The Significance of Serum Selenium Level in Prostatic Diseases: Comparing Prostate Cancer Versus Benign Prostate Hyperplasia

**ABSTRACT**

Prostate cancer (PCa) is the most common cancer among men and also a significant cause of mortality. Over one million new cases were diagnosed in 2020 and over 300,000 deaths from prostate cancer were recorded in the same year. Trace metals like Selenium have also been studied with respect to prostate cancer. The effect of selenium on angiogenesis, cell death, androgen receptor signaling has been a subject of research. We are comparing the serum Selenium (Se) levels of patients diagnosed with prostate cancer versus those diagnosed with Benign Prostate Hyperplasia (BPH).

A total of 81 patients who gave their consent, and had lower urinary tract symptoms were recruited over a 6 months period. 40 patients had Benign prostate enlargement while 41 patients had prostate cancer. Blood samples were collected and analyzed for Se using Atomic absorption spectrophotometer.

The mean age of respondents in this study was 60(9) and 62(9) for BPH and PCa respectively. The mean BMI was 25.81 (2.04). The mean PSA of the BPH and PCa groups were 2(1) and 18(5) respectively P <0.001. The serum selenium level for those with BPH was 0.17 (0.07) , while that for those with PCa was 0.14 (0.07) with a p-value of 0.073.

In this study we found that serum Se was lower in patient with PCa compared with controls(BPH) but this difference was not statistically significant. The role of Se in prostate diseases and indeed prostate cancer still requires further research.

**Key words:** *Selenium, Prostate cancer, Benign prostate hyperplasia, Mortality*

**INTRODUCTION**

Prostate cancer is the most common cancer among men and also a significant cause of mortality. Over one million new cases were diagnosed in 2020 and over 300,000 deaths from prostate cancer were recorded in the same year.1 The aetiology of most cancers and in this case prostate cancer is a still a subject of debate and has been linked to some risk factors including, genetics, race, environmental factors, diet and lots more.2,3 A towering challenge in the management of prostate cancer, is to identify, control or modify factors that may prevent or affect disease progression of prostate cancer. Literature is replete with research on studies alluding to life style modifications that altered the prostate cancer progression.4-7

Trace metals like selenium have also been studied with respect to prostate cancer. The effect of selenium on angiogenesis, cell death, androgen receptor signaling have also been evaluated.8,9 Selenium (Se) has been documented to be preventive for prostate cancer. The risk of aggressive or advanced prostate cancer reduces by 10% for every 10ng/ml increase in plasma Se 10,11 but the doses to achieve response or ideal range of intake for optimum risk reduction has not been estimated. 12,13.

Studies have found increase in the incidence of prostate cancer in the African population14 therefore the need to identify factors that may affect this disease is necessary. We are comparing the serum selenium level of patients diagnosed with prostate cancer versus those with Benign Prostate Hyperplasia (BPH).

**METHODOLOGY**

This is a prospective study of patients who presented with bladder outlet obstruction (BOO) and had prostate biopsy. It was carried out in the University of Port Harcourt teaching Hospital (UPTH) and Gbeye hospital. Both centers are located in Port Harcourt, Rivers State in Southern Nigeria. The centers attended to patients with urological conditions. Both centers saw 356 patients with suspected prostate cancer within the study period of six months, 146 of them gave consent to be recruited into the study, 24 patients were excluded because they were on anticoagulants and had significant risk for severe bleeding. 14 of those that gave consent had been commenced on presumptive treatment for PCa at referring hospital and so were also excluded from the study. A total of 108 patients who met the inclusion criteria were fit to have prostate biopsy.

All patients presented with symptoms suggestive of prostate cancer or biochemical/ radiological evidence indicating prostate cancer had prostate biopsy done For every PCa diagnosed histologically, the next case of histologically diagnosed BPH was included. Forty (40) cases of BPH and 41 cases of PCa were included in the study, their blood samples were collected for Se level analysis.

