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ORIGINAL ARTICLE

Clinico-Pathologic Characteristics of Patients with Prostate Cancer and Outcome of Prostate Biopsy in a Nigerian Tertiary Hospital

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ABSTRACT

Background: Prostate cancer is considered the second most common malignancy worldwide and the fifth leading cause of cancer death. Its greatest mortality is among men of African descent. This study assessed the clinical and pathologic characteristics of patients diagnosed with prostate cancer and the outcome of prostate biopsy.

Methods: This was a cross-sectional study carried out from January 2015 to December 2016. Consecutive patients presenting to Urology clinic with elevated prostate specific antigen >4ng/ml and /or abnormal digital rectal examination findings were included in this study and had digitally guided biopsy. Specimen were sent for histopathology and outcome recorded. The patients were also followed up, and complications of prostate biopsy documented. Data analysis was done using SPSS version 20.0.

Results: A total of 191 patients participated in this study. The majority (35.1%) of study participants were in the 60-69 age group with mean age of 68.2 ± 9.4 years. One hundred and eighty-one (94.8%) of patients had lower urinary tract symptoms. Forty-three patients (22.5%) had metastatic symptoms, with low back pain being the commonest (51.2%). Digital rectal examination findings were abnormal in 49.2% of patients. The cancer detection rate in the study was 40.3%. The majority (51.9%) of patients with adenocarcinoma of the prostate had Gleason score 5-7. The commonest complication of prostate biopsy was hematuria occurring in 36.1% of patients, with 1% developing post biopsy sepsis.

Conclusion: A notable proportion of patients diagnosed of prostate cancer had advanced disease. Gleasons' score parallels disease aggressiveness.

Keywords: Biopsy complications; Clinical characteristics; Gleasons score; Lower urinary tract symptoms; Prostate cancer.

INTRODUCTION

Prostate cancer (PCa) is the second most common malignancy worldwide, with 1.460 million men diagnosed of this cancer in 2022.[1] Incidence rates are highest in Northern Europe, Australia, New Zealand, the Carribean and North America, lowest in Asia and Africa. Regional pattern of mortality does not follow that of incidence, despite high incidence in parts of Europe and North America, mortality rates are highest in sub-Saharan and the Caribbean indicative of late detection and treatment.[1] In Nigeria, prostate cancer is the most common cancer among men and the incidence is on the increase. In a study carried out by Ogunbiyi et al, the prevalence was put at 11%[2], while a 2013 community-based study by Ikuerowo et al[3] put the prevalence at 1046 per 100,000 patients. In 2020, 18019 cases were recorded with age standardised incidence rate (ASR) of 30.7 per 100,000.[4]

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Generally, prostate cancer are thought to be indolent, some tend to be invasive and are diagnosed either when they have already metastasized or rapidly spread beyond the prostate resulting in prostate cancer specific mortality,[5] which is described as the fifth leading cause of death worldwide and the greatest mortality is among men of African descent.[1] Early diagnosis , has improved outcome in treatment of prostate cancer as witnessed in Western and European countries.[6] This is contrary to what obtains in Nigeria where there are no guidelines for screening coupled with the attendant poor awareness, knowledge and attitude towards prostate cancer.[7-9]

Critical to diagnosis of (PCa) is prostate biopsy. The indications for prostate biopsy include abnormal digital rectal examination (DRE) or elevated prostate specific antigen (PSA) level.[10] Prostate biopsy is usually well tolerated, it has low risk of major complications, however frequently encountered complications include pain and bleeding.[11-12]

The incidence, mortality of PCa is widely believed to vary from region to region which is dependent on genetic variations, disparity in screening programs where they exist, detection

and treatment. Anecdotally, it is widely believed that diagnosis is usually late in our environment due to these factors as well as health seeking behaviour amongst blacks, hence the need for this study. The aim of this study was to assess the clinical and pathologic characteristics of patients with prostate cancer, and the outcome of prostate biopsy.

METHODOLOGY

Study setting

This study was conducted in the urology unit of University of Benin Teaching Hospital over a 2-year period from January 2015 to December 2016. University of Benin Teaching Hospital is a tertiary multi-specialty hospital with 800 bed capacity and an established urology unit which serves as a referral centre for patients in the state and neighbouring states of Delta, Kogi, Ekiti and Ondo states offering basic and high - end urologic services. Its outpatient clinic operates twice weekly, Mondays and Fridays. Tuesdays are scheduled for prostate biopsy it is usually an outpatient procedure carried out at the urology procedure clinic. The Urology unit operates multiple theatre sessions in a week scheduled for Mondays, Wednesday, Thursdays and Fridays.

