Clinicopathological Correlates of Patients with Prostate Cancer in a Tertiary Hospital in Northwestern Nigeria

Emmanuel U OYIBO, Mohammed A UMAR, Khalid ABDULLAHI, Sadiq A MUHAMMAD, Peter N AGWU

ABSTRACT

Background: Worldwide, prostate cancer is a common cause of significant morbidity and mortality in ageing men. Digital rectal examination(DRE) and serum total prostate specific antigen(tPSA) are widely used tools for prostate cancer(CaP) screening and diagnosis before transrectal ultrasound (TRUS)-guided prostate biopsy. **Objectives:** This study aimed at finding the clinical, biochemical, radiological and pathological correlates in patients with an enlarged prostate and elevated serum tPSA. **METHODOLOGY**: This is a 12-month cross-sectional study of 80 male patients aged 50 years and above with lower urinary tract symptoms(LUTS), abnormal digital rectal examination and/or elevated PSA greater than 4ng/mL. Aged-matched males were also included as a negative biopsy group with serum levels of tPSA determined using ELISA methods among both groups. Clinical, procedural (TRUS guided biopsy) assessment, transrectal ultrasound-guided biopsies of the prostate for histological characterisation of all patients and Gleason score categorization for prostate in cancer group were done. The relationship between serum tPSA and Gleason score of prostate cancer patients was determined using Spearman's correlation. **Results**: The mean serum total PSA in patients with prostate cancer and the negative biopsy group was 82.93 ± 35.02 and 28.85±30.92 ng/ml respectively. The majority of the patients in the prostate cancer group (90.0%) had suspicious findings on DRE compared to the negative biopsy group (46.2%). There is a positive correlation between serum tPSA and Gleason score in patients with prostate cancer. Serum tPSA levels were significantly lower in the negative biopsy group. The Gleason score pattern of distribution among patients with Prostate cancer showed that the majority had a score greater than 8 and ISUP Grade V. **Conclusion**: Findings of elevated total serum PSA and abnormal digital rectal examinations in patients with an enlarged prostate in our practice are predictive of high Gleason score prostate cancer on TRUS-guided biopsy of the prostate.

Keywords: Clinicopathological, Digital rectal examination, Gleason score, Prostate cancer, Serum total prostate specific antigen (tPSA), Transrectal ultrasound guided biopsy.

OPEN ACCESS

Affiliation
Urology Unit,
Department of Surgery, Usmanu Danfodiyo University Teaching Hospital, Sokoto, Sokoto State, Nigeria.

***Correspondence**
Emmanuel Ugbede Oyibo
Tel: *+2348069669973*
Email: *ugbedeoyibo@gmail.com*

Article Metrics
Date Submitted: 9 July 2022
Date Accepted: 19 Sept 2022
Date Published: Jan-June 2023

Journal Metrics
E- ISSN: *1115-0521*
Website: *www.orientjom.org.ng*
E-mail: *editorojm@gmail.com*

Publisher:
cPrint, Nig. Ltd
E-mail: cprintpublisher@gmail.com

Access to the article
Website: http://www.orientjom.org.ng
: DOI: 10.5281/zenodo.7126985

How to cite this article
Oyibo EU , Umar MA, Abdullahi K, Muhammad SA and Agwu PN. Clinicopathological Correlates of Patients with Prostate Cancer in a Tertiary Hospital in Northwestern Nigeria. Orient J Med, 2023;35(1-2):1-10. DOI:10.5281/zenodo.7126985

INTRODUCTION

Prostate cancer ranks the second most common malignancy in men and the fourth most common cancer in males and females with an estimate of about 1.1 million men diagnosed with this cancer in 2012, and 70% of the diagnoses occurred in developing nations.[1] The incidence of prostate cancer varies worldwide, with the highest rates in Australia, New Zealand, Northern America, and Western and Northern Europe due to the widespread practice of screening for cancer using prostate specific antigen test and then a subsequent prostate biopsy.[2]

In men, prostate cancer is the fifth leading cause of death, and the greatest mortality has been found among men of African descent[1]. However, the 2012 age-standardised incidence rate for prostate cancer estimated for Nigeria was 30.7 per 100,000.[3] Contrary to the World Health Organization reports, several other studies indicate a higher incidence of prostate cancer in Nigerian men. Studies from Northwestern Nigeria suggest that 6.0% of male cancers are due to prostate cancer corroborated by other hospital-based studies from across other geopolitical zones of Nigeria with a rising incidence of 6.2% in certain regions to 16.5% in others.[4-9]