Se level was analyzed using Atomic Absorption Spectrophotometer (AAS), Atomic absorption spectrometer's working principle is based on the sample being aspirated into the flame and atomized when the AAS's light beam is directed through the flame into the monochromator, and onto the detector that measures the amount of light absorbed by the atomized element in the flame. Since metals have their own characteristic absorption wavelength, a source lamp composed of that element is used, making this method relatively free from spectral or radiational interferences. The amount of energy of the characteristic wavelength absorbed in the flame is proportional to the concentration of the element in the sample. The wave length of Se is 196.0nm using nitrous oxide acetylene flame.

A series of standard metal solutions in the optimum concentration range are prepared, the reference solutions were prepared daily by diluting the single stock element solutions with water containing 1.5ml concentrated nitric acid/litre. A calibration blank was prepared using all the reagents except for the metal stock solutions.

Standards are intermediately included as samples to check for accuracy of the machine. Calibration curve for Se was prepared by plotting the absorbance of standards versus their concentrations

The patients’ biodata, Prostate specific antigen (PSA) and Se levels were recorded and collated using Microsoft Excel 2016 version (Microsoft Corporation, Redmond, WA, USA), and they were subjected to analysis using SPSS version 20.

**RESULTS**

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TABLE 1: Age and BMI of study population

| **Characteristic** | **N = 81** |
| --- | --- |
| **Age** | 60 (9) |
| **BMI** | 25.81 (2.04) |
| **BMI CATEGORY** |  |
| Normal weight | 27 (33%) |
| Obese | 2 (3%) |
| Overweight | 52 (64%) |

Fig 1. Place of Residence for the past 10 years

## Table 2: selenium and Prostate specific antigen in both groups

| **Characteristic** | **control**  N = 401 | **PCa**  N = 411 | | **p-value**2 | |
| --- | --- | --- | --- | --- | --- |
| **Se (µmol/L)** | 0.17 (0.07) | | 0.14 (0.07) | | 0.073 | |
| **PSA** | 2 (1) | 18 (5) | | <0.001 | |

**DISCUSSION**

The burden of prostatic diseases is a global concern, especially in African population where disease morbidity and mortality has been recorded to be higher.15 There are several studies that aim to identify risk factors of prostate cancer. There are myriads of research that provide persuasive reports on the role of non-genetic factors in the aetiology of PCa3,16,17

The influence of selenium in the prevention, prognostication and treatment of prostate cancers has been a subject of research with varying outcomes.18,19.

The mean age of respondents in this study was 60(9) years for BPH and 62(9) years for the PCa group, there was not statistically significant difference when the ages of both groups were compared. The age group with the highest frequency in a study by Padmapriya et all was 60-70 and this is agreement with our study20. This also agrees with prior studies of patients with prostatic diseases done in the same geographical area3,16. The mean BMI was 25.81 (2.04). Most of the study population were overweight, only three percent (3%) were obese. Obesity has been associated with PCa,3 so the low number of obese respondents reduces the influence of obesity as a confounding factor in this study.

In our study, most of the study subject population 49(60%) were urban dwellers. Those who live in developed countries and cities (urban) have been demonstrated to have a higher risk for prostate cancer.3 The mean PSA for respondents in both groups were compared and found to be statistically significant P < 0.001. The significant difference in PSA of both study groups show that the group with PCa had a higher risk for prostate cancer compared to those who had BPH.

Se has been shown to have antioxidant effects21, effects on the cell cycle22 and angiogenesis23. The sources of Se can be from food, water or supplements. These sources provide seleninium as Selecysteine (SeCys), methylselenocyteine, sodium selenite, Selenomethione (SeMet) and selenite. Cereals are the primary source of Selenium, other sources are vegetables, fruits and nuts.24 Se is primarily absorbed in the small intestine.25

Se is incorporated into proteinlike selenium binding proteins 1 (SBP-1) and selenium binding proteins 2 (SBP-2). The role of these proteins is not well established but there is evidence to show that high nuclear levels of SBP-1 was associated with lower tumor grade.26 Se supplementation has been found to act synergistically when combined with chemotherapy and radiotherapy for prostate cancer treatment 27.

Se supplementation has also been shown to reduces the post radiotherapy diarrhea that occurs following treatment of prostate cancer. These indicate that Se may be beneficial in the prognosticating and even treatment of patients with PCa.

