

Retrospective Analysis of Complications from Prostate Cancer among Nigerians

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Abstract

Background: Prostate cancer (PCa) may be asymptomatic at an early stage and may run an indolent course that requires minimal or no treatment. Early diagnosis through screening reduces the rate of advanced diseases. Whereas, in the western countries where screening is more prevalent, many presents early with a chance for curative treatment. In Africa, late presentation is often the case with palliative treatment sadly the only choice. **Objective:** To evaluate the associated complications in patients with prostate cancer and assess the Gleason's grade as a risk factor for complications observed in patients with prostate cancer, in Port Harcourt, Rivers, Nigeria. **Method and Methodology:** This was a retrospective study carried out over ten years, between January 2011 and December 2020. All patients with histologically confirmed prostate cancer who presented to the University of Port Harcourt Teaching Hospital, Sophia clinic, and Rosivylle clinic were evaluated. The folders were retrieved and their age, presenting complaints, skeletal survey, and biopsy reports were evaluated. Patients with incomplete records were excluded from the study. These data were collated using Microsoft Excel 2016 version and they were analyzed using SPSS version 20. **Results:** There were 335 patients with PCa with a mean age of 68.71 year. The commonest complication was urinary symptoms observed in 192 with urine retention 119(35.5%) and nephropathy 73(21.8%). The spine was the commonest site of bone spread observed in 160(47.8%) followed by the femur 62(18.5%). Anaemia was the next common. There was an association between age, presence of urinary symptoms, and bone involvement with the Gleason's Grade. However, there was a strong association of the overall presence of complications with Gleason's score. **Conclusion:** Men with prostate cancer tend to present with advanced disease in Port Harcourt. The most common presentation was lower urinary tract symptoms followed by low back pain. Complications are associated with high Gleason's grade cancers. Screening may aid in early diagnosis and cure of the disease especially for men of African descent.

Keywords: Prostate cancer, complication, bone spread, vertebra, femur, anaemia.

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INTRODUCTION

Prostate cancer is the second most frequent malignancy (after lung cancer) in men worldwide, counting 1,276,106 new cases and causing 358,989 deaths (3.8% of all deaths caused by cancer in men) in 2018 [1, 2]. In Nigeria, prostate cancer is the leading cause of cancer-related deaths in men 40 years and above [3]. It is common in Port Harcourt with a hospital incidence of 114/100,000[4]. The incidence of prostate cancer is increasing [5, 6]. The cost of managing cancer of the prostate is expensive [7]. Risk factors associated with prostate cancer include increasing age, family history of prostate cancer, and black race. The treatment of Prostate cancer would depend on the stage and grade

of the disease at presentation, the fitness of the patient, and facilities available. Risk stratification is important in management [8]. This study aims to highlight the associated complications in patients with prostate cancer and assess Gleason's grade as a risk factor for complications observed in patients with prostate cancer.

MATERIALS AND METHODS

This was a retrospective study carried out over ten years, between January 2011 and December 2020. All patients with histologically confirmed prostate cancer who presented to the University of Port Harcourt Teaching Hospital, Sophia clinic, and Rosivylle clinic were evaluated.

The folders were retrieved and their age, presenting complaints, skeletal survey, and biopsy reports were evaluated. Patients with incomplete records were excluded from the study. These data were collated using Microsoft Excel 2016 version and they were analyzed using SPSS version 20.

RESULTS

There were 335 patients with PCa with a mean age of 68.71year. The commonest complication was urinary symptoms observed in 192 (with urine retention 119(35.5%) and nephropathy 73(21.8%). The spine was the commonest site of bone spread observed in 160(47.8%) followed by the femur 62(18.5%). There

was an association between age, presence of urinary symptoms, and bone involvement with the Gleason’s Grade. However, there was a strong association of the overall presence of complications with Gleason’s score.

Table-1: Age Characteristics of Prostate Cancer Patients.

