Biochemical Characteristics of Liver Enzymes, Prolactin, Zinc and Selenium in Benign Prostatic Hyperplasia and Cancer of the Prostate Patients Attending Urology Clinic at Nnamdi Azikiwe University Teaching Hospital, Nnewi.

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Abstract: Prostate disorder is any of the abnormalities that afflict the prostate gland in the male reproductive system, often characterized as prostatitis, benign prostatic hyperplasia (BPH) and cancer of the prostate (CaP) with a rising incidence in Nigeria. Objective: This study was designed to assess biochemical characteristics of liver enzymes, prolactin, zinc and selenium in benign prostatic hyperplasia and cancer of the prostate patients in Nnamdi Azikiwe Teaching Hospital (NAUTH) Nnewi. Materials and methods: A total number of 55 men diagnosed with CaP, 52 men diagnosed with BPH and 55 apparently healthy men attending the urology clinic in NAUTH were recruited for this study. Total Prostate Specific Antigen (PSA), free Prostate Specific Antigen (fPSA) and prolactin were analysed by Enzyme Linked immunosorbent assay method. Alanine amino transferase (ALT), Aspartate amino transferase (AST) and Alkaline Phosphatase (ALP) were estimated using IFCC (International Federation of Clinical Chemistry and Laboratory Medicine) method. Zinc and Selenium were determined using Atomic Absorption Spectrophotometer (AAS). Results: The mean serum levels of prolactin, ALT and ALP were significantly higher (P<0.05) in CaP subjects (5.08±2.19, 45.76±22.61, 100.91±70.39) when compared with BPH (4.03±1.73, 41.33±14.37, 85.83±18.97) and control subjects (2.59±1.11, 33.96±5.86, 68.42±19.90) respectively. Whereas, the serum levels of Zinc and Selenium were significantly decreased (P<0.05) in BPH (0.41±0.16 and 0.27±0.09) compared with CaP (0.55±0.34 and 0.30±0.15) and control group (0.85±0.42 and 0.65±0.59) respectively. Also, the mean values of TPSA and FPSA were of significant positive correlation with prolactin, ALT and ALP and significant negative association with Zinc and Selenium in both BPH and CaP subjects (P<0.05). Conclusion: This suggests that prostatic disorders (BPH and CaP) are associated with significant proliferation of the mammary and liver cells; and depletion of trace elements.

Keywords: Benign hyperplasia, Cancer of the prostate, Liver enzymes, Prolactin, Trace elements.

1. Introduction

Prostate disorders are disease conditions of the prostate gland, a walnut-shaped gland that is part of the male reproductive system which functions to make fluids that goes into semen. The Prostate fluid is essential for a man’s fertility. Therefore, diseases of the prostate namely, prostatitis, benign prostatic hyperplasia (BPH) and prostate cancer is a major risk factor to man’s infertility. Prostatitis is defined as an increased number of inflammatory cells within the prostate gland. The inflammatory process may be infectious or inflammatory in origin. It is a common condition which can affect men of any age, but it’s most common in younger and middle aged men, typically between 30 and 50. Benign Prostatic Hyperplasia (BPH) is an age-related non-malignant enlargement of the prostate gland. Anatomically, BPH is most strongly associated with the posterior urethral glands (PUG) and transitional zone (TZ) of the prostate. In men over the age of 60 years,
enlargement (hyperplasia) of the prostate is relatively common. In the vast majority of cases it causes no symptomatic difficulties, though infection may occur, as may rupturing of blood vessels. Enlargement may cause compression of the urethra with progressive obstruction of the flow of urine, incomplete emptying, or inability to void; there may also be a constant dribbling of urine. The bladder is never totally emptied, however, and the remaining urine becomes stagnant and infection sets in. The stagnant urine may cause the precipitation of stones in the bladder; the bladder muscle thickens to overcome this obstruction. If urine begins to back up in the kidney, progressive damage may ensue, which can lead to kidney failure and subsequent uremia (the toxic effects of kidney failure). In severe cases, BPH may lead to sepsis, irreversible bladder damage, renal failure or even death.5