A study comparing among 116 Caucasians with late onset prostate cancer showed low levels of serum Se in patients with PCa, when compared with controls28 however the Danish diet cancer and health cohort comparing prostate cancer and controls showed comparable levels of Se and Seleno-proteins in prostate cancer patient and the controls.29

Se level for patient with PCa was 0.14 (0.07) µmol/L which was lower than that for people with BPH 0.17 (0.07) µmol/L. This difference was however not statistically significant with a p value of 0.073. This agrees with Dhillhon et al 19, in their study they reported lower Se levels in patients with PCa versus the controls (BPH). A weak evidence of the positive effect of Se on PCa has also been recorded in other studis.26,27 Cui et al 30 also reported low Se in patients with prostate cancer compared to the control group just as we found in this study. This may be due to the effective scavenging of reactive nitrogen oxide by selenium and it’s anti-inflammatory activity30-32. There is also data to suggest that Selenium reduces cell multiplication and reduced cell cycle progression by the reduction of cyclin in PCa cell lines.30 These go to say that Selenium plays a role in PCa though our study has not shown significant difference when comparing serum Se levels in patients with PCa and BPH

There are studies that analyzed the impact of selenium intake in the development to PCa with opposing outcomes, The Nutritional Prevention of Cancer (NPC) trial done in 198333 showed that after Se supplementation, there was reduced risk for prostate cancer in patients who initially had low Se level.32 The SELECT trial 34 showed Selenium supplementation at 200 micro grams in 35,533 men with PSA < 4ng/ml and normal digital rectal examination findings did not reduce the risk of prostate cancer. The disparity in outcomes of these studies may be because the NPC trial considered patients with low Se as opposed to the SELECT. Jiang et al 35 compared the data from both studies and concluded that Se supplementation did not prevent PCa in healthy men.

There are however other researches that show that Se is involved not just in the development but also in the progression of prostate cancer. The mechanisms by which it achieves this include the androgen receptor signaling pathway36 Animal models have demonstrated that methyl selenium compounds showed changes in proteins with evidence of functional prostate differentiation and signaling of androgens.37 Monomethylated selenium (MeSe) has shown decrease in PSA and prostatic androgen receptors.109 Se has also be also been shown to increase break down of androgen receptor proteins diminished its nuclear presence in LNCAP110. Recent drugs that target androgen receptors demonstrated that Se nanoparticles suppress growth of PCa by its effect on androgen receptors.38

Abnormal cell proliferation is characteristic of cancers and is also found in prostate cancer. Prostate cells exposed to 100nM of sodium selenite reduced selenoproteins which caused G1 arrest through increasing BCL2 mRNA expression and decreased transcripts related to G2/M and S-phase genes causing blockage of G1/S transition. These show that selenoprotein is likely to prevent cell arrest and so preserve prostatic function.39

Feeding mice with different forms of Se has been shown to impede angiogenesis. Angiogenesis is regulated by vascular endothelial growth factor (VEGF) and transforming growth factor. Hypoxia induced growth factor -1α (HIF-1α) induces a cascade of events that leads to increased VEGF production and so promoting cell growth. Studies have revealed that methylated selenic acid (MSeA) administration to men with hormone refractory PCa reduces the production of VEGF.40 hence reducing angiogenesis required for PCa growth.

In our study we did not consider Se supplementation because these were patients presenting with clinical symptoms that needed some form of treatment. A lot of the studies on the effect Se on PCa were not carried out in West Africa. A Nigerian study like this one with larger sample size is required to determine the role of Se in PCa and indeed other malignancies.

**CONCLUSION**

In this study we found that serum Se was lower in patient with PCa compared with controls (BPH) but this difference was not statistically significant. The role of Se in prostate diseases and indeed prostate cancer still requires further research to determine its role, this will also help identify those who will benefit from Se supplementation, dose and duration of supplementation required. This is particularly important in West-Africa where the burden of prostate cancer is high.

**Consent**

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

**Disclaimer (Artificial intelligence)**

Option 1:

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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Details of the AI usage are given below:

1.

2.

3.

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