N	=	335
Mean		68.71
Median		69.00
Std. Deviation		10.21
Range		73.00
Youngest		44.00
Oldest		117.00

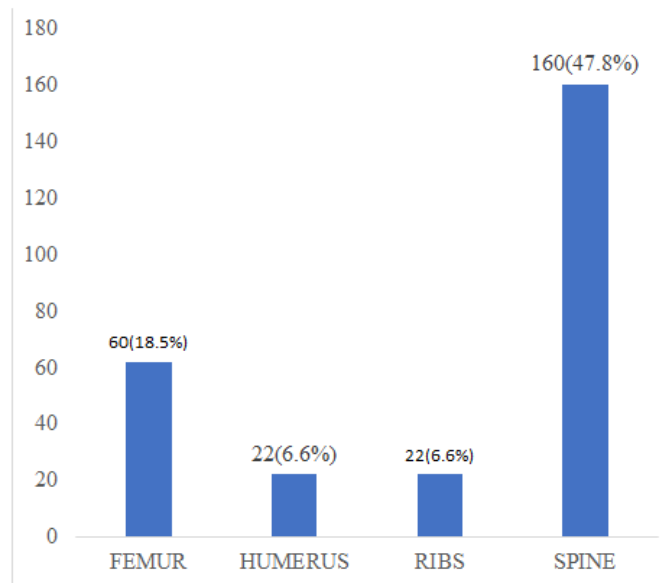


Fig-1: Bones involvement among prostate cancer patients.

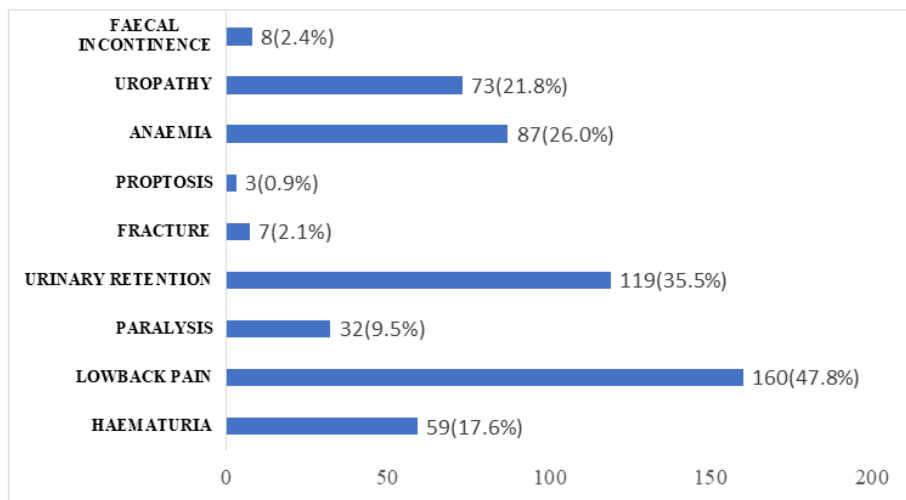


Fig-2: Complications of prostate cancer patients.

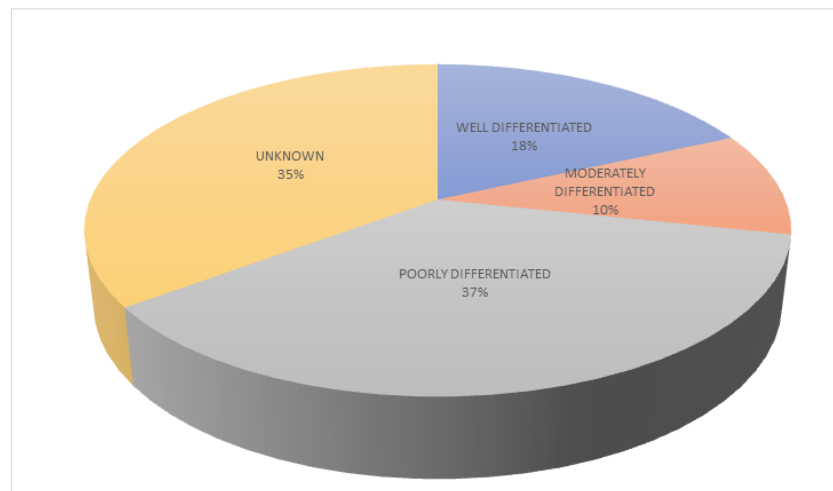


Fig-3: Gleason's scores distribution among prostate cancer patients.

