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Evaluation of some Renal Biomarkers, Interleukin-4 and Troponin Among Patients with Prostate Cancer Attending Chukwuemeka Odumegwu Ojukwu University Awka

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Abstract

Background: *Prostate cancer and benign prostatic hyperplasia (BPH), Common in aging men with overlapping clinical features, have been increasingly linked to renal dysfunction and inflammatory responses, underscoring the need to assess different markers alongside traditional prostate-specific antigens for improved diagnosis and disease monitoring.*

Study design: This study aimed to evaluate and compare the levels of Total Prostate-Specific Antigen (TPSA), Free PSA (FPSA), Troponin I and T, Interleukin-4, and renal function markers in patients with prostate cancer, BPH, and healthy controls. A total of three groups were studied: prostate cancer patients, BPH patients, and age-matched healthy controls.

Result: The mean serum levels of TPSA, FPSA, Troponin I and T, and Interleukin-4 were significantly elevated in both prostate cancer and BPH patients compared to the controls ($P < 0.05$). Additionally, serum creatinine, urine microalbumin, urine creatinine, albumin-creatinine ratio (ACR), and Cystatin C were significantly higher in prostate cancer patients than in controls ($P < 0.05$), but not significantly different in BPH patients compared to the prostate cancer group ($P > 0.05$). Strong positive correlations were observed between TPSA and Cystatin C, ACR, and microalbumin, as well as between microalbumin and ACR ($P < 0.05$). However, no significant correlation was found between serum creatinine and either Cystatin C or microalbumin.

Conclusion: *These findings suggest that renal and inflammatory biomarkers, particularly Cystatin C and ACR, may offer additional value in prostate cancer assessment beyond conventional PSA testing.*

Keywords: Prostate cancer, Benign prostatic hyperplasia, TPSA, Cystatin C, Microalbumin, Biomarkers, Inflammatory markers

Introduction

Prostate cancer (PCa), a malignant tumor of the prostate gland, is a major public health issue among men worldwide, especially in aging populations. Prostate cancer is the most common cancer among men in Africa, with Nigeria recording the highest number of deaths, 8,382 out of 14,334 cases (58.5%) in men aged 0-84 years. Benign prostatic hyperplasia (BPH) accounts for 78.3% of prostate-related diagnoses, increasing in prevalence from 20% at age 40 to 90% by age 80, while prostatic adenocarcinoma makes up 92.4%-96.7% of all malignant prostate tumors [1]. This rising incidence is due to late presentation and limited screening infrastructure. Though BPH does not metastasize like PCa, both conditions often present with similar lower urinary tract symptoms, making early and accurate diagnosis challenging [2, 3].

Obstruction from prostate enlargement-either due to BPH or

PCa-can lead to bladder dysfunction and renal complications. Chronic urinary obstruction may contribute to the development of acute kidney injury (AKI) and progress to chronic kidney disease (CKD) if undetected. This underscores the clinical importance of assessing renal function in men with prostate disorders. Early diagnosis through sensitive renal markers could improve patient outcomes and help prevent irreversible kidney damage [4, 5].

Cystatin C, a cysteine protease inhibitor filtered by the glomeruli and catabolized in the proximal tubules, has become a sensitive biomarker for glomerular filtration rate (GFR). It may rise earlier than creatinine in cases of renal impairment and is less affected by age or muscle mass. Cystatin C also has emerging relevance in oncology, where it may function as either a tumor suppressor or promoter, depending on the cancer type [6, 7].

Recent investigations by Wegiel et al. and Jiborn et al. reported downregulation of Cystatin C (Cys-C) in prostate cancer (PCa) tissue samples [8,9]. In contrast, other studies have shown that serum Cys-C levels may differentiate PCa from BPH and serve as a potential marker for monitoring treatment response in metastatic PCa, particularly in patients receiving zoledronic acid. Overall, the literature presents conflicting evidence regarding the role of serum Cys-C in malignancy prediction, highlighting ongoing debate about its reliability and clinical utility in cancer detection [10, 11].

Troponin I and T, while widely used to detect cardiac injury, have shown emerging links to systemic inflammation in malignancies, while Interleukin-4 (IL-4), an anti-inflammatory cytokine, may reflect immune dysregulation in prostate cancer [12, 13].