Patients with an enlarged prostate may present with complaints of lower urinary symptoms, necessitating physical examination and digital rectal examination(DRE), serum prostate specific antigen assay which may be elevated often culminating in prostate biopsy to reach a diagnosis and the subsequent need to provide suitable treatment.[7,10-13]

Early detection and improved treatment in patients with cancer of the prostate are associated with declining mortality in most Western and European countries.[14] However, this is contrary to what obtains in developing countries like Nigeria where no institutionalized screening protocol coupled with poor awareness, knowledge and attitude toward the disease.[15-17] Prostate biopsy and histology have remained the gold standard for prostate cancer diagnosis after the detection of an anomaly on the digital rectal examination(DRE) though not the only indication for such procedure. Tumour biomarkers elaborated in the body have played a vital role in the early diagnosis, treatment and follow-up of patients with prostate cancer. These biomarkers may be present in the blood or urine samples of patients and these samples may be obtained with minimal or no complications as the sample collection is minimally invasive. [18]

Since the late 80s, serum prostate specific antigen assay has revolutionized the screening and diagnosing of prostate cancer. Despite the controversies surrounding its application, the introduction of PSA as a screening tool has reduced the rate of diagnosis of advanced disease and mortality from prostate cancer due to earlier detection of apparently asymptomatic stage.[19,20] On the other hand, the Gleason grade and score of the biopsy specimen is an objective assessment of the degree of differentiation of the malignant prostate tissue and has been applied as a surrogate indicator of the aggressiveness of the tumour.[21,22]

METHODOLOGY

The study was a hospital-based prospective cross-sectional study conducted following the approval of the Health Ethics and Research Committee(HERC) of the Usmanu Danfodiyo University Teaching Hospital,Sokoto. It included consecutive patients presenting to the urology clinic of our hospital from March 2019 to February 2020 with clinical, radiological, and biochemical features suggestive of prostate cancer.

The inclusion criteria were patients aged 50 years and above with: elevated PSA and/or Lower urinary symptoms (LUTS), abnormal digital rectal examination (DRE) findings, and/or abnormal TRUS/transabdominal scan findings or those with histologically confirmed prostate cancer before the commencement of treatment.

Those patients who have had a digital rectal

examination in less than a week, a biopsy of the prostate in less than three weeks, urethral instrumentation(urethrocystoscopy) or stones in the urethra or the bladder in less than three weeks, prostate cancer patients on 5α-reductase inhibitor drugs, hormonal or radiation therapy and those who have had the previous prostatectomy for benign prostatic hyperplasia or radical prostatectomy for malignant prostatic conditions were excluded from the study.

The sample size calculation for the prospective cross-sectional study[23] is as follows:

$$n = \frac{\left[Z_{1-\alpha/2}\sqrt{P_0(1-P_0)} + Z_\beta\sqrt{P_1(1-P_1)}\right]^2}{(P_1 - P_0)^2}$$

- Z1-α/2 = percentage point of the normal distribution corresponding to the required (two-sided) significance level (α) of 0.05 = 1.96.
- Zβ = one sided percentage point of the normal distribution corresponding to 100% -the power, example if power = 80% (100% - power) = 20% (i.e. p- value of 0.2) = 0.84
- P_0 = Null hypothesis proportion (i.e. no increase expected, which means that the proportion will remain as previously obtained i.e.sensitivity of prostate specific antigen from the previous study, 89.8%.[24, 25]=0.898
- P_1 = Alternative hypothesis proportion = 89.8% baseline + 10% increase = 99.8% = 0.998
- P_1 P_0 = The difference (i.e. expected increase in the proportion of microseminoprotein - beta, new biomarker in the diagnosis of CaP) = 0.998-0.898 = 0.1

$$n = \frac{\left[1.96 \times \sqrt{0.898(1-0.898)} + 0.84\sqrt{0.998(1-0.998)}\right]^2}{(0.998 - 0.898)^2}$$

n = 32.67 = 33 Patients or subjects.

The sample size includes attrition of 20% {that is 6.30 approximately 7}. The minimum sample size for this research was forty(40). Out of the eighty patients(80) recruited, forty(40) patients returned with adenocarcinoma of the prostate on histology while the remaining forty(40) patients had a negative biopsy. All the patients had TRUS-guided biopsy of the prostate.A structured proforma was used to collect relevant data, including demographics, clinical history, physical examination, clinicopathological variables, results of the relevant investigation and prostate biopsy findings on TRUS examination. The data were entered into the Statistical Package for the Social Sciences (IBM SPSS) for Windows, Version 20.0. Armonk, NY: IBM Corp, 2011. The mean of serum total prostate-specific antigen (tPSA) in both groups was determined and compared using the Students' t-test. The relationship between serum levels of total prostate-specific antigen (tPSA) and Gleason scores of patients with prostate cancer was calculated using Spearman's correlation. The level of significance was set at $p < 0.05$. After informed consent, under aseptic conditions, 4mls of the venous blood sample was collected from the upper extremity and put into plain red top venipuncture tubes without additives and anticoagulants. The assay for total PSA(tPSA) was done using the enzyme-linked immunosorbent assay (ELISA) method based on the manufacturer's (Monobind Inc- AccuBind ELISA Microwells Product Code:2125-300) instruction.

