Original Research Article

Estimation of selected metals in the tissues of prostate carcinoma patients: A Research

ABSTRACT

It Indicated that the Prostate cancer is common it affects nearly one-third of male over the age of 45. For two fundamental reasons, prostate cancer (PCa) is a serious health issue and a good prospect for tissue-scale, individualized modeling of cancer progression. In vivo validation might be allowed due to its compact size and the ability to measure serum PSA, a for prostate cancer blood biomarker can be diagnosed with support if certain markers identified by immunohistochemistry on tissue sections can aid in the diagnosis of adenocarcinoma that is primary in the prostate gland or metastatic. The biology of prostate cancer can be deeply understood by the gene identification and gene patterns expression. Using the Affymetrix Uranium95a, U95b, and Uranium95c chip sets (37,777 genes and expression sequence tags), Comprehensive gene expression is performed study on 152 hompsapien samples, which were from men of all ages and included cancer tissues, prostate tissues next to tumors, and prostate tissue of donor. In the prostate tissues, the majority of metals show a random distribution; nevertheless, patients show comparatively more unpredictability than controls. However, our findings indicate that the pattern of gene expression in cancer-related tissues is altered to such an extent that it resembles the effects of a cancer field. In contrast to controls, PCA and CA demonstrated how hazardous metals interfered with the critical metals' normal physiological and metabolic roles in the prostate tissues of both patient groups. In comparison to hyperthyroid patients and controls, hypothyroid patients' prostate tissues had greater mean levels of Fe, Ni, Cr, and Hg. Additionally; we discovered that by employing a unique model, Prostate cancer aggressiveness can be predicted by gene expression patterns.

Keywords: Prostate cancer, tissue-scale, patients, gene expression**.**

1. Introduction

Metals are solid, shiny, conductive elements known for their malleability, ductility, and high reflectivity [1] .Most are found in ores, though some like copper and gold occur freely due to low reactivity [2]. Lithium, zinc, iron, and copper are essential metal traces that are necessary for the functioning of enzymes and proteins, which support a variety of metabolic processes [3]. Heavy metals like chromium, mercury, arsenic, and cadmium are toxic even at low concentrations, with industrial use raising health and environmental concerns [4]. Cadmium disrupts cellular respiration and DNA repair, contributing to oxidative stress and apoptosis [5]. Chromium affects immune functions, with high levels reducing alveolar macrophage activity [6]. Cobalt exposure can cause respiratory diseases and cancer [7]. Copper, while essential, can be toxic in excess, affecting antioxidant functions and DNA integrity Copper (Cu) an Essential Redox-Active Transition, Mercury, liquid at room temperature, is highly toxic and requires careful handling to prevent contamination [8]. Magnesium, crucial for industrial applications, can cause toxicity if not properly excreted [9]. Iron is key for oxygen transport and cellular respiration, with deficiencies leading to anemia and excess intake potentially increasing cancer risk [10]. Tin, mainly extracted from cassiterite, is generally non-toxic, though certain organotin compounds are highly toxic [11]. Cancer is a disease where cells grow uncontrollably and spread to other body parts. There are over 100 types, commonly categorized by origin and cell type. Benign Tumors are Non-cancerous growths that do not spread but may press on vital structures . Causes include environmental toxins, genetics, and stress with treatments varying from "watchful waiting" to surgery [12]. Malignant Tumors are Cancerous and can spread (metastasize) to other body parts, maintaining their original

[13]. Diagnosis involves imaging tests and biopsie,Carcinoma are most common cancer, originating in epithelial cells. Sarcoma Develops in bone and soft tissues. Leukemia is Cancer of blood-forming tissues, resulting in abnormal white blood cells. Lymphoma begins in lymphocytes, affecting lymph nodes and vessels. Multiple Myeloma starts in plasma cells, forming tumors in bones. Melanoma originates in melanocytes, usually on the skin but can also occur in other pigmented tissues [14]. The spinal cord and brain Benign or malignant tumors are identified by their location within the central nervous system and kind of cell. Genetic alterations that impair

normal cell division and growth are the root cause of cancer. Errors in cell division, environmental damage (such as UV radiation and tobacco smoke), or inherited genes can all result in these alterations. The body's capacity to remove damaged cells is weakened with age, which raises the risk of cancer. Each cancer has a unique set of genetic alterations, with different cells in the same tumor potentially having distinct changes. Cancer staging involves determining the extent of the disease, historically done through clinical examination and limited imaging. Advances in diagnostic tools like CT, MRI, ultrasound, and PET have largely replaced invasive procedures for staging [15].