Study design

This was a cross-sectional study

Study population

The study involved patients referred to the urology clinic, who were 50 years and above and either asymptomatic or symptomatic of lower urinary tract symptoms, with elevated prostate specific antigen (PSA) level >4ng/ml or had abnormal digital rectal examination (DRE) on evaluation. All patients who had previous diagnosis of prostate cancer (PCa), those on anticoagulant and, patients with urinary tract infection/prostatitis were excluded from the study.

Sample Size Determination

Sample size (n) = ((Z_1-α/2) ^2 (P)(q))/d^2 where n = sample size; Z1 = α/2 critical value and a standard corresponding level of confidence (at 95% CI or 5% level of significance (type 1-error) it is 1.96; P= prevalence; q = 1-p; d = margin of error or precision; Z1 = α/2 = 1.96.

P = 11% = 0.11 according to a study by Ogunbiyi et al[4]; q = 1-0.11 = 0.89; d=5% = 0.05

Sample size = 150; providing for attrition rate at 10%, the eventual sample size became 165.

Study procedure

Eligible patients had evaluation of their medical history and physical examination carried out. Digital rectal examination was considered abnormal when the prostate gland exhibited nodules, hard in consistency, asymmetry, irregularity of the lateral sulci and fixity of gland to the rectal mucosa. A venous blood sample was taken for pre- treatment total PSA determination. Collected samples were kept at 4 degrees Celsius after centrifugation by a dedicated laboratory scientist within 24 hours of analysis or at -25 degrees Celsius when analysis was done after 24 hours. Prostate specific antigen level was determined by the enzyme-linked fluorescent assay (ELFA), using biomerieux mini VIDAS immunoassay system analyser (2010). Participants with abnormal DRE and /or PSA >4 ng/ml had digitally guided prostate biopsy. All patients had a course of Ciprofloxacin and Metronidazole antibiotics which commenced on the morning they were scheduled for prostate biopsy.

Patients were previously instructed to empty their bowel on the morning of the biopsy. At presentation, the patients were positioned in the left lateral position with both knees flexed with 20mls of 2% xylocaine gel instilled into the rectum before the biopsy. An 18G trucut biopsy needle in a spring -loaded Bard monopty biopsy gun (Bard urological, Covington GA) was then introduced with the aid of the gloved index finger.

Under digital guidance, sextant biopsies were obtained for each patient. Specimen were collected in a bottle containing 10% formalin and sent for histopathology analysis. All patients were allowed home after observation for one hour following biopsy. Patients were instructed to report back to the hospital if any complications such as prolonged hematuria, rectal bleeding, clot retention of urine, and sepsis occurred. Patients were also followed up with telephone calls to ascertain if there were any complications. At the histopathology laboratory, formalin- fixed paraffin -blocked tissues were cut on a microtome to the thickness of 4 microns, and tissue sections stained with hematoxylin-eosin (H&E) were examined a histopathologist dedicated to this study. Gleason's grade and score were assigned by the pathologist.

Statistical analysis

Statistical analysis was done using the IBM SPSS (Statistical Package for Social Sciences) software version 25.0. Data that are numerically distributed such as age were expressed as mean ± standard deviation. Data that are categorical were expressed as frequencies and proportions such as level of education, prevalence of lower urinary tract symptoms, metastatic symptoms, digital rectal examination findings and complications of prostate biopsies.

Ethical consideration

The approval of the institutions ethics and research committee was obtained before commencement of the study with protocol number ADM/E 22/A/VOL.V11/1101. Informed consent was obtained from all patients before enrolment into the study. This study was carried out at no extra financial cost to the patient. Participants were informed of their right to decline participation or even opt out whenever they deemed it necessary, and patient selection was within set inclusion criteria.

RESULTS

A total of two hundred and one patients who satisfied the inclusion criteria were recruited for this study. Only 191 (95%) patients presented for prostate biopsy, after clinical evaluation.

All patients in this study were Nigerians with age range between 50-85 years. The mean age of the study population was 68.2± 9.4 years, about a third of the study population, 67 (35.0%) patients were between 60 and 69 years followed by the 70-79year age range accounting for 49 patients (25.7%). Most of the patients who formed the study population had exposure to formal education,177 (92.7%) Table 1)

Table 1: Patient's characteristics

Variable	Frequency (n = 191)	Percent
Age group (years)		
50 – 59	43	22.5
60 – 69	67	35.0
70 – 79	49	25.7
≥80	32	16.8
Level of education		
None	14	7.3
Primary	77	40.3
Secondary	58	30.4
Tertiary	42	22.0

