



Determination of Prostate Specific Antigen Level among Male Patients with Bacterial Urinary Tract Infections Attending Kuje General Hospital Abuja, Nigeria

Authors

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Abstract

Recent hospital and cancer registry data shows increasing prostate cancer incidence in Nigeria, which was previously regarded as a low incidence region. Prostate cancer is the leading cause of cancer death among men in Nigeria and second most common cancers of men worldwide and sexual history has been a consistent risk factor. Prostate specific antigen (PSA) test is still the single most important test for early detection of prostate cancer worldwide. However, not much is reported about prostate cancer in relation to urinary tract infections in Africa. This study investigates the prevalence of prostate cancer risk in and bacterial urinary tract infections among men in Abuja, Nigeria. One Hundred (100) samples each of blood and urine were collected, from fifty (50) male patients suffering from urinary tract infections and fifty (50) apparently healthy males attending Kuje General Hospital Abuja, Nigeria. All the blood samples were subjected to PSA analysis using Enzyme-linked Immunosorbent Assay procedure (Diagnostic Automation/ Cortez Diagnostics, Inc, USA) while urine analysis (microscopy, culture and biochemical identification) was performed on the urine to isolate and identify the common bacteria associated with urinary tract infections among the study population. Structured questionnaire seeking information on possible socio-demographic and risk factors as well as clinical manifestations was also issued. Results obtained from laboratory analysis and data generated from questionnaires were subjected to statistical analysis. Our findings revealed a prevalence of 24.00% PSA and *Escherichia coli* (64.0%), *Enterococcus spp.*(29.41%), *Klebsiella spp* (18.82%) and *Staphylococcus aureus* (14.12%) were the common bacteria implicated. A significantly higher level ($P=0.02$) of PSA level (34.00%) was observed among patients with UTI than in the apparently healthy group (14.00%). Further stratification by age shows that those in the age group of 60-69 years had the highest level of PSA (45.5%) while the least PSA level was observed in the age group of 30-39 years old (11.1%), and this difference is statistically significant ($P=0.008$). In conclusion, the proportion of men especially young men (30-39 years) with UTI and by extension elevated PSA level is on the increase and given that increased levels of PSA is an important risk factor for prostate cancer, we therefore, recommend early diagnosis and treatment of UTI to avoid complexity on the level of PSA and subsequent development of prostate cancer.

Keywords: Determination, Prostate Specific Antigen, Urinary Tract Infections, Male, KGH, Abuja, Risk factors, Jos.

Introduction

Prostate cancer is a common urological malignancy and an important health challenge among males in Nigeria. The prevalence of prostate cancer is increasing in Africa. Although the exact mechanism of transformation of prostate glands into cancer cells is not clearly understood, there is growing epidemiological evidence suggesting that prostate tissue cells are prone to sexually transmitted and urinary tract infections (Chantal *et al.*, 2014). Currently, the common tools for diagnosis of prostate cancer are prostate specific antigen (PSA) test and digital rectal examination. The combination of both PSA and DRE tests leads to a greater detection of prostate cancer (Saleh Altuwaijiri, 2012).

Prostate specific antigen is a glycoprotein that is mainly produced from prostatic epithelial cells. It liquefies semen and allows sperm to swim freely. Besides this well-known physiological function of liquefying seminal clot, PSA is also involved in tumor growth, invasion and metastasis of prostate cancer (Saleh Altuwaijiri, 2012). In healthy men, PSA can be found at high concentration of 0.2-2.0mg/ml in seminal fluid and low concentration in serum usually less than 4.0ng/ml and the serum concentration increase steadily with advancing age (Ali *et al.*, 2013). Prostate Specific Antigen (PSA) expression is androgen dependent and therefore less sensitive in older population. Obesity has been reported to reduce serum PSA levels, while increase has been found in prostate infection, irritation, benign prostatic hyperplasia (BPH), and ejaculation. Limitations of PSA as a biomarker for monitoring response to therapy have been identified, as increase in serum level not correlating with tumour regression following radiotherapy has been reported in some instances (Karin, 2001)

With contradictory opinions regarding who and when to screen for prostate cancer even in developed countries; or even after knowing who to screen, the choice of appropriate procedure that will be effective in terms of cost, access, level of sophistication and minimal piercing with yet

reliable results is a bigger challenge to prostate cancer eradication strategy (Maurad *et al.*, 2014)). Thus, the use of blood PSA test is used to identify candidates needing prostate biopsy. A blood test to measure PSA is considered the most effective test currently available for the early detection of prostate cancer (Karin, 2001). Being a protease, it appears to be involved in the initiation and growth of prostate cancer by abnormal release of growth factors or proteolysis of growth factors binding proteins. It may also have a role in invasion and metastases through the degradation of collagen and laminin (Anant *et al.*, 2010).

