Original Article

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Thyroid function test evaluation in prostate cancer patients in Khartoum State

Abdallah Eltoum Ali[1], Sejood Eshag Mohamed Abdalla[1], Ibrahim Ahamed Ali Karti[2], Haidar Eltayeb Saleh[3]

[1]Department of Clinical Chemistry, Faculty of Medical Laboratory Sciences, Al Zaiem al Azhari university, Khartoum, Sudan. [2]Program of Medicine, Alofoug College of Science & Technology, Khartoum, Sudan. [3]Sylvester Comprehensive Cancer Center (SCCC) Clinical Research Laboratory Services, Miami University, Miami FL 33136, USA.

ABSTRACT

Background: Thyroid hormones (TH) are key regulators of essential cellular processes, including proliferation, differentiation, apoptosis, and metabolism. They play an important role in the development of prostate cancer (PCa). Therefore, this study aimed to assess thyroid function tests among PCa patients in Khartoum State. **Methods**: The study comprised 100 male participants, including 50 PCa patients as a case study and 50 healthy men as the control group. Blood samples were collected for thyroid function test and prostate-specific antigen (PSA) using Tosoh™ device (China) and enzyme-linked immunosorbent assay (ELISA) using the device Fortress™. **Results**: Statistical analysis of the test results of the case study demonstrated mean and standard deviation (SD) ± PSA = (31.8 ± 12.5 nmol/l), triiodothyronine (T3) = (3.3 ± 1.3 nmol/l), thyroxine (T4) = (119.58 ± 46.21 nmol/l), and thyroid-stimulating hormone (TSH) = (4.6 ± 3.4 nmol/l). At P-value 0.0001, when compared to the control group, the frequencies among the case study participants for hyperthyroidism, euthyroidism, and hypothyroidism were 33 (66%), 14 (28%), and 3 (6%), respectively. **Conclusions**: Hyperthyroidism is the most common thyroid disorder among patients with PCa.

Keywords: Prostate cancer (PCa), thyroid hormones (TH) namely T3, T4, TSH, and prostate-specific antigen (PSA)

Corresponding author: Abdalla Eltoum Ali. E-mail: abdalla.ali2087@yahoo.com . Tel: +249912375933

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INTRODUCTION

Prostate cancer develops when the rates of cell division exceed those of cell death, leading to uncontrolled tumor growth. Following the initial transformation event, further mutations of a multitude of genes, including the genes for retinoblastoma, can lead to tumor progression and metastasis. Most prostate cancers are adenocarcinomas.[1-3] Triiodothyronine (T3) and its prohormone thyroxine (T4) are hypothesized to promote carcinogenesis through their important roles in cell differentiation, growth, and metabolism.[4] These hormones also promote tumor-induced angiogenesis[5] and have been shown to increase prostate cancer cell proliferation in vitro.[6,7] Thyroid-stimulating hormone (TSH) is produced by the anterior pituitary gland to regulate T4 secretion from the thyroid and is an important laboratory measure for determining thyroid status.[8] In individuals with normal thyroid function, T4 and TSH act in a negative feedback loop[5]; thus, a

hypothyroid state is defined as having low T4 but high TSH, and hyperthyroid status is defined as having high T4 but low TSH.[9] It is hypothesized that hypothyroid men may be at a decreased risk of prostate cancer, whereas hyperthyroid men may have an increased risk. Serum PSA measurement has been widely used in screening (early detection), diagnosis, and monitoring of treatment response in various stages of PCa.[4] A major disadvantage of PSA-based PCa detection is the considerable number of false positive results that occur; many patients undergo unnecessary prostate biopsy procedures due to the false positive elevation in the serum PSA level. Various diagnostic and therapeutic procedures, as well as benign and physiological conditions, have been shown to increase serum PSA concentrations (2-7).[10] The intricate connection between the prostate and thyroid gland is widely recognized. Although it has been established that thyroid hormone regulates thyrotropin-releasing hormone levels in the male reproductive system, including the prostate, the direct impact of thyroid hormones on the prostate remains uncertain. This study assessed the association between serum T3 levels and the risk of recurrence in patients treated for localized PCa.[11]

MATERIALS AND METHODS

Study Group: A cross-sectional study was conducted at Khartoum Oncology and Isotopic Treatment Hospital. Fifty patients diagnosed with prostatic cancer PCa were taken aged 26-66 years as cases , with an additional 50 healthy men as controls.