Non-invasive biomarkers such as urinary microalbumin and creatinine are also valuable for detecting early renal injury [14]. Microalbuminuria, an early indicator of glomerular damage and systemic inflammation, is elevated in prostate cancer. The albumin-to-creatinine ratio (ACR) offers a standardized way to evaluate renal function in random urine samples [14, 15, 16].

Despite their potential, these markers are under-researched in African populations, including Nigeria, creating a gap in early detection and disease monitoring in prostate cancer and BPH patients. Previous studies at COUTH have not evaluated renal status or assessed Cystatin C and microalbumin (MALB) levels in prostate cancer and benign prostatic hyperplasia.

This study aims to evaluate renal biomarkers (Cystatin C, urinary microalbumin, creatinine), along with Interleukin-4 and Troponin I, in prostate cancer patients attending Chukwuemeka Odumegwu Ojukwu University Teaching Hospital, Awka. It also seeks to compare these findings with those from BPH patients and healthy individuals. By identifying early physiological and renal changes associated with prostate diseases, the research intends to contribute to improved diagnostic strategies, reduce renal complications, and enhance clinical management of prostate conditions in Nigeria.

Methodology

Study Design and Area

This study adopted a comparative cross-sectional design to evaluate selected renal biomarkers (Cystatin C, microalbumin, creatinine), Interleukin-4 (IL-4), and Troponin I & T among patients diagnosed with prostate cancer, benign prostatic hyperplasia (BPH), and a control group of apparently healthy individuals. The study was conducted at Chukwuemeka Odumegwu Ojukwu University Teaching Hospital, Awka, Nigeria.

Study Population

This cross-sectional study involved 210 adult male participants aged 40 years and above, including 70 with benign prostatic hyperplasia (BPH), 70 with prostate cancer (PCa), and 70 age-matched healthy controls. Subjects were selected through a convenient sampling method, and relevant clinical information was obtained from their medical records.

Participants were categorized into three groups:

1. Prostate Cancer Group – Individuals with histologically confirmed prostate cancer.
2. BPH Group – Individuals diagnosed with benign prostatic hyperplasia based on clinical and radiological findings.
3. Control Group – Healthy males with no clinical or laboratory evidence of prostatic or systemic disease.

Eligibility required participants to be male and aged ≥40 years. Exclusion criteria included individuals with a history of chronic illnesses such as diabetes mellitus, cardiovascular disease, liver or kidney disease, and any malignancy other than prostate cancer. Also excluded were those undergoing chemotherapy or radiotherapy, recent infections, or use of anti-inflammatory medications.

Sample Size Determination

The minimum sample size was determined using G*Power statistical software, with an effect size of 0.35, power of 80%, and a significance level of 0.05. A total of 180 participants (60 per group) was calculated, and this was increased to 210 participants (70 per group) to accommodate potential attrition.

Ethical Consideration

Ethical approval was obtained from the Chukwuemeka Odumegwu Ojukwu University Teaching Hospital Ethics Committee. Written informed consent was obtained from all participants after providing full details about the study's purpose, procedures, and confidentiality measures.

Sample Collection and Preparation

Each participant provided a 5 mL fasting venous blood sample, collected under aseptic conditions. The samples were allowed to clot, centrifuged at 3000 rpm for 10 minutes, and the serum was separated and stored at −20°C until analysis.

Additionally, 10 mL of midstream, clean-catch morning urine was collected in sterile containers. A preservative (0.02% sodium aside) was added to prevent bacterial growth. Urine samples were stored at 4°C if analyzed shortly or frozen for delayed analysis.

Laboratory Analysis

- Cystatin C levels were analyzed using the immunoturbidimetric method on a Roche Cobas 8000 analyzer, using reagents from BioSino Bio-Technology & Science Inc., Beijing, China [10].
- Total PSA and Free PSA were determined by sandwich enzyme immunoassay [17].
- Urea and creatinine were determined by the modified Urease–Berthelot and Jaffe-Slot alkaline picrate methods, respectively [18].
- Urinary microalbumin was measured by the immunoturbidimetric method, and urinary creatinine was determined using the Jaffe colorimetric method [19, 20].
- Interleukin-4 (IL-4) was evaluated using enzyme-linked immunosorbent assay (ELISA) kits standardized for human cytokine measurement [13].
- Albumin-to-Creatinine Ratio (ACR) was calculated as: ACR = urine albumin (mg/L) ÷ urine creatinine (mmol/L).
- Troponin I and T levels in serum were analyzed using high-sensitivity chemiluminescent immunoassay, following the manufacturer's protocol [13].