Prostate cancer is a malignant (cancerous) tumour (growth) that consists of cells from the prostate gland. Prostate cancer is the most common malignant tumour in men over the age of 65 years. Thus, prostate cancer under age 40 is extremely rare, while it is common in men older than 80 years of age. As a matter of fact, some studies have suggested that among men over 80, between 50 and 80 percent of them may have prostate cancer.6 It has been declared a public health epidemic in black American men because of its high incidence. Prostate cancer most commonly metastasizes to the bones, lymph nodes, and may invade rectum, bladder and lower ureters after local progression. Prostate cancer has the potential to advance loco-regionally to adjacent organs. This spread can take place via different routes, including direct invasion and through lymphatic channels.7

Africa was reported in the past to have a low incidence of this disease,8 however past studies indicated a high and rising incidence in Nigerians.5,10 As much as 11% of all cancers in Nigeria are reported to be of the prostate1 whereas as many as 25% and 12% of adult male Nigerians were reported to have BPH11 and prostatitis12 respectively. The prevalence of prostate cancer in Nigeria was formerly put to be about 15.7%.13,14 It was also reported that Prostate Cancer is the most common cancer in Nigerian males; having overtaken lung cancer.15 Furthermore, another study carried out later reported that the incidence of Prostate cancer in Nigeria is 18.2% and prostate cancer accounts for about 9.6% of all mortality from Cancer cases in Nigeria.16 The trend at which prostate cancer is growing is alarming and attention needs to be paid to this.

The current screening method for prostate cancer relies on a combination of Prostate specific antigen (PSA) assay including free and total Prostate specific antigen (fPSA and tPSA) while biopsy is done to confirm it if there is suspicion of cancer. However the interest of this study is to ascertain if some other methods could be of diagnostic value.

Prostate Specific Antigen (PSA) is a serine protease in the kallikrein family of proteases; it is also called human kallikrein 3 17 produced in high concentrations by prostatic epithelium, PSA is secreted mainly into seminal fluid, where it dissolves the gel that forms after ejaculation by digesting the major gel-forming proteins, thereby resulting in increased sperm motility.18 In prostate cancer, however, the architecture and polarization of epithelial cells are deranged, disrupting normal secretory pathways and causing PSA to “leak” or to be actively secreted into extracellular space and escape into the circulation. As a result, PSA is found in the serum in concentrations 30 times higher per unit weight of cancerous tissue than of normal tissue, and 10 times higher per unit weight of cancerous tissue than of the epithelial tissue in benign prostatic hyperplasia (BPH).17,19

Prolactin is a peptide hormone, encoded with the PRL gene. Prolactin (Prl) is a peptide hormone of numerous and distinct bioactive and immunoreactive variants.20 Its versatile functions are known to include effects on the immune system, on osmoregulation, and on behavior. Furthermore, prolactin stimulates lactation and growth in mammary gland by activating the expression of milk protein genes 21 and genes presumably necessary for proliferation of mammary cells.22,23 In prostate, prolactin has been presumed to have a role in the regulation of prostatic development, growth, and differentiation 24,25 In Humans, receptors for prolactin are expressed in the Prostate and particularly abundant in the pre-cancerous lesions.25

The liver is the largest organ in the body and serves many vital functions such as remove damaged red blood cells from the blood in coordination with spleen, produces bile, clotting factors, stores vitamins, minerals, protein, fats and glucose from diet.26,27 Most liver diseases cause only mild symptoms initially, but these diseases must be detected early. Hepatic (liver) involvement in some diseases can be of crucial importance. AST, ALT, and alkaline phosphatase are liver enzymes and they typically are used to detect damage or injury to the liver.28
Trace elements are inorganic molecules which are essential for life. Although these elements constitute a relatively small amount of total body tissues, they are very essential in many physiological and biochemical processes. In states of absolute deficiency, death results and in limited intake biological functions are impaired.\(^29\)