Inclusion criteria and exclusion criteria: The study on thyroid function test evaluation in Prostate Cancer PCa patients included criteria comprised males diagnosed with PCa, patients undergoing thyroid function tests, and a minimum age requirement(18 yers). Exclusion criteria included females, patients with a history of thyroid disorders or thyroid surgery, and individuals on medications that may interfere with thyroid function.

Ethical consideration: The study was revised and approved by the ethics and scientific committee of the Faculty of Medical Laboratory Sciences, Al Zaiem al Azhari University. Samples were taken with verbal consent from the patients or their relatives.

Data collection: The data collection was carried out using a single, well-constructed questionnaire. The questionnaire included parameters such as age, gender, and duration of the disease to ensure comprehensive and accurate data collection.

Collection of specimens: Venous blood samples were collected by using sterile, dry, plastic syringes and a tourniquet to make the veins more prominent. The puncture sites were cleaned with 70% ethanol and 5 ml of blood collected in lithium heparin containers. The lithium heparin blood samples were centrifuged at 4000 rpm to obtain the plasma and then stored at -4 degrees Celsius until the analysis.

Measurement of biochemical parameters: Whole blood samples were collected in heparinized blood containers, and plasma was used for measurement of thyroid function test to determine T3, T4, TSH, and prostate-specific antigen (PSA) using Tosoh™ device (China) and enzyme-linked immunosorbent assay (ELISA) using the device Fortress™. Thyroid function tests are designed to distinguish hyperthyroidism and hypothyroidism from the euthyroid state. To accomplish direct measurements of the plasma level of hormones, the TSH ELISA test on the principle of solid phase enzyme-linked immunosorbent assay is carried out,which utilizes a unique monoclonal antibody directed against a distinct antigen determinant on the intact TSH molecule.

Normal Range: T3 (1.3–3.1 nmol/l), T4 (63–141 nmol/l), TSH (0.5–5 nmol/l).

PSA: Normal (0–4), Border (4–10).

Data analysis Statistical analysis of the results was performed using the Statistical Package for Social Sciences (SPSS) version 15.0 for Windows. A Student's t-test was used to assess the significance of differences between groups, and a Pearson's correlation test was performed to determine the relationship between variables, with the r-value reported as the correlation coefficient. A p-value less than 0.05 was considered statistically significant. Pearson's correlation, also known as Pearson's correlation coefficient, is a statistical measure of the strength and direction of the linear relationship between two variables. It is denoted by the letter "r." **Range of Values:**

The Pearson correlation coefficient ranges from -1 to +1.

An r-value of +1 indicates a perfect positive linear relationship.

An r-value of -1 indicates a perfect negative linear relationship.

An r-value of 0 indicates no linear relationship between the variables.

RESULTS

This case-control study involved 50 professionally diagnosed patients with PCa as the case group.

Measuring PSA as well as Thyroid Function Test (TFT) among the case and control groups showed a greater elevation of each parameter (T3, T4, TSH, and PSA) among the case than in the control group, with significant differences when data for both groups were compared using the p-value at <0.000 (see Table 1).

The mean+SD age of the participants was 66.5±6.52 years, with a group of 50 healthy men set as the control group. The patients were recruited from Khartoum Oncology Hospital, with most of them (56%) originating from the West , followed by Middle (22%), North (18%), and South (4%) of Sudan. .

