding from the study tends to support earlier observations by Carter *et al*.(1992) and Chemberlein *et al*.(1997), that the rate of increase of prostate specific antigen (PSA) with age was greater in men with prostate cancer than in healthy men or those with benign prostate hyperplasia (BPH). Oesterling *et al.* (1995) had earlier reported that increase in serum prostate specific antigen (PSA) value was age dependent.

A comparison of serum prostate specific antigen (PSA) concentrations of patients diagnosed with prostate cancer and control subjects showed that prostate specific antigen (PSA) level was higher in patients across the various age ranges when compared with the controls. This corresponds with the studies of Carter *et al*.(1992) and Chamberlein *et al*.(1997). Similarly a comparative analysis of serum selenium concentrations in patients diagnosed with prostate cancer and control subjects showed that the selenium level of patients were significantly ($p<0.05$) lower than that of the control subjects which agrees with the works of Brooks *et al*. (2001). The result of the present study is therefore in agreement with previous studies on the subject and indicates that serum prostate specific antigen (PSA) and selenium levels are reliable indicators for prostate cancer assessment and evaluation in suspected individuals.

5. Conclusion

Despite the differences in environmental, nutritional and social factors in the various studies, the results of the present study conducted in Aba metropolis agrees with results of previous studies on the incidence of prostate cancer and the inverse relationship of serum prostate specific antigen (PSA) and selenium concentrations in patients diagnosed with prostate carcinoma. It is therefore imperative that men with or without family history of prostate carcinoma should regularly determine serum selenium and prostate- specific antigen (PSA) from the age of 40 years for early detection of prostate cancer.There is need to carry out further studies possibly on other factors likely to affect serum prostate specific antigen (PSA) and selenium levels such as drugs, occupations, and social habits.

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