Urinary tract infections can spike PSA level because of the close proximity of the urinary tract with the prostate, the infection can irritate and inflame prostate cells and cause PSA concentration to rise reflecting and innate defense mechanism of the prostate (Saleh Altuwaijiri, 2012).

We hypothesized that men with urinary tract infections will have higher level of serum prostate specific antigen, predisposing them to higher risk of prostate cancer. And to test this hypothesis therefore, we screened men with and without urinary tract infections for the level of prostate specific antigen in Kuje General Hospital Abuja, Nigeria.

Materials and Methods

Study Design

The effectiveness of treatment of prostate cancer largely depends on the stage upon which it was detected. The earlier any sign is detected, the better the chances for effective treatment. We therefore, conducted a case-control study involving 100 men aged 35 years and above attending urinary tract infections unit of Kuje General Hospital, Abuja, Nigeria to determine the association between their UTI status and PSA levels. Their mean age was 54.3 years and slight majority of them were civil servants. Cases (n=50) were those with confirmed bacterial urinary tract infections during their hospital visit. Controls (n=50) were those not diagnosed with bacterial

UTI. Standard questionnaire was administered to consenting participants to obtain information on socio-economic status, clinical manifestations and possible risk factors of UTI and prostate cancer. Blood and urine samples were collected from each of the study participants. The mean time between blood draw and diagnosis was 3 months while urine samples were analyzed immediately after collection.

Ethical Consideration

The protocol for the study was considered and approved by the ethical committee of Kuje General Hospital Review Board.

Sample Processing

Sera were tested for the presence and level of prostate specific antigen using enzyme-linked immunosorbent assay (Diagnostic Automation/Cortez Diagnostics, Inc, USA) and a PSA value of $\geq 4.0\text{ng/ml}$ was regarded as positive while values less than 4.0ng/ml was regarded negative. On the other hand, urine samples were subjected first to urine analysis, microscopy and culture to isolate and identify the commonest bacteria associated with urinary tract infections in male patients. These isolates were identified based on morphological characteristics and biochemical tests. Samples with colony counts of $\geq 10^5$ CFU/mL bacteria were considered significant and therefore positive.

Statistical Analysis

Data generated from questionnaires including background information, clinical information and information on risk factors as well as results obtained from laboratory analysis were entered into statistical package for social sciences version 21 to test for significant difference between variables using chi-square and student t- test. Statistical significance was determined at ($P < 0.05$) at 95% Confidence interval and results were reduced to frequency tables, ratios and percentages.

Results

The overall prevalence of elevated prostate specific antigen ($\geq 4.0\text{ng/ml}$) among men 35 years and above in Kuje General hospital Abuja,

Nigeria was 24.0% with the highest frequency occurring within the age group of 60-69 years 10(45.5%) while the least was observed among those in the age group of 30-39 years old 2(11.1%) as shown in Table 1. Analysis on the correlation between urinary tract infection and PSA level showed significant difference ($P=0.02$) in the level of prostate specific antigen between cases (male patients with UTI) and controls (male patients without UTI) as shown in Table 2. Analysis of the frequently observed clinical manifestations among the participants indicated that although there is no significant relationship between PSA level and frequently observed clinical presentations ($P > 0.05$), difficulty in urination, Abdominal pain and frequent urination were the most frequently observed clinical manifestations (Table 3). Of the major risk factors for prostate cancer and bacterial UTI analysed, significant association was observed between history of urinary tract infection and elevation of prostate specific antigen level ($P < 0.05$). More so, analysis of PSA level in relation to number of sexual partners showed that those who currently had no sexual partners have higher PSA level 3 (60.0%) and those with multiple (≥ 2) sexual partners had strangely less elevation in the level of their PSA 15 (23.4%) as shown in Table 4. The result from urine analysis that is, microscopy, culture and biochemical characteristics showed that the predominant bacteria associated with UTI among the sampled population are *Escherichia coli*, *Enterococcus* spp. *Klebsiella* spp. and *Staphylococcus aureus* as shown in Table 5.