Pearson's correlation showed a negative association between all measured parameters (T3, T4, TSH, and PSA) and the patient age and disease duration. The only significant difference was obtained with TSH, with duration p-value at <0.05 (see Table 2).

Positive correlation of PSA and TFT with T3 and TSH was observed with a significant difference, while a negative correlation was obtained with T4 with no significant difference (see Table 3; Figures 2, 3, and 4).

Most of the patients suffered from hyperthyroidism (66%) due to increased production of T3 and T4 from the thyroid gland and decreased production of TSH from the pituitary gland. A significant percentage (28%) of the patients had normal thyroid functions, while 3% had hypothyroidism (see Figure 1). The comparison of the mean levels of TFTs and PSA and p-value 0.00 in hyperthyroidism patients is shown in Table 4.

Table 1: Comparison of mean levels of TFTs and PSA among study groups

	Case group N=50	Control group N=50	p-value
T3 nmol/l	3.3 ± 1.3	1.6 ± 0.67	0.000
T4nmol/l	119.58 ± 46.21	101.6 ± 17.95	0.045
TSH nmol/l	4.6 ± 3.4	1.7 ± 0.7	0.000
PSA nmol/l	31.8 ± 12.5	1.85 ± 2.1	0.000
p-value less than 0.05 was considered statistically significant			

Table 2: Correlation of age and duration of disease with TFTs and PSA

Parameters	Values	Age	Duration
T3	R	-0.033	-0.117
	P	0.819	0.418
T4	R	-0.092	-0.024
	P	0.526	0.870
TSH	R	-0.051	-0.317*
	P	0.725	0.025
PSA	R	-0.109	-0.259
	P	0.452	0.070
r=Pearson's correlation between 1 and -1			

Table 3: Correlation of PSA with TFTs

Variable		T3	T4	TSH
PSA	Pearson's correlation	0.343	0.033	0.280
	p-value	0.007	0.803	0.029

Table 4: Comparison of mean levels of TFTs and PSA and p-value in hyperthyroidism patients

Variable	Hyperthyroidism N=33	Control group N=50	p-value
T3	3.1 ± 1.0	1.6 ± 0.67	0.000
T4	139.8 ± 15.4	101.6 ± 17.95	0.000
TSH	0.4 ± 0.1	1.7 ± 0.7	0.000
PSA	12.3 ± 10.4	1.85 ± 2.1	0.000

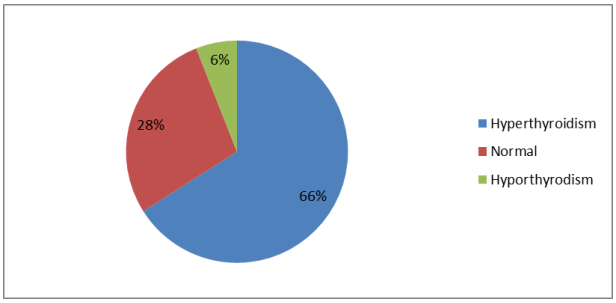

Figure 1: Frequency of thyroid disorders among case group

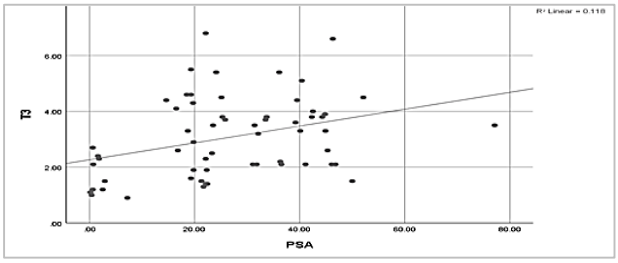

Figure 2: Correlation between PSA and T3 among case studies (p-value=0.007, r=0.34)