Zinc is an important constituent of prostatic fluid and is known to play an important role in the development and normal functioning of prostate.\(^30,31\) Normal prostate tissues from healthy individuals accumulate the highest levels of zinc in the body.\(^32\) Malignant prostate cells that develop in the peripheral zone do not contain the high zinc levels that characterize the normal secretory epithelial cells.\(^33\)

Selenium is an essential trace element present in foods such as bread, cereals, nuts, meat, fish and other seafood are found predominantly as the amino acid derivatives, selenomethionine and selenocysteine.\(^34\) There is a relatively narrow margin between selenium intakes that result in deficiency or toxicity, with health effects being related to level of exposure and selenium status.\(^35\) Moreover, in humans there are 25 selenoproteins and many of these are enzymes that act to protect the body against oxidative damage. Without selenium, the function of the selenium-requiring proteins can be compromised which results in the signs and symptoms of deficiency. Certain diseases such as cancer and cardiovascular disease as well as aging process, is associated with an increase in oxidative damage. Maintaining adequate selenium intakes may provide some protection against these processes.\(^36\) There is a growing interest in selenium in relation to possible protective effects against cancer and other chronic diseases. In a large-scale supplementation trial, selenium had an anticarcinogenic effect.\(^37\)

The most frequent metastatic sites in prostate cancer are bone, lymph nodes and visceral metastases including the liver, central nervous system and the lungs.\(^38\) Thus, assessment of liver function of males with prostate disorders may be of good value. Also, plasma Prolactin rises sharply at puberty and continues to increase in parallel with age-related increase seen in the incidence of Benign Prostatic Hyperplasia and Prostatic Cancer.\(^39\) However prolactin is postulated to be implicated in the most cancerous cases in women with little or no input on its progression of in men with cancer related cases such as BPH and CaP. It has also been proven that some trace elements have inhibitory roles in cancer biology; however, there is still a deficient data regarding the relationship between trace elements functions and initiation, advancement and inhibition of carcinogenic process in prostatic gland.\(^40,42\) Hence, this study was designed to evaluate the biochemical characteristics of liver enzymes, prolactin, zinc and selenium in patients with BPH and CaP attending urology clinic in NAUTH, Nnewi.

2. Materials and methods

2.1. Study site and ethical clearance

This was a cross-sectional survey that was carried out in the Surgical Out-patients Department of Nnamdi Azikiwe University Teaching Hospital Nnewi (NAUTH). Ethical clearance was obtained from the Ethics Committee of Nnamdi Azikiwe University Teaching Hospital, Nnewi before the commencement of the study and informed consent was obtained from the subjects.

2.2. Study subjects and design

This study comprised of a total of 162 subjects which consist of 52 individuals with Benign Prostate hyperplasia, 55 subjects with Prostate cancer and 55 apparently healthy men that served as control group.

2.3. Sampling Technique

Random sampling technique was used during sample collection and 7 ml of venous blood was collected from subjects as they visited the Urology unit at Nnamdi Azikiwe University Teaching Hospital using a plain specimen container. The serum obtained after centrifugation was stored at 2-8°C until analyzed.

2.4. Inclusion criteria

Individuals within the age of 50-80 with Benign Prostate Hyperplasia or cancer of the Prostate were recruited.

2.5. Exclusion criteria

Subjects that have disease conditions such as alcoholic liver disease; liver cirrhosis were excluded from this study.

2.6. Statistical analysis

The version 22 of Statistical Package for Social Sciences (SPSS) was used in statistical analysis. The results were expressed as (Mean±SD). Comparisons were made using one way analysis of variance (ANOVA). Pearson correlation analysis
was used to establish possible correlation between PSA and other analytical parameters in BHP and CaP. P<0.05 was taken as significant.

3. Results

3.1. Anthropometric data of subjects with prostate disorder and control subjects

The height, weight and body mass index (BMI) of the BPH, CaP and control subjects are shown in table 4.1. The result showed that there was no significant differences (P>0.05) in weight (72.56±10.97, 75.85±12.87 and 75.79±11.94), height (1.68±0.06, 1.70±0.08 and 1.71±0.08) and BMI (25.55±3.54, 26.11±3.27 and 25.92±3.13) of the BPH, CaP and control subjects respectively.