Table-2: Relationship between Age, Lower Urinary Tract Symptoms, bone involvement, and Complication in Patients with Prostate Cancer

Variables	Grading (Gleason's score)								P-value	
	Well-differentiated (1-6)		Moderately differentiated (7)		Poorly differentiated (8-10)		Unknown			
	N	%	N	%	N	%	N	%		
Age group										0.575
40-49	1	(1.6)	1	(2.9)	1	(.8)	2	(1.7)		
50-59	9	(14.8)	5	(14.7)	17	(13.9)	22	(18.6)		
60-69	22	(36.1)	15	(44.1)	43	(35.2)	40	(33.9)		
70-79	19	(31.1)	7	(20.6)	49	(40.2)	34	(28.8)		
80-89	7	(11.5)	6	(17.6)	8	(6.6)	17	(14.4)		
≥90	3	(4.9)	0	(.0)	4	(3.3)	3	(2.5)		
LUTS										0.861
Yes	59	(96.7)	33	(97.1)	120	(98.4)	116	(98.3)		
No	2	(3.3)	1	(2.9)	2	(1.6)	2	(1.7)		
Bone affected										0.780
Yes	12	(19.7)	6	(17.6)	30	(24.6)	25	(21.2)		
No	49	(80.3)	28	(82.4)	92	(75.4)	93	(78.8)		
Presence of complications										0.001*
Yes	40	(65.6)	20	(58.8)	90	(73.8)	106	(89.8)		
No	21	(34.4)	14	(41.2)	32	(26.2)	12	(10.2)		

*Complication = Presence of any complications.

DISCUSSION

Prostate cancer is usually a disease of the elderly, PCa incidence and mortality rates are strongly related to age with the highest incidence being seen in elderly men (> 65 years of age)[2]. In this study the mean age was 68.71years. Several other studies have a similar mean age [4, 5]. The age, stage, and Gleason's grade are important factors that are considered in treatment selection. Prostate cancer can be managed by active surveillance [9], Watchful waiting [9, 10] radical prostatectomy [11], and radiotherapy [12-14]. Cryotherapy [15-17] and high intensity focused ultrasound is an option for well-selected patients [18, 19]. Hormonal manipulation [20-22] and palliative care is used for metastatic disease [22].

Prostate cancer may be asymptomatic at the early stage and run an indolent course that could require minimal or no treatment. Early diagnosis through screening reduces the rate of advanced diseases [23]. Whereas, in the advanced world patients present early without symptoms or mild symptoms, in Africa, late presentation is common [4, 5].

Though PCa affects mainly the elderly [24, 25], the youngest patient in this study was 44years. Salinas and colleagues [26] also noted the risk factor for early prostate cancer which includes African- American descent and family history. In this study, all the patients were Blacks from and reside in the southern part of Nigeria.

Bone metastasis impacts negatively on the quality of life of the patient and is associated with increased morbidity such as pathological fracture, and reduced mobility is a risk factor for pulmonary embolism and mortality [27] and provides a hospitable microenvironment that enhances tumor cells proliferation. Bony metastasis is driven by the interaction between invading tumor cells, osteoblasts, and osteoclasts [27, 28]. Prostate cancer spreads directly to the bones [28, 29]. Two hundred and forty-six patients had osseous metastasis in this study which represents 73.42% of the total number of patients, with the lumbar vertebrae having the highest incidence.

Ondo *et al.* [30] in their study on prostate cancer noted that bone metastasis was observed in 82.6% of patients, and the lumbar vertebrae and pelvic bone were the most common bones that were involved. The higher incidence of bony metastasis in the Ondo *et al.* study maybe because of the late presentation with more severe disease. Bony metastasis usually is a poor prognostic indicator [31].

Lower urinary tract symptoms were the most common clinical presentation of the prostate cancer patients in our study. These include nocturia, frequency, urgency, poor stream, intermittency, incomplete bladder emptying, and urinary retention. A hundred and nineteen (35.5%) presented with urinary retention and seventy-three presented with lower urinary tract symptoms. A hundred and ninety-two patients presented with urinary symptoms. Ekeke *et al.* [5] also noticed the high presentation with LUTS. Patients with prostate cancer presenting with urinary symptoms may be a sign of late presentation, PCa usually starts in the peripheral zone and less from the periurethral transitional zone. The spread of prostate cancer directly to the bladder neck and the enlarging prostate gland can account for the obstruction of urine flow, hence the lower urinary tract symptoms [32]. These symptoms can progress over time leading to retention. Treatment of these patients with androgen deprivation therapy also improved symptoms as noted in a study conducted by Akpayak *et al.* [33] at Jos, Nigeria.

The second most common presentation in this study was low back pain observed in a hundred and sixty patients (47.8%). The reason for this may not be unconnected to the high frequency of metastases to the vertebral spine. Metastatic deposits to the spine can cause pain [34]. However, it is worthy of note that low back pain is common in the elderly from poor posture, radiculopathy, osteoporotic vertebral fractures, de novo degenerative lumbar spondylosis, spinal infections, visceral diseases, and cauda equina syndrome [34].