Prostate Biopsy

Transrectal ultrasound(TRUS) guided prostate biopsy was done using Mindray Digi/Prince®(DP-6600)-Germany 2007/2008 for all patients recruited. The frequency of the transrectal probe was set at 6.5 MHz to scan the prostate and for biopsy. Twelve (12) biopsy cores were obtained from lateral to medial parts of each prostate lobe, targeting suspicious nodules visualized on TRUS. The specimen was appropriately labelled and sent in 10% formaldehyde to the Histopathologist. Haematoxylin and Eosin (H&E) slides were prepared and examined under the microscope (Olympus BX51 with low power X40 and medium power X200) for tissue diagnosis. The histopathologist determined the histology and the Gleason grade/score of the benign and malignant prostate tissue respectively.

RESULTS

Forty men with histological diagnosis of prostate cancer and forty age-matched adult males with negative biopsy were recruited for this study.

Patients' age distribution in the CaP group ranged from 50 to 89 years, with a mean of 69.38±8.08 years. The peak age incidence in the CaP group was in the 8th decade (71-80 years). Similarly, patients' age range in the negative biopsy group was 50 to 99 years, with a mean of 65.43±9.68 years). There was a statistically significant difference in the age distribution of both groups(p=0.003).

Table 1: Clinical parameters of study participants

Variables		Prostate Cancer Group n=40(%)	Negative biopsy Group n=40(%)	p-value
LUTS				
	Yes	30(75.0)	34(85.0)	0.264
	No	10(25.0)	6(15.0)	
Family history of	**Prostate cancer**			
	Negative	4(10.0)	11(27.5)	0.898
	Positive	2(5.0)	2(5.0)	
	Unaware	34(85.0)	27(67.5)	
Digital rectal examination				
	Benign	4(10.0)	22(53.8)	<0.001
	Suspicious	36(90.0)	18(46.2)	

Table 2: Procedural (TRUS Guided biopsy) assessment

Variables	Prostate Cancer Group n=40(%)	Negative biopsy Group n=40(%)	p-value
Prostate capsule Integrity			
Intact/Uniform	6(15.0)	22(55.0)	
Breech/Irregular	34(85.0)	18(45.0)	
Prostatic Nodules			
Yes	31(77.5)	15(37.5)	<0.001
No	9(22.5)	25(62.5)	
Echogenicity of Prostate			
Hyperechoic	0(0.0)	5(12.5)	0.003
Hypoechoic	22(55.0)	11(27.5)	
Isoechoic	5(12.0)	14(35.0)	
Mixed	13(32.5)	10(25.0)	
TRUS Prostate Volume(g)	67.32±52.50	57.19±34.06	0.382

Serum Total PSA Levels and Histopathological Characteristics of Study Participants

Among the Prostate cancer patients, the serum total PSA ranged from 6.25 to 114.67 ng/ml with a mean of 82.93±35.02, while the serum total PSA in the negative biopsy group ranged from 0.88 to 115.17ng/ml with a mean of 28.85±30.92 which was significantly lower than the CaP group (p<0.001). The majority of the CaP group patients (34, 90%) had PSA values greater than 20ng/ml.

All the patients in the study group had a histological diagnosis of adenocarcinoma of the prostate. The Gleason score of CaP patients in this study ranged from 6 to 10, with a modal score of 6. Twenty-one (52.5%) of these patients had a score of 8 and above (Figure 1). The least Gleason score was 6, accounting for 13(32.5%) men in the CaP group.

Table 3: Gleason s core distribution and ISUP Grading among patients with Prostate Cancer.