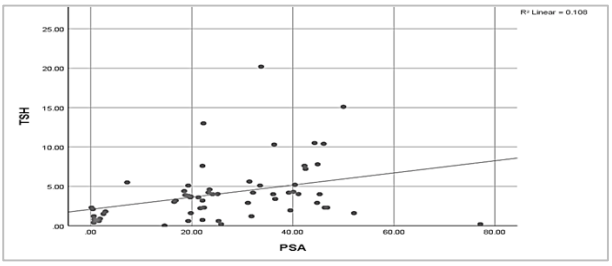

Figure 3: Correlation between PSA and TSH among case studies (p-value=0.029, r=0.282)

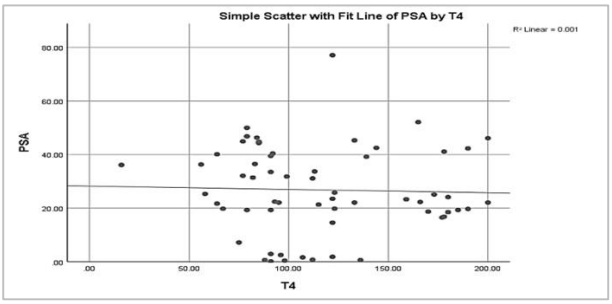

Figure 4: Correlation between T4 and PSA among case studies (p-value=0.803, r=0.001)

DISCUSSION

Prostate cancer arises from an imbalance between cell division and cell death, leading to unchecked tumor growth. Genetic alterations, such as those affecting the retinoblastoma gene, can drive further tumor progression and metastasis. Adenocarcinoma is the predominant form of prostate cancer. Prostate-specific antigen (PSA) is a key biomarker used in the screening, diagnosis, and monitoring of prostate cancer, initially believed to be specific to the prostate and elevated in benign conditions. While thyroid hormone is known to influence thyrotrophic-releasing hormone levels in the male reproductive system, including the prostate, the direct impact of thyroid hormones on the prostate remains unclear. They assessed the connection between serum T3 levels and the probability of recurrence.[12] Nearly every tissue in the body is observed to develop, differentiate, and grow in response to thyroid hormones.[13] According to Bilek et al.,[14] the thyroid gland and the rat ventral prostate have a close association. The direct impact of thyroid hormones on the prostate is still unknown, despite the fact that thyroid hormone is widely known to modulate thyrotropin-releasing hormone levels in the male reproductive system, including the prostate.[15] In patients receiving treatment for localized PCa, Lehrer et al. examined the association between serum T3 levels and the likelihood of recurrence in patients receiving treatment for locally advanced prostate cancer, assessing the connection between these levels and the probability of recurrence .They classified the 68 individuals in their study into three risks, namely identified, moderate, and high risk. In the present study, patients diagnosed with PCa were set as case group. In measuring PSA as well as TFT, the case group showed a greater elevation of each parameter than in the control group with a significant difference, indicating the need for additional research to further investigate the relationship between evaluation of TFTs and PCa. The inclusion criteria for the research could also involve patients with confirmed cases of hyperthyroidism. This would allow for a more focused analysis on how this specific thyroid disorder may increase the risk of developing PCa. A prospective cohort study of a community-dwelling population in Western Australia between the ages of 25 and 84 found some agreement. Tests, including the TSH and free thyroxin (FT4), were performed on the archived. Along with the 41 prostate malignancies, other cancers were also included. In a previous study, a significant association was observed between lower thyroid-stimulating hormone (TSH) levels and a decreased risk of PCa (P = 0.005); conversely, higher levels of FT4 were associated with an increased risk of PCa (P = 0.009).[17] Middle-aged males with benign prostatic hyperplasia were given hormones hormones such as testosterone and dihydrotestosterone. 4o