Mean age= 68.2 ± 9.4 years

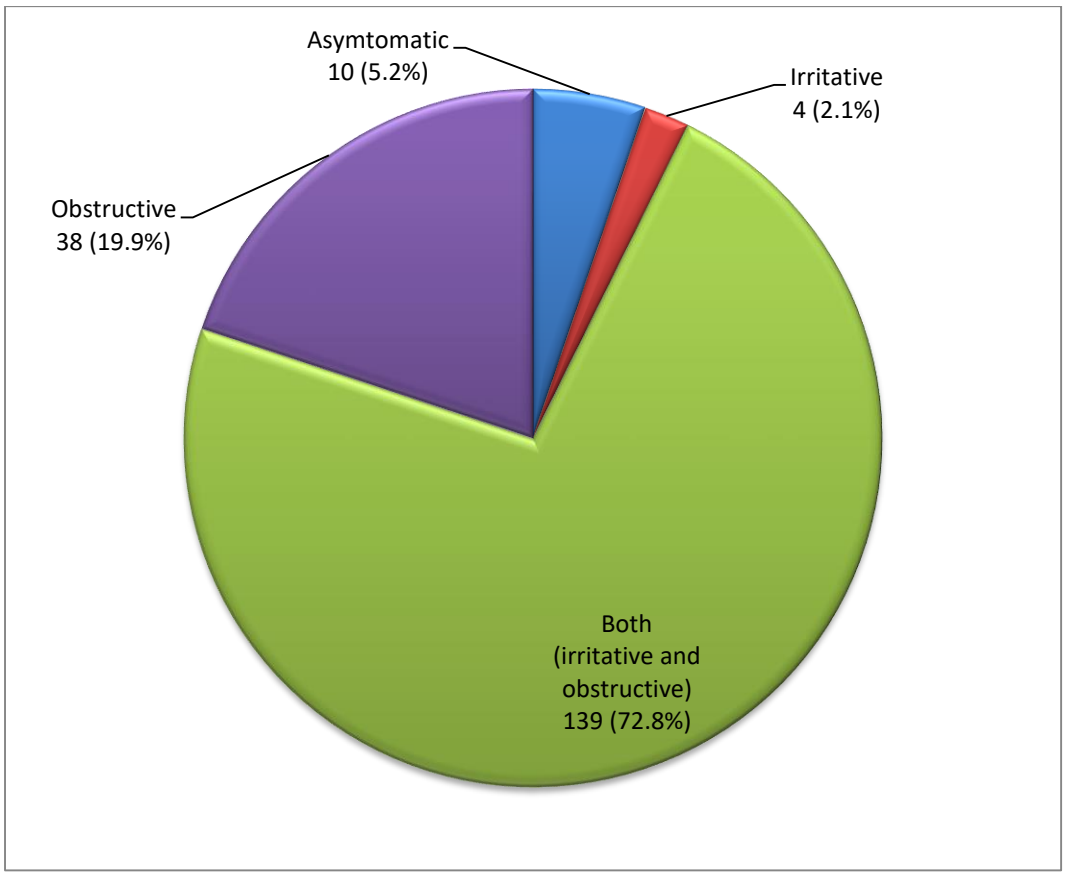

Figure 1: Prevalence of lower urinary tract symptoms among the patients

Of the 191 patients, 10 (5.2%) were asymptomatic while 4 (2.1%) and 38 (19.9%) had irritative and obstructive symptoms respectively. Majority, 139 (72.8%)`of patients had both obstructive and irritative symptoms. (Figure 1)

Of the symptomatic patients, 43 had metastatic symptoms with low back pain accounting for highest proportion 22 (51.2%) of symptoms while cough and yellowness of the eyes accounted for the least proportion of metastatic symptoms 1 (2.3%) respectively. (Table 2) Ninety-seven (50.8%) patients had normal DRE findings while others had abnormal DRE findings. Hard consistency of the prostate was the most common abnormal DRE findings occurring in 86 (91.5%) patients who had abnormal DRE. As shown in table 3. Seventy-seven (40.3%) of the study population were diagnosed of adenocarcinoma of the prostate. The mean ages of patients diagnosed with CaP and benign prostatic disease were 68.9±9.4 years and 67.7±9.2 years, respectively and the difference was not statistically significant (p= 0.394). A higher proportion 51.9% (40) of the study population with adenocarcinoma had Gleason's score 5-7 (moderately differentiated adenocarcinoma), as shown in table 4. Amongst patients with post biopsy complications, sixty-nine (36.1%) patients had haematuria, with rectal bleeding occurring in 22 (11.5%) patients, while 7 (3.6%) patients had urinary tract infection, 5 (2.6%) patients had acute urinary retention and 2 (1%) patients had sepsis. (table 4)

Table 2: Metastatic symptoms of study population

Metastasis	Frequency (n = 191)	Percent
No	148	77.5
Yes	43	22.5
Metastatic symptoms (n=43)*		
Low back pain	22	51.2
Weight loss	15	34.8
Paraparesis	11	25.9
Bone pains	4	9.3
Cough	1	2.3
Yellowness of the eyes	1	2.3