Variable		Frequency	Percentage
Gleason Score	6	13	32.5
	7	6	15.0
	8	6	15.0
	9	12	30.0
	10	3	7.5
	Total	**40**	**100**
ISUP Gleason Categories	[illegible]	13	32.5
	II(3+4)	1	2.5
	III(4+3)	5	12.5
	IV(8)	6	15.0
	V(≥9)	15	37.5
	Total	**40**	**100**

***ISUP**: International Sciety of Urological Pathology*

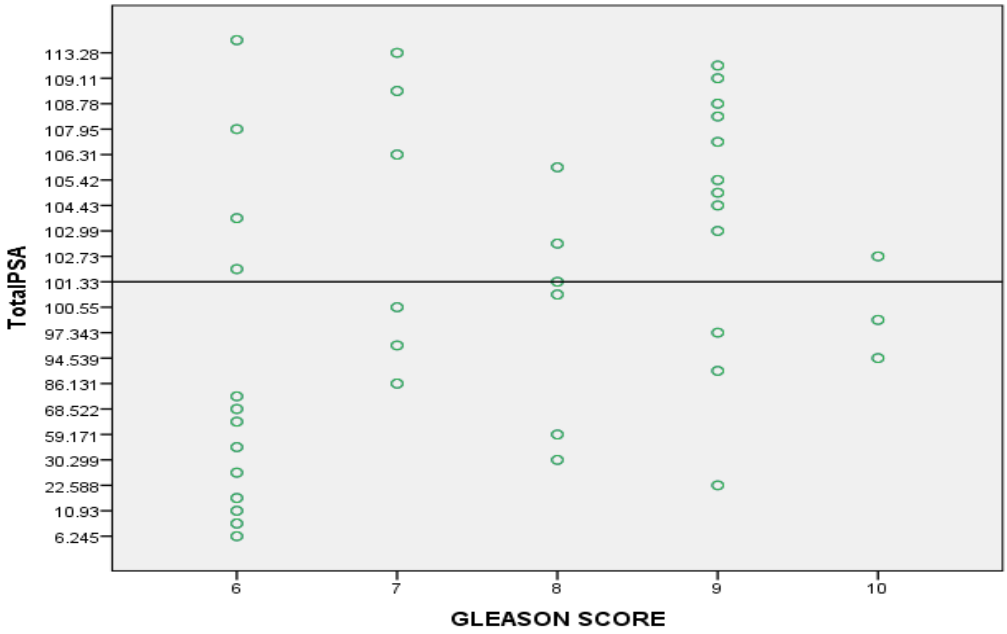
Correlation between Serum levels of Total Prostate Specific Antigen (tPSA) to Gleason Score in patients with Prostate Cancer.

Forty (40) study patients with adenocarcinoma of the prostate had an assessment of their Gleason's score (Mean = 7.65 ± 1.41) and assayed serum levels of prostate-specific antigen (PSA) (Mean = 82.93 ± 35.02). Spearman's correlation analysis showed a moderate positive correlation (rs = 0.442) between Gleason's score and assayed serum levels of total prostate-specific antigen (tPSA). Therefore, there was a strong positive association between Gleason score and assayed serum levels of total PSA and was statistically significant (p = 0.004).

However, there was a moderate positive correlation between serum total PSA and the Gleason score among men with CaP with higher total PSA levels found

* Correlation is significant at the 0.05 level (2- tailed)

Figure 1 : Correlation between serum level of Total PSA and Gleason Score in Patients with Prostate cancer.



among men with higher Gleason scores (Table 4) (R^2=0.442, p=0.004).

DISCUSSION

The manifestation of prostate disease is usually amongst the middle-aged and elderly groups. The development of adenocarcinoma of the prostate increases with age, peaking at 60-69 and 70-79 years, respectively.[26, 27] The highest incidence of prostatic diseases in this study was in the 6th and 7th decades but among patients with negative biopsy occurred a decade earlier than the Prostate cancer group. This is because prostate diseases occur in the elderly population. These findings were similar to global surveys and studies in other parts of Nigeria, Ghana and South Korea.[28-31]

The serum total PSA was significantly higher in patients with prostate cancer than in those with negative biopsy. This finding is comparable to studies by Prcic *et al.*[32], Froehner et al.[33] and Orakwe et al.[34], where the malignant prostate tumour group had a significant increase in the mean serum level of total prostate-specific antigen(PSA) compared with the controls($p<0.0001$). This is due to the abnormal leakage of PSA into the circulation further influencing its expression in malignant epithelium following a distorted prostatic glandular architecture.[35]

In this study, prostate cancer patients had a Mean Gleason's Score and tPSA of 7.65 ± 1.41 and 82.93 ± 35.02, respectively. Amongst the CaP group, twenty-one (52.5%) patients with a Gleason score of 8 and above, with thirteen (32.5%) patients having a Gleason score of 6 and below. This study showed a high Gleason score in most patients, similar to a survey by Okolo *et al*., Nakandi *et al.* and Jalloh *et al.*[36] reporting that prostate cancer patients in sub-Saharan countries have high Gleason scores when compared to those in developed countries. The high Gleason score found in

the current study underscores the more aggressive behaviour of prostate cancer in men of African descent irrespective of place of birth or residence and this observation may be due to the genetic susceptibility of people of this race to the disease.[37] However, it may just be due to the peculiar cultural and religious practices leading to late presentation to the hospital for treatment.[16]