All laboratory analyses were conducted in duplicate, and standardized protocols with internal and external quality controls were strictly observed. Laboratory personnel were blinded to participant groupings to reduce observer bias.

This study was limited by its single-center and cross-sectional design, which may affect generalizability and preclude the observation of temporal trends in biomarker levels. Furthermore, subclinical or undiagnosed conditions in the control group may have introduced unrecognized biases.

Data Analysis

Data were analyzed using SPSS version 25. Descriptive statistics, including mean and standard deviation, were computed for biomarker levels. One-way Analysis of Variance (ANOVA) was used to compare mean values across the three groups, followed by post-hoc multiple comparison tests where applicable. Pearson's correlation analysis was performed to explore relationships between biomarkers. A p-value < 0.05 was considered statistically significant.

Result

The mean levels of **Total Prostate-Specific Antigen (TPSA)**, **Free Prostate-Specific Antigen (FPSA)**, **Troponin I and T**, and **Interleukin-4** were significantly elevated in patients with **prostate cancer** and **benign prostatic hyperplasia (BPH)** compared to the control group (**P < 0.05**), as presented in **Table 1**.

This suggests that these biomarkers may be useful indicators of prostate-related pathologies.

Furthermore, the mean levels of **urine microalbumin**, **urine creatinine**, **albumin-creatinine ratio (ACR)**, **serum creatinine**, and **Cystatin C** were significantly higher in prostate cancer patients when compared to the control group (**P < 0.05**), as shown in **Table 2**.

However, in patients with **BPH**, the levels of **urine microalbumin**, **urine creatinine**, and **ACR** were not significantly different from those observed in prostate cancer patients (**P > 0.05**). This indicates that while these markers are elevated in prostate cancer, they may not effectively distinguish between prostate cancer and BPH.

A strong positive correlation was observed between **TPSA and Cystatin C** ($r = 0.868$, $p = 0.000$), **TPSA and ACR** ($r = 0.838$, $p = 0.000$), **TPSA and microalbumin** ($r = 0.786$, $p = 0.001$), and **microalbumin and ACR** ($r = 0.789$, $p = 0.002$) across the three study groups, which included prostate cancer patients, individuals with BPH, and healthy controls, as illustrated in **Table 3**. These findings suggest a potential interrelationship between TPSA, renal function markers, and disease progression.

In contrast, no significant correlation was found between **Cystatin C and serum creatinine** ($r = 0.268$, $p = 0.106$) or between **microalbumin and serum creatinine** ($r = 0.178$, $p = 0.456$). This lack of association suggests that while Cystatin C and microalbumin may serve as independent markers, they do not necessarily correlate with serum creatinine levels in this patient population.

Table 1: Mean ± standard deviation concentrations of serum Troponin I, Troponin T, Interleukin-4, TPSA, and FPSA in people with prostate cancer, Benign prostate hypertrophy, and healthy male subjects (control)

	Troponin I (ng/ml) Mean ± SD	Troponin T (ng/ml) Mean ±SD	Interleukin 4 (pg/ml) Mean ±SD	TPSA (ng/ml) Mean ±SD	FPSA (ng/ml) Mean ±SD
Prostate Cancer N = 70	0.084 ± 0.025	0.061 ± 0.03	4.58 ± 1.3	47 ± 15.9	5.9 ± 1.7
Benign Prostate Hypertrophy (BPH) N = 70	0.046 ± 0.012	0.031 ± 0.006	2.5 ± 0.74	6.8 ± 1.5	3.4 ± 1.2
Healthy Male Subject N = 70	0.017 ± 0.006	0.006 ± 0.003	1.0 ± 0.20	0.95 ± 0.32	0.55 ± 0.21
P-Value	P-Value		P-Value		
A V B	0.000*	0.000*	0.000*	0.000*	0.000*
A V C	0.000*	0.000*	0.000*	0.000*	0.000*
B V C	0.000*	0.000*	0.000*	0.273	0.000*

Table 2: Mean ± standard deviation concentrations of serum cystatin C, creatinine, urine Microalbumin, and Creatinine in people with prostate cancer, Benign prostate hypertrophy, and healthy male subjects (control).