Vertebral spread is one of the earliest osseous manifestations of skeletal metastasis. This has been attributed to the peculiar relationship between the prostatic and vertebral venous systems. The valveless

veins enhance the spread of cancer cells to the lumbar vertebrae from the prostate and are postulated to be responsible for the high incidence of low back pain in patients with advanced prostate cancer. Vertebral metastasis may result in metastatic spinal cord compression and stenosis which can lead to paralysis seen in thirty-two (9.5%) of our patients. Metastasis to bone can weaken the bone leading to pathological fractures [27]. Seven (2.1%) patients had pathological fractures.

Anaemia was also a common presentation in this study observed in eighty-seven (26%) of the patient. Multiple factors could account for the anemia that is observed in patients with prostate cancer [35]. In our study, fifty-nine patients (17.6%) presented with haematuria. Blood loss from haematuria is not uncommon as many of the patients may present with coexisting benign enlargement from the transitional zone of the prostate. Urinary tract infection which is associated with bladder outlet obstruction can make the prostate bruise easily and lead to haematuria. Uraemia can also cause haematuria by impairing platelet aggregation. Additionally, reduced red cell production because of bone marrow infiltration and cytokine effects from the tumor can contribute to anaemia [35].

Anorexia is a constitutional symptom that is observed in most advanced malignant processes and is also a systemic manifestation of advanced prostate cancer. The cause of anorexia is believed to be multifactorial [36]. Peripherally, substances released from the tumour such as pro-inflammatory cytokines, lactate, and parathormone-related peptides cause anorexia. Central causes of anorexia include depression, pain, and decreased desire to eat [36].

Tumors that more commonly affect the orbit include breast, and lung, with the prostate being the third most common [37]. Orbital metastasis from prostate cancer is generally uncommon [28, 37]. Three patients presented with proptosis. This may be due to metastasis to the orbit [37]. Metastasis to the orbit is usually via the haematogenous route through the carotid and ophthalmic arteries. Early intervention to preserve the function of the eye is important. Metastasis to the orbit is a poor prognostic indicator [28].

Prostate-Specific Antigen (PSA) is a glycoprotein that is produced by both normal and neoplastic tissues of the prostate and is useful for diagnosis, risk stratification, evaluating recurrence, and also as a screening tool [38]. In this study, the mean PSA could not be ascertained because a hundred and two of the patients' PSA was recorded as greater than 100ng/ml. At the time of this study, the majority of the laboratories do not provide PSA results above 100 – 200ng/ml. The highest PSA recorded was 1167ng/ml and the lowest was 45ng/ml. Our finding is similar to

the findings by Salako *et al.* [32] who also noticed a high mean PSA amongst the patients in their study.

Every patient in this study had a biopsy. Most of the patients (37%) presented with poorly differentiated adenocarcinoma. This high-grade cancer may be responsible for the attendant widespread metastasis. Previous studies have also noticed the relationship between poorly differentiated adenocarcinoma and poor prognosis [39]. Thirty-five percent of patients had no Gleason score, especially at the early stages of the study periods, as many pathologists were not providing the Gleason's grade in their pathology reports. An analysis of the Gleason grade and complications showed a statistically significant association between Gleason's score the risk of developing complications such as anaemia, pathologic fractures, paraparesis, and paraplegia ($p=0.001$). Rusthoven *et al.* [39] also noticed a similar finding in his study. Gleason grade 5 is an independent poor prognostic factor.

In developed countries, screening even though controversial, has produced a dramatic stage migration from mostly incurable to mostly curable disease, this provides men the opportunity for early detection and curative treatment of potentially lethal prostate cancer and has reduced mortality rate by 53% [4]. Screening significantly reduces pain and suffering from advanced prostate cancer. Screening programs are rarely carried out in resource-poor countries, hence the late presentation with advanced disease.

Treatment of prostate cancer depends on numerous factors. No patient had a radical prostatectomy or active surveillance because the patients presented late.

CONCLUSION

Men with prostate cancer tend to present with advanced disease in Port Harcourt. The most common presentation was lower urinary tract symptoms followed by low back pain. Complications are associated with high Gleason's grade cancers. Screening may aid in early diagnosis and cure of the disease especially for men of African descent.

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