Table 1: Age-related Prevalence of Elevated level of Prostate Specific Antigen (PSA) among men 35 years and above attending Kuje General Hospital Abuja

Age	Number tested	Positive (%)	P Value
30-39	18	2 (11.1)	0.008*
40-49	30	2 (6.7)	
50-59	23	8 (34.8)	
60-69	22	10 (45.5)	
≥ 70	07	2 (28.6)	
Total	100	24 (24.0)	

Key: Significant at $P \leq 0.05$, %=percentage, Positive=PSA value $\geq 4.0\text{ng/ml}$ (normal range=0-3.99ng/ml)

Table 2: Comparison between Urinary Tract Infection and PSA level among men 35 years and above attending Kuje General Hospital Abuja

Cohorts	Number tested	Positive (%)	P Value
Cases	50	17 (34.0)	0.02*
Control	50	07 (14.0)	
Total	100	24 (24.0)	

Key:Key: Significant at $P \leq 0.05$, %=percentage, Positive=PSA value ≥ 4.0 ng/ml (normal range=0-3.99ng/ml)

Cases= Patients with urinary tract infection

Controls= apparently healthy population

Table 3: Prevalence of Elevated PSA in relation to Clinical Manifestation among men 35 years and above attending Kuje General Hospital Abuja

Clinical Manifestations	No. Tested	Positive (%)	P Value
Difficult Urination			
Yes	32	10 (31.3)	0.24
No	68	14 (20.6)	
Total	100	24 (24.0)	
Abdominal Pain			
Yes	25	10 (40.0)	0.03*
No	75	14 (18.7)	
Total	100	24 (24.0)	
Frequent Urination at night			
Yes	38	15 (39.5)	0.25
No	62	9 (13.5)	
Total	100	24 (24.0)	

Key: Significant at $P \leq 0.05$, %=percentage, Positive=PSA value ≥ 4.0 ng/ml (normal range=0-3.99ng/ml)

Table 4: Prevalence of Elevated level of PSA in relation to major Risk Factors among men 35 years and above attending Kuje General Hospital Abuja

Risk factor	No. Tested	Positive (%)	P Value
Occupation			
Civil servant	33	8 (24.2)	0.37
Farmer	16	5 (31.3)	
Trader	18	4 (22.2)	
Unemployed	24	3 (12.5)	
Retiree	9	4 (44.0)	
Total	100	24 (24.0)	
Family History of PCa			
Yes	29	9 (31.0)	0.29
No	71	15 (21.0)	
Total	100	24 (24.0)	
No. of Sexual Partners			
0	5	3 (60.0)	0.34
1	31	6 (19.4)	
2	29	6 (20.7)	
3	15	3 (20.0)	
4	18	6 (33.3)	
5	2	0 (0.0)	
Total	100	24 (24.0)	
History of UTI			
Yes	38	15 (39.5)	0.005*
No	62	9 (14.5)	
Total	100	24 (24.0)	

Key: Key: Significant at $P \leq 0.05$, %=percentage, Positive=PSA value ≥ 4.0 ng/ml (normal range=0-3.99ng/ml), PCa= Prostate cancer, UTI= Urinary tract infections

Table 5: Occurrence of Bacterial isolates in patients with Urinary Tract Infection attending Kuje General Hospital, Abuja

Bacterial isolates	No. of isolates	%
<i>Staphylococcus aureus</i>	12	24.0
<i>Enterococcus</i> spp.	25	29.41
<i>Klebsiella</i> spp.	16	18.82
<i>Escherichia coli</i>	32	64.0
Total	44	88.0

Key: Significant at $P \leq 0.05$, %=percentage, Positive=PSA value ≥ 4.0 ng/ml (normal range=0-3.99ng/ml)

Discussion

From this study, the overall prevalence of elevated prostate specific antigen level (PSA ≥ 40 ng/ml) among men attending Kuje General Hospital was 24.0%. This result agrees with the findings of Ali *et al.* (2013) in Iraq who also conducted similar research and found a prevalence of 28.9% among men aged 36-55 years. This is also similar to findings of Uller *et al.* (1999); Hara *et al.* (2004) and Alex *et al.* (2012) who have found the prevalence rates of 26.0%, 25.0% and 24.0% respectively. However, these men with abnormal PSA are yet to present for prostate biopsy, primarily because they do not understand the need for investigation, especially when they are symptom free. There has been no significant public awareness campaign about prostate cancer in the country and having been told that the prostate is one of the male reproductive glands, irrational fear of impotence resulting from any surgery or procedure in the anorectal region sets in (Ali *et al.*, 2013). The situation, however, is different for a condition like breast cancer where the awareness level has been raised by recent campaign in Nigeria, the breast being more accessible for examination and biopsy, and availability of fine needle aspiration technique, which is less invasive. Until public awareness of the necessity and safety of prostate biopsy is raised enough for symptom free men to accept the procedure for diagnostic purposes, the rate of abnormal PSA will have to serve as a crude index of the prevalence of prostate cancer risk (Ukoli *et al.*, 2003).