Tissue is a group of cells with similar structure and function, filled with intercellular matrix. The four main types are epithelial, connective, muscle, and nervous [16]. Epithelial tissue lines organs and blood vessels, providing protection, secretion, absorption, and sensation [17]. It lacks blood vessels and relies on diffusion for nourishment [13]. Connective tissue supports and connects other tissues, consisting of fibers, ground substance, and cells like fibroblasts and macrophages . It provides structural support and mediates the exchange of nutrients and waste [18]. There are three forms of muscle tissue that allow for movement through contraction: skeletal, cardiac, and smooth muscle, all containing actin and myosin . Nervous tissue forms the nervous system, composed of neurons and glial cells, conducting electrical signals for communication and processing information in the CNS and PNS [19].

Prostate Tissue develops from epithelial outgrowths in the urogenital sinus and mesonephric.It is a walnut-sized gland below the bladder, surrounding the urethra. The prostate produces fluids that enhance male fertility and is prone to cancer, with about 1 in 7 men diagnosed during their lifetime. Prostate cancer is a leading cancer among men, with increasing global prevalence. Modifications in lifestyle, like giving up smoking, exercising, and keeping a healthy weight, may lower the risk [20]. Screening and managing early prostate cancer are complex and controversial [21].

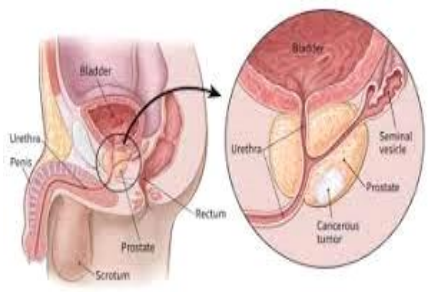

Figure 1: Developmentof Prostate Cancer

There were three categories of risk inducing factors: non-modifiable, which included genetic polymorphisms and situations in which no specific gene(s) has identified yet; blood-based markers; and external exposures, which included lifestyle where modification is possible. Age is the most important non-modifiable factor. Among all cancers, prostate carcinoma has the sharpest age-incidence arc in unscreened populations, rising at about the sixth age power. Of all malignancies, 25% are discovered prior the age of 65 [22]. Men are more likely to develop prostate cancer overall if they have a first-degree relative who has the disease (RR = 2.48; 95% CI 2.25–2.74) due to **genetic factors**. In comparison to older men, men under 65 had a higher risk (RR = 2.87; 95% CI 2.21–3.74), and if the affected person was a brother not a father (RR = 3.14; 95% CI 2.37–4.15), this risk is higher. 6. While family history is undoubtedly significant, known genes presently account for just 35% of the familial risk [22]Prostate cancer has been linked to both UV radiation from sun exposure (13), and ionizing radiation 12 in **external exposure,** however, more research and precise risk assessments are required [22].

Some studies suggest a potential link between urinary tract infections and increased prostate cancer risk due to chronic inflammation. However, more research is required to clarify this association [22].

Photometers are used by spectrophotometry, called spectrophotometers, to extent a light beam's intensity at different wavelengths [23]. AAS is a sensitive method for detecting metals in samples, often at picogram levels, using techniques like GC and LC separations (Butcher et al., 2005). A corresponding, measurable signal is produced when electromagnetic radiation at a specific wavelength is absorbed by free gaseous atoms. AAS, or atomic absorption spectrometry, is the term for this procedure. The absorption signal $\propto$ to the concentration of free atoms in the channel. By measuring the amount of light absorbed, the amount of analyte element present can be quantitatively quantified [24]. Atomic absorption spectrometry (AAS) can be very helpful for the examination of clinical samples, which typically involves identifying the presence of metals in fluids and tissues for toxicological investigation or therapeutic purposes [25].