*multiple response

Table 3: Digital rectal examination findings of the patients

Findings	Frequency (n = 191)	Percent
Normal DRE findings		
No	94	49.2
Yes	97	50.8
Abnormal DRE findings (n = 94)*		
Hard prostate	86	91.5
Asymmetry	78	83.0
Nodules	74	78.7
Fixity	14	14.9

*multiple response

Table 4: Clinic-pathologic outcomes of the patients

Variable	Frequency (n = 191)	Percent
Benign	113	59.2
Malignant	77	40.3
HGPIN	1	0.5
Gleason score		
2-4	8	10.4
5-7	40	51.9
8-10	29	37.7
Biopsy related complications		
Haematuria	69	36.1
Rectal bleeding	22	11.5
UTI	7	3.6
Urinary retention	5	2.6
Sepsis	2	1.0

Mean ± Standard deviation Age: Benign = 67.7 ± 9.2 years, Malignant = 68.9 ± 9.8 years, p = 0.394

DISCUSSION

Age is considered a common risk factor for prostatic diseases, particularly with prostate cancer (PCa),[13]this reflects in the age distribution amongst participants in this study, majority of the participants were between 60-69 years followed by the 70-79 years age group, this is in agreement with previous studies documented in the literature. [14,15] The mean age of the study population was 68.2 ± 9.4 years. In Nigeria several studies have shown mean age ranging between 61.2 and 71.4 years.[15-19]

Most of the patients in this study were symptomatic with 94.8% presenting with lower urinary tract symptoms, similar to finding in previous studies[6,17,18-20] in addition, symptoms suggestive of metastasis such as low back pains, weight loss, paraparesis and bone pains occurring amongst of participants as in Table 2, were also documented. Also noted are DRE findings suggestive of advanced disease in 49.2% of the study population, the trend has been corroborated by findings in previous studies.[18-20]This may be attributed to lack of guidelines for prostate cancer screening, hence precluding early diagnosis.

The cancer detection rate in this study was 40.3%,this is similar to the detection rate recorded by Odubanjo et al in Lagos who recorded a detection rate of 39.7%,[6] but was at variance with earlier studies conducted in Nigeria,[16,17,21] the reason adduced for this increase was the rising awareness about the disease and the increasing utility of PSA.[2] This study revealed that over one -third of the prostate cancer population were Gleasons' 8-10 which underpins the conceived fact about the aggressiveness of prostate cancer amongst blacks irrespective of location as documented by Jackson MA et al,[22] demonstrating the greater significance of genetic factors over environment in determining aggressiveness of prostate cancer disease in blacks. Similar findings were noted by Odubanjo et al,[6] this amongst other reasons maybe attributed to why its greatest mortality occurs in men of African descent.[1]

In this survey biopsy was digitally guided and 6 cores were taking, the most common complication reported like similar studies conducted in the past was bleeding.[23-26]Commonly encountered was hematuria which ranged from 10-84%,[27,28] findings in this study revealed hematuria rate of 36.1% which is within the range documented in the literature, though the range is noted to be wide because of the varying connotation given to hematuria by authors in their research work, other reasons adduced for the wide range include being either prospective or retrospective study.[29] Ghani et al,[30] found out that the prevalence of hematuria was not related to the number of cores taking. The second most common complication in this study was rectal bleeding, with an incidence rate of 11.5%, rectal bleeding as recorded in previous studies was between 1.3-45%,[31,32]as obtainable in this study rectal bleeding is considered minor and of no consequence for appropriately counselled patients. When rectal bleeding becomes massive, it is usually life threatening.[23]

Despite antibiotic prophylaxis, infectious complications is a well -documented risk of prostate biopsy, the urinary tract infection rate in this study was found to be 3.6%, similar to values recorded by Loeb et al[23] and Mbaeri et al[26], only 1% developed sepsis requiring hospitalization, in this study, there are varying rate of sepsis reported in the literature.[33-35] Similar to findings by Mbaeri et al,[26] in this study only one participant had syncope representing 0.52% of the population, placement in Trendelenburg position was all that was required to achieve relief, and then patient was observed for an hour, this complication is attributed to pain of biopsy.[24]

Limitations: This study lacked imaging studies of patients to corroborate symptoms suggestive of metastasis. The biopsies were digitally guided with the possibility of missed lesions.

Conclusion: This study revealed that most patients diagnosed of prostate cancer in our environment are symptomatic with a significant number presenting with features of advanced disease. The Gleasons score points to high tumour grade attributable to tumour aggressiveness amongst blacks. Most biopsy complications are minor not requiring hospitalization.

It is therefore recommended that policies should be initiated aimed at Prostate cancer screening amongst black men, this will aid early detection, stage migration and reduce mortality.

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Authors' contributions: OE was involved in the conceptualization and design of this work, OE and EO were both involved in acquisition of data, analysis and interpretation of data. OE was involved in drafting the article and revising critically for important intellectual content, while OE and EO gave approval for final version for publication.

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