In this study bacteriuria (defined as presence of infectious bacteria in the urinary tract) was presented in 50.0% of specimens analyzed. This is similar to 67.2% bacteriuria observed by Ali *et al.* (2013) and 57.1% found by Al-Yassery (2011) in Iraq. The result however, disagrees with the results of Khadhum (2006), who found the prevalence of 8% bacteriuria in general urine examination of patients in Iraq. This difference in findings could be due to the fact that while his population comprised general patients, our study was conducted among men with similar medical need (Urinary tract infection) and while their studies included younger generation who may not yet be exposed to risk factors of UTI. And since it is known that increase in the size of the prostate due to age significantly raises the chances of acquiring bacterial UTI. Clinically, urine analysis that reveals both bacteriuria and pyuria is diagnostic of urinary tract infection (Ali *et al.*, 2013).

On the other hand, the most common bacteria isolated were *E. coli* (37.65%), *Enterococcus* spp.(29.41%), *Klebsiella* spp. (18.82%) and *Staphylococcus aureus* (14.12%) respectively. This result agrees with the findings of Al-Yassery, (2011) who found that the most common bacteria in UTI patients was *E. coli* (40.8%), *Enterococcus* spp. (16.7%), and *Staphylococcus* spp. (2.5%) and Sohail *et al.* (2015) who found that *E. coli* (89.13%) was the most occurring bacteria among UTI patients followed by *Klebsiella* spp. (11.7%) in Jordan. More so, our result also agrees with the findings of Al-Amedi, (2003) which confirmed that *E. coli* was the commonest uropathogen (33.6%) in UTI in Iraqi population. This consistent finding that *E. coli* is the commonest uropathogen among UTI patients may in part be due to the fact that the Pili, capsule and some specific surface protein of *E. coli* may give it the adherence characteristics which confer the bacterium with the ability to adhere to epithelial cells and mucoid membranes lining the urinary tract (Ali *et al.*, 2013). This is because adherence (using adhesive molecules) is a key event in each

step in the pathogenesis of urinary tract infections as UTI typically starts with periurethral contamination by uropathogens residing in the gut, followed by colonization of the urethra and subsequent migration of the pathogen to the bladder, an event that requires appendages of flagella and pilli. In the bladder, the consequences of complex host-pathogen interactions ultimately determine whether uropathogens are successful in colonization or elimination. It may be partly due to their ability to form biofilms that significantly enhances their survival in the urinary tract (Bien *et al.*, 2012).

The current study demonstrated that the number of patients with urinary tract infections (cases) had significantly higher total prostate specific antigen level 17 (34.0%) than those without UTI referred to as control 7 (14.0%), a finding that is consistent with many literature findings that places people with urinary tract infections at far greater risk of having elevated concentrations of prostate cancer. A similar finding was observed by Alex *et al.* (2012) in Barcelona, Spain who reported that PSA levels were significantly higher patients with urinary tract infection 26 (24.0%) than those without UTI 6(11.2%). This is possible because urinary tract infection can cause an increase of PSA level due to the close proximity of urinary tract with the prostate. As such, infection of the urinary tract can irritate and inflame prostate cells and cause PSA level to rise. Also, the increasing PSA level in patients with UTI reflects an innate defense mechanism of the prostate (Ali, *et al.*, 2013). More so, abdominal pain and difficulty in urination are among the most frequently observed clinical manifestation of PSA elevation among the participants and coincidentally are similar clinical findings in urinary tract infections making definitive diagnosis difficult. This is perhaps, part of the challenge being experienced in making specific diagnosis of prostate cancer, PSA level and bacterial tract infections based on clinical presentations.

In conclusion, the finding of this research has shown that elevated prostate specific antigen

concentrations were observed among male patients with urinary tract infections than in those without urinary tract infections, more worrisome, is the fact that PSA levels increased steadily with advancing age. By extension, it could mean that UTI could predispose men to increased chances of prostate cancer. However, this need to be investigated further given that the number of samples in this study is few.

We therefore recommend routine UTI check up and prompt treatment when necessary to minimize the chances of an individual's PSA level going up which may also increase their chances of developing prostate cancer. Furthermore, we recommend definitive diagnosis be made only when clinical findings are combined along with laboratory results as a matter of policy to avoid misleading assumption as evidenced by similarities in critical manifestations from different infections.

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Appendix



**HEALTH AND HUMAN SERVICES SECRETARIAT
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Our Ref:

Your Ref:

Date:.....

11th January, 2017

The Project Supervisor,
UniJos,
Plateau State.

ETHICAL CLEARANCE

We the ethical Committee of Kuje General Hospital has sat and reviewed the proposal of Ogaji Nanbam Danladi Mat No.UJ/2010/NS/0440 from University of Jos department of Microbiology. On the topic bellow.

Determination of Prostate Specific Antigen (PSA) among patients with Bacterial urinary tract infection Attending Kuje General Hospital.

We have agreed that she should proceed with her research work as long as no damage or any injuries will be inflicted on the researched subject.

Sign: 
Hospital Secretary