Figure 2: Spectrophotometer

The aims and objectives are to establish baseline data for essential and toxic element concentrations in prostate carcinoma patients compared to healthy subjects, considering factors like environment, gender, diet, and smoking habits [26]. Investigate correlations among essential and toxic elements in tissues of both patient and control groups. Identify viable correlations between element levels in tissues of prostate carcinoma patients and controls [27]. Determine significant differences in element concentrations across various types and stages of prostate carcinoma. Explore the use of tissue analysis as a clinical study's diagnostic instrument [28].

2. Material and Method

Demographic and lifestyle data was collected, including age, sex, height, weight, financial status, and diet, from about 110 healthy individuals and prostate cancer patients [29] [30]. The participants, mostly family members, relatives, and neighbors, filled out forms to provide this information for comparison between the two groups [31] [32].

3. Sample Collection

- The Trial to Prevent Prostate Cancer, conducted from 1993-1997, enrolled 18,882 men to evaluate if finasteride could prevent prostate cancer. Eligible participants were at least 55 years old with specific health criteria. Cancer specimens, containing at least 80% cancer, were analyzed, excluding those with transition zone cancer. Participants provided demographic, lifestyle, and medical information, and their BMI was calculated. Tissue samples, including transition zone (TZ), peripheral zone normal (PZ-N), and peripheral zone cancerous (PZ-C), were randomly selected from patients with varying prostate gland masses and were stored at -270°C until analysis.

- The study involved 741 men who, between 1982 and 1989, experienced radical prostatectomy at J.H Hospital. Tissue specimens, including transition zone (TZ), peripheral zone normal (PZ-N), and peripheral zone cancerous (PZ-C) samples were taken from the tissue for the prostate cancer and serum, research excellence in the Baylor Specialized program. Cancer specimens contained at least 80% cancerous tissue, and transition zone cancer was excluded. Controls were the patients' spouses or female companions, selected for their awareness of prostate cancer and similar lifestyle factors. All samples were frozen at -270°C for storage and analysis.
- This prospective single-institution trial, approved by the local IRB, enrolled 26 prostate cancer patients between July 2011 and April 2012. The prostate cancer tissue and serum research excellence in the Baylor Specialized program. Patients with intermediate- or high-risk prostate cancer as determined by biopsy were included, and those with transition zone cancer or significant imaging artifacts were excluded. Six patients were removed from the study due to imaging artifacts or lack of significant peripheral zone cancer, leaving a final group of 20 patients.
- Fresh prostate tissues were collected immediately after surgery and dissected to ensure purity, with samples matched for transition zone (TZ), peripheral zone normal (PZ-N), and peripheral zone cancerous (PZ-C) specimens. Only tumor less than 30% stromal component samples and normal tissues with at least 60% glandular components were selected. Transition zone cancer was excluded. Within 30 minutes of removal, tissues were processed, frozen, and kept at -270°C. The institutional review board gave its approval to these methods.
- In stage 1 of the study, prostate cancer cases from the UKGPCS were analyzed. The prostate cancer tissue and serum research excellence in the Baylor Specialized program. The tissue samples were donated by the Baylor Program of Research Excellence in Prostate Carcinoma Tissue and Serum Bank, with matched transition zone (TZ), peripheral zone normal , and peripheral zone cancerous specimens. Transition zone cancer, non-white participants, and those diagnosed through asymptomatic PSA screening were excluded. Samples were frozen at -270°C for storage and analysis.
- With approval from the University of Illinois Institutional Review Board, this study analyzed 114 prostate cancer tissue samples from the prostate cancer tissue and serum research

excellence in the Baylor Specialized program. The samples, including transition zone, peripheral zone normal, and peripheral zone cancerous specimens, were nominated from patients with varying prostatectomy specimens and contained at least 80% cancerous tissue. Transition zone cancer was excluded. Hematoxylin and eosin (H&E) staining, FT-IR imaging, and freezing at -270°C were the steps taken to prepare the tissues for analysis.