	Microalbumin, (mg/L) Mean ±SD	Urine Creatinine (mmol/L) Mean ±SD	Albumin/Creatinine Ratio (ACR) (mg/mmol/l) Mean ±SD	Cystatin-C (mg/L) Mean ± SD	Serum creatinine umol/l) Mean ± SD
Prostate Cancer (A) N = 70	99.7 ± 40	22.7 ± 5.6	4.8 ± 2.7	3.94 ± 1.2	119 ± 11.7
Benign Prostate Hypertrophy (BPH) N = 70 (B)	28.5 ± 9.8	10.9 ± 2.1	2.7 ± 0.82	2.37 ± 0.66	102 ± 16
Healthy Male Subject (C) N = 70	16.8 ± 3.8	9.4 ± 2.3	2.0 ± 0.74	0.99 ± 0.16	81 ± 23
P-Value					
A V B	0.000*	0.000*	0.000*	0.000*	0.043*
A V C	0.000*	0.000*	0.000*	0.000*	0.000*
B V C	0.400	0.662	0.663	0.000*	0.008*

Table 3: Correlation of the level of association between the variables

VARIABLES	R	P - value
TPSA vs cystatin C	0.868	0.000*
TPSA vs ACR	0.838	0.000*
TPSA vs microalbumin	0.786	0.000*
Microalbumin vs serum creatinine	0.178	0.456
Microalbumin vs ACR	0.789	0.002*
Cystatin C vs serum creatinine	0.268	0.106

Discussion

Prostate cancer (PCa) and benign prostatic hyperplasia (BPH) are increasingly recognized as systemic diseases with possible renal and inflammatory involvement beyond the prostate [5]. This study explored renal and inflammatory biomarkers-Cystatin C, microalbumin, creatinine (serum and urinary), ACR, Troponin I and T, IL-4-and their associations with PSA levels in men with PCa, BPH, and healthy controls.

Consistent with previous findings, TPSA and FPSA levels were significantly elevated in both PCa and BPH groups, supporting their established role in prostate disease diagnosis, though their lack of specificity limits differentiation between malignant and benign conditions [4]. To improve diagnostic accuracy, this study integrated renal and inflammatory markers, revealing that IL-4 and Troponins were significantly raised in both PCa and BPH, indicating systemic inflammation and possible cardiovascular stress. These findings align with those of Nguyen et al. and Tommaso et al., but differ from Toriola et al., possibly due to differences in study design and sample characteristics [12].

Renal markers, including microalbumin, serum creatinine, ACR, and Cystatin C, were significantly elevated in PCa compared to controls, suggesting subclinical renal involvement. This is partly in agreement with Ogueze et al., who found elevated BMG and MALB in PCa/BPH, although their observed strong correlation between MALB and ACR across all groups was not replicated in this study.[4] Findings also aligned with Oluboye et al [23]. who reported increased serum creatinine, but contradicted Cox et al [24]. who observed lower Cystatin C levels in PCa. Such discrepancies may result from differences in assay methods, population characteristics, and disease staging.

Interestingly, although urinary microalbumin, urinary creatinine, and ACR were elevated in PCa compared to controls, they did not significantly differ between BPH and PCa groups, suggesting limited utility in distinguishing between these conditions. However, the significant elevations of serum creatinine and Cystatin C in PCa support their potential as indicators of renal involvement in malignancy.

Correlation analysis revealed strong positive relationships between TPSA and Cystatin C, microalbumin, and ACR, suggesting a possible link between prostate pathology and early renal dysfunction. The lack of correlation between serum creatinine and these markers reinforces the utility of Cystatin C and microalbumin as early and sensitive indicators of renal stress, consistent with existing literature on their diagnostic advantages [4].

This study's limitations-including its cross-sectional, single-center design and potential selection bias due to undiagnosed comorbidities in the control group-restrict causal interpretation and generalizability. Nonetheless, the findings underscore the value of integrating renal and inflammatory markers with PSA screening to enhance the diagnostic and prognostic framework for prostate disease.

Conclusion

Combining prostate-specific, renal, and inflammatory markers may improve diagnostic accuracy and early detection of systemic involvement in prostate disorders. Cystatin C and ACR, in particular, show promise as adjunct biomarkers for assessing renal function in prostate cancer. Further multicenter longitudinal studies with larger sample sizes are needed to validate these findings and clarify the mechanisms linking prostate pathology with renal and inflammatory changes.

Conflict of Interest

None

Funding

None

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