In this study, a moderate positive correlation (r_s= 0.442) was observed between Gleason's score and assayed serum levels of total prostate-specific antigen among patients with CaP. This moderate positive correlation was statistically significant (p=0.004). This finding is in keeping with a previous study by Okolo *et al.*[38] from Ibadan-South western Nigeria, who also observed a moderate positive correlation(r_s=0.400) between Gleason's score and assayed serum levels of PSA, which was also statistically significant at p=0.001.

Patients presenting with suspicious findings were more likely to have a histopathological diagnosis of prostate cancer. Most of the patients in the CaP group had suspicious DRE findings (p<0.001), giving a cancer detection rate of 90% when compared to studies by Lee *et al*.[39] and Cooner[40] with a detection rate of 43.8% and 32.6% respectively. Thus the value of DRE in detecting prostate cancer in this study was higher than in previous studies which may be a result of the late presentation among our patients with advanced disease. Although 46.2% of the patients in the negative biopsy group had suspicious findings on DRE, a previous study had explained similar occurrences with a significant proportion of patients with DRE findings suggestive of malignancy turning out to be negative for malignancy after histological evaluation.[41]

This study supports the utility of DRE as an important and simple adjunctive bedside or office procedure in the diagnostic workup of patients with an enlarged prostate. This may be a trigger for prostate biopsy and thus a diagnosis of prostate cancer as has been reported from other parts of the world among family care physicians.[42-44]

Digital rectal examination may thus be a handy tool for the general practitioner and the urologists, especially in most Sub-Saharan Africa hospitals, where there are no organized screening programs or advanced diagnostic tools for the detection of prostate cancer. This observation is pertinent as most patients in the region of study present late with advanced disease that induce changes in the prostate adjourning and rectal mucosa are usually remarkable and can easily be detected during DRE.

Transrectal ultrasonography (TRUS) since its introduction into clinical practice four decades ago has been an important armamentarium in the evaluation of the patient with a symptomatic enlarged prostate as it enables the assessment of prostate volume, echotexture, capsular integrity, changes in the urinary bladder as well as a tool for guided biopsy.[45,46]

This study revealed a mean prostate volume of 67.32g with a range of 13.0-282g with the majority of patients having hypoechoic echogenicity (55.0%). Ahmed *et al.*[47] in Zaria-Nigeria found a mean prostate size of 66.8g with a range of 15-219g while Isiwele *et al.*[48] reported a mean prostate volume of 88.5cm^3 with a range of 13.0cm^3 376.0 cm^3. These were at variance with a similar study done in Norway by Eric *et al.*[49] with a mean prostate volume of 58.0g and a range of 26.6164.8g. In this study, lower prostate volumes were noted in the negative biopsy compared with the prostate cancer group, which is at variance with a previous study [50] however it was not statistically significant(p>0.005). Therefore, it is logical to take a higher number of core biopsies in larger prostates to detect cancerous foci as prostate cancer may coexist with benign prostate hyperplasia. TRUS is the most commonly available and utilized imaging modality in the diagnosis of prostate cancer with sonographic features such as hyperechoic, isoechoic and

hypoechoic though malignancy mostly demonstrates hypoechoic lesions, especially in the peripheral zone .[46, 51, 52] More than half of the CaP group patients had prostate glands with hypoechoic features, followed closely by mixed echogenic elements. The highest proportion (55.0%) of patients with hypoechoic nodules had CaP compared with none and 32.5% (hyperechoic and mixed echogenicity) respectively. The highest predictive value in detecting prostate cancer is associated with peripherally located hypoechoic nodules[53] The correlation of hypoechoic nodules to the histological diagnosis of CaP was noted in a previous study.[48] This was corroborated by a study done by Ahmed *et al.* [47] and Lee *et al.*[39] with hypoechoic lesions correlating more with a histologic diagnosis of CaP however, this current study revealed that all the hyperechoic lesions were benign. Performing a biopsy of only hypoechoic lesions would have misdiagnosed 27.5% of the patients with prostate cancer whose results were negative on histology.