3.1 Methodology

- Only benign areas of biopsy cores were analyzed for inflammatory response, with samples processed similarly to HIC-HPLC for high-quality evaluation [33]. Inflammatory cell types (acute and chronic) and their proportion in benign tissues were recorded [34] [35]. Inflammation was scored based on extent (focal, multifocal, diffuse) and grade (mild, moderate, severe) across different tissue compartments (luminal, intraepithelial, stromal). Intensity scores were calculated by multiplying extent by grade and summing for each compartment, then aggregated for each patient [36]. A single pathologist, blinded to cancer status, reviewed all images to ensure consistency [37]

- HIC-HPLC was used to analyze proteins in formalin-fixed, paraffin-enclosed human prostate tissues [38] [18]. A 4.6 × 250 mm polypropylaspartamide column with a 1000 Aangstrom pore size was employed for separation, with samples taken in 1.5 M $(NH_4)_2SO_4$ and eluted with buffers A and B. Immunostaining with anti-methylacyl-CoA racemase (AMACR) antibodies and anti pi (GSTpi) was performed. Using a Varian 9070 fluorescence sensor with emission at 334 nm and excitation at 232 nm, proteins were detected.

- A 4.6 × 250 mm polypropylaspartamide column with a 1000 Angstrom pore size was utilized for HIC-HPLC. Using buffers A (1.2 M Na_2SO_4, 25 mM Na_3PO_4 and B (50 mM Na_3PO_4, 5.0% 2-propanol), samples were added to 1.5 M $(NH_4)_2SO_4$ and then eluted. Using a Varian 9070 fluorescence sensor with emission at 334 nm excitation at 232 nm, proteins were found. Using a 5º-nuclease assay (Taqman) on an ABI Prism 7900HT system, genotyping was carried out accurately by including duplicates and negative controls [39].
- 4. A 4.6 × 250 mm polypropylaspartamide column with a 1000 Angstom pore size was utilized in HIC-HPLC. Using buffers A (1.2 M Na_2SO_4, , 25 mM Na_3PO_4) and B (50 mM

sodium phosphate, 5% 2-propanol), samples were added to 1.5 M $(NH_4)_2SO_4$ and then eluted. Varian 9070 fluorescence detector was used to detect proteins at excitation wavelengths of 232 nm and release wavelengths of 334 nm. To describe the tissue architectural characteristics, nine criteria were developed: gland roundness, nuclear grade, clefts, lumen/gland ratio, stromal reaction, cell gland continuity, separation, and Gleason score.

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3.2 Statistical analysis

We applied generalized linear models to assess tissue and health characteristics, accounting for baseline age, family background of prostate cancer, and race [40] We assessed tissue inflammation by evaluating prevalence (e.g., any core with inflammation), extent (e.g., percentage of tissue area with inflammatory response), and intensity scores for chronic inflammation. Logistic reversion was applied to evaluate OR and 95% CI for the interaction between inflammatory signs and prostate cancer, with adjustments made for BMI, smoking, and diabetes [41] [42]. To account for potential detection bias, we analyzed PSA levels at biopsy and conducted repeated analyses with lower PSA concentrations and under specific biopsy conditions [43] [31].

4. Results and discussions

The measure of selected metals (Fe, Sn, Co, Cu, Mg, Cr, Ni, and Cd) in prostate tissues of carcinoma patients were compared with those in healthy donors/controls. The analysis focused on their distribution, correlations, and multivariate apportionment. Metal levels were reported in units of µg/g, wet weight.. Apart from the overall distribution, the chosen metal is also assessed for differences according to gender, dietary preferences, and tobacco usage.

Current study involved males as the substantial donors; male subjects patients and controls were 73%. Out of the 48 male subjects included in this study, 7% were the smokers. The odds ratios for reporting the majority of classical symptoms were significantly higher in patients with more severe hyperthyroidism. Weight increase, palpitations, and neck enlargement were more common in men than in women, whereas other symptoms showed similar patterns in both sexes.