. In another study on FT4 and TSH, the FT4 quartile demonstrated a large increase whereas no statistically significant difference was seen with regard to TSH.[18] A previous study also found an association between thyroid hormones and the pathophysiology of several cancer forms.[19] The results from case-control and population-based studies were inconclusive in determining the link between thyroid hormones and

cancer. Numerous pieces of evidence pointed to an increased risk of various solid tumors in people with asymptomatic and clinical hyperthyroidism.[19] The results of a study agreed that there is a link between thyroid hormones and PCa case-control.[20] According to our research, elevated serum PSA levels were related to higher serum T3, T4 levels and low serum TSH levels, as well as physiological interactions between thyroid hormones and PSA levels. Thyroid hormones, including T3 and T4, play a role in regulating the metabolism and growth of cells, including prostate cells. Thyroid hormones are known to influence the production and activity of PSA, a protein produced by the prostate gland. Low levels of TSH, which is indicative of high levels of T3 and T4, may be associated with increased cell proliferation in the prostate, leading to higher PSA production. This relationship between thyroid hormones and PSA levels has been suggested in some studies, although the exact mechanisms are not fully understood, and further research is needed to establish a definitive link.[21-23]

Previous research demonstrated lower serum TSH and greater serum T3 levels in men with benign prostatic hyperplasia and PCa. Additionally, a number of factors are known to affect PSA, the most widely used being biomarker, which is used for the diagnosis of PCa.[24] Increased T3 levels have been linked to a number of markers of PCa histopathological aggressiveness, according to a prior study.[25] According to new endocrinological guidelines,[26] men with clinical or subclinical hypothyroid status had a lower chance of developing PCa than men with normal thyroid function.[27] The present study found that males with the highest TSH levels (which indicate a hypothyroid state) had a decreased risk of developing PCa. These results are in line with earlier laboratory and epidemiologic evidence supporting the influence of thyroid hormones on the PCa incidence.[28-30] Another cross-sectional investigation had similarly revealed that PCa cases had more circulating T3 than controls.[31] The association between thyroid hormones or status and incidence of PCa was only explored in two prospective studies.[32,33] One study found that males who self-reported with thyroid disease had a higher chance of developing PCa,[32] but this study did not distinguish between hypothyroid and hyperthyroid conditions. TSH concentration and risk were found to be negatively correlated in the other study, which looked at circulating thyroid hormone levels and PCa (advanced cases were not looked at individually)[33]. T4 and TSH were observed to interact negatively in individuals with normal thyroid function.[8] Accordingly, a hypothyroid state is characterized by low T4 and high TSH, and a hyperthyroid state by high T4 and low TSH. Indeed, T4 and T3 binding to the plasma membrane receptor integrin avb3 stimulates several pro-carcinogenic pathways, including PI-3K and MAPK/ERK1/2, and boosts cell proliferation and angiogenesis, which is a well-known biological mechanism via which this may occur in case of prostate cancer .[5] Importantly, integrin avb3 has been linked to the spread of PCa.[34] Nearly every tissue in the body develops, differentiates, and grows in response to thyroid hormones.[13] The direct impact of thyroid hormones on the prostate is still unknown, even though it is widely known that thyroid hormone modulates thyrotropin-releasing hormone levels in the male reproductive system, including the prostate.[15] According to Lehrer S et al.,[16] hypothyroid men may be at a decreased risk of PCa, whereas hyperthyroid men may have an increased risk. In the current study, most of the patients (66%) had secondary hyperthyroidism, Hyperthyroidism is associated with an increased risk of specific diseases, such as cardiovascular diseases, osteoporosis, and certain cancers, including prostate cancer (PCa). Elevated thyroid hormone levels may influence the growth and metabolism of prostate cells, potentially leading to an increased risk of prostate cancer.

CONCLUSIONS

According to our findings, elevated serum PSA levels were linked to decreased serum TSH and elevated serum T3 and T4 levels. The study also found that hyperthyroidism is more common than hypothyroidism among patients with PCa. Although the mechanism of how thyroid hormones affect patients with prostate cancer is still unknown, further research are needed to corroborate the results of our study.

Informed Consent: All participants provided informed consent.

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