A higher proportion of patients with an irregular prostate outline have CaP than 15.0% of those with intact/uniform capsules. This implies that the presence of irregular prostate outlines on TRUS strongly suggests the presence of CaP. The majority of the patients in the CaP group had a TRUS diagnosis of prostate cancer, giving a cancer detection rate of 77.5%. In a similar study by Lopes et al. [54] in Brazil, most of the patients with suspicious nodules in the CaP group had a malignant prostate on histology with a positive predictive value of 74%. A similar study by Gupta et al. [55] in India confirms identical inferences.

CONCLUSION

There is a significantly higher serum total PSA and Gleason score in the patients with prostate cancer in our population. Furthermore, suspicious findings on digital rectal examination and TRUS-guided biopsy were suggestive of malignancy in patients with prostate cancer suggesting the role of DRE in an environment like ours.

Limitations of the Study

Some of the patients included in the negative biopsy group may have prostate cancer despite the negative TRUS biopsy result.

Declarations

Ethical approval and patient consent to participate in the study were sought from the institution's health and research committee and a copy is attached. All authors have their signatures appended.

Availability of data and material for the study: The datasets used and/or analyzed during the current study are available from the corresponding author on request.

Competing interests: The authors declare that they have no competing interests.

Funding: No source of funding.

Authors' contributions: EUO conceptualized the study, and analyzed and interpreted the patient data regarding prostatic diseases and biopsy. UA/KA/ASM/NPA thoroughly reviewed the manuscript and made corrections.
All authors read and approved the final manuscript.

Acknowledgements: I want to acknowledge Drs. KJ Awosan, Bilkisu Gulma and Ijapa Adamu for their assistance concerning statistical analysis. Mr Kabiru and Mr Mustapha assisted with the laboratory analysis.

REFERENCES

1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, *et al.* Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *International Journal of Cancer.* 2015;136:E359-386.
2. Ferlay J,Parkin DM, Steliarova-Foucher E. Estimates of cancer incidence and mortality in Europe in 2008. *European Journal of Cancer (Oxford, England : 1990).* 2010;46:765-

781.

3. Saibu GM, James BA, Adu OB, Faduyile F, Adedayo OF, Morounke SG, *et al.* Epidemiology and Incidence of Common Cancers in Nigeria. J*ournal of Cancer Biology and Research*. 2017;1105.
4. Yawe KT, Tahir MB, Nggada HA. Prostate cancer in Maiduguri. *West African Journal of Medicine*. 2006;25:298-300.
5. Akang EE, Aligbe JU, Olisa EG. Prostatic tumours in Benin City, Nigeria. *West African Journal of Medicine.* 1996;15:56-60.
6. Afolayan EA. Five years of Cancer Registration at Zaria (1992-1996).*The Nigerian Postgraduate Medical Journal.* 2004;11:225-229.
7. Mohammed AZ, Edino ST, Ochicha O, Gwarzo AK, Samaila AA. Cancer in Nigeria: a 10-year analysis of the Kano cancer registry. *Nigerian Journal of Medicine.* 2008;17:280-284.
8. Akinremi TO, Ogo CN, Olutunde AO. Review of prostate cancer research in Nigeria. *Infectious Agents and Cancer.* 2011;6(Suppl 2):S2-S8.