On the average basis, the prostate tissue of arthritis patients unveiled the following decreasing trend of metal levels: Fe > Calcium> Magnesium > Hg > Zinc> Co > Chromium > Cu > Mg > Cadmium.

The concentration spread in the cases of Calcium, Mg, Iron, and Hg was observed to be relatively large. A more typical distribution pattern was seen for several metals (Cobalt, Cr, Copper, Mg, and Zinc), which were bolstered by relatively low SE and SD standards. In the prostate tissue of normal presenters, following decreasing order was seen in the selected metals average concentrations : Ca, Fe, Mg, Hg, Cr, Co, Cu, Mg, and Cd.

The prostate tissues of patients showed significantly different fluctuations in specific metal proportions compared to controls, suggesting that the distribution of certain metals depends on the health status of the subjects. Most metals exhibited similar distributions, except for Cd, Mg, and Cr, which showed slight variations. Notable positive connections were observed between Cr-Magnesium (r= .547), Calcium-Mg (r= .516), Copper-Mg (r= .426), Cu-Magnesium (r= .412), Copper-Cr (r= .351), Cd-Magnesium (r= .349), and Mg-Mg (r= .341). In contrast, Cd-Zn (r= - .380) demonstrated a significant negative connections.

An accumulation of the chosen metals in the patients prostate tissue was shown by an apparent positive connection between the selected metals and macronutrients.Strong correlations were noted between following metal pairs; Calcium-Mg (r= .753), Calcium-Mg (r= .677), Mg-Magnesium (r= .620), Cr-Calcium (r= .600), Mg-Cr (r= .580), and Cr-Magnesium (r= .579). Some other significant correlations were recorded for Cr-Cd (r= .468), Cd-Magnesiun (r= .481), Iron-Cd (r= .355), Co-Iron (r= .328), Cobalt-Mg (r= .315) and Fe-Magnesium (r= .308). The remaining metal pairs showed very little evidence of a positive or negative association.

The average intensities of Ni, Iron, Hg, Zn, and Cr were significantly raised in prostate tissues. However, the levels of Co, Magnesium, and Cd were particularly raised in the prostate tissues of patients compared to other donor groups. When comparing the prostate tissues of both patient groups to controls, PCA and CA indicated that toxic metals interfere with the normal physiological and metabolic functions of essential metals.

In the selected metals, Nickel, Iron, Cobalt, and Hg were relatively raised in the prostate tissues of vegetarian patients, though the average intensities of the other metals (Copper, Zn, Mg, Cd, and Cr) were nearly the same in both vegetarian and non-vegetarian patients. In the prostate tissues of non-vegetarian patients, Mg and Cd levels were nearly identical, while Zn and Cu levels were slightly higher.

The prostate tissues of vegetarian controls had significantly greater average concentrations of Zn, Hg, and X, whereas the prostate tissues of non-vegetarian controls had significantly higher average concentrations of Fe, Ni, and Co. Patients who did not smoke had considerably higher amounts of Fe, Ni, Cr, and Hg in their prostate tissues, whereas patients who smoked had higher levels of Fe. Almost comparable levels in the prostate tissues of smokers and non-smokers of the patients were noted for Cu, Co, Mg and Cd . Prostate tissues from smokers had greater levels of Co, Fe, Cr, Ni, Hg, and Cd, but there were negligible variations in Cu, Mg, and Zn.

5. Conclusion

In patients, a notable accumulation of particular metals in the prostate tissue such as Mercury (Hg), Iron (Fe), and Nickel (Ni) indicates elevated levels of certain macronutrients. A comparison of hypothyroid patients with hyperthyroid patients showed lower levels of harmful metals in the latter. Intricate interactions between different metals, e.g., calcium-chromium, Magnesium-calcium may impact cancer stringency. This study highlights a relatively higher concentration of toxic metals in vegetarian patients than in non-vegetarians, illustrating the dietary influence. Depending on the impact of metal exposure on gene expression, a predictive model is developed to observe the cancer stringency.

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