Table 1: (Mean ± SD) of the anthropometric data of subjects with prostate disorder and control subjects.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>BPH (n=52)</th>
<th>CaP (n=55)</th>
<th>Control (n=55)</th>
<th>F value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>72.56±12.18</td>
<td>75.79±11.99</td>
<td>71.80±12.04</td>
<td>1.31</td>
<td>0.34</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.68±0.17</td>
<td>1.70±0.17</td>
<td>1.67±0.15</td>
<td>0.43</td>
<td>0.02</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.55±3.13</td>
<td>26.11±3.27</td>
<td>25.92±3.13</td>
<td>0.39</td>
<td>0.37</td>
</tr>
</tbody>
</table>

KEYS: BMI= Body Mass Index, CEA = Carcino-Embryonic Antigen, BPH = Benign Prostatic Hyperplasia, CaP = Cancer of the Prostate. Mean difference is significant when P is <0.05. * = mild significance and ** = marked significance.

3.2. Variations of the serum levels of TPSA, FPSA, Prolactin, ALT, AST, ALP, Zinc and Selenium in BPH, CaP and Control Subjects.

The mean levels of TPSA and FPSA which were used as markers in identifying and selecting the BPH and CaP subjects shows a significant increase (P<0.05) in CaP subjects (83.92±4.74 and 29.33±1.37) when compared with BPH (26.85±11.37) and control subjects (22.05±7.72 and 25.84±25.80) respectively but did not show any significant difference when compared between BPH (26.85±11.37) and CaP subjects (22.05±7.72 and 25.84±25.80) respectively.

Table 2: Variations of the serum levels of TPSA, FPSA, %FPSA, Prolactin, ALT, AST, ALP, Zinc and Selenium in BPH, CaP and Control Subjects.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>BPH (n=52)</th>
<th>CaP (n=55)</th>
<th>Control (n=55)</th>
<th>F value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TPSA (ng/ml)</td>
<td>16.63±1.74</td>
<td>83.92±4.74</td>
<td>29.33±1.37</td>
<td>140.00</td>
<td>0.00</td>
</tr>
<tr>
<td>FPSA (ng/ml)</td>
<td>4.74±0.24</td>
<td>4.89±0.25</td>
<td>6.90±0.34</td>
<td>479.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Prolactin (ng/ml)</td>
<td>5.34±0.84</td>
<td>8.51±6.83</td>
<td>0.49±0.34</td>
<td>37.00</td>
<td>0.00</td>
</tr>
<tr>
<td>ALT (iu/L)</td>
<td>41.33±2.61</td>
<td>45.76±2.96</td>
<td>33.96±7.76</td>
<td>22.05±2.94</td>
<td>0.05</td>
</tr>
<tr>
<td>AST (iu/L)</td>
<td>26.85±1.26</td>
<td>29.84±2.95</td>
<td>22.05±2.94</td>
<td>2.05±2.94</td>
<td>0.05</td>
</tr>
<tr>
<td>ALP (iu/L)</td>
<td>85.83±2.85</td>
<td>100.91±3.25</td>
<td>68.42±19.90</td>
<td>22.05±7.72</td>
<td>0.05</td>
</tr>
<tr>
<td>Zinc (iu/L)</td>
<td>0.41±0.55</td>
<td>0.55±0.34</td>
<td>0.55±0.34</td>
<td>25.02±2.95</td>
<td>0.05</td>
</tr>
<tr>
<td>Selenium (iu/L)</td>
<td>0.27±0.30</td>
<td>0.30±0.17</td>
<td>0.30±0.17</td>
<td>19.40±4.64</td>
<td>0.05</td>
</tr>
</tbody>
</table>

KEYS: BPH = Benign Prostatic Hyperplasia, CaP = Cancer of the Prostate. Mean difference is significant when P is <0.05. * = mild significance and ** = marked significance.

3.3. Relationship between serum levels of TPSA, FPSA, Prolactin, ALT, AST, ALP, Zinc and Selenium among BPH Patients.

In BPH patients, the mean serum level of TPSA correlated positively with the serum levels of FPSA (r = 0.826), Prolactin (r = 0.722), ALT (r = 0.921) and ALP (r = 0.824) (<0.05) respectively but correlated negatively with the serum levels of Zinc and Selenium (r = -0.985 and -0.951) (P<0.05) respectively. More so, the serum level of FPSA correlated positively with the serum levels of Prolactin (r = 0.672), ALT (r = 0.439) and ALP (r = 0.633) and in the same vein, correlated negatively with the serum levels of Zinc and Selenium (r = -0.721 and -0.940) (P<0.05) respectively. However, the mean values of TPSA and FPSA did not show significant association when correlated with the mean value of AST (r = 0.018 and 0.011) (<0.05) respectively.
Mean serum levels of Zinc and Selenium (r = -0.400 and (P<0.05) respectively but correlated negatively with the
serum levels of Prolactin (r = 0.522), ALT (r = 0.401) and ALP (r = 0.317) but correlated negatively with the
mean value of AST (r = 0.021 and 0.007) (P>0.05) respectively. However, the mean values of TPSA and
FPSA did not show significant association when P is <0.05. * = mild significance and ** = marked significance.

Table 3: Relationship between serum levels of TPSA, FPSA, Prolactin, ALT, AST, ALP, Zinc and Selenium among BPH Patients.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>BPH Patients</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>TPSA Vs FPSA</td>
<td>-0.128</td>
<td>0.000**</td>
</tr>
<tr>
<td>TPSA Vs Prolactin</td>
<td>-0.477</td>
<td>0.000**</td>
</tr>
<tr>
<td>FPSA Vs Prolactin</td>
<td>0.314</td>
<td>0.001</td>
</tr>
<tr>
<td>FPSA Vs TPSA</td>
<td>0.442</td>
<td>0.000**</td>
</tr>
<tr>
<td>FPSA Vs AST</td>
<td>0.467</td>
<td>0.000**</td>
</tr>
<tr>
<td>FPSA Vs ALP</td>
<td>0.343</td>
<td>0.001</td>
</tr>
<tr>
<td>Zinc Vs TPSA</td>
<td>0.423</td>
<td>0.000**</td>
</tr>
<tr>
<td>Selenium Vs TPSA</td>
<td>0.432</td>
<td>0.000**</td>
</tr>
</tbody>
</table>

CaP Patients

<table>
<thead>
<tr>
<th>Parameters</th>
<th>r-value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TPSA Vs FPSA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TPSA Vs Prolactin</td>
<td></td>
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<tr>
<td>FPSA Vs Prolactin</td>
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<tr>
<td>FPSA Vs TPSA</td>
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<tr>
<td>FPSA Vs AST</td>
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<tr>
<td>FPSA Vs ALP</td>
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<td></td>
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<tr>
<td>Zinc Vs TPSA</td>
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<td></td>
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<tr>
<td>Selenium Vs TPSA</td>
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</table>

In the present study, it was observed that the mean levels of TPSA and FPSA of BPH and CaP subjects were significantly higher than that of apparently healthy individuals. This is consistent with earlier studies.45,46 Furthermore, the mean level of TPSA was significantly higher in CaP subjects in comparison with BPH subjects. The increased TPSA may be as a result of stronger expression of alpha-1-antichymotrypsin (ACT) in prostate cancer tissue than in BPH tissue.45

3.4. Relationship between serum levels of TPSA, FPSA, Prolactin, ALT, AST, ALP, Zinc and Selenium among CaP Subjects.

In CaP subjects, the serum level of TPSA correlated positively with the serum levels of FPSA (r = 0.728), Prolactin (r = 0.491), ALT (r = 0.379) and ALP (r = 0.511) (P<0.05) respectively but correlated negatively with the mean serum levels of Zinc and Selenium (r = 0.400 and -0.591) (P<0.05) respectively. Also, the mean level of TPSA correlated positively with the serum levels of Prolactin (r = 0.522), ALT (r = 0.401) and ALP (r = 0.317) but correlated negatively with the serum levels of Zinc and Selenium (r = -0.612 and -0.503) (P<0.05) respectively. However, the mean values of TPSA and FPSA did not show significant association when correlated with the mean value of AST (r = 0.021 and 0.007) (P>0.05) respectively. When P is <0.05, * = mild significance and ** = marked significance.

Table 4: Relationship between serum levels of TPSA, FPSA, Prolactin, ALT, AST, ALP, Zinc and Selenium among CaP Patients.

4. Discussion

The incidence of benign prostate hyperplasia and prostate cancer is rapidly increasing worldwide. However, drastic attention is needed in order to reduce the rate of mortality and morbidity emanating from prostate diseases.

In addition, Asare-Anane et al.,47 observed in a study that prostatic fluids in prostate cancer patients have higher prolactin levels than the controls. Epidemiological studies exploring a correlation between serum prolactin levels and prostate cancer incidence or severity have been equivocal, with some reporting no difference while others found a higher incidence of hyperprolactinemia in patients with metastatic prostate cancer than those with hormone responsive tumours.48,49 Studies by several groups have shown that Prolactin is one of the non-steroidal factors involved both in prostate...
cell proliferation and in the development of benign prostate hyperplasia and prostate cancer. In vitro, prolactin induces proliferation and antagonizes apoptosis in prostate organ culture and in some tumor cell lines. Prolactin hormone is an additional growth factor to the prostate gland, and rising prolactin levels correlate with progression in advanced prostate cancer cases. Prolactin receptors are found on prostate cancer cells, and it is postulated that these receptors may facilitate the entry of testosterone into the cell. The expression of the receptors is particularly elevated in prostate cancer and carcinoma in situ. This suggests that up-regulation of prolactin receptor and local production of prolactin in prostate could be important in increased risk of prostate cancer and treatment resistance. Indeed, Prolactin serum levels increase with age, whereas androgen levels decrease, suggesting that the role of prolactin in the development of prostate hyperplasia and cancer becomes more important with age. Although it is unknown whether prolactin causes the disease or the disease causes prolactin increase, what is known is that after inducing an increase in serum prolactin, the possibility of prostate pathology is significantly increased. Hence, Prolactin is now considered as a risk factor in the etiology of prostate pathologie (Eaton et al., 1999). However, a conclusive demonstration has not been easy to demonstrate due to experimental protocols in use, as well as the possible role of androgens. In spite of this, it has been found that Prolactin can promote prostate cell growth by activating a mechanism dealing with the inhibition of apoptosis.

In this study, the mean values of ALT and ALP of prostate cancer patients and Benign prostatic hyperplasia were significantly higher compared to that of the control group. This corroborated with a recent study done by, Guntupalli et al., who reported that liver enzymes were significantly higher in BPH and CAP subjects compared to the control group. However, AST mean values did not show any significant difference. Increase in enzyme activities suggests either hepato-cellular damage or cholestasis. This study suggests that liver disease may be associated with patients with prostate disease.

Moreover, a significant decrease in mean levels of zinc was observed in subjects with prostate cancer and BPH subjects compared with the control group. Some researchers have earlier reported that plasma and tissue zinc were substantially lowered in the cancerous prostate and BPH than in normal prostate. Studies have also observed that total zinc levels in the prostate are much higher than in other soft tissues in the body, and those with prostate cancer have been shown to have exceedingly low levels of zinc in the prostate and prostatic secretions in men with prostate disease compared with healthy men. Nevertheless it was suggested that Zinc deficiency could be a risk factor for prostate cancer. It is well documented that tumor cells undergo metabolic transformations that are essential for their malignant existence but are not the cause of malignancy. The accumulation of zinc in normal prostate glandular epithelial cells results in two important effects, a metabolic effect, and a proliferative effect. Its metabolic effect is the inhibition of citrate oxidation, which is necessary for prostate function. A second effect of zinc is its inhibition on prostate-cell proliferation. Zinc is of importance for the functions of many transcription factors and proteins involved in the recognition of specific DNA sequences and regulation of gene transcription. Zinc has a protective effect against free-radical injury. Zn may play a key role in the prevention of prostatic disease by ameliorating oxidative stress, which can subsequently result in DNA damage, increasing the risk of mutation and malignant transformation. In fact, dietary Zn deficiency has been associated with increased DNA damage in the prostate during oxidative stress. Specifically, Zn deficient prostate cells have greater DNA damage and altered expression of genes associated with this damage, indicating that marginal Zn intake may sensitize the prostate to oxidative damage. As oxidative stress increases, so does the cellular Zn requirement for protective mechanisms, thus perpetuating the harmful effects of Zn deficiency. The intramitochondrial accumulation of high zinc levels inhibits aconitase activity which inhibits citrate oxidation. This essentially truncates the Kreb’s cycle and markedly decreases ATP production (normally coupled to citrate oxidation). These relationships form the basis of a new concept of the role of zinc and citrate related energy metabolism in prostate malignancy. The inability of carcinoma cells to accumulate high zinc levels results in increased citrate oxidation and the coupled ATP products essential for progression of malignancy. Feng et al. showed similar effects of high intracellular accumulation levels of zinc in prostate cells inducing mitochondrial apoptogenesis.

This study reported that the mean selenium level was significantly lower in prostate cancer and BPH subjects when compared with the control subject. This is in agreement with two meta-analyses of observational studies from diverse populations that reported the potential effect of selenium against the development of prostate cancer. It was also discovered that higher serum selenium levels may reduce prostate cancer risk in men with high intake of vitamin E, in multivitamin.
users, and in smokers.\textsuperscript{67} Interventions with selenium have shown benefit in reducing the risk of cancer incidence and mortality in all cancers combined, and specifically in liver, prostate, colorectal and lung cancers.\textsuperscript{68} In contrast certain studies observed that there was no significant difference in mean selenium levels in BPH and CaP subjects \textsuperscript{67,69,70} carried out a study on 235 prostate cancer cases and 456 controls and found no association between prostate cancer risk and serum selenium concentrations in a cohort from the Carotene and Retinol Efficacy Trial (Goodman et al., 2001).\textsuperscript{69} In 2004, Lipsky et al.,\textsuperscript{71} evaluated 150 participants (70 cases and 80 controls) and reported toenail selenium levels may not influence prostate cancer incidence. Similarly, Allen and colleagues suggested that selenium concentration, as measured in nails of 300 case control pairs, did not strongly associate with prostate cancer risk. Peters et al.\textsuperscript{70} observed no inverse association between prediagnostic serum selenium concentration and the risk of prostate cancer in a large cohort study with 724 cases and 879 matched controls. The prostate gland is androgen sensitive hence, the prostate may be susceptible to oxidative damage because androgens increase oxidative stress, partly by increasing the mitochondrial and decreasing the glutathione.\textsuperscript{72,73} Prostate cancer risk is an age-related disease and oxidative stress increases with age,\textsuperscript{74} through generation of reactive oxygen species and reduced activity of antioxidative enzymes.

5. Conclusion

We therefore conclude that the prostatic depletion of serum levels of Zinc and Selenium in both BPH and CaP subjects may be the reason behind the mammary (Prolactin) and liver (ALT and ALP) cells proliferation as recorded in this study. This is substantiated by the fact that the prostate gland is androgen sensitive hence; the prostate may be susceptible to oxidative damage due to the reduced protective mechanisms thereby increase oxidative stress, partly by increasing the mitochondrial and decreasing the glutathione activities.

Thus, the serum levels of Prolactin, Zinc and Selenium estimation in conjunction with the established markers (TPSA, FPSA, %FPSA etc) can be of good diagnostic/prognostic value in the identification of adult men at risk for development of prostatic complications. Dietary supplements rich in Zinc and Selenium should also be encouraged relatively healthy adult men and in the management of prostate disorders so as to reduce oxidative stress associated with reduced levels of zinc and selenium.

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