9. Sahabi SM, Abdulahi K. Epidemiological Survey of Malignant Neoplasms in Sokoto,Nigeria. *World Journal of Research and Review*. 2017;4:10-15.
10. Mohammed AZ, Edino ST, Ochicha O, Gwarzo AK, Samaila AA. Cancer in Nigeria: a 10-year analysis of the Kano cancer registry. *Nigerian Journal of Medicine.* 2008;17:280-284.
11. Halpern JA, Oromendia C, Shoag JE, Mittal S, Cosiano MF, Ballman KV, *et al.* Use of Digital Rectal Examination as an Adjunct to Prostate Specific Antigen in the Detection of Clinically Significant Prostate Cancer. *The Journal of Urology*. 2018;199:947-953.
12. Song JM, Kim CB, Chung HC, Kane RL. Prostate-specific antigen, digital rectal examination and transrectal ultrasonography: a meta-analysis for this diagnostic triad of prostate cancer in symptomatic korean men. *Yonsei Medical Journal.* 2005;46:414-424.
13. Odubanjo MO, Banjo AAF, Ayoola S, Abdulkareem FB, Anunobi CC, Olayinka AA. The Clinicopathologic Pattern of Prostatic Carcinoma in Lagos, Nigeria. *North American Journal of Medicine and Science.* 2013;6:71-75.
14. Odubanjo MO, Banjo AAF, Ayoola S, Abdulkareem FB, Anunobi CC, Olayinka AA. The Clinicopathologic Pattern of Prostatic Carcinoma in Lagos, Nigeria. *North American Journal of Medicine and Science.* 2013;6:71-75.
15. Ajape A, Ibrahim K, Fakeye J, Abiola O. An overview of cancer of the prostate diagnosis and management in Nigeria: The experience in a Nigerian tertiary hospital. *Annals of African Medicine.* 2010;9:113-117.
16. Bowa K, Kachimba J, Labib M, Mudenda V, Chikwenya M. The changing pattern of urological cancers in Zambia. *Medical Journal of Zambia.* 2008;35:157-159.
17. Awosan KJ, Yunusa EU, Agwu NP, Taofiq S. Knowledge of prostate cancer and screening practices among men in Sokoto, Nigeria. *Asian Journal of Medical Sciences*.2018;9:51-56.
18. Wu JT, Liu GH. Advantages of replacing the total PSA assay with the assay for PSA-α1- antichymotrypsin complex for the screening and management of prostate cancer.*Journal of Clinical Laboratory Analysis.*1998;12:32-40.
19. Bul M, Schröder Fh. Screening for prostate cancer The controversy continues, but can it be resolved? *Acta Oncologica*. 2011;50(Suppl 1):4-11
20. Humphrey PA, Andriole GL. Prostate cancer diagnosis. Missouri medicine. 2010;107:107-112.
21. Gordetsky J, Epstein J. Grading of prostatic adenocarcinoma: current state and prognostic implications. *Diagnostic Pathology.* 2016;11:25.
22. Jędroszka D, Orzechowska M, Hamouz R, Górniak K,Bednarek Ak. Markers of epithelial-to-mesenchymal transition reflect tumor biology according to patient age and Gleason score in prostate cancer. *PLOS ONE*. 2017;12:e0188842.
23. Ibrahim T.Sample size determination. In: Research Methodology and Dissertation Writing for Health and Allied Health Professionals.Abuja, Nigeria: Cress Global Link Limited;2009:70-75
24. Amayo A, Obara W. Serum prostate specific antigen levels in men with benign prostatic hyperplasia and cancer of prostate. East African Medical Journal. 2004;81:22-26.
25. Ojewola RW, Tijani KH, Jeje EA, Ogunjimi MA, Anunobi CC, Adesanya AO. An evaluation of usefulness of prostate specific antigen and digital rectal examination in the diagnosis of prostate cancer in an unscreened population:

experience in a Nigerian teaching hospital. West Afr J of Med. 2013;32:8-13.

26. Chodak GW, Keller P, Schoenberg HW. Assessment of screening for prostate cancer using the digital rectal examination. *The Journal of urology.* 1989;141:1136-1138.
27. Parsons JK, Kashefi C. Physical activity, benign prostatic hyperplasia, and lower urinary tract symptoms. *European Urology*. 2008;53:1228-1235.
28. Olajide A, Eziyi A, Kolawole O, Sabageh D, Ajayi I, Olajide F. A comparative study of the relevance of digital rectal examination, transrectal ultrasound, and prostate-specific antigen in the diagnostic evaluation of patients with advanced carcinoma of the prostate in a resource poor environment. *Sahel Medical Journal.* 2016;19:27-31.
29. Lee SWH, Chan EMC, Lai YK. The global burden of lower urinary tract symptoms suggestive of benign prostatic hyperplasia: A systematic review and meta-analysis. *Scientific reports.* 2017;7:7984.
30. Chokkalingam AP, Yeboah ED, Demarzo A, Netto G, Yu K, Biritwum RB, *et al.* Prevalence of BPH and lower urinary tract symptoms in West Africans. *Prostate cancer and prostatic diseases.* 2012;15:170-176.
31. Goh HJ, Kim SA, Nam JW, Choi BY, Moon HS. Community-based research on the benign prostatic hyperplasia prevalence rate in Korean rural area. *Korean Journal of Urology.* 2015;56:68-75.
32. Prcic A, Begic E, Hiros M. Usefulness of Total PSA Value in Prostate Diseases Diagnosis. *Acta Informatica Medica.* 2016;24:156-161.
33. Froehner M, Hakenberg OW, Koch R, Schmidt U, Meye A, Wirth MP. Comparison of the clinical value of complexed PSA and total PSA in the discrimination between benign prostatic hyperplasia and prostate cancer. *Urologia Internationalis*. 2006;76:27-30.
34. Orakwe DE, Tijani KH, Jeje EA, Ogunjimi MA, Ojewola RW. Comparison of the pre-treatment testosterone levels in benign prostatic hyperplasia and prostate cancer patients. *African Journal of Urology*. 2017;23:105-108.
35. Nogueira L, Corradi R, Eastham JA. Prostatic specific antigen for prostate cancer detection. *International Brazilian Journal of Urology.* 2009;35:521-529.
36. Jj Y. Clinical and Histopathological Profile of Patients with Prostate Cancer in Kampala, Uganda. *Medical Journal of Zambia.* 2019;46:19-27.
37. Ahmed RO, Sewram V, Oyesegun AR, Ayele B, Van Wyk A,Fernandez P. A comparison of clinicopathologic features of prostate cancer between Nigerian and South African black men. *African Journal of Urology.* 2022;28:1-8.
38. Okolo CA, Akinosun OM, Shittu OB, Olapade-Olaopa EO, Okeke LI, Akang EEU, et al. Correlation of serum PSA and Gleason score in Nigerian men with prostate cancer. *African Journal of Urology.* 2008;14:15-22.
39. Lee F, Gray JM, Mcleary RD, Mchugh TA, Solomon MH, Kumasaka GH, et al. Prostatic evaluation by transrectal sonography: criteria for diagnosis of early carcinoma. *Radiology*. 1986;158:91-95.
40. Cooner WH, Mosley BR, Rutherford Cl Jr, Beard JH, Pond HS, Terry WJ, et al. Prostate cancer detection in a clinical urological practice by ultrasonography,digital rectal examination and prostate specific antigen. *The Journal of Urology*. 1990;143:1146-1152.
41. Simmons MN, Berglund RK, Jones JS. A practical guide to prostate cancer diagnosis and management. *Cleveland Clinic Journal of Medicine.* 2011;78:321-331.
42. Jones D, Friend C, Dreher A, Allgar V, Macleod U. The diagnostic test accuracy of rectal examination for prostate cancer diagnosis in symptomatic patients: a systematic review.*BMC Family Practice.* 2018;19:79.
43. Soares SCM, De Camargo Cancela M, Migowski A, De Souza DLB. Digital rectal examination and its associated factors in the early detection of prostate cancer: a cross-sectional population-based study. *BMC Public Health*. 2019;19(1):1573.
44. Walsh AL, Considine SW, Thomas AZ, Lynch TH, Manecksha RP. Digital rectal examination in primary care is important for early detection of prostate cancer: a retrospective cohort analysis study. *The British Journal of General Practice.* 2014;64:e783-787.
45. Muhammad AS, Abdulwahab-Ahmed A, Agwu NP, Yunusa G, Abdullahi K, Mungadi IA. Use of transrectal ultrasound in the management of urologic diseases in a tertiary hospital in North-Western Nigeria. *The Nigerian Postgraduate Medical Journal.* 2018;25:172-176.
46. Shariat SF, Roehrborn CG. Using biopsy to detect prostate

cancer. Reviews in Urology. 2008;10:262-480.

47. Ahmed M, Maitama H, Bello A, Kalayi G, Mbibu H. Transrectal ultrasound findings in patients with advanced prostate cancer. *Annals of Nigerian Medicine.* 2010;4:59-61.

48. Isiwele EM, Ikpeme AA. Predictive Value of Transrectal Ultrasound in the Diagnosis of Prostate Cancer. *International Journal of Contemporary Medicine Surgery and Radiology.* 2018;3:C66-69.

49. Eri LM, Thomassen H, Brennhovd B, Håheim LL. Accuracy and repeatability of prostate volume measurements by transrectal ultrasound. *Prostate Cancer and Prostatic Diseases*. 2002;5:273-278.

50. Doluoğlu ÖG, Öztekin ÇV, Karabakan M, Akdemir AÖ, Çetinkaya M. The importance of prostate volume in prostate needle biopsy. *Turkish Journal of Urology.* 2013;39:74-77.

51. Akduman B, Crawford ED. Transrectal ultrasound-guided prostate biopsy: current approach. *Turkish Journal of Urology.* 2010;36:25-32.

52. Chen FK, De Castro Abreu AL, Palmer SL. Utility of Ultrasound in the Diagnosis, Treatment, and Follow-up of Prostate Cancer: State of the Art. *Journal of Nuclear Medicine*. 2016;57:13-18.

53. Pinto F, Totaro A, Palermo G, Calarco A, Sacco E, D'addessi A, et al. Imaging in prostate cancer staging: present role and future perspectives. *Urologia Internationalis.* 2012;88:125-136.

54. Lopes PM, Sepúlveda L, Ramos R, Sousa P. The role of transrectal ultrasound in the diagnosis of prostate cancer: new contributions. Radiol Bras. 2015;48:7-11.

55. Gupta S, Gupta DK, Lamba H. Histopathological Study of 100 Cases of Prostatic Nodules. International Journal of Medical Science and Education. 